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- 1 2-FLUORO-3-(4-NITRO-PHENYL) DESCHLOROEPIBATIDINE, A NOVEL COMPETITIVE ANTAGONIST OF HUMAN NEURONAL $\alpha 4\beta 2$ nAChR, WITH POSSIBLE UTILIZATION IN TREATMENT OF NICOTINE DEPENDENCE**
G. Abdrakhmanova(1), M.I. Damaj(1), F.I. Carroll(2) and B.R. Martin(1), (1) Virginia Commonwealth University, Richmond, VA and (2) Research Triangle Institute, Research Triangle Park, NC
- A series of 2-fluoro-3-(substituted phenyl)deschloroepibatidine analogs possess high binding affinity to $\alpha 4\beta 2$ but not to $\alpha 7$ nAChR, and inhibit nicotine-induced analgesia without affecting nicotine-induced hypothermia (Carroll et al., J. Med. Chem., 2004). We hypothesized that these epibatidine analogs would be potent neuronal nAChR antagonists with possible nAChR subtype selectivity. Patch-clamp technique in a whole-cell configuration was used to examine functional activity of tested epibatidine analogs on recombinant $\alpha 4\beta 2$ and $\alpha 3\beta 4$ nAChRs. The 2-fluoro-3-(4-nitro-phenyl)deschloroepibatidine analog (4-nitro-PFEB) exhibited the most pronounced antagonist activity among these analogs when tested electrophysiologically on $\alpha 4\beta 2$ nAChRs (IC₅₀~0.1 μ M; 17-fold more potent than dihydro- β -erithroidine). The inhibitory effect of 4-nitro-PFEB on ACh-induced current amplitude was voltage- and use-independent, only partially reversible after complete inhibition at its 1 μ M concentration, and was not accompanied by alterations in the current kinetics. The concentration-response curve for ACh showed a shift to the right in the presence of 0.1 μ M 4-nitro-PFEB without altering maximum ACh-induced response; the EC₅₀ for ACh was increased from 23 to 106 μ M. In contrast to $\alpha 4\beta 2$ nAChRs, 4-nitro-PFEB did not affect $\alpha 3\beta 4$ nAChR mediated currents at ≤ 1 μ M (IC₅₀~64 μ M). Overall, our binding, behavioral and functional data suggest that 4-nitro-PFEB is an effective competitive antagonist of $\alpha 4\beta 2$ versus $\alpha 7$ and $\alpha 3\beta 4$ nAChRs. The fact that 4-nitro-PFEB possesses low toxicity, can cross the blood-brain barrier and has low probability of affecting peripheral neuronal nAChR function indicates that it may serve as potential candidate for treatment of nicotine dependence acting through selective inhibition of $\alpha 4\beta 2$ nAChRs. Supported by DA-12001.
- 2 SENSE OF COHERENCE AS A STABLE PREDICTOR FOR METHADONE MAINTENANCE TREATMENT OUTCOME**
Y. Abramsohn, E. Peles and M. Adelson, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
- Aims: to determine whether sense of coherence (SOC) can serve as a predictor for success in Methadone Maintenance Treatment (MMT). Methods: A total of 44 patients who admitted between December-2003 and December-2004 filled the SOC questioner on admission to MMT clinic. Patients who stayed at least 1y underwent repeated SOC questionnaire. SOC defined as "A global orientation that express the extent of person confidence and ability to cope with pressures in life". Drugs abuse for cocaine, amphetamine, THC, opiates and benzodiazepines in month prior to second SOC evaluation after 1y was recorded, and defined as positive if at least one urine of any drug was positive Results: Of the 44 patients, 35(79.5%) stayed at least one year. The SOC on admission was 122.6 \pm 24.8 in those who stayed and 104.6 \pm 25.9 in those who left (ANOVA F=3.7, p=0.06). Repeated SOC questionnaire evaluation a year later found similar score compared to the baseline (122.6 \pm 24.7 and 119.9 \pm 27.7, paired t-test 0.8 p=0.4). Mean scores however were significantly lower in 18 (51.4%) patients who abused any drugs (113.2 \pm 25.0 at baseline and 104.1 \pm 22.0 after 1y), compared with the 17(48.6%) who did not abuse (132.5 \pm 20.9 at baseline and 136.6 \pm 23.4 after 1 year, Repeated measures, Groups: F=13.9, p=0.001; Time effect F=0.5, p=0.5). Conclusions: These findings suggest that SOC can be used as a possible tool in predicting MMT success in abstinence from drug abuse. It also extends previous studies that found SOC to be a stable personality factor in other population, to out group - former heroin addicts currently in MMT.
- 3 DRUG AND ALCOHOL INTOXICATION IN VIOLENT VICTIMIZATIONS ON THE SOUTHERN UTE INDIAN RESERVATION**
J. C. Abril, Medical and Health Research/National Development and Research Institutes, New York, NY
- Problem: Little empirical data documents violent victimization among Indians on reservations. Tribal authorities report that Indians had higher incidents of violence than non-Indians living on the Southern Ute Indian reservation. Background: The Southern Ute Indian Tribe is a federally-recognized American Indian Tribe located in the southwest corner of Colorado. It has tribal police, court, jail, and substance abuse treatment facility serving Indian clients sentenced for substance-induced domestic violence and substance abuse. Hypothesis: Violent victimization occurring among Southern Ute Indian tribal members is precipitated and worsened by instant drug and/or alcohol use by either the victim of violence and/or the person being violent. Methods: A 72-item survey questionnaire was distributed to all adult Southern Ute Indians (n=891) and to a larger (n=1,100) sample of non-Indians living within the boundaries of the Southern Ute reservation; 312 Indians and 355 non-Indians responded to the survey. Eighty-five 1-2 hour personal interviews were conducted with Indians subjects. Statistical analyses of the survey responses were conducted. Qualitative data also illustrate examples of incidents of violence. Findings: Southern Ute women were victimized more often than any others in this study (p<.05). Victims of physical violence were often victimized by people who were under the influence of drugs and/or alcohol at the time of the attacks. Subjects also reported their own intoxication while engaging in mutual violence and while acting as the sole aggressor in such. While females were victimized more by an intoxicated person, they too, reported they were under the influence when they were the violent person. Conclusions: Drug and/or alcohol use, both among victims and those who are behaving violently, may be a reliable predictor variable associated with future violent victimization among Native American Indians living on this reservation.
- 4 EXAMINER-RATED BEHAVIOR IN MALE AND FEMALE CHILDREN WITH IN UTERO COCAINE EXPOSURE**
V.H. Accornero, L. Xue, C.E. Morrow, M.W. Stuhlman, J.C. Anthony, C.B. McCoy and E.S. Bandstra, University of Miami Miller School of Medicine, Miami, FL, and Michigan State University, East Lansing, MI
- Objective: To examine the impact of prenatal cocaine exposure on facets of behavior as rated by examiners at ages 5 and 7 years. Design/Methods: Data were collected as part of the ongoing longitudinal Miami Prenatal Cocaine Study (MPCS). 476 African-American full-term infants (253 cocaine-exposed, 223 non-exposed) were enrolled prospectively at birth and assessed serially through age 7. Analyses are based on 424 children (224 cocaine-exposed, 200 non-exposed) with available behavioral ratings from the 5- and/or 7-year neurodevelopmental assessments. Behavior was assessed using the Behavior Observation Record (BOR), an investigator-developed rating scale assessing dimensions of behavior as observed during the structured testing session. Raters were trained research psychometricians blinded to drug exposure status. The relationships between prenatal cocaine exposure and facets of behavior were estimated using generalized estimating equations within the general linear model (GLM/GEE). Results: Borrowing information across the age 5- and age 7-year ratings and holding constant the child's age and prenatal exposure to other drugs, prenatal cocaine exposure was associated with greater temper/anger outbursts (estimated difference D = 0.7; p = 0.014) and uncooperative behavior (D = 0.7; p = 0.024). In follow-up male/female subgroup analyses, prenatal cocaine exposure was related to uncooperative behavior for males only, whereas cocaine-associated increases in temper/anger outbursts were evident only in the females. Conclusions: Relative to non-cocaine-exposed comparisons, prenatally cocaine-exposed children were rated by blinded examiners as more uncooperative and as displaying more temper/anger outbursts during testing sessions. Exploratory subgroup analyses revealed possible male/female differences in the association between in utero cocaine exposure and specific facets of behaviors. K01DA16720; R01DA06556; M01RR16587; T32HD07510; Health Foundation of South Florida

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5 DEXTROPHAN TARTRATE PRODUCES TOLERANCE AND PHYSICAL DEPENDENCE IN RHESUS MONKEYS

M.D. Aceto, E.R. Bowman and L.S. Harris, Virginia Commonwealth University, Richmond, VA

Dextrophan (DX) is a major metabolite of dextromethorphan, an ingredient commonly found in many cough preparations. Both substances are used recreationally by humans and are subject to abuse. Our objective was to determine the physical dependence capacity of this metabolite using nonhuman primates. DX was given subcutaneously (s.c.) to 3 rhesus monkeys (*M. mulatta*) 4 to 6 times a day for 30 days. The starting dose was 3 mg/kg. Over the course of the study, the dose was gradually raised so that on the last 2 days of the study it was 13 mg/kg. Initially, DX produced severe ataxia and body sag. Tolerance developed rapidly to these effects by day 10. Eight to 12 hours after DX was abruptly discontinued, a withdrawal syndrome was observed. It was characterized by the signs designated lying on side or abdomen, rubbing face, repeated touching of genital area, restlessness and drowsiness. One hour later, the monkeys were challenged with a single dose of naltrexone (1 mg/kg, s.c.). The withdrawal syndrome worsened. In addition, 2 of the monkeys retched and vomited. Withdrawal signs were no longer evident 5 hours later. In sharp contrast with the withdrawal syndrome produced by mu-opioid receptor agonists such as morphine, allodynia associated with abdominal palpation was not observed. The results indicate that repeated use of relatively low doses of DX or by extension, dextromethorphan, can produce tolerance and physical dependence. Supported by NIDA DA 1-7725.

7 PSYCHIATRIC AND SUBSTANCE ABUSE COMORBIDITY INFLUENCES TREATMENT OUTCOMES IN OPIOID-ABUSING PAIN PATIENTS

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We explored the relationship between psychiatric and substance use disorders and treatment outcomes for patients with Rx opioid abuse and pain participating in a 12-week behavioral/pharmacological treatment. At week 12, patients were either maintained on (success) or tapered off (failure) RX opioids for pain (based on an algorithm). "Success" required decreased pain, improved functioning, Rx opioid adherence, and decreased other drug use. 36 randomized patients completed the SCID at baseline; high rates of current and lifetime mood (current=47.2%, lifetime=25.0%) and anxiety disorders (current=41.7%, lifetime=19.4%) and lifetime alcohol (current=2.8%, lifetime=36.1%) and non-opioid drug disorders (current=5.6%; lifetime=41.7%) were found. We hypothesized that comorbidity would predict poorer treatment outcomes. Patients with a current mood disorder had poorer completion rates (47.1% completed) vs. those with a lifetime mood disorder (100% completed) or no mood disorder (80% completed; chi-square=7.9, $p<.05$). A similar pattern was found for anxiety disorders (chi-square=7.2, $p<.05$); 42.9% of patients with a current anxiety disorder completed treatment vs. 85.7% with lifetime and 85.7% with no anxiety disorder. Neither current nor lifetime mood/anxiety disorders were associated with success at wk 12. Conversely, neither alcohol nor non-opioid SUDs were associated with treatment completion; however both were significantly associated with success at wk 12. Only 50% of patients with lifetime or current AUDs were successful vs. 92.9% without AUDs (chi-square=5.7, $p<.05$). Similarly, only 58.3% with lifetime or current non-opioid SUDs were successful vs. 91.7% with SUDs (chi-square=3.6, $p=.06$). Findings suggest that Rx opioid abusers with psychiatric comorbidities are more difficult to retain in treatment but, if retained, have comparable outcomes to those without psychiatric disorders. Conversely, patients with non-opioid SUDs (mostly lifetime) are retained in treatment just as well as those without SUDs, but their drug abuse is not as amenable to change.

6 EFFECTS OF SLEEP DEPRIVATION ON COGNITION, DECISION-MAKING AND IMPULSE CONTROL

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Sleep disturbances are common in abstinent substance abusers and have been strongly linked to relapse in recovering alcoholics (Brower, Aldrich, & Hall, 1998; Friedmann et al., 2003). It is possible that sleep loss increases susceptibility to relapse through its effects on cognition, decision-making and/or impulse control. To characterize the effects of sleep loss on cognitive performance we are testing the effects of 36 hours of sleep deprivation on cognitive tasks in healthy volunteers. To date, eight males and six females have completed a two-session study in which they remained awake for a full night and following day, or were allowed to sleep normally during the night. At 8 am and 6 pm on the day after the monitored sleep deprivation or normal sleep, participants completed mood questionnaires and measures of attention and cognitive efficiency, behavioral inhibition, delay discounting and risk taking. Sleep deprivation increased subjective ratings of fatigue and decreased ratings of elation, vigor, and positive mood. Sleep deprivation also impaired attention and cognitive efficiency on the Automated Neuropsychological Assessment Matrix battery. On the Stop Task, sleep deprivation marginally increased stop reaction time, indicating impaired behavioral inhibition, but it did not affect delay or probability discounting or risk taking. These preliminary findings indicate that sleep deprivation impairs certain cognitive processes while not affecting others. These impairments may play a role in the increased susceptibility to relapse in recovering substance abusers. Supported by DA09133, T32DA07255, M01RR00055.

8 CHOLINERGIC RECEPTOR SYSTEMS IN COCAINE-ADDICTED SUBJECTS: ALTERATIONS IN REGIONAL CEREBRAL BLOOD FLOW

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Reinforcement behaviors depend upon a balance between nucleus accumbens dopamine and acetylcholine (ACh). In preclinical studies, cocaine induces marked changes in the cholinergic system, and drugs acting upon cholinergic receptors alter cocaine self-administration. This study was therefore designed to assess cholinergic receptors systems in cocaine-dependent subjects. Cocaine-only addicted male subjects (25 to 45 y/o) were studied at two to six-weeks abstinence and compared to age-similar controls. On three separate study days, subjects were administered i.v. (1) the muscarinic/nicotinic ACh agonist physostigmine (2) the muscarinic ACh antagonist scopolamine, or (3) saline. Single photon emission computed tomography (SPECT) was used to compare the regional cerebral blood flow (rCBF) response of drug vs. saline ($p<0.01$). Following physostigmine infusion, control subjects ($n=9$) demonstrated an increase in left orbitofrontal cortex (OFC), right thalamic, and left parahippocampal rCBF and a decrease in the rostral anterior cingulate and right DLPFC rCBF. Cocaine-dependent subjects ($n=10$) showed an increase in the left and right OFC and hypothalamus. Following scopolamine infusion, controls ($n=10$) showed a decreased rCBF in the rostral anterior cingulate, left lateral OFC, and left thalamus. Cocaine-dependent subjects ($n=11$) demonstrated an increase in rCBF in the left DLPFC and a decrease in the left thalamus, brainstem, anterior (non-amygdalar) temporal cortex. The identification of highly localized and functionally relevant regions of muscarinic and nicotinic receptor dysregulation may provide specific targets for cholinergic pharmacologic treatments. These findings further imply that hypotheses suggesting ubiquitous, cortical-wide increases or decreases in receptor changes may be overly simplistic. This work was funded by NIDA R01DA011434.

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9 EFFECTS OF ACUTE "BINGE" COCAINE ON MU OPIOID RECEPTOR MRNA LEVELS IN THE FRONTAL CORTEX OF DOPAMINE D1 OR D3 RECEPTOR KNOCKOUT MICE

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In humans, an elevation of mu opioid receptor (MOP-r) binding potential in the frontal cortex (FC) is associated with cocaine craving during early abstinence. In studies of rats, decreases in dopaminergic (DAergic) transmission in medial prefrontal cortex are associated with increased cocaine-seeking behavior. Dopamine D1 or D3 receptor knockout (D1^{-/-} or D3^{-/-}) mice offer the opportunity to test the roles of these specific receptors' deficiency in regulation of MOP-r gene expression in response to acute "binge" cocaine administration. In the present studies, we found an increase in basal MOP-r mRNA levels in the FC of either homozygous D1^{-/-} or D3^{-/-} mice, with no difference in the nucleus accumbens (NAc) core, caudate-putamen (CPu), amygdala or ventral tegmental area. Acute "binge" cocaine (3 × 15 mg/kg for 2.5 h) returned the high FC MOP-r mRNA baseline in D1^{-/-} or D3^{-/-} mice back to that in wild type controls. In the NAc core, the MOP-r mRNA response to acute "binge" cocaine was opposite between the two knockout mice: a decrease in D1^{-/-} mice and an increase in D3^{-/-} mice. Further, stress hormone corticosterone response to acute "binge" cocaine was blunted in D1^{-/-} mice and enhanced in D3^{-/-} mice. Taken together, our findings suggest that: (1) both D1 and D3 receptor deficiency is involved in the FC MOP-r gene regulation; (2) neither D1 nor D3 receptor is required for inhibitory effects of cocaine on the FC MOP-r gene regulation; and (3) D3 receptors mediate an inhibitory effect on the action of cocaine on NAc MOP-r gene expression and stress responsivity.

11 CONTRASTING GENETIC MODELS FOR LIFETIME COMORBIDITY OF CANNABIS AND OI D USE AND PROBLEM USE IN AUSTRALIAN ADULT TWINS

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Causal and correlative processes may contribute to the association between cannabis and other illicit drugs (OID). Genetically informative studies support the role of heritable and environmental influences on the liability to use or misuse illicit drugs. We contrast mechanisms by which these genetic and environmental risk factors contribute to the association between cannabis and OID use and problem use (one or more symptoms of abuse/dependence) using a large dataset (N=4179) of adult (mean age= 30 yrs) male (42%) and female twins. We evaluated thirteen possible mechanisms to explain the lifetime comorbidity of cannabis and OID use and problem use. Substantial heritability was found for cannabis use (46%) and problem use (53%) and OID use (38%) and problem use (62%) with modest evidence for shared environmental influences (10-36%) on use. Latent genetic ($R_g=0.66-0.95$) and environmental factors ($R_e=0.04-0.51$) influencing cannabis and OIDs were correlated. An alternative model, where the liability to cannabis use and problem use had a reciprocal causal influence on the liability to OID use and problem use, could not be rejected. For comorbid drug use, and especially in women, using cannabis resulted in an independent increase in the likelihood of using OIDs, even in women that were not otherwise vulnerable to using OIDs. No other quantitative sex differences were noted. Despite support for a correlated vulnerabilities model, consistent with the "gateway" hypothesis, high-risk cannabis users were at increased risk for OID use, implying that a combination of correlative and causal processes govern this association. These results were also similar to previous findings from an independent sample of adult twins from Virginia, U.S.A. Despite cultural differences in perceptions regarding cannabis use in the U.S. and Australia, similar mechanisms may be contributing to the comorbidity across these drug classes in both populations. Support: AA07728, AA11998, AA13321, DA12854 & AA10249

10 RELIABILITY OF DIAGNOSTIC INFORMATION AND VALIDATION BY TOXICOLOGICAL TESTING IN POSTMORTEM DRUG ABUSE CASES

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The potential for microarray technology to identify molecular mechanisms that are altered in human drug abuse has increased interest in studies using postmortem brain samples from drug abuse cases; however, there are often barriers to obtaining adequate historical data concerning drug abuse. We evaluated medical examiner's reports, toxicology (general toxicology screening using blood in most cases, separate assays of hair, and assays for cocaine and metabolites in brain), and a telephone interview with the next-of-kin for postmortem evaluation of drug abuse. Forty-two cases of potential drug abuse were identified from the NIMH brain bank. Of these, 8 were initially identified as drug abuse cases from the medical examiner's report, and the remainder were identified by family telephone interviews (n=23) and detection of drugs by toxicological analyses (n=35). There were differences between drugs in the reliability of detection by various methods. For cocaine abuse, only three cases were identified on the basis of the medical examiner's report, but cocaine use was identified by the telephone interview in eight cases and by general toxicology in 13 cases. No cases of cannabis use were identified by the medical examiner's report, but the telephone interview identified 13 cases and general toxicology identified six cases. In 3 cases, cocaine and metabolites were present in brain, but cocaine was not detected either by general toxicology or in hair. In 8 cases, delta 9-tetrahydrocannabinol was detected by hair toxicology, but was not found by general toxicology. For postmortem studies, toxicological testing of multiple tissues (brain, hair, and blood) appears to be necessary for identifying current or recent drug use. Therefore, extensive toxicology should form a cornerstone of the postmortem assessment of drug abuse.

12 ANABOLIC STEROIDS: USERS' AND EXPERTS' PERSPECTIVES

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The objective of this study wants to analyze the use of anabolic steroids, its principal causes within the Autonomous Region of Valencia, Spain. Qualitative methodologies were combined with focus groups and interviews. The sample of interviews included 30 young men of the city of Valencia, and the focus groups also integrated 8 specialists in subjects ranging in Sociology, Anthropology, Psychology, Medicine, etc. The interviews and focus groups were digitally recorded and analyzed using the software Answer Tree. The experts agreed that there is a social perception that considers the non-prescribed use steroids as a grave social problem that is currently unregulated at an institutional level. They note that sports are very popular and that the "culture of the body", is major factor that influences people to change their body. The objective is to have a body that corresponds with the image they want to project. Starting from the point of view that the addiction to these products is strictly psychological, its use is the result of a physical suggestion that has surpassed the sports scene. The profile of a consumer is a young male, between 20 and 35 years old, with the routine of daily gym workouts, low perception of risk and consumption without any type of control or medical prescription who projects their persona image as something now known as being "metrosexual". The sale of these products in pharmacies lacks any judicial regulation and its sale through the rising Internet black market and gyms has not ceased to grow. Parallel to steroid use, are psychological problems such as Adonis Complex. Further studies are needed on the use of anabolic steroids taking into account its side-effects. We also point to the need to create political means for its control, such as establishing an ethical code for gyms. Supported by Generalitat Valenciana; Dirección General de Drogodependencias and Dirección General de Salud Pública-CSISP.

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13 CEREBRAL METABOLIC DIFFERENCES BETWEEN COMPLETERS AND DROPOUTS IN COCAINE DEPENDENCE TREATMENT

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Imaging studies indicate cerebral metabolic differences in drug abusers relative to non-drug using controls particularly in the orbitofrontal cortex (OFC), lateral prefrontal cortex (LPFC) and the anterior cingulate cortex (ACC). Chronic cocaine use is hypothesized to produce some of these metabolic changes. Because these alterations are localized within circuitry mediating cognitive functions, they could contribute to poor treatment adherence and/or outcome. This study examined the relationship of functional imaging data to outcome of treatment for cocaine dependence. Method: Cocaine dependent patients (N=23) in outpatient clinical trials of cognitive behavioral treatment (CBT) plus medication Underwent FDG PET imaging. All had monitored inpatient abstinence for 3 days prior to PET scans so as to limit the impact of recent cocaine use on imaging data. All were medication-free on admission and no psychotropic medications were prescribed during the 3-day stay. PET scans of regional glucose metabolism were obtained with subjects in eyes-open resting condition. Analysis: Based on prior studies, four major brain areas were examined: OFC (medial and lateral); dorsolateral PFC (superior, middle and inferior gyri); parietal cortex (superior and middle) and ACC (infrageneal, perigeneal and subgeneal). We compared treatment completers (remaining in CBT at least 12 weeks without missing ≥ 2 consecutive weeks, n=8) to dropouts (n=15). Results: Dropouts had significantly higher relative metabolism than completers in the medial OFC (left and right) and in the ACC (left infrageneal). Completers showed a tendency toward higher relative metabolism than dropouts in left parietal cortex. Exploration outside of these regions using SPM showed additional areas of metabolic differences, including the cerebellar vermis (completers > dropouts). These data indicate functional markers that predict retention, possibly consequent to cognitive impairment, in treatment for cocaine dependence.

14 COCAINE DECREASES PROGESTERONE SYNTHESIS IN PLACENTAL CELLS AND ELEVATES PROSTAGLANDIN LEVELS IN THE AMNIOTIC FLUID DURING PREGNANCY IN HUMANS

B. Ahluwalia, Howard University, Washington, DC

Balwant Ahluwalia, Wanzheng Pei, Shakuntala Rajguru, Olanrewaju Adeyiga. Howard University College of Medicine, Washington D.C. 20060 To assess fetal placental endocrine axis functions in cocaine users, studies were conducted in vitro and in situ. For in vitro study, placentas were obtained immediately following delivery from subjects (10) who were drug free (licit or illicit) throughout pregnancy (control subjects). Placental cells (cytotrophoblast cells 1×10^6) were isolated and incubated in media containing $1-3 \mu\text{molar}$ cocaine along with either substrate (25 hydroxycholesterol or low density lipoprotein). Progesterone was isolated from the incubate and quantitated using radioimmunoassay. The data show that progesterone synthesis was significantly decreased in the cocaine treated cytotrophoblast cells ($p < 0.01$) in cocaine treated cytotrophoblast cells. The results of this study show that 1) progesterone synthesis in cytotrophoblast cells decreased significantly ($p < 0.01$) in the presence of cocaine and 2), PGE2 and PGF2 α levels were significantly increased in the amniotic fluid in cocaine user ($p < 0.01$) and cocaine caused decrease in cAMP levels in cocaine treated cytotrophoblast cells. It is concluded that adverse outcome of pregnancy in cocaine users in humans is caused by altered placental-fetal endocrine functions.

15 DECREASED ALCOHOL/SMOKE/DRUG USE FREQUENCY WITH INCREASING AGE

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In 1665 the French moral philosopher Francois Duc de La Rochefoucauld wrote: "When we age it is not we who leave our vices it is the vices that leave us". In order to investigate the hypothesis that the frequency of drug use declines with age we employed a dataset of 4462 male veterans examined at an age between 31 and 49 years with respect to a row of physiological and life style measures. The relationship of frequency of current drug use [None Marijuana; Hard] to age was analyzed using a generalized linear model with a logit link i.e. $\log(\text{Odds of drug use [None; Marijuana; Hard]}) = a_0 + a_1 * \text{Age}$ Independent variables were standardized by z-transform. Both marijuana and hard drug use showed similar, negative and significant slopes of $a_1 = -0.681$ and $a_1 = -0.605$, respectively, supporting the idea that the drug use frequency drops with age. Both alcohol use and smoking showed a significant and similar decline ($a_1 = -0.182$ and $a_1 = -0.207$, respectively), this rate of decline is substantially lower than that for marijuana and hard drug use. We have previously demonstrated that the frequency of drug use increased with increased plasma levels of testosterone; we therefore analyzed the interaction between aging and testosterone by adding testosterone to the model. Both age and testosterone showed a similar sized and significant effect on the frequency of drug use, but with an opposite direction as testosterone increased the frequency of hard drug use ($a_1 = 0.362$) and marijuana use ($a_1 = 0.492$), whereas age decreased the frequency for hard drugs ($a_1 = -0.456$) and for marijuana ($a_1 = -0.544$). Further a significant interaction between age and testosterone was found for hard drugs ($a_1 = -0.216$) and for marijuana ($a_1 = -0.121$). A similar pattern was seen for alcohol use ($a_1 = -0.121$; $a_1 = 0.211$; $a_1 = -0.103$), but with less powerful effects. In contrast smoking did not show a significant interaction between age and testosterone, but was still significantly affected by age ($a_1 = -0.132$) and testosterone ($a_1 = 0.475$).

16 EFFECTS OF NICOTINE AND MECAMYLAMINE ADMINISTRATION ON NEUROTENSIN SYSTEMS IN THE RAT VENTRAL TEGMENTAL AREA

M.E. Alburgess, A.J. Hoonakker and G.R. Hanson, University of Utah, Salt Lake City, UT

Prior research suggests that neuropeptides have been implicated in the psychopathology of stimulants of abuse. In addition, the ventral tegmental area (VTA), a midbrain region implicated in the rewarding effects of most, if not all, addictive drugs, appears to be a critical target for nicotine action. Because the neuropeptide neurotensin (NT) has been linked with both mesolimbic and mesocortical dopamine function, we previously determined that nicotine treatment profoundly affects NT systems by decreasing neurotensin-like immunoreactivity (NTLI) content in the VTA. The present study was designed to investigate the effects of selective DA receptor antagonists and nicotinic receptor antagonist on nicotine-induced changes in VTA NTLI levels. Male Sprague-Dawley rats received multiple administrations of nicotine (0.8 mg/kg, i.p.) in the presence or absence of selective dopamine receptor (D1; SCH23390 or D2; eticlopride) or nicotinic receptor (mecamylamine) antagonists, and were sacrificed 18h after drug treatment. The NTLI changes induced in the VTA by nicotine administration were prevented by pre-treatment with either dopamine D2 receptor antagonist or the nicotinic receptor antagonist, but pre-treatment with dopamine D1 receptor antagonist did not affect the nicotine-induced changes on NTLI in the VTA. These results suggest that a combination of dopamine D2 and nicotinic receptors activity are important for the NTLI reduction in VTA caused by nicotine. Supported by NIDA grants DA09407 and DA00378.

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- 17 PRELIMINARY FINDINGS OF THE WHO ASSIST PHASE III STUDY IN AN AUSTRALIAN SETTING: A FIVE-MINUTE BRIEF INTERVENTION FOR ILLICIT DRUGS LINKED TO ASSIST SCORES**
R. Ali, R. Humeniuk and D. Newcombe, University of Adelaide, Adelaide, South Australia
The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) is an eight item pencil and paper questionnaire developed in 1997 by World Health Organisation in response to the overwhelming burden of disease caused by substance use. The ASSIST screens for problem or risky use of tobacco, alcohol, cannabis, cocaine, amphetamine-type stimulants, sedatives, hallucinogens, inhalants, opioids and other drugs. The test was devised for use in primary health care settings. The findings from the WHO ASSIST Phase I and II studies demonstrated that the ASSIST is a feasible, reliable and valid screening instrument for use in primary health care settings across various cultures. Phase III, which is currently in progress, involves a randomised controlled trial investigating the effectiveness of a brief intervention for illicit drugs (cannabis, cocaine, amphetamine-type stimulants and opioids) linked to ASSIST scores in approximately 900 subjects worldwide. A five minute brief intervention was developed using the ASSIST Feedback Form to give personalised feedback and advice to clients about their ASSIST scores and their associated level of risk. Preliminary findings from the Australian site based on recent analysis of 100 subjects demonstrated a significant reduction in illicit drug use ($F=12.0$; $df=1,98$; $p=0.001$) for those subjects receiving a brief intervention compared with control subjects not receiving an intervention. These results demonstrate that ASSIST screening and brief intervention is a timely and effective way of identifying and intervening with substance-using clients in primary health care settings. *On behalf of the WHO-ASSIST Study Group for Phase III: R. Ali (Australia), T. Babor (USA), M. Farrell (UK), M. Formigoni (Brazil), R. Humeniuk (Australia), J. Jittiwutikarn (Thailand), R. de Lacerda (Brazil), W. Ling (USA), J. Marsden (UK), B. McRee (USA), M. Monteiro (WHO Geneva), D. Newcombe (Australia), H. Pal (India), V. Poznyak (WHO Geneva), S. Simon (USA), J. Vendetti (USA)
- 18 DIFFERENCES IN HEROIN-INDUCED BEHAVIORS IN C57BL/6J AND 129P3/J MICE**
J.M. Allen, M.J. Swift, N.M. Dankert, S.D. Schlussman, Y. Zhang, A. Ho and M.J. Kreek, The Rockefeller University, New York, NY
We have reported that 129P3/J (129) mice formed conditioned place preference (CPP) to 5, 10 or 20 mg/kg doses of heroin, while C57BL/6J (C57) mice did not (Dankert et al. CPDD 2005). In the present report, we describe the home cage behavior in the same mice studied for conditioned place preference, following each heroin conditioning session. Methods: Male 129 and C57 mice were individually housed in a room dedicated to these studies and allowed to acclimate for 2 weeks before the study. On study days, mice were transported to an adjacent room, injected with heroin (5, 10 or 20 mg/kg) or saline (on alternate days) and confined to the CPP chamber for 30 minutes. All mice were then immediately returned to their home cage and moved back to the housing room where they were individually videotaped for 2 minutes for behavioral observation. Results: 129 mice routinely showed prolonged periods of inactivity in the home cage. This immobility took two distinct forms. The most common was a typical "freezing" behavior, in which animals became immobile, and apparently, rigid, in mid-step, similar to the catatonia described by Amalric et al (Br. Res. 386, 1986, Psychopharm. 91, 1987). The other type of inactivity was more subtle. Animals sat immobile, frequently in the center of the cage, clearly not in the nest and clearly not asleep. Occasionally an animal would move its head slightly, but this movement had a lethargic quality. Of 15 129 mice injected with heroin, 14 demonstrated these behaviors at least once during the 4 heroin conditioning sessions; 4 of the 5 mice injected with the highest dose of heroin studied displayed this behavior on all days and the other displayed this inactivity on 3 of the 4 days studied. In contrast, of the 15 C57 mice studied, only 2 mice showed "freezing" behavior, but most C57 mice did show a pronounced hind-limb rigidity, which resulted in a marked ataxia, characterized by a distinctive "duck walk". These observations demonstrate that heroin has strain specific behavioral effects. Supported by NIH DA-P60-05130 and DA-K05-00049 to MJK.
- 19 INTEGRATING EVIDENCE-BASED COUNSELING WITH ROUTINE BUPRENORPHINE TREATMENT FOR OPIATE DEPENDENCE**
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There is growing empirical evidence of buprenorphine's effectiveness in treating opiate dependence across a wide range of patient populations even when compared with the long-standing methadone maintenance approach. As it becomes more widely available, buprenorphine has the advantage of reaching a larger population of opiate dependent patients because it may be offered in a variety of clinical care settings. In order for buprenorphine to have a sizable effect, its expansion must be rapid, comprehensive, and appropriately integrated with other treatment and prevention programs. The treatment of opiate dependence, however, like the treatment of other addictive disorders, is likely to be bolstered by the inclusion of appropriate behavioral counseling. In this study, we describe the substance abuse and HIV risk-taking outcomes following the addition of a manualized, evidence-based, cognitive-behavioral counseling approach that we have adapted to complement routine buprenorphine treatment for opiate-dependent patients. The manualized counseling sessions were designed to enhance personal motivation for recovery and to improve skills for coping with and preventing relapse to illicit drug use. Though the counseling approach was designed to impose structure on treatment, it is sufficiently flexible to allow tailoring to meet individual treatment needs, particularly with the less structured use of buprenorphine. The content of counseling sessions was recorded and coded to determine clinicians' adherence to the manual and to assess the feasibility of integrating the counseling sessions with routine buprenorphine treatment. In addition, focus group interviews were conducted with clinicians to obtain additional detailed information regarding the utility and usability of the manualized counseling approach. Results indicate the promise and feasibility of incorporating evidence-based cognitive-behavioral counseling with buprenorphine treatment for opiate dependence.
- 20 FACTORS ASSOCIATED WITH HEAVY ALCOHOL USE AMONG WOMEN IN RESIDENTIAL DRUG TREATMENT**
A. A. Alvanzo, D. Svikis and D. Langhorst, Virginia Commonwealth University, Richmond, VA
Background: Patients with comorbid alcohol and drug use disorders tend to have more severe substance use disorders and often have poorer treatment outcomes than those with a single disorder. The primary aim of this study was to examine factors related to heavy alcohol use in women in residential drug treatment. Methods: Participants were 159 women in a residential drug treatment facility. Data was collected using the Addiction Severity Index (ASI), a semi-structured interview performed at study intake. All women provided informed consent as part of a larger research study on the effects of behavior incentives on attendance and retention in residential drug treatment. Demographically, women were in their late 30's (mean age 37.2, SD 7.19), had completed 11.3 years of school (SD 2.01), and were predominantly African American (74.8%). Defining heavy alcohol use as > 3 drinks/day, we analyzed the number of days of heavy alcohol use in the previous 30 days and total alcohol consumption in the previous 30 days. Covariates included age, race, years of education, as well as 30 day history of depression, anxiety, suicidal thoughts, medical problems, abuse (physical, sexual, or emotional), cocaine use, and heroin use. Bivariate analyses were performed using student's t-tests and Pearson's correlation coefficient for linear regression. Results: Heavy alcohol use was present in 27.7% of women. Days of heavy drinking was associated with depression (7.7 days vs. 2.2 days, $p < .0001$), and days of cocaine use ($r = 0.308$, $p < .0001$). Total alcohol consumption in 30 days was associated with depression (62.1 drinks vs. 16.8 drinks, $p .017$). Implications: Results suggest that heavy alcohol use in drug abusing women is associated with depression and cocaine but not heroin use. Study findings support the importance of screening for and treating depression in women in substance abuse treatment. This research was supported by NIDA DA 11476 and NIAAA AA 11802

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- 21 ESTIMATED RISK OF COCAINE DEPENDENCE SOON AFTER ONSET OF USE: UNITED STATES, 2002-2003**
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BACKGROUND & AIMS: Analyzing epidemiological data from 2000-2001, our research team previously estimated that roughly 6% of recent-onset cocaine users in the US become cocaine dependent within 24 months after first use of cocaine. In addition, we found excess risk associated with crack-smoking, being female, and (independently) with being of African-heritage. Here, with more recent data, we seek to strengthen and confirm these findings. **METHODS:** The new estimates are based on data from the National Surveys on Drug Use and Health (NSDUH) conducted in 2002-2003, with representative samples of community-dwelling US residents age 12+ (n=109,309). The key response variable in this study is first onset of cocaine dependence among recent onset cocaine users (i.e., those who starting cocaine use within 24 months of assessment). **RESULTS:** A total of 1638 respondents, 1.5% of the total sample, qualified as recent-onset cocaine users. An estimated 6%-7% of these developed the cocaine dependence syndrome within 24 months after onset of use. With respect to male-female differences, there was a 2 fold excess risk for females (p<0.10). **DISCUSSION:** The estimated 6%-to-7% risk of becoming cocaine dependent within 24 months after onset of cocaine use is not appreciably different from the previously reported estimate of 6%, and we have confirmed excess risk associated with being female and (independently) with smoking crack. Associations with other characteristics (e.g., African-heritage) were not confirmed in these new data, and require additional study. **SUPPORT:** NIDA/NIH/FIC D43TW05819; T32DA07292; K05DA015799.
- 22 N-ACETYL-CYSTEINE AND BACLOFEN AS PHARMACOTHERAPIES FOR CUE- AND DRUG-INDUCED COCAINE CRAVING**
S.L. Amen, R.C. Risinger, L.B. Piacentini and S.J. Li, Medical College of Wisconsin, Milwaukee, WI
N-acetylcysteine (NAC, Mucomyst®), a cysteine prodrug, and baclofen (BLF), a GABA-B agonist, reduce reinstatement in rodent cocaine self-administration models (Baker, 2003; Roberts, 1997). Clinically, these drugs have also been shown to reduce human cocaine use measured by dollars spent (LaRowe, 2004) and positive urine tests (Shoptaw, 2003). Therefore, we sought to examine the effects of NAC vs BLF vs PBO in a 3-week, single-blind crossover study of cue- and drug-induced cocaine craving in experienced, non-treatment seeking, cocaine-dependent volunteers. Participants remained inpatient for 3 separate 4-day stays, each with one study medication: NAC 400 mg tid, BLF 20 mg tid or PBO. For each visit, volunteers underwent identical 1-hr sessions on Days 1 and 4, where they completed visual analog scale ratings of HIGH, CRAVING, RUSH and ANXIOUS each minute throughout the session while observing videos depicting household (non-affective) scenes or cocaine-related scenes. The videos were then followed by an injection of 20 mg/70 kg i.v. cocaine. Participants remained inpatient for Days 2 and 3 and were monitored for side-effects, sleepiness, cravings, and cigarette usage. Analysis of the initial participants suggests that NAC produces a significant and robust reduction in baseline CRAVING, maximum and mean cue-induced as well as drug-induced CRAVING, and cocaine CRAVING measured by post-injection area under the curve. There is a trend for half of the participants in both treatment groups to rate a significant decrease in HIGH. Interestingly, analysis suggests a 30% decrease in the Questionnaire of [Cigarette] Smoking Urges (Tiffany, 1991) on Day 4 after NAC. Treatments were well tolerated; side-effects were minimal and consistent with literature reports. We will present a comprehensive analysis of the effects of NAC and BLF on both cue- and drug-induced high and craving and their potential roles as a pharmacotherapy for cocaine dependence. Supported by NIDA RO1 DA10214 and GCRC M01 RR00058.
- 23 DISCRIMINATIVE STIMULUS EFFECTS OF SR 141716A IN RHESUS MONKEYS TREATED WITH 2 MG/KG/DAY OF Δ9-THC**
M.R. Amin and L.R. McMahon, University of Texas Health Science Center San Antonio, San Antonio, TX
One strategy for examining drug dependence and withdrawal involves training agonist-dependent animals to discriminate an appropriate antagonist. To examine the neuropharmacology of dependence and withdrawal that can occur to cannabinoids, this study has begun to characterize the discriminative stimulus effects of i.v. SR 141716A (1 mg/kg) in monkeys receiving s.c. Δ9-THC (2 mg/kg/day). In addition to SR 141716A, the cannabinoid antagonists AM 251 and SLV 326 occasioned high levels of responding on the SR 141716A lever, whereas midazolam, triazolam, cocaine, ketamine, and morphine did not. Acute pretreatment with Δ9-THC before the experimental session, in addition to the dose of Δ9-THC administered daily, attenuated the SR 141716A discriminative stimulus. In addition, the cannabinoid agonists CF 55940 and WIN 55212-2 attenuated the discriminative stimulus effects of SR 141716A. Morphine attenuated the effects of SR 141716A in some monkeys, whereas triazolam did not. When daily Δ9-THC treatment was suspended for 6 days, all monkeys responded predominantly on the SR 141716A lever within 2-3 days; thereafter, in some monkeys, responding on the SR 141716A lever was diminished from 4-6 days after discontinuation of treatment. This study demonstrates that, in monkeys receiving a relatively large dose of Δ9-THC, cannabinoid antagonists have qualitatively similar effects, cannabinoid agonists attenuate the effects of SR 141716A, and the discriminative stimulus effects of SR 141716A are qualitatively similar to discontinuation of Δ9-THC treatment. The discrimination is consistent with cannabinoid withdrawal and, in addition to its sensitivity to cannabinoids, appears to have utility for evaluating other drug classes that do (Δ opioid agonist) and do not (a benzodiazepine) modify this particular measure of cannabinoid withdrawal. Supported by DA15468 and DA19222.
- 24 PCP-INDUCED REGULATION OF THE NMDAR AND DEVELOPMENT OF LOCOMOTOR SENSITIZATION**
N.C. Anastasio and K.M. Johnson, University of Texas/Galveston, Galveston, TX
Phencyclidine (PCP) was originally developed for use as a surgical anesthetic, but was abandoned due to post-operative hallucinations. It was a significant drug of abuse in the mid-1960s and early 1970s known as "angel dust". PCP has many pharmacologic effects, but elicits its major actions by noncompetitively blocking the NMDA receptor ion channel. The NMDAR is a member of the ionotropic glutamate family of receptors and is composed of multiple subunits including NR1, NR2A-D, and NR3A/B. PCP treatment to perinatal rats results in neurodegeneration and sensitization to the locomotor activating effects of PCP challenge. The purpose of this study was to investigate the effects of PCP treatment on the composition of the NMDAR subunits and its relationship to the development of locomotor sensitization in young rats. Sprague-Dawley rat pups were treated on PN7, 9, and 11 with saline or PCP (10mg/kg). Animals were sacrificed on PN12 for biochemical studies or tested for sensitization to PCP at PN28-35. Western analysis showed that sub-chronic PCP treatment results in a significant increase in NR1 and NR2A protein but no change in NR2B levels in the frontal cortex. PCP treatment results in down-regulation of NR1 in the striatum with no effect on the levels of NR2A or NR2B. Additional experiments examined the effects of pretreatment with risperidone (5-HT2A/D2 receptor antagonist) or the selective D2 receptor antagonist, sulpiride. Risperidone and sulpiride prevented the up-regulation of NR1 and NR2A in the frontal cortex induced by PCP, but were ineffective at inhibiting the PCP-induced down-regulation of NR1 in the striatum. On PN28-35 animals were challenged with 4 mg/kg PCP and total horizontal activity was measured. Sub-chronic PCP treatment resulted in locomotor sensitization that was inhibited by risperidone and sulpiride. These studies suggest that up-regulation of the NR1 and NR2A subunits in the frontal cortex induced by PCP treatment is correlated with the development of locomotor sensitization and that D2 receptors may play a regulatory role in both processes. Supported by DA-07287, DA-02073 and MH-63871.

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- 25 TOBACCO USE IN A RESIDENTIAL SAMPLE OF DRUG-DEPENDENT WOMEN**
L. M. Anderson, D. Svikis, D. Langhorst and S. Meshburg-Cohen, Virginia Commonwealth University, Richmond, VA
The present study identified correlates of smoking in a sample of drug dependent women in residential treatment. Participants were 163 women who provided informed consent to participate in a behavioral incentive drug abuse research study. They had a mean age of 37.2 years (SD= 7.2) and 73% were African American. Approximately three-fourths of the sample reported lifetime history of depression (76.7%) and anxiety (71.8%). Participants were categorized as smokers (N=124; 76%) or nonsmokers (N=39; 24%) based on Addiction Severity Index (ASI) data. On average, smokers used cigarettes 28 days out of the last 30, smoked 16 cigarettes per day, had been smoking regularly for 16 months, and began smoking at age 20. Smokers reported a higher lifetime prevalence of depression (81% vs. 64%; $F[161, 55]= 10.3, p < .001$) and anxiety (76% vs. 59%; $F[161, 57]= 13.1, p < .05$) than nonsmokers. Smoking frequency in the past 30 days was significant with cigarettes per day (cpd) ($F[15,142]= 24, p < .001$), age of first cigarette use ($F[14,145]= 3.4, p < .001$), and months of regular cigarette use ($F[15,147]= 6.1, p < .001$). Smokers increased their frequency of smoking from intake into the program to discharge from the program by 4.3 days per month (20.1 days vs. 25.6 days out of the past 30; $p < .05$). However, cpd decreased from intake to discharge by 5 cpd (15 cpd vs. 10 cpd; $p < .001$). Findings suggest that drug dependent women with comorbid smoking are more likely to report a lifetime prevalence of anxiety and depression. Results also suggest that female smokers in a residential drug abuse treatment program will increase the number of days per month that they smoke cigarettes, but decrease cigarettes smoked per day. This research was supported by NIDA DA 11476 CORRESPONDING AUTHOR: Lynn Anderson, VCU, Box 980343 Richmond, VA 23298 USA.
- 26 RECIPROCAL T2RT FLUCTUATIONS IN STRIATUM AND CEREBELLAR VERMIS CORRELATE WITH SUBJECTIVE DESIRE FOLLOWING ORAL METHYLPHENIDATE**
C.M. Anderson, M.H. Teicher, M.M. Silveri, S.E. Lukas, P.F. Renshaw and M. J. Kaufman, Brain Imaging Center, McLean Hospital/Harvard Medical School, Belmont, MA
We recently reported that the cerebellar vermis may contain dopamine transporter (DAT) (Neuropsychopharmacology, in press). Vermis exerts influence over dopamine (DA)-rich basal ganglia (BG) regions governing reward processes (Hoshi et al., Nat. Neurosci. 2005). This study assessed vermal and BG activations in 11 healthy adults (7 men) in response to an oral methylphenidate (MPH) challenge (0.5 mg/kg). Vermis and BG activations were measured at baseline and periodically following MPH administration using transverse relaxometry (T2RT), a surrogate marker for cerebral perfusion. Subjective measures of drug effect also were acquired after each T2RT dataset using Likert scales. Data were analyzed with a principal component (PC) analysis. Ten vermal regions of interest (ROI) measures were reduced to 4 PCs accounting for 68% of the T2RT variance. Eight striatal ROIs were reduced to 4 PCs accounting for 81% of the T2RT variance. Six subjective ratings were reduced to 4 PCs accounting for 82% of ratings variance. Correlation analyses indicated associations between regional T2RT and subjective PCs. Desire/liking PC ratings were correlated negatively and positively with vermis region VIII PC ($r=-0.479, p<0.01$) and putamen PC ($r= 0.384, p<0.01$), respectively. Thus, vermis and putamen PCs were oppositely correlated with desire/liking PC, resulting in a strong correlation between desire/liking ratings and the vermis minus putamen PC ($r=0.61, p<0.0001$). We conclude that MPH activates vermis regions thought to contain DAT and that there is a reciprocal relationship between vermis and putamen activations and subjective desire/liking. These data provide additional support for vermis participation in and possible modulation of BG responsively to MPH and perhaps other stimulants. The nature of this interaction may reflect individual differences in self-reports of desire for or aversion to MPH. Supported by NIH grants DA00343, DA16746, DA14674, DA17324, DA09448 & DA14178.
- 27 EFFECTS OF ACUTE AND REPEATED NICOTINE ADMINISTRATION, AND SUBSEQUENT TERMINATION, ON DELAY DISCOUNTING IN LEWIS AND FISCHER 344 RATS**
K. G. Anderson and R. A. Dover, West Virginia University, Morgantown, WV
A previous study (Anderson & Woolverton, 2005) reported strain differences between Lewis and Fischer 344 rats in impulsive versus self-control choices (delay discounting). To further investigate strain differences in delay discounting and effects of nicotine on impulsive choice, eight Lewis and eight Fischer 344 rats were allowed to choose between one, immediate food pellet and three food pellets delivered after a delay. The delays to the larger alternative (0, 5, 10, 20, 40 s) were increased across five blocks of trials in daily sessions. For all subjects, choice for the larger reinforcer decreased as the delay to its presentation increased. Strain differences were observed in mean control (non-drug) indifference points (delay where choice for the large and small reinforcers are equal, 50%). Following acute nicotine administration (0.1, 0.3, 1.0 mg/kg, s.c.), mean indifference points were increased relative to control values for both strains after the highest doses. This increase was greater for the Fischer 344 rats, i.e., they emitted more larger reinforcer choices. Following repeated exposure to 1.0 mg/kg nicotine, choice for the larger reinforcer returned to near control levels for both groups. Upon termination of nicotine administration, mean indifference points decreased to below control values for both groups. Differences in genetics and/or neurochemistry may influence delay discounting and impulsive choice, and how drugs of abuse affect such behavior.
- 28 LATE INSOMNIA AS A PREDICTOR OF TREATMENT RETENTION IN NALTREXONE MAINTENANCE FOR HEROIN DEPENDENCE**
S.J. Anen, M.A. Sullivan, S. Shakibaie, S.K. Vosburg and E.V. Nunes, New York State Psychiatric Institute, New York, NY
These data are from a Stage 1B randomized, double-blind, outpatient trial designed to test the efficacy of a behavioral therapy and depot naltrexone in combination with oral naltrexone. Seventy-three heroin-dependent participants were administered a Hamilton Depression Scale by a research psychiatrist prior to detoxification. Given the frequency of insomnia as a post-detoxification complaint, both in the treatment literature and in our clinical experience, we identified an insomnia subscale. Items 9-11, which focus upon early, middle, and late sleep insomnia, were examined in order to determine the potential role of sleep disturbances upon study retention. The sample was divided into three groups according to the following strategy: patients were assigned to the Late Insomnia group if any late insomnia was reported, the No Insomnia group if none was noted, and the Other Insomnia group if early and/or middle insomnia was present without late insomnia. Regression analysis showed that late insomnia was a significant predictor of retention ($R=.29, R^2=.08, p=.01$). In the Late Insomnia group, 23.3% failed to complete detoxification, compared to 18.2% in the No Insomnia group and 10.5% in the Other Insomnia group. Those within the Late Insomnia group were also less likely to complete six months of naltrexone treatment (9.3%) versus those with No Insomnia (26.3%) and those with Other Insomnia (18.2%). These findings suggest that late insomnia is a distinct sleep phenomenon, which serves as a marker for poor retention in the treatment of heroin dependence and deserves clinical attention, including research to assess more aggressive interventions targeting sleep disturbance. These results also reinforce the utility of the Ham-D as a tool to guide clinical care. More research is needed to examine whether late insomnia reflects more severe opioid withdrawal, concurrent affective or anxiety disorder, or some other, perhaps opioid-induced, phenomenon. Future research should also examine whether insomnia predicts poor outcome for other treatment modalities such as agonist maintenance.

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29 EFFECTS OF PROGESTERONE AND ESTROGEN ON REINSTATEMENT OF COCAINE-SEEKING BEHAVIOR IN FEMALE RATS

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Phase of estrous cycle modulates i.v. cocaine self-administration in rats. Estrogen facilitates the acquisition and reinstatement of cocaine self-administration when administered to ovariectomized (OVX) rats. Recently, it has been shown that progesterone (P) decreases the rate of cocaine acquisition in female rats (Hu et al. 2004). The purpose of the present study was to study the short-term effects of estrogen (0.05 mg/kg estradiol benzoate, EB) and P (0.5 mg/kg) on the reinstatement of cocaine-seeking behavior in female rats. Rats were implanted with i.v. catheters, and they received a bilateral ovariectomy. They were then placed in operant chambers and trained to lever press for 0.4 mg/kg cocaine infusions under a FR 1, 20-sec, timeout schedule of reinforcement during daily 2-hr sessions until behavior was stable for 14 days. The cocaine reservoir was then replaced with saline, and a 21-day extinction period began. After extinction, rats were separated into one of three treatment groups (i.e., OVX+EB, OVX+EB+P, or OVX+VEH). At this time the house light, lever lights, and pump were disconnected and VEH, EB, or EB+P was administered 30 min prior to the onset of each daily session until the completion of the study. After three days of hormone treatment rats received a reinstatement procedure in which alternating days of a single saline or cocaine (5, 10, or 15 mg/kg in mixed order) i.p. priming injection was administered at the beginning of each experimental session for six consecutive days. Responding during the maintenance and extinction phases was similar across all groups. Estrogen treatment in the OVX+EB group increased reinstatement at the 10 mg/kg dose relative to the OVX+EB+P and the OVX+VEH groups that had similar low levels of responding. The suppression of cocaine induced reinstatement responding following an injection of progesterone and estrogen suggests a possible role for progesterone in the therapeutic prevention of relapse of cocaine seeking behavior. Supported by R01 DA03240 and K05 DA15267 (MEC).

30 DYNAMIC REINFORCING ENVIRONMENTS AND THE ANHEDONIC HYPOTHESIS

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The idea that dopamine mediates the reinforcing effects of positive stimuli subsist in the field of neurosciences. The present study will show that haloperidol does not interfere with the rat's behavior of pressing on a lever to obtain food reinforcers that varied in magnitude and probability of occurrence. Within sessions the ratio of reinforcers changed seven times in two levers, modeling a dynamic environment. Magnitude of reinforcement was manipulated independently of the ratio of reinforcer provided by the levers. Four doses of haloperidol were assessed (ip) over periods of twelve days. Haloperidol did not stop the discrimination that the rats established between rich and lean levers, response distributions favored the lever associated with the highest probability of reinforcement and the largest number of pellets. The parameters of the generalized matching law (bias and sensitivity to reinforcement) indicated that haloperidol acted upon the motor system, but it did not affect the rat's motivation for food reinforcers.

31 SUBSTITUTION IN ROUTINE CARE IN GERMANY: RETENTION RATES AFTER 12 MONTHS OF FOLLOW-UP (COBRA)

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Background: Keeping the patient in substitution treatment is a core challenge. Retention rates are a crude measure for indicating how well treatment works. In controlled clinical trials the retention rates vary between 30 to 80% depending upon type of substitution drug and duration of treatment. Little is known about the influence of the kind of substitution drug, provider model (size of facility) and intensity of care. Questions: What proportion of patient on methadone and buprenorphine is retained after 12 months in routine care? What are the most common reasons for dropout? Do retention rates differ by type of substitution drug (methadone vs. buprenorphine), provider model (small, medium, large practice) and duration of substitution therapy? Method: COBRA baseline sample of N=2,694 patients of an overall of N=223 substitution doctors was followed-up over a period of 12-months. Retention rates are based on the subset of patients that were still eligible (N=2,158). Detailed examination of plausibility of the data of the 12-months follow-up and alignment with the baseline, 6- and 9-months follow-up was done. Data analyses of survival rates with STATA. Results: Retention rates in routine care are at least as high as in clinical trials. Primary care settings with few patients and no specialisation reveal slightly better retention rates than large scale specialised centers. Methadone and buprenorphine patients show similar retention rates in the 12-month follow-up, if accounting for prior treatment duration. The retention rate is lowest among patients who just started the substitution treatment and highest among those who are receiving the substitution drug already for a longer time. The data indicate differences in drop-out reasons among methadone and buprenorphine patients: Buprenorphine patients remained more frequently with their physicians, had less often significant concomitant drug use, became more frequently clean and are less often imprisoned compared to methadone patients.

32 PERCEIVED MEDICAL EFFECTIVENESS AND BUPRENORPHINE USE

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Physicians' perceived limitations of a new medication can greatly affect its use. This is especially relevant when the medication must be prescribed in a regulated environment, such as buprenorphine. Perceived limitations may be related to physicians' experience with the medication and training. Using an ongoing survey of physicians certified to prescribe buprenorphine for the treatment of opioid dependence, we examined if limitations were associated with physicians' experience and training, with special attention to limitations that appear to question the medication as opposed to the regulations. The surveys (n=1,753) asked physicians to select from a list of 13 possible limitations. The responses ranged from a high of 41.9% who saw the 30 patient regulatory limit on physicians as a problem to a low of 1.3% who thought medical complications were problematic. Medical effectiveness (either "limited effectiveness" or "medical complications") were selected by 3.9% of the physicians. These physicians were more likely to specialize in Internal Medicine and less likely to specialize in Psychiatry, but they did not differ on having addiction medicine certifications, type of practice, number of years practicing, region of the country, urbanicity or the mean number of patients with substance abuse problems they saw in the past 90 days. The physicians who selected medical effectiveness as a limitation, however, had treated fewer patients with buprenorphine in the last 90 days than other physicians. Examining the 31.8% of physicians who were surveyed more than once revealed no temporal trend in identifying medical effectiveness as a limitation, suggesting that just time would not change their perception. Although not a widespread problem, the tendency for physicians with more general training to treat fewer patients with buprenorphine suggests that efforts to expand access to treatment need to address this concern. The use of mentor physicians to counsel physicians with less experience treating opioid dependent patients may be one approach to address this limitation.

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33 DEVELOPING TRAINING MODULES AND OTHER TOOLS FOR INTERNATIONAL DRUG ABUSE RESEARCHERS

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The National Institute on Drug Abuse (NIDA) seeks to support international cooperative research, training, and the exchange of scientific information by drug abuse scientists around the globe. Currently, not one specific Web site contains training modules for international application of drug abuse research and other resources created specifically for those working in international drug abuse research. Danya International, Inc. (Danya) is addressing these needs by developing the Drug Abuse Research Training Program for International Investigators (DART-I). This highly interactive and user-friendly Web site for the international drug abuse research community will include training modules and links to other relevant resources, including funding opportunities, a partnering database, and a roadmap to NIDA resources tailored for an international audience. Danya proposes a Web site that will consist of three primary components: (1) training modules designed to improve research skills of foreign investigators; (2) a partnering database to facilitate the development of collaborative proposals; and (3) a guide to funding opportunities for international substance abuse research. Over the course of Phase I and Phase II, Danya will develop this Web site designed to respond to the ever-increasing need of enhancing research skills of foreign investigators and stimulating state-of-the-science collaborative research between investigators from domestic U.S. institutions and researchers in other countries. This presentation discusses the following Phase I activities: a needs assessment with international researchers, NIDA grantees, and other NIDA stakeholders; the development of two training modules; the development of a Website prototype; and a pilot feasibility study.

35 PATTERNS OF NON-MEDICAL USE OF PRESCRIPTION STIMULANTS IN COLLEGE STUDENTS: ASSOCIATIONS WITH ADHD AND POLYDRUG USE

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This study describes initial findings from the College Life Study (CLS) on the patterns of non-medical use of prescription stimulants among college students. Face-to-face interviews were administered to 1,253 first-time first-year college students that included questions about the presence of attention-deficit hyperactivity disorder (ADHD), prescribed medications for its treatment, non-medical use of prescription stimulants, and history of use of alcohol, tobacco and nine classes of other illicit drugs, as well as a wide array of other behavior and personal characteristics. Among the 47 students who reported that they were diagnosed with ADHD (ADHD+) and had a prescription for a stimulant for its treatment, 28% (n=13) took the medication more than was prescribed. Among students without ADHD (ADHD-), 18% (n=217) had used a prescription stimulant non-medically at some point in their life, 79% of whom had used it in the past year. Adderall was the most common prescription stimulant (89%), followed by Ritalin (26%) and Concerta (12%) reported by these students, and an overwhelming majority (89%) obtained their drug(s) from a friend with a prescription. The most commonly reported reasons for non-medical use among ADHD- students were to improve focus to study (75%), curiosity (19%), to stay awake longer to party (13%), and to get high (5%). Regardless of the presence of an ADHD diagnosis, lifetime use of other illicit substances was much more likely in non-medical users of prescription stimulants. For example, the prevalence of lifetime cocaine use among ADHD+ and ADHD- students who used prescription stimulants non-medically was 36% and 18%, as compared to 12% and 3% among their non-using counterparts. In conclusion, non-medical use of prescription stimulants appears widespread among college students primarily for the purpose of enhancing academic performance, and co-exists frequently with polydrug histories.

34 PSYCHIATRIC DISORDERS AND DEPENDENCE IN CANNABIS USERS THAT SEEK TREATMENT VS. A RANDOM POLICE-SELECTED GROUP OF USERS

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Objective: Compare prevalence of psychiatric disorders and cannabis dependence in cannabis users that seek treatment, and cannabis users that do not seek treatment. Methods: Two groups were selected: 1) cannabis users seeking treatment (CST), 2) cannabis users selected by the police on random controls (RC). These police controls were not motivated by disruptive behaviors. All participants were administered the Mini International Neuropsychiatric Interview for the DSM-IV (MINI) current and lifetime. Results: 167 cannabis users (57 CST, 110 RD) were assessed. No statistical difference between groups was found on age (19.9, SD=6.1), sex ratio, social status (mostly students) or age of first cannabis use (15.5 years, SD=2.5). Both groups differed ($p < .05$) on cannabis dependence criteria: 74% of CST and only 26% of RC. In both groups over 40% met alcohol abuse criteria. Other substances abuse or dependence was anecdotic. Over 70% of CST group reported more than two current or lifetime non-substance psychiatric disorder in addition to cannabis dependence and they were 30% in the RC group. CST users met significantly more anxiety (35%) and mood (20%) disorder criteria than RC users (respectively 12% and 8%). Conclusion: Cannabis users who sought treatment met more often cannabis dependence criteria and had higher prevalence of anxiety and depression. In this sample, cannabis users who were selected on random controls had low prevalence of cannabis dependence and anxiety and depression. Cannabis users seeking treatment have comparable prevalence of anxiety and depression than other treatment seeking substance users.

36 REGIONAL DIFFERENCES IN THE EFFECTS OF WITHDRAWAL FROM REPEATED COCAINE UPON CC-HOMER PROTEIN EXPRESSION: A TWO-SPECIES COMPARISON

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The constitutively expressed (CC) Homer protein Homer2 actively regulates behavioral and neurochemical sensitivity to cocaine in rodents. While withdrawal from repeated cocaine down-regulates the expression of the CC-Homer Homer1b/c selectively in the nucleus accumbens (NAC) shell of rats, the effects of cocaine upon Homer2 expression in rodent brain are not known. The present study employed standard immunoblotting techniques to compare the effects of repeated cocaine (7 X 30 mg/kg + 3 weeks withdrawal) upon Homer1b/c and Homer2a/b expression in the NAC and prefrontal cortex (PFC) of rats. As the majority of work characterizing a role for Homer2 in cocaine addiction-related behaviors involved mice, a parallel immunoblotting experiment employed C57BL/6J mice to assess for potential inter-species differences in CC-Homer regulation by repeated cocaine. As reported earlier by Swanson et al. (2001), withdrawal from repeated cocaine administration down-regulated Homer1b/c expression in the NAC shell, but not in the NACcore or PFC of rats. Identical cocaine treatment to mice down-regulated Homer1b/c in the NAC (shell + core) but not in the PFC. Similar to Homer1b/c, Homer2 was also down-regulated in the NAC shell of rats and in the NAC of mice. In contrast to Homer1b/c, Homer2 was also down-regulated in the PFC of both species. Thus, withdrawal from repeated cocaine down-regulates the expression of different CC-Homer isoforms in a regionally-distinct manner that is independent of the species of the rodent studied. These data, coupled with earlier evidence for a critical role for both Homer1 and Homer2 in determining sensitivity to psychomotor stimulant drugs, strongly implicate cocaine-induced regulation of CC-Homer proteins in the etiology of psychomotor stimulant addiction and the development of stimulant-induced psychosis. Supported by a NARSAD Young Investigator Award and a UCSB Faculty Career Award to KKS.

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37 GENDER DIFFERENCES IN SEX TRADE BEHAVIOR AND INJECTION DRUG USE AMONG SOUTH AFRICAN DRUG USERS

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There is a major gap in research findings related to HIV transmission in Sub-Saharan Africa given the magnitude of the pandemic in the region. The present study sought to examine gender differences in sex trade behavior and injection drug use among South African drug users as an initial step in a line of investigation aimed at reducing HIV in the region. This study is based on data from the International Neurobehavioral HIV Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of HIV, and Hepatitis A, B, and C in the U.S, South Africa, and Russia. The present study is based on the South Africa sample comprised of 144 drug users between 18 and 50 years of age in the Pretoria region. The Pretoria baseline sample was 91% Black and 65.3% male with 33.3% of the baseline sample testing positive for HIV. Multinomial logistic regression indicated that females (OR = 18.49; 95% CI = 7.47; 45.80) were significantly more likely than males to engage in sex trade behavior while controlling for age. Specifically, 66% of females in the sample reported trading sex for money compared to 9.6% of males. There was no gender difference in the rate of injection drug use. There is a lack of research elucidating risk factors associated with the transmission of HIV and other STDs in South Africa. A small base of extant research suggests that HIV transmission among South African women is largely attributable to sexual behavior rather than other risk factors, such as sharing needles to inject drugs. The present study suggests that an alarmingly high prevalence of sex trade behavior among women in South Africa may explain, in part, extremely high HIV rates among women in Sub-Saharan countries.

39 HIPPOCAMPAL REGULATION OF CONTEXT-INDUCED COCAINE-SEEKING BEHAVIOR

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Brain areas involved in cognition regulate behaviors related to cocaine addiction and relapse. We hypothesized that inactivation of the ventral subiculum (vSUB) of the hippocampal formation would impair context-induced reinstatement of cocaine-seeking behavior. Rats were implanted with jugular catheters and bilateral cannulae into the vSUB and trained to self-administer cocaine. They then underwent 3 days of conditioning, during which they had 1-hr access to cocaine in the presence of one set of novel visual, olfactory, and auditory contextual cues (context A) and 1-hr access to saline with a different set (context B). A novel flashing light stimulus that differed for cocaine and saline was delivered concurrently with infusions, serving as a conditioned cue. The experimental group (n=4) was given lidocaine infusions into the vSUB temporarily inactivating it, before each conditioning session, and the control group (n=5) was given saline. Responding was extinguished in a third context (context C). Rats were then given a series of 3 reinstatement tests, and number of responses on the previously cocaine-paired lever was measured. Rats were first tested in contexts A and B in the absence of conditioned cues. Next, rats were given conditioned cues in context C. For the third test, rats were given the cues in contexts A and B. Number of responses on the cocaine-paired lever was higher in the cocaine condition than in the saline or extinction conditions [$F(2,14)=14.9, p<.001$], and this did not differ between groups. This shows that all rats were able to discriminate between cocaine and saline and responding was successfully extinguished. For the cocaine reinstatement tests, the control group had significantly higher responding above extinction levels in the context only and the context + cues conditions [$F(3,12)=4.0, p=.035$], whereas the lidocaine group did not have higher responding above extinction levels in any reinstatement test. This shows that lidocaine treatment blocked context-induced reinstatement, which suggests that the vSUB plays a role in associating cocaine with cues in the environment. Supported by DA11716.

38 HCV SERVICE AWARENESS AMONG DRUG TREATMENT STAFF: PROGRAM BARRIERS TO CLIENTS' OPTIMAL UTILIZATION OF HCV SERVICES

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In order for staff in drug treatment programs to optimally support clients' HCV-related needs, they need to encourage their clients to utilize HCV services available to them through the program. Therefore, it is critical that staff be aware of these services. Using data collected from staff in 2 residential drug-free treatment programs and 2 methadone maintenance treatment program (MMTPs) in New York City, we examined the extent to which staff were aware of the their programs' HCV education, testing and medical services offered on-site or through referral. We found that staff in both modalities were especially likely to be aware of referrals to off-site physicians. In addition, staff in drug free residential programs were most aware of programs' support with medical appointments and with HCV medication. Staff in MMTPs were most aware of the availability of antibody testing and literature provided to educate clients about HCV. Regrettably, there were many services that the great majority of staff in both modalities were unaware that their programs offered. For example, only 15% of the staff in each of the MMTPs were aware that their program offered support for clinical trials and only 35% of the staff in the drug free programs were aware that group education about HCV was available. Implementing an effective staff training that makes all staff aware of the HCV services offered at their program is an important step in order to increase clients' utilization of critical HCV services (Funded by NIDA grant RO1-DA13409).

40 CONDITIONED COGNITIVE AND PSYCHOMOTOR EFFECTS OF CAFFEINE IN HUMANS

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Drug-paired stimuli can acquire the ability to elicit drug craving and drug-seeking behaviour via Pavlovian conditioning processes. Such processes have been considered particularly important in relation to the occurrence of relapse after long periods of drug abstinence. Conditioned drug effects have been demonstrated in the laboratory; for example, cocaine-like physiological effects have been reported following exposure to cues previously associated with cocaine. However, little research has examined whether stimulant effects on cognitive and psychomotor performance can also be conditioned to previously neutral stimuli in humans. The present study addressed this issue using caffeine as a model stimulant drug. Ten moderate-to-high caffeine consumers (intake >200 mg/day) were deprived of caffeine overnight before attending eight conditioning trials in which either 400 mg of caffeine (four sessions) or placebo (four sessions) were paired with two visually distinct computer cubicles. These eight sessions were followed by tests for conditioned responding, in which placebo was administered in both cubicles. It was hypothesized that participants would show caffeine-like performance and mood enhancement in the caffeine-paired cubicle when placebo was given in that cubicle. During the conditioning phase, caffeine significantly improved performance on a rapid visual information processing task and it increased self-reported measures of arousal relative to placebo. Caffeine also improved simple and choice reaction times relative to placebo on the early conditioning trials, but the significant difference was lost over subsequent trials due to systematic performance gains in the placebo condition. These results may reflect the early development of conditioned responses in the caffeine-associated cubicle, which then generalised to the broader context of the experimental setting during subsequent trials. Such an interpretation would also explain why performance in the two cubicles was similar on the tests for conditioned responding.

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41 ESTRADIOL MODULATION OF THE BEHAVIORAL EFFECTS OF D-AMPHETAMINE IN PREMENOPAUSAL WOMEN

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Previous research suggests that d-amphetamine alters impulsive and psychomotor behavior in humans. There is also evidence that estrogen modulates the effects of dopaminergic drugs, such as d-amphetamine, in women. This ongoing study explores the behavioral effects of d-amphetamine, alone and in combination with estradiol, in healthy, premenopausal women. Volunteers complete 10 experimental sessions during the early follicular phase of their menstrual cycle and are administered estradiol (0.00 or 0.25 mg, sublingual) and d-amphetamine (0 or 16 mg, p.o.) in combination under double-blind, double-dummy conditions. Prior to (baseline) and subsequent to (1, 2, 3 hours) drug administration, volunteers complete assessments consisting of cardiovascular measures, verbal reports of drug effect (Visual Analog Scale and Profile of Mood States), and computer tasks designed to assess psychomotor (Digit Symbol Substitution) and impulsive (Delay Discounting and Stop-Signal) behavior. The effects of these two compounds, alone and in combination, will be analyzed using a repeated measures ANOVA with amphetamine dose, estradiol dose and time as factors. Thus far, 6 of 10 subjects have completed or are completing the study. Typical stimulant-like effects of d-amphetamine have been observed on all measures, including significant increases in heart rate and blood pressure, as well as verbal reports of arousal and vigor. In contrast, estradiol, alone, has not engendered any significant effects. It is hypothesized that estradiol will significantly increase the magnitude of the stimulant effects of d-amphetamine. Supported by RR-15592.

43 CELL CYCLE EVENTS ASSOCIATED WITH METH-INDUCED ASTROGLIOSIS

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Methamphetamine (METH) is a powerfully addictive psychostimulant that has a pronounced effect on the central nervous system. Although the overall mechanism of METH-induced toxicity is not fully understood, prolonged use of METH causes severe neurotoxic effects, as well as the development of astrogliosis via the dopaminergic system. The present study was designed to examine if METH-induced astrogliosis is related to apoptosis or necrosis using flow cytometry. The rat C6 glioma cells were used as an in vitro model to assess the development of METH-induced astrogliosis by performing a dose response curve for METH at the following concentrations (0.5, 1.0, 2.0, 3.0, 4.0 and 5 mM) at 1, 24 and 48 hrs. The cytotoxicity was determined by the non-radioactive cytotoxic assay kit (MTS). The lethal dose (LD50), where 50% of the cells were killed, was determined to be 2.2 mM after 48 hrs exposure to METH. In order to investigate the nature of cell death, the rat C6 glioma cells, were treated with METH at similar concentrations and time points stated above. After drug treatments, the rat C6 glioma cell were stained with propidium iodide (PI)-annexin V and analyzed by flow cytometry to determine the stage of METH-induced apoptosis or necrosis. Further studies were carried out to determine the stages of cell cycle inhibition by METH. Flow cytometry data suggests that the astrogliosis induced by METH using its LD50 (2.2 mM) is associated with apoptosis. The overall data collected from these experiments will further assist in our understanding of METH-induced astrogliosis. This research project was supported by NIH/RCMI RR03020, NIH/MBRS GM08111, and COE.

42 EFFECTS OF COGNITIVE-BEHAVIORAL STRESS MANAGEMENT ON STRESS REACTIVITY IN SUBSTANCE-DEPENDENT INDIVIDUALS: A PILOT STUDY

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Human and animal studies show that stress is associated with initiation, maintenance, and relapse to substance use (Goeders, 2004; Sinha, 2001). In order to better understand this relationship, clinical researchers have begun to examine stress reactivity in human laboratory paradigms. The findings reveal that acute psychological stress can increase negative emotions, physiological and biological reactivity, and craving, and that stress reactivity may be predictive of relapse (Breese et al., 2005). The specific aims of this pilot study were to 1) tailor an existing, 2-session cognitive-behavioral stress management (CBSM) intervention (Gaab et al., 2003) to be used with substance-dependent individuals, and 2) evaluate the effects of the CBSM intervention on subjective and physiological stress reactivity in response to experimentally-induced psychological stress (i.e., Mental Arithmetic Task given pre and post CBSM) among substance-dependent individuals. To date, 10 individuals have completed the CBSM intervention and the preliminary results show significant within session declines in self-reported craving, desire to use, inability to resist using, stress, and negative mood, particularly during the first CBSM session ($p < .05$). The findings also show a significant decrease in frequency of substance use during the study ($p < .03$), and a marginally significant decline in the desire to use and improvement in the ability to resist using when exposed to the psychological stressor following completion of the CBSM intervention ($p < .09$). Thus far, 2 individuals have completed a no-treatment control condition. The study is ongoing and a comparison of the two groups will be presented.

44 MIXED OUTCOMES FROM BRIEF SUBSTANCE USE INTERVENTIONS WITH HOMELESS ADOLESCENTS

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Outcomes for a brief feedback and motivational intervention for substance use among homeless adolescents are presented. Homeless adolescents use substances at extremely high rates compared to other youth, and experience considerable negative consequences as a result. Yet homeless adolescents are not reached by, or are not responsive to, traditional prevention and treatment programs for substance use and abuse. In a previous study (Peterson, Baer Wells, Ginzler, & Garrett, 2006), youth who completed a brief intervention and who were rated as engaged in the intervention by study clinicians reported greater reductions in substance use rates compared to youth in a control condition and youth given the intervention but rated as less engaged. The current study sought to increase the magnitude and frequency of positive response to brief interventions among homeless youth via better integration within a local drop-in agency, the use of vouchers to encourage attendance at up to four short sessions, and by allowing counselors greater flexibility in the structure of the short feedback sessions. Analyses to date suggest that previous study results were not replicated. Although reductions in substance use rates were reported, differences between intervention and control conditions were not observed. Counselor ratings of participant engagement did not identify a more responsive subgroup as in the previous study, but did identify youth who were more drug-involved at baseline. Differences in sample recruitment and in the context for intervention across the two studies are discussed. Considerable change in the control condition suggests that youth were ready to reduce risks when recruited, and/or assessment is reactive and possibly beneficial for homeless youth.

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- 45 PREVALENCE OF CHRONIC FLASHBACKS IN HALLUCINOGEN USERS: A WEB-BASED QUESTIONNAIRE**
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Background: The DSM-IV category hallucinogen persisting perception disorder (HPPD) is a syndrome of chronic flashbacks occurring in hallucinogen users. Very little research has attempted to document its prevalence or correlates and it is believed by users and some scientists to be very rare. HPPD may be under-reported because only a minority of those affected seeks treatment. Methods: A questionnaire on a drug information website recruited individuals to complete a "visual experiences survey." Questions concerned medical and drug use histories and presence and phenomenology of any flashback-like visual abnormalities while not intoxicated. Inclusion criteria and specific questions were designed to identify and exclude unserious or unreliable responses, including those describing acute drug effects. Analyses used descriptive statistics and multiple regression. Results: 3139 completed the questionnaire (19.4% out of 16192 who viewed the information sheet). 2678 (85.3%) met inclusion criteria. 1652 (61.7%) reported visual experiences reminiscent of hallucinogen effects while not intoxicated. 107 (4%) reported both that (a) symptoms were initially or currently sufficiently troublesome to have prompted thoughts of treatment and (b) that they did not have medical histories known to produce unusual visual experiences. Only 27 had actually sought treatment. Commonly endorsed symptoms included seeing illusory movement of still objects (82%), illusory repetitive patterns (71%), and seeing auras or halos around objects (67%). 51 (48%) believed a specific episode triggered their symptoms and reported using cannabis (56.9% of these 51), LSD (25.5%), psilocybin (23.5%), high dose dextromethorphan (19.6%) and MDMA (15.7%) in the week before onset. Conclusions: Although diagnosis of HPPD would require formal assessment, these data suggest visual changes may be relatively common in hallucinogen users. Objective testing of visual functioning in this population is warranted.
- 46 EFFECT OF TOBACCO CRAVING ON LAPSE TO SMOKING AMONG ADOLESCENT SMOKERS UNDERGOING CESSATION TREATMENT**
K.S. Bagot, S.J. Heishman and E.T. Moolchan, NIDA/Intramural Research Program, Baltimore, MD
Previous research indicates a positive association between withdrawal symptoms and relapse to smoking among abstinent adult smokers. We hypothesized a similar relationship between craving and lapse in a population of adolescent smokers during the treatment phase of a cessation trial. A visit was defined as a lapse visit when the participant reported smoking or had a CO ≥ 7 ppm subsequent to an abstinent visit. Craving was assessed using the Questionnaire of Smoking Urges (QSU). Thirty-four adolescent participants (mean \pm SD, age 15.2 ± 1.05 years, cigarettes per day 13.9 ± 4.12 , Fagerström Test for Nicotine Dependence 6.36 ± 0.982 , 66% female), over a combined total of 167 treatment visits were included in the current analysis. Logistic regression analyses showed that adolescents who experienced higher craving (QSU score) were more likely to lapse during smoking cessation treatment ($p = 0.018$). If replicated in a broader group of adolescent smokers, these findings suggest that degree of craving predicts lapse during cessation treatment and might serve as a clinical marker for the efficacy of tobacco cessation interventions among dependent adolescent smokers.
- 47 MEASUREMENT PROPERTIES OF THE DSM-IV SUBSTANCE DEPENDENCE AND ABUSE CRITERIA**
A.J. Baillie, M.R. Teesson and K. Richardson, Macquarie University, and National Drug and Alcohol Research Centre, University of New South Wales, Sydney, New South Wales, Australia
Hypothesis: Two studies which evaluate the measurement properties of the DSM-IV Substance Dependence and Abuse Criteria are described i) a confirmatory factor analysis of cannabis diagnostic criteria from a population sample and ii) a meta-analysis of published literature examining the factor structure of the criteria. Species: Human Number of Subjects: 722 Cannabis users Procedures: Data from cannabis users were obtained from a cross-sectional study of a large and representative sample of the Australian general population. The DSM-IV criteria for cannabis abuse and dependence were assessed using the CIDI-AUTO. Published literature was collected from searches of Medline and Psycinfo and from the reference lists of relevant publications. Information was extracted from published reports and subjected to meta-analysis. Results: Within the adult population, 2.2% met criteria for a cannabis use disorder (0.7% abuse and 1.5% dependence). Confirmatory factor analysis indicated that both a one- and two- factor model for cannabis use disorder provided an adequate fit to the data. However, the estimated correlation between the abuse and dependence factors in the two-factor model was extremely high (0.99) suggesting a single factor is the most parsimonious account. Continuing to use cannabis despite knowledge of psychological or physical problems, a great deal of time spent obtaining, using or recovering from the effects of cannabis, and withdrawal were the criteria most strongly related to the underlying dimension, however withdrawal, tolerance, and persistent desire, or unsuccessful efforts to cut down provided more information around the diagnostic threshold. This finding is consistent with results of meta-analysis of similar published research. Statistical analyses: confirmatory factor analysis, meta-analysis Conclusion: A one-factor model provided the most parsimonious model of the cannabis abuse and dependence criteria. Suggestions for the revision of the criteria are discussed.
- 48 EFFECT OF COCAETHYLENE ON ACUTE RESPONSES TO COCAINE**
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One approach to addiction pharmacotherapy is to administer a drug that can induce tolerance to the abused drug. Cocaethylene (EC) is a pharmacologically active cocaine (COC) homolog, with greater selectivity for the dopamine transporter, formed by transesterification of COC in the presence of alcohol. Human laboratory studies show that EC evokes subjective and cardiovascular (CV) effects similar to COC, but is less potent with a longer elimination half-life than COC. This study reports results of a randomized, double-blind, placebo-controlled, within-subject study to 1. determine the ability of EC to modulate acute responses to COC 2. identify pharmacokinetic interactions between COC and EC. Method: Non-treatment-seeking, COC-dependent, volunteers (n=8) received an EC bolus followed by an infusion calculated to produce plasma concentrations of 0, 50 or 200 ng/ml followed by intravenous COC (0, 0.25 or 0.5 mg/kg) injected over 1 minute after 240 min. of EC. Blood samples, subjective, and physiological measures were collected. Results: EC bolus produced a significant response and target EC concentrations were obtained. No differences were found when baseline responses were compared to those 240 min following initiation of the EC infusion for any CV or subjective effect indicating that tolerance occurred for EC. Although not statistically significant, there was a decrease in "COC high", "any high", "rush", "craving", "stimulated", "bad drug effects", "good drug effects", "nervous", duration of "rush" and duration of "COC high" when subjects received a COC challenge during EC infusion. COC pharmacokinetics were not altered by EC. Conclusions: No toxic interaction occurred when COC was administered during EC infusion. COC responses were modestly diminished with EC indicating that partial tolerance may have been produced for COC. These results indicate that higher doses of EC may be safely given and might produce more robust tolerance to COC in humans. Induction of tolerance to COC with C2 substituted benzyloxypropane analogs could be a promising pharmacotherapy for cocaine dependence.

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- 49** **DISRUPTION OF THE NEURONAL NITRIC OXIDE SYNTHASE GENE PREVENTS NEUROADAPTATIONS INVOLVED IN THE MAINTENANCE AND REINSTATEMENT OF COCAINE CONDITIONED PLACE PREFERENCE IN M.A. Balda, K.L. Anderson and Y. Itzhak, University of Miami School of Medicine, Miami, FL**
- Ample evidence exists for the remodeling of the mesocorticostratial and mesolimbic dopamine and glutamate systems during adolescence. These circuits are major substrates for psychostimulants and, consequently, exposure to drugs during adolescence may disrupt normal neural development. Additionally, the role of nitric oxide (NO) as an important modulator of DAergic and glutamatergic neuronal function suggest that it may be involved in the neuroplasticity underlying the addictive properties of psychostimulants. The present study investigated the induction, maintenance, extinction, and reinstatement of cocaine-induced conditioned place preference (CPP) in WT and nNOS KO mice in order to determine age-sex-dependent differences in drug-seeking behavior. All animals developed marked cocaine CPP (20mg/kg), regardless of genotype, age and/or sex. WT adolescent males and females (PD24) maintained CPP for one and two weeks post-conditioning, respectively, and WT adult animals (PD89) maintained CPP for four weeks. A priming injection of cocaine (5mg/kg) to the WT adolescent groups (both sexes) reinstated CPP in adulthood (PD70), suggesting the development of long-lasting sensitivity to cocaine. Likewise, cocaine priming reinstated CPP in WT adult animals (both sexes). In contrast to WT adolescent, KO adolescent mice (both sexes; PD26) did not maintain CPP expression nor did they respond to a cocaine priming injection. KO adult males like their adolescent counterparts neither maintained CPP nor responded to a cocaine prime. Results of KO adult females, however, were indistinguishable from WT adult females. The present results demonstrate that the nNOS gene is required in adolescence for the development of neuroadaptations that enable the maintenance and reinstatement of CPP, and suggest that the nitrenergic system may be critically involved in the development of persistent drug seeking behavior from adolescence through adulthood. Supported by NIDA DA19107.
- 50** **DOPAMINE AGONISTS AND ANTAGONISTS IN THE DYNAMICS OF CHOICE**
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- Research in neuroscience suggests that dopamine (DA) determines the reinforcing effects of primary stimuli such as food. This idea received support from data showing that DA antagonists (e.g., haloperidol) suppress operant behaviors maintained with positive reinforcement. Paradoxically, the same effect has been obtained with DA agonists (e.g., methylphenidate), questioning the role of DA in determining the reinforcing value of positive stimuli. The present study used the generalized matching law (Baum, 1974) to estimate the effects of d-amphetamine and haloperidol on food reinforcers; particularly, on sensitivity to reinforcement. A variable reinforcing environment was modeled by arranging seven reinforcer ratios to occur in two levers within the same session. A local analysis was conducted to determine the effects of these drugs on choice behavior. As it was predicted, response distribution favored the lever associated with the highest probability of reinforcement. The drugs affected total response output, but they did not affect sensitivity to reinforcement. The discrimination that rats established between the rich and the lean levers was not affected by methylphenidate, nor was it affected by haloperidol. The implications for a general model of anhedonia will be discussed.
- 51** **INHIBITION OF ANTIBACTERIAL RESPONSE PATHWAYS BY THC**
G. C. Baldwin, S.M. Kiertcher, S. Uh, K.M. Whittaker, D.P. Tashkin and M.D. Roth, David Geffen School of Medicine at University of California/Los Angeles, Los Angeles, CA
- Ligand binding to Toll-like receptors (TLR) provides an important stimulus for activating innate immunity. Inflammatory and antimicrobial responses induced by TLR/ligand interactions include cytokine production, intracellular bacterial killing, and production of nitric oxide (NO). We previously reported that alveolar macrophages (AM) from the lungs of marijuana (MJ) and cocaine smokers were impaired in their ability to phagocytose and kill bacteria, effects related to their inability to upregulate iNOS mRNA or produce nitric oxide (NO). To characterize the mechanisms involved, we recently established and validated a rapid *in vitro* assay for monitoring the production of NO by human macrophages and found that human monocyte-derived macrophages (MACS) produce NO when stimulated by *S. aureus*. Furthermore, exposure of these cells to THC led to a dose-dependent impairment in killing and NO production. In order to investigate mechanisms, we first compared *S. aureus* and LPS for their ability to stimulate NO from cytokine-primed MACS. A positive response was only observed in cells exposed to *S. aureus*, not LPS, suggesting that triggering through TLR-2 is pivotal for inducing NO from human cells. Consistent with this, pretreatment of MACS with anti-TLR-2 antibody significantly inhibited the production of NO. We have also shown that stimulation of human MACS via TLR-2 resulted in time-dependent phosphorylation of I-kappa-B-alpha as well as an increase in phospho-p38 MAPK-alpha. THC appears to target the MAPK signaling cascade, as we have observed a dose-dependent decrease in phospho-p38 in THC-exposed MACS following stimulation by *S. aureus*. Overall, our results suggest that both NF-kappa-B as well as MAPK signaling cascades may be required for the induction of iNOS and NO production in human macrophages, and that the deleterious effects of THC on antibacterial responses may result from inhibition of these signaling pathways. Supported by NIDA grant DA03018.
- 52** **ENDURING STRUCTURAL PLASTICITY IN NUCLEUS ACCUMBENS FOLLOWING MDMA (ECSTASY) ADMINISTRATION IN RATS**
K.T. Ball, C.L. Wellman and G.V. Rebec, Indiana University, Bloomington, IN
- Repeated exposure to the indirect dopamine agonists amphetamine and cocaine is associated with increases in dendritic length, branch number, and spine density on medium spiny neurons in nucleus accumbens (NAc). In this study we examined whether repeated exposure to non-neurotoxic doses of the amphetamine derivative MDMA, which increases release of dopamine and serotonin, also results in long-lasting morphological changes in NAc. Adult, male rats received 2 daily injections of either 5.0 mg/kg (\pm)-MDMA or saline vehicle, ~6 hr apart, for 3 consecutive days, followed by 4 drug-free days for a total of 3 weeks. Following a 4-week withdrawal period, brains were removed and processed using a modified Golgi method. For each animal, an experimenter (blind to condition) reconstructed 10 medium spiny neurons each from NAc core and shell subregions in each animal. To assess overall changes in dendritic morphology, total length and number of dendritic branches were compared between groups, and differences in the amount and location of dendritic material were assessed with a 3-dimensional version of a Sholl analysis. In NAc core, the number of spines was determined on 1st through 4th order branches, and the overall density of multiple-headed spines also was quantified. MDMA treatment produced no significant changes in overall dendritic length or branch number in NAc core or shell compared to saline-treated animals. In addition, the Sholl analysis indicated no significant differences in dendritic organization across the dendritic arbor in either subregion. MDMA-treated rats, however, displayed large increases in spine density across all branch orders. Additionally, MDMA treatment resulted in an especially large increase in the overall number of multiple-headed spines. Although the exact functional consequences of these changes are unknown, they could reflect altered patterns of excitatory synaptic connectivity, thus contributing to the long-lasting behavioral plasticity that occurs after exposure to MDMA and related drugs. Supported by NIH grants DA 02451 (G.V.R.) and DA 020209 (K.T.B.)

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53 COUNSELOR EXPERIENCES WORKING WITH METHADONE-MAINTAINED CHRONIC PAIN PATIENTS: AN EXPLORATORY STUDY

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Opioid treatment programs have witnessed a dramatic increase in the number of patients with co-occurring chronic pain and opioid dependence (POD). Untreated, unrelieved chronic pain can have deleterious health and psychosocial consequences. Despite recent calls for improved counseling interventions for POD, little is known about counselors' experiences working with this clinical population. The purpose of this study was to explore counselors' experiences working with methadone-maintained POD patients, including counselors' descriptions of their POD patients, POD management issues, and their willingness to receive specialized POD training. Twenty-five substance abuse counselors completed a survey developed by the authors. Mean counselor age was 46.2 years(SD, 10.7); 18(72%) were women, 16(64%) described themselves as white, and their mean years of clinical experience was 12.2(SD, 5.6). Approximately 27% of counselors' caseloads comprised POD patients. The most frequent adjectives used by counselors to describe typical POD patients were: needy/difficult(30%), sad/hopeless(24%), frustrated(18%), manipulative(10%), and rigid/close-minded(10%). The most common management issues encountered by counselors with POD patients included: monitoring appropriate use of pain medications(50%), making appropriate pain management referrals(36%), patients' non-compliance with counselor recommendations(16%), and coordinating counseling and external pain management services(16%). Of the 22 counselors who completed the question concerning willingness to receive specialized POD training, 86% responded in the affirmative. We conclude that counselors frequently encounter POD patients, who are typically viewed negatively and who pose many clinical management issues. Counselors' reports of difficulties working with POD patients, combined with a high willingness to receive specialized training, suggests that the introduction of specialized chronic pain counseling into opioid treatment programs might be well-received. Supported by 2 K24 DA000445 (RS)

55 CONTRIBUTION OF THE FIBROSCAN® TO HEALTHCARE ACCESS FOR DRUG USERS AND PRECARIOUS POPULATION: OBSERVATIONAL STUDY

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Drug treatment programs are well situated to provide hepatitis C (HCV) services to their patients. This study aimed to propose a liver stiffness measurement (LSM) with FibroScan® (Echosens, Paris) to patients coming to the Liberty Clinic (Bagneux) and the Moulin-Joly Center (Paris) and evaluate its acceptability and usefulness. The examination was proposed to 136 patients (108 men, mean age 41 +/- 8 years). All of them accepted to undergo LSM immediately and none of them complained about discomfort or pain. LSM values ranged from 2.8 to 75 kPa with 108 (79%) patients below the 8.7 kPa and 10 (7%) patients above 14 kPa (significant and cirrhosis cut-off values [1]). The Spearman correlation coefficients were 0.78 ($p < 0.001$, $n = 30$) and 0.66 ($p < 0.001$, $n = 34$) between LSM and METAVIR fibrosis or Fibrotest value, respectively. The population was split into four groups: A-no alcohol excess HIV and HCV negative; B-alcohol abuses, HIV and HCV negative; C-HIV and HCV positive; D-HIV positive. The mean (standard deviation) LSM were 7.6 (7.6), 7.0 (3.8), 14.1 (17.0) and 11.7 (14.8) for the A, B, C and D group, respectively. The fact that this examination is non invasive and gives immediate results strengthens the therapeutic alliance. This new examination allows an objective assessment of the liver fibrosis extent which is not impaired by extra hepatic conditions. This information thus added to clinical and biological picture allow not waiting for the stressing verdict of liver biopsy. The therapeutic collaboration between the patient and the physician is strengthened. Good results, such as the decrease of liver stiffness, encourage alcohol abstinence and treatment compliance. In conclusion, FibroScan® could be used as a first line examination in the assessment of liver disease like ECG for heart disease. [1] Ziol et al. Hepatology 2005;41(1):48-54.

54 HIGHLY SUCCESSFUL OUTCOME WITH LOW-DOSE REQUIREMENTS IN METHADONE MAINTAINED HMONG

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The Hmong are a closely knit ethnic group from the mountains of Laos, where for centuries they have cultivated opium poppies. The prevalence of opium dependence in the Hmong is estimated to be approximately 5-7%. Over the past twenty-five years, tens of thousands of Hmong have immigrated to the United States. Nearly 200 Hmong participate in our urban hospital-affiliated methadone maintenance treatment program (MMTP). The purpose of this study was to evaluate treatment outcome (measured as one year retention and reduction of illicit opiates in urine toxicology tests) in Hmong compared to non-Hmong attending a single MMTP. All clinic admissions from February 2002 through December 2004 were evaluated for one year retention in treatment, reduction in illicit opiate positive urine toxicology, and comorbid psychiatric illness. A total of 363 (75 Hmong) patients were evaluated. Women comprised 48.6% of the non-Hmong and 32.0% of the Hmong admissions ($p < 0.05$). Mean age (range) in years was 43 (20-72) for non-Hmong and 51 (22-91) in the Hmong ($p < 0.05$). One year retention was 68.4% in the non-Hmong and 73.3% in the Hmong (n.s.). The median (range) maximum daily methadone dose during treatment was 80mg (20-200mg) for patients retained at least one year and 68mg (10-140mg) for patients retained less than one year ($p < 0.05$). In patients retained for at least one year, the median maximum daily methadone dose was 90mg (20-200mg) in the non-Hmong and 55mg (25-100) in the Hmong ($p < 0.05$). Gender did not influence retention overall or in the non-Hmong and Hmong populations. Patients remaining in treatment for at least one year were older than those who dropped out ($p < 0.05$). This effect was not observed, however, in the Hmong population ($p = .97$). Differences in prevalence of psychiatric comorbidities and urine toxicology results were also noted between the non-Hmong and Hmong populations. In conclusion, the Hmong have higher treatment success on lower doses of methadone than the non-Hmong attending the same MMTP.

56 MATERNAL BLOOD AND ORGAN TOLUENE LEVELS AFTER ACUTE AND REPEATED BINGE EXPOSURES

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Inhalant abuse is an increasing form of drug abuse. Of particular concern is the abuse of inhalants during pregnancy. While postnatal outcomes in offspring exposed prenatally to inhalants are being assessed, little is known about impact of inhaled toluene on pregnant women. The present study assessed the distribution of toluene in blood and body tissues of pregnant rats after brief, high-dose, 15-min toluene exposures modeling maternal binge inhalant abuse. Timed-pregnant Sprague-Dawley rats were exposed to toluene at 0, 8000, 12000, or 16000 parts per million (ppm) for 15 min/exposure. Exposures occurred twice each day from gestational day 8 (GD8) thru GD20. Immediately following the 2nd exposure on GD8 and GD14, blood was taken from the saphenous vein. Following the final exposure on GD20, animals were sacrificed and trunk blood was collected along with maternal tissue specimens from cerebellum, heart, lung, kidney and liver. Results demonstrate that peak toluene blood concentrations (TBCs) increased as the inhaled concentration of toluene increased. TBCs observed in cerebellum and lung at GD20 were higher than in blood suggesting these tissues concentrate toluene. TBCs in heart and liver at GD20 were similar for all toluene doses suggesting that these organs may become saturated. Overall, TBCs in blood and other tissues following repeated toluene exposure demonstrate that toluene readily reaches many potential sites of action. Prior studies in non-pregnant animals report decreasing TBCs with repeated toluene exposure suggesting a metabolic tolerance that was not seen in these pregnant animals. These results imply that factor(s) related to pregnancy may alter development of tolerance. The relationship of maternal tolerance to fetal outcome remains to be determined. (Supported by grants DA15095 and DA15951 to SEB).

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57 QUALITY OF LIFE IN MMT PATIENTS WITH UNTREATED HCV INFECTION

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Objective: To describe baseline quality-of-life (QOL) measures and predictors for MMT patients with untreated chronic hepatitis C (HCV) infection entering a NIDA-funded HCV treatment study. Method: For the first 44 subjects, hierarchical multiple regression techniques were used to assess model improvement using four domains/blocks of predictors: demographics, HCV viral load, substance use severity by the ASI, depression using SCID and BDI. These blocks of predictors were regressed on QOL scales by the SF-36. Results: Subjects were mostly male (64%) with a mean age (\pm SD) of 44 (\pm 7.4). 64% were white. Mean viral load by HCV RNA was 4.6 E6 (\pm 7.6 E6). Mean ASI alcohol severity was .03 (\pm .07), drug severity was .13 (\pm .07) mental health severity was .35 (\pm .26). 74% had a lifetime diagnosis of depression; mean BDI was 16.6 (\pm 11.1). Mean SF-36 physical score (PCS) was 45 (\pm 10.8), mental health score (MCS) was 38.2 (\pm 12.9). Preliminary regression results suggest a consistent pattern whereby depression severity increased predictive accuracy over simpler models for QOL measures. Overall regression for SF-36 MCS, using all blocks, produced a model r^2 of .33 ($p=.06$), representing significant improvement ($p<.05$) over a model without depression severity. Similar patterns were found for other SF-36 subscales with varying levels of significance; however, the regression for SF-36 PCS, using all blocks, was not significant. Conclusions: Quality of life variables for MMT patients with HCV were lower than reported in healthy normals. After demographics, HCV viral load, and substance use severity were accounted for, depression severity was associated with decreased quality of life. These results suggest that psychiatric intervention to improve depression may be an important target in improving quality of life in these subjects. In light of the small sample size, these results should be considered preliminary in nature. Acknowledgments: NIDA RO1 DA 016764-01

58 CHRONIC EXPOSURE TO ANALGESIC DOSES OF OXYCODONE DOES NOT ALTER FEMALE REPRODUCTIVE FUNCTION IN RATS

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Oxycodone is a potent mu opioid receptor agonist used in chronic pain management. Although oxycodone is an effective analgesic, the long-term consequences of chronic use especially in females of reproductive age have not been adequately studied. This objective served as the basis for our present study. Adult female Sprague-Dawley rats were used ($n=8$ per group). During the 10 day pretreatment phase, rats were adapted to an oral gavage procedure with water to minimize stress effects. Baseline measures of nociception were recorded using a hotplate set at 52 degrees C and estrus cycle was monitored via histological assessment of vaginal smears. This was followed by a treatment phase wherein doses of 5 or 10 mg/kg/day were orally gavaged for 5 days. The dose was then escalated by 0.25 or 0.5mg/kg/day for 10 days to a final dose of 7.5 or 15mg/kg/day which was maintained for 15 days. Vaginal smearing was done daily and hot plate latency was assessed 3 times a week. After 30 days of treatment, rats were bred and their pregnancy was monitored. Statistical analysis revealed that both doses of oxycodone were effective analgesics. The latency for low dose oxycodone treated rats nearly doubled from a baseline of 9.5 sec to approximately 16 sec, while the high dose rats' latencies increased 3 fold from 8.1 sec to approximately 24 sec. In contrast, oxycodone treatment did not affect % of estrus cycles that were normal (75-85%), average cycle length (4.0-4.4) and pregnancy rate (75-100%). These data suggest that chronic exposure to analgesic doses of oxycodone did not interfere with the normal reproductive function of the female rat, including the ability to become pregnant. Supported, in part by the Board of Regents, State of Louisiana, LEQSF RD-A-19.

59 A SINGLE EXPOSURE TO COCAINE PRODUCES WITHDRAWAL-ASSOCIATED INCREASES IN 5-HT_{2A} SEROTONIN RECEPTOR FUNCTION IN RATS

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Withdrawal associated changes in neuronal systems are typically observed following repeated exposure to drugs of abuse. We have previously shown that withdrawal from repeated administration of cocaine produces supersensitivity of hypothalamic 5-HT_{2A} serotonin receptors and increases 5-HT_{2A}-associated G-proteins (EJP 221:121,1992 & JPET 307:1012,2003). However, the minimum duration of cocaine exposure that can induce neuroadaptive increases in 5-HT_{2A} receptor function during withdrawal has not been determined. This study investigated the effects of single vs repetitive injections of cocaine on withdrawal-induced increases in 5-HT_{2A} receptor function. Adult male rats were injected with cocaine (15 mg/kg, ip, bid) for 0, 1, 3, 5 and 7 days and tested following 2 days of withdrawal. Changes in G-protein stimulated- and 5-HT_{2A} receptor-stimulated phospholipase C (PLC) activities in frontal cortex were determined by GTP γ S-increases in PLC activity and serotonin(5-HT)-stimulated activity above GTP γ S-stimulated PLC activity, respectively. Seven days of cocaine exposure produced withdrawal-associated increases in both 5-HT_{2A}- and G protein-stimulated PLC activities in frontal cortex (160 and 180 pmol/mg protein/min over control, respectively). While similar increases were found after 1, 3 or 5 days of cocaine treatment it is notable that a single injection of cocaine also produced a significant effect. Withdrawal from only a single injection of cocaine markedly increased both 5-HT_{2A}- and G protein-stimulated PLC activities (110 and 130 pmol/mg protein/min over control, respectively). None of the increases in 5-HT_{2A}- and G protein-stimulated PLC activities were associated with changes in the levels of 5-HT_{2A} receptors, G α_q or G α_{11} G-proteins, as measured by Western blots. In summary, our results reveal unique cocaine withdrawal-associated increases in cortical 5-HT_{2A} receptor function that occur after only a single exposure to cocaine. Supported by USPHS DA13669 & DA07741.

60 INTERACTION OF MDMA AND ITS METABOLITES AT MONOAMINE TRANSPORTERS IN RAT BRAIN

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Background. \pm -3,4-Methylenedioxymethamphetamine (MDMA, or Ecstasy) is a 5-HT releasing agent, which causes long-term depletion of brain 5-HT. Evidence suggests that MDMA metabolites are involved in the mechanism of 5-HT depletion. Hypothesis. We suspected that metabolites of MDMA would be potent substrates for 5-HT transporters (SERT), thereby entering neurons to cause damage. Methods. MDMA and its metabolites were tested for their ability to interact with SERT and DA transporters (DAT) in rat brain. The dihydroxy analog (\pm -3,4,-dihydroxymethamphetamine, HHMA) and the 4-methoxy-3-hydroxy analog (\pm -4-methoxy-3-hydroxymethamphetamine, HMMA) were synthesized by standard methods. Effects of drugs were examined using in vitro release assays in synaptosomes and in vivo microdialysis in nucleus accumbens of conscious rats. Results. As expected, MDMA was a potent substrate at SERT (90 \pm 7 nM) and DAT (249 \pm 19 nM). HHMA was a potent DAT substrate (130 \pm 6 nM) but weaker at SERT (1729 \pm 134). HMMA displayed weak activity at both SERT (607 \pm 50 nM) and DAT (3652 \pm 252 nM). An i.v. dose of 1 mg/kg MDMA produced significant elevations in extracellular 5-HT (8-fold) and DA (2-fold). HHMA increased dialysate DA (2-fold) and HMMA increased dialysate 5-HT (5-fold), but only after administration of high i.v. doses (10 mg/kg). Conclusions. HHMA is more potent than MDMA as a DAT substrate, while HMMA is weaker than MDMA at both transporters. Neither metabolite displays potent CNS effects in vivo, possibly due to high polarity and lack of penetration through the blood-brain-barrier. Our findings suggest that HHMA is more apt to be toxic for DA neurons than 5-HT neurons. Thus, the purported role of these metabolites in mediating 5-HT neurotoxicity remains enigmatic. Acknowledgement. This research was generously supported by the NIDA IRP.

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61 EFFECTS OF NMDA AND NMDA ANTAGONISTS ON COCAINE-ASSOCIATED CONDITIONED REINFORCER-INDUCED REINSTATEMENT IN RATS

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The N-methyl-D-aspartate (NMDA) subtype of glutamate receptor plays a significant role in many cocaine related behaviors, including its reinforcing effects and the environmental factors that influence cocaine-seeking behavior. The purpose of this study was to examine the role of the NMDA receptor or conditioned reinforcer (CR)-induced reinstatement in rats. NMDA, the prototypical agonist for this receptor, and the antagonists phencyclidine (PCP) and memantine were examined. Rats were trained to self-administer 0.5 mg/kg/infusion cocaine associated with the onset of a tone and flashing stimulus lamps according to a fixed ratio-5 (FR 5) reinforcement schedule. Subsequently, rats' behavior was extinguished during which cocaine and stimuli were withheld. Upon observing extinction of lever pressing (maximum of 5 responses in 10 min), rats were presented with response-contingent CR presentation during a 10-min response-initiated test period. Rats were tested twice, once following vehicle pretreatment and once following administration of a dose of NMDA, memantine, or PCP. Levels of responding obtained during the 10-min periods following extinction, drug and vehicle pretreatments and the latencies to begin responding were compared. Response-initiated presentation of cues significantly induced reinstatement in all groups pretreated with drug vehicles. PCP significantly augmented CR-induced reinstatement at an intermediate dose, but suppressed behavior at higher doses. Conversely, when memantine had effects it only attenuated reinstatement. NMDA also decreased reinstatement relative to vehicle injection. Latency to initiate responding was increased following administration of high doses of each drug. The results from the present study further support the role the NMDA receptor may play in mediating conditioned reinforcing effects of cocaine and relapse to cocaine abuse. Supported by NIDA grants F31 DA-16845 (JLN) and DA-01442 (PMB)

63 RISK FACTORS ASSOCIATED WITH NON-MEDICAL PRESCRIPTION OPIOID USE: RESULTS FROM A NATIONAL SURVEY

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The non-medical use of prescription opioids (NMUPO) has risen in recent years, and surpasses illicit heroin use. To identify demographic and clinical characteristics associated with NMUPO in a national sample of U.S. adults, we performed an analysis on the 2003 National Survey of Drug Use and Health. In a sub-sample of respondents 18 years and older (n=37,026), we investigated variables associated with NMUPO (defined as taking an opioid only for the feeling it causes or taking an opioid prescribed for someone else) in the past year. Each variable was examined for bivariate association with past-year NMUPO and in a multivariable logistic regression model. 52% of respondents were female and ages ranged from 18 to 80. The prevalence past-year NMUPO was 4.56%. On multivariable analysis, the following risk factors were associated with past-year NMUPO: younger age (18-25 years old, OR 6.29; 2.63-15.06); past-year alcohol abuse or dependence (OR 1.62; 1.12-2.32); past-year marijuana use, abuse or dependence (OR 2.27; 1.87-2.76); past-year cocaine use, abuse or dependence (OR 1.81; 1.31-2.51); past-year inhalant and/or hallucinogen use, abuse or dependence (OR 2.00; 1.54-2.61); past-year non-medical tranquilizer and/or sedative use, abuse or dependence (OR 12.77; 9.62-16.96); past-year non-medical stimulant use, abuse or dependence (OR 3.06; 2.24-4.19); initiating illicit substance use before age 13 (OR 2.34; 1.54-3.55); mental illness (OR 1.44; 1.17-1.78) and missing at least one day of work in the past 30 days for either absenteeism and illness (OR 1.37; 1.01-1.87). Past-year NMUPO occurs in nearly 5% of the U.S. population over age 18. Clinicians should consider NMUPO of higher potential risk in young patients with prior illicit and licit drug or alcohol abuse/dependence, those who initiated illicit substance use before age 13, those with mental illness, and those with poor employment attendance.

62 PROTRACTED WITHDRAWAL IN MORPHINE-DEPENDENT RHESUS MONKEYS: PHYSIOLOGICAL AND BEHAVIORAL EFFECTS

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Upon discontinuation of morphine treatment in humans and nonhumans characteristic withdrawal signs can emerge such as lacrimation and vomiting. Typically, withdrawal signs peak in 1-3 days and decrease markedly within 1 week; however, physiological changes (e.g., tachycardia) have been reported to persist for longer. In order to characterize the physiological and behavioral effects of protracted withdrawal, telemetry was used in combination with behavioral observation and drug discrimination procedures in three rhesus monkeys that received 5.6 mg/kg/12 hr of morphine for at least 1 year before discontinuation of morphine treatment for 21 days. Monkeys discriminated 0.0178 mg/kg naltrexone from saline while responding under a fixed-ratio schedule of stimulus-shock termination. Frequency of withdrawal signs such as lip protrusion and vocalizations, which were not observed prior to discontinuation, peaked 2-3 days following discontinuation of treatment. Most of the behavioral changes dissipated within 5 days, although some (e.g., lip protrusion) were still evident 18 days after discontinuation of treatment. Normal circadian patterns in heart rate, body temperature and activity were disrupted for up to 14 days after discontinuation of morphine treatment and returned to pre-discontinuation values by 21 days. In contrast to long-lasting physiological and directly observable effects of morphine withdrawal, responding occurred on the naltrexone lever 1-4 days following discontinuation of treatment; thereafter, responding was exclusively on the saline lever. To the extent that discriminative stimulus effects of withdrawal in non-humans are predictive of subjective reports of withdrawal in humans, these data indicate that effective treatments for opioid dependence must address not only the short-term subjective components of withdrawal but also, and perhaps more importantly, lingering behavioral and physiological effects that might contribute to relapse long after chronic drug use is discontinued. Supported by DA05018 and Senior Scientist Award DA17918 (CPF).

64 HIV RISK BEHAVIORS IN HEPATITIS C- POSITIVE AND NEGATIVE POLYDRUG ABUSERS IN DRUG TREATMENT

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HCV and HIV are transmitted by many of the same routes, though HCV has a higher incidence than HIV in the US. We tested whether rates of HIV risk behaviors are higher in HCV positive (HCV+) than HCV negative (HCV-) drug abusers. Polydrug-abusing participants (N=647) were tested for HCV antibodies on admission to an outpatient clinical treatment trial. Participants filled out the HIV Risk-Taking Behavior Scale (HRTBS) every 2 weeks during treatment (daily methadone, weekly counseling, and protocol-specific behavioral interventions). Urine samples collected 3 times per week were tested for heroin and cocaine to assess drug use. Baseline HCV test results (+ or -) were the predictor in analyses comparing changes across time in HRTBS scores [repeated-measures linear regression (SAS Proc Mixed)] and urine test results [repeated-measures logistic regression (SAS GLIMMIX macro)]. HCV+ participants (N=356, 55%) had significantly higher total HRTBS scores than HCV- participants (mean \pm SEM: HCV+, 3.97 \pm 0.09; HCV-, 2.77 \pm 0.10), $F(1,645) = 86.4$, $p < .0001$. This difference was accounted for by a difference on the drug-risk subscore (HCV+, 2.30 \pm 0.05; HCV-, 0.81 \pm 0.06), $F(1,645) = 369.8$, $p < .0001$. For the sexual-risk subscore, there was a smaller difference in the opposite direction (HCV+, 1.70 \pm 0.06; HCV-, 1.99 \pm 0.07), $F(1,645) = 9.75$, $p < .01$. For both groups, all scores decreased throughout the study; Tukey-Kramer pairwise comparisons showed that group differences in drug-risk behaviors were no longer significantly different after the tenth week of the 35-week trial. Preliminary analysis of the urine test results suggest that the initially higher risk scores in the HCV+ group were not reflected in significantly higher rates of heroin or cocaine use. This study suggests that infection with HCV in polydrug-abusing patients is associated with higher rates of drug-related HIV risk behaviors and that such behaviors decrease over the course of treatment. Supported by Intramural Research Program, NIH NIDA.

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65 RATES OF POSITIVE DRUG TEST SCREENS OF OPIATE, COCAINE AND MARIJUANA USE AMONG URBAN AFRICAN-AMERICAN AND WHITE DRUG USERS

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Epidemiological studies of drug use often rely exclusively on drug use self report when examining risk factors of HIV and other disease statuses. The present study sought to examine gender and ethnic differences in rates of opiate, cocaine, and marijuana use as defined by positive urine drug test screens for these substances among adult injection and non-injection drugs users. This study is based on data from the International Neurobehavioral HIV Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of HIV, and Hepatitis A, B, and C in the U.S., South Africa, and Russia. The present study is based on the U.S. sample comprised of 610 injection and non-injection drug users between 15 and 50 years of age in the Baltimore metropolitan region. The Baltimore baseline sample was comprised of 312 African American (51.1%) and 298 White (48.9%) subjects and was 56.4% male. Multinomial logistic regression indicated that Whites (OR = 3.32; 95% CI = 2.19; 5.03) and males (OR = 1.48; 95% CI = 1.03; 2.13) were significantly more likely to use opiates than were African Americans or females, respectively while controlling for age and education. A significant interaction between ethnicity and gender was also indicated for opiate use such that rates of opiate use among male (72.4%) and female (70.2%) Whites were equivalent while rates of opiate use was significantly higher among African American males (56.0%) than females (40.3%) (OR = 1.78; 95% CI = 1.10; 2.89). Rates of cocaine and marijuana use as measured by positive urine drug test screens did not differ by ethnicity or gender. The majority of the present study sample was comprised of drug users with low socioeconomic status. The present study findings suggest that inner city Whites are using injection and non-injection drugs at equivalent or higher rates than inner-city African Americans. The study findings may help to identify sub-groups of drug users at elevated HIV risk.

67 THERMOREGULATORY INTERACTION BETWEEN CANNABINOIDS AND MDMA

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A major feature of cases presenting with acute MDMA toxicity is hyperthermia. The combination of MDMA with various other drugs is a frequent pattern of MDMA use in humans. The drug most commonly taken with MDMA in human users is cannabis, more than 90% of ecstasy users taking it regularly. In contrast to the hyperthermia seen with MDMA, acute administration of cannabinoid agonists produces hypothermia in rats. Thus, an important issue is whether acute exposure to cannabinoids may have a preventive effect on MDMA-induced hyperthermia. To determine the effects of cannabinoids on MDMA-induced hyperthermia, a biotelemetry system (Mini-Mitter) with calibrated transmitter (series 4000), implanted intraperitoneally (i. p.) under anesthesia 5-7 days before testing, was used to measure body temperature in a controlled environmental room at an ambient temperature of 22 C. Injection of adult male Sprague-Dawley rats (250-300 g) with MDMA induced a dose-related hyperthermia compared to control saline ($P < 0.05$), with a maximum increase of 1.3 ± 0.3 C (10 mg/kg, i.p.), 1.9 ± 0.14 C (20 mg/kg, i. p.) and 2.2 ± 0.10 C (30 mg/kg, i.p.) at 120 min after injection of MDMA. The injection of WIN 55,212-2 at doses of 1 to 5 mg/kg produced hypothermia in a dose-dependent manner. The injection of the synthetic cannabinoid agonist WIN 55,212-2 ((R)-(+)-[2,3-dihydro-5-methyl-3-[(4-morpholino)methyl]pyrrolo-[1,2,3-de]-1,4-benzoxazin-6-yl](1-naphthyl)methanone, (1-5 mg/kg, i. p.) attenuated significantly the MDMA-induced hyperthermia in a dose-related fashion. This inhibitory effect was not due to a nonspecific interaction with hydrophobic regions of functional proteins or their lipid surroundings in the cell membrane, because WIN 55,212-3, an enantiomer of WIN 55,212-2, did not affect the MDMA-induced hyperthermia, indicating that the effect of WIN 55,212-2 on MDMA-induced hyperthermia is stereoselective. Thus, these data show that cannabinoids can interact with MDMA in antagonizing its hyperthermic effect. (Supported by Grants DA06650, DA13429 and DA00973).

66 ECSTASY PRICE EXPECTATIONS AND THEIR IMPACT IN CURRENT ECSTASY CONSUMPTION

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The economic theory of rational addiction (RA) assumes that drug users' behavior is rational in that it is forward-looking and consistent over time. Within this perspective, future monetary prices and the availability of addictive drugs influence current consumption decisions. Current consumption of a drug depends not only on users' needs and preferences, but also on their willingness to pay which is in turn a function of their beliefs about how the price of a drug will fluctuate. It is surprising that such a basic principle of RA has not been addressed adequately in the existing literature. By explicitly incorporating a price-expectations equation into the standard RA framework, this study contributes to our understanding of how expectations affect current price and therefore current consumption. Specifically, we derived and then estimated a reduced form equation for Ecstasy prices based on data from the NIDA-funded Tri-City study (DA14854) examining diagnostic nosology for Ecstasy (MDMA), Ketamine, GHB, and Rohypnol. The parent study collected data from current MDMA users in St. Louis, Miami and Sydney. Recreational MDMA users (Total N=602) were recruited and interviewed twice, one week apart, with the same survey questionnaires. Users were asked to report the cost of the last MDMA pill bought and how much they would be willing to pay for it right now. Information from both waves provided data for measuring current, expected, and future prices for an Ecstasy pill in the three markets. Preliminary results showed strong evidence (Adjusted $R^2=0.83$) of a forward-looking addictive behavior to use Ecstasy. Current unit price ($\beta=0.879$, $p \leq 0.001$) and expected price ($\beta=0.049$, $p \leq 0.001$) were optimal predictors of next time purchase price. The estimated model indicated a significant role for motivation to use Ecstasy and the number of symptoms from Ecstasy use. Our findings extend and clarify the important contribution of the RA theory. Increased efforts to monitor economic factors in drug abuse research are necessary.

68 THERAPEUTIC ALLIANCE WITH RESEARCH ASSISTANTS AND WITH COUNSELORS AMONG METHADONE MAINTENANCE PATIENTS RECEIVING AN ABSTINENCE-BASED REINFORCEMENT INTERVENTION IN A L. A. Benishek(1,2), S. E. Shealy(1), B. J. Rosenwasser(1), M. L. Kerwin(1,3) and K. C. Kirby(1,2), (1) Behavioral Interventions, Treatment Research Institute, (2) University of Pennsylvania School of Medicine, Philadelphia, PA and (3) Rowan University, Glassboro, NJ

Research suggests that therapeutic alliance between a counselor and patient can predict success in drug abuse treatment. Abstinence-based reinforcement interventions are effective treatments to initiate cocaine abstinence. When these procedures are applied as an adjunct to usual treatment in community-based treatment settings, they usually are administered by a research assistant (RA). This study examined the degree to which therapeutic alliance was present during an abstinence-based reinforcement intervention administered by RAs with minimal counseling experience. Cocaine-dependent methadone maintenance patients who were receiving an escalating schedule of voucher-based reinforcement for cocaine abstinence were asked to complete the Working Alliance Inventory (WAI) with respect to the RAs and again with respect to their counselors within 2 weeks of entry into the study and again at 2 months. Ratings were significantly higher for the RAs than for counselors on the overall WAI score and on each of the 3 subscales, although these effect sizes were small on the bond subscale, which is believed to most closely estimate therapeutic alliance ($F(1,50) = 4.18$, $p = .05$, $ES = .08$). The task subscale had the largest effect size ($F(1,49) = 41.43$, $p < 0.001$, $ES = .46$). There was a significant correlation between urinalysis-verified cocaine abstinence and working alliance with the RAs (WAI total score; $r = .35$, $p = .04$), but not with the counselors ($r = .28$, $p = .09$). Cocaine abstinence did not correlate with the bond subscale for either relationship. These results suggest that therapeutic and working alliance develop with RAs during abstinence-based reinforcement interventions at levels that are at least similar to those established by counselors in community-based treatment settings.

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69 DISCRIMINATIVE-STIMULUS EFFECTS OF ADENOSINE ANTAGONISTS IN METHAMPHETAMINE-TRAINED MONKEYS

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The present studies were undertaken to compare the effects of adenosine antagonists in groups of monkeys trained to discriminate either 0.056 mg/kg (n=4) or 0.32 mg/kg (n=3) of i.m. methamphetamine (MA) from saline. Subjects initially were trained under a 10-response fixed-ratio schedule to press one lever after i.m. injection of the training dose of MA and another lever after i.m. injection of vehicle. When responding was stable, cumulative i.m. dosing procedures were used to study the effects of test drugs including methamphetamine (0.003-0.32 mg/kg), caffeine (0.1-18 mg/kg), DMPX (0.1-3.2 mg/kg), CGS 15943 (0.1-10 mg/kg), and 8-PT (0.32-10 mg/kg). Additional experiments were conducted to determine the effects of pretreatment with caffeine on methamphetamine dose-effect functions. Results currently show that methamphetamine and caffeine produced dose-related increases in responding on the MA-associated lever in both groups of monkeys. The training doses of methamphetamine produced full substitution (>90%) in both groups, and a 0.75 log unit separation was evident in the position of the two dose-effect functions. Caffeine also produced dose-related increases in MA-appropriate responding, with a 0.75 log unit separation in the position of the dose-effect functions. However, caffeine did not fully substitute for MA, engendering approximately 70% responding in both groups of monkeys at the highest doses. Over the range of doses studied, 8-PT had no MA-like effect in either group whereas DMPX and CGS 15943 had varying effects among individual subjects, regardless of MA training dose. Pretreatment with doses of caffeine, DMPX, or CGS 15943 that did not reproduce effects of MA moderately increased its potency (≤ 3 -fold). These findings support the view that the discriminative stimulus effects of caffeine incompletely overlap those of MA, regardless of training dose. The 0.75 log unit separation in potency of MA in the two groups was preserved with caffeine, suggesting a mechanistic basis for these behavioral effects. (supported by NIH/NIDA DA03774, DA10566)

71 EX-VIVO STUDY OF LONG-LASTING ACTIVITY OF THE KAPPA-ANTAGONIST JDTC

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JDTC is a long-lasting opioid antagonist with high affinity for each of the opioid receptors (K_i 0.96, 29.6, 0.41 nM for mu, delta, and kappa respectively), but with great selectivity for kappa (K_e 0.01 nM) over mu (K_e 3.4 nM) or delta (K_e 79.3 nM) receptors with respect to inhibition of [35S]GTPγS activity. JDTC has interesting biological activity, as it has been demonstrated to have antidepressant activity in the forced swim test model of depression, block some signs of withdrawal in morphine dependent animals, and reduce footshock stressor but not cocaine-induced reinstatement of cocaine self-administration. In addition, kappa-mediated antinociceptive activity was shown to be inhibited by JDTC for greater than 45 days. To better understand the nature of this ultra long-lasting activity, we have looked at reversibility in cell culture and in ex vivo experiments in guinea pigs. When incubated with CHO cells transfected with mu or kappa receptors, JDTC was found to be wash resistant at kappa but not mu receptors, completely inhibiting both receptor binding and [35S]GTPγS activity after multiple membrane washes. When guinea pigs were dosed with 0.1, 1.0 and 10 mg/kg JDTC (i.p.), both kappa receptors and U69,593-mediated inhibition of electrically induced contractions of the longitudinal muscle myenteric plexus preparation were blocked in a dose dependent manner. Mu receptors and DAMGO-mediated inhibition of contractions were also reduced but to a much lesser extent than kappa-mediated activities. The length of time for which JDTC can block these ex vivo activities is under investigation. These studies show that JDTC is an exceedingly potent kappa-antagonist that maintains antagonist activity long after dosing and when target tissues are removed from the animal.

70 CHANGES IN COCAINE CRAVING, MOOD AND STRESS IN COCAINE-DEPENDENT INDIVIDUALS DURING INPATIENT TREATMENT AND OUTPATIENT FOLLOW-UP

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OBJECTIVE: Prior research has shown that cocaine dependent individuals report decreases in cocaine craving and cocaine abstinence symptoms over the course of inpatient treatment, but less is less known about drug craving and mood symptomatology after discharge. Therefore, the purpose of this study was to examine cocaine craving, mood, perceived stress and depressive symptoms in cocaine dependent adults during inpatient treatment and repeatedly 14, 90 and 180 days after discharge. **METHOD:** Seventy cocaine dependent adults seeking inpatient treatment were assessed using the Cocaine Craving Questionnaire (CCQ), Beck Depression Inventory (BDI), Perceived Stress Scale (PSS), and the Profile of Mood States (POMS). Subjects were assessed weekly during the 4-week inpatient treatment stay and during outpatient follow-up appointments after 14 days, 90 days, and 180 days post-discharge. **RESULTS:** Paired t-tests showed that cocaine craving, perceived stress, depression, anxiety and anger significantly decreased during the inpatient stay. However, cocaine craving significantly increased by day 14 after discharge and continued to rise until day 90 (p<.01). On the other hand, there was a delayed rise in stress levels, anger and anxiety symptoms which increased significantly by day 90 and were maintained at day 180 assessments. No differences by gender were observed. Increases in cocaine craving during follow-up were not significantly different among relapsed versus non-relapsed patients, despite high rates of relapse (70% at 90-days). **CONCLUSIONS:** Findings replicate previous work indicating decreases in cocaine abstinence symptoms during inpatient treatment, but also indicate that cocaine craving, stress and negative mood increases when patients return to their natural environments. These findings support the need to address cocaine craving, negative mood and perceived stress in behavioral and pharmacological treatments for cocaine dependence. (Supported by P50-DA16556 and K02-DA17232).

72 ROLE OF THE THERAPEUTIC ALLIANCE IN THE TREATMENT OF PAIN PATIENTS WHO ABUSE PRESCRIPTION OPIOIDS

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Therapeutic alliance is an important predictor of treatment outcomes among substance abusers. We examined therapeutic alliance in patients who completed a Stage 1 trial comparing 2 behavioral interventions to treat pain and prescription opioid abuse concurrently. The interventions were Adherence Therapy (AT) and Motivational Adherence Therapy (MAT), which consisted of AT enhanced with Motivational Interviewing (MI) and cognitive-behavioral (CBT) strategies. Both interventions were delivered in conjunction with methadone, q6h along with prn "rescue" doses. We assessed alliance for both patients and therapists at each session, using the Haq-II; 24 patients completed treatment with 6 receiving AT and 18 MAT. At treatment's end, patients were either maintained on opioid analgesics (successes) or tapered off (failures) based on an algorithm taking changes in pain, functioning, opioid adherence, and other drug use into account. Overall, patients and therapists reported high alliance scores across treatment groups and sessions. For patients, alliance grew significantly over time [Session 1 M = 96.9, SD = 8.3; Session 8 M = 101.3, SD = 11.5; F(7,119) = 3.0, p < .01] and was not impacted by treatment group or treatment outcome. For therapists, a significant interaction between time and treatment outcome was observed [F(7,119) = 6.5, p < .01]; post-hoc analyses indicated that for treatment failures, therapist alliance ratings did not change significantly over time. However, for treatment successes, alliance ratings increased over time, with significant increases from baseline alliance seen in sessions 4-8. Interestingly, patient and therapist alliance scores were not correlated with VAS ratings of pain and functioning. Findings support that patients developed strong alliances with their therapists in both novel treatments. It is promising that patients were able to make a healthy connection that, in most instances, was reciprocal. Finally, therapist alliance may be an important indicator of patient success.

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73 PSYCHOLOGICAL MANIPULATIONS OF INDICES OF CARDIOVASCULAR AND CEREBROVASCULAR BLOOD FLOW VELOCITY IN COCAINE ABUSERS

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Illicit cocaine abuse is a major public health problem. In addition to reported neurological and neuropsychiatric side-effects, chronic cocaine abuse is associated with a significant reduction in resting cerebral blood flow. In the present study, we sought to determine if the chronic abuse of cocaine abuse might influence physiological responses induced by psychological stimuli. The subjects of the study were 13 non-drug using and 16 cocaine abusers. We compared cardiovascular (heart rate and blood pressure) and transcranial Doppler (TCD) measures obtained before (at 90 sec intervals for 4.5 minutes) and during (at 90 sec intervals for three minutes) three psychological tasks (reading, defending oneself against a shoplifting allegations and anger) known to increase cardiovascular responses. We found that baseline resting heart rate was significantly higher ($p < 0.05$) in the control subjects compared to cocaine abusers. In contrast, TCD measures (primarily pulsatility index (PI), a measure of resistance to flow) were significantly higher ($p < 0.05$) for the cocaine abusers compared to the control subjects. Nevertheless, changes in cardiovascular and TCD measures induced by the psychological tasks were similar for both group of subjects, except for the shoplifting task which showed greater increases ($p < 0.05$) in blood pressure in the control subjects (systolic, 16.0; diastolic, 9.3; MAP, 13.0) compared to the cocaine abusers (systolic, 9.3; diastolic, 7.6; MAP, 6.6). These observations suggest that, although chronic cocaine abuse might significantly alter baseline cerebrovascular indices, the drug might not influence autoregulatory cerebrovascular systems.

75 FUNCTIONAL ACTIVITY OF SMOKERS AND NON-SMOKERS IN A DELAY-DISCOUNTING TASK

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Smokers discount the future more than non-smokers in delay discounting tasks and are therefore considered more impulsive. Given that prior studies have demonstrated a relationship between decision making and the prefrontal cortex and the anterior cingulate, we hypothesized that smokers engaged in a discounting task would exhibit decreased cortical and cingulate activity compared with non-smokers in an event-related fMRI study. Thirty subjects were enrolled in this study and 18 completed (9 smokers). During the scan subjects made a choice between receiving \$x now (4 values of X) and \$10(later (4 later times). At the end of the session, one of the questions was randomly selected and the subject received payment according to their choice for that question. A gradient echo EPI sequence was used to collect T2* data on a 1.5T GE Echosped LX 9.1 system. Imaging data for each subject was corrected for motion, normalized into a standardized Talairach template and spatially smoothed using SPM2. An event-related analysis was done using the General Linear Model in SPM2 with signal changes modeled as delta functions located at stimulus presentation onsets and convolved with a canonical hemodynamic response function. A t statistical map was generated for each subject, which was used in a second level analysis to contrast smokers and non-smokers. The results show greater activation in several brain regions in non-smokers relative to smokers during a discounting task. Specifically, non-smokers relative to smokers showed statistically significant increases in activity in medial BA 32, left parietal lobe (BA40), left caudate, right cerebrum (BA31), and right inferior frontal gyrus (BA45). The activated areas are known to be involved in decision-making and impulse control, particularly the frontal cortex and cingulate. These findings demonstrate that smokers use these regions less than non-smokers and are consistent with the lack of consideration of the future documented among cigarette smokers.

74 DESPITE PROLONGED ABSTINENCE FUNCTIONAL ACTIVITY IN RESPONSE TO COCAINE SELF-ADMINISTRATION REMAINS REDUCED IN THE TEMPORAL LOBE OF RHESUS MONKEYS

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Previous studies from our lab have shown substantial decreases in functional activity, as measured by rates of glucose utilization, in the temporal neocortex, hippocampus, and amygdala of rhesus monkeys following chronic cocaine self-administration. However, the response of these brain regions following a period of abstinence and then re-exposure to a single session of cocaine self-administration is presently unknown. We hypothesized that the changes observed following chronic cocaine exposure would be diminished following abstinence, indicating recovery, and the functional activity of these animals following reinstatement would resemble that of animals that had self-administered cocaine for only a short time. Monkeys self-administered cocaine (0.3 mg/kg/infusion under a fixed-interval schedule) for a period of 100 days followed by either 1 month (n=4) or 3 months (n=3) of abstinence and were compared to food-reinforced controls (n=4) whose responding had been maintained by food under identical schedules and were abstinent for a similar time period. Following abstinence, animals were exposed to a single session of cocaine or food self-administration in which all monkeys obtained the full number of available reinforcers. Immediately following the final reinforcer, functional activity within the temporal lobe was assessed via the quantitative 2-[14C]deoxyglucose method. In contrast to our hypothesis, following both 1 and 3 months of abstinence, cocaine self-administration produced significant decreases in cerebral metabolism in amygdala, hippocampus, and portions of the temporal cortex, similar to those observed immediately following 100 days of cocaine exposure. The absence of any change in functional response to cocaine following a prolonged period of abstinence would suggest that the neuroadaptations that occur as a result of chronic cocaine exposure have not diminished. Supported by DA09085 and DA06634.

76 EFFECTS OF MEMANTINE AND BUPROPION ON CIGARETTE-SMOKING BEHAVIOR IN THE HUMAN LABORATORY

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It is postulated that modulation of NMDA neurotransmission may be effective in the treatment of tobacco addiction. The purpose of this ongoing study is to evaluate the effect of an NMDA receptor antagonist, memantine, on the choice to smoke cigarettes in the human laboratory. For comparison, effects of placebo and bupropion, a smoking-cessation medication, are also assessed. To date, eleven nicotine dependent, non-treatment seeking volunteers (64% male) completed three phases of the study, during which they received placebo, bupropion 300 mg/d, or memantine 40 mg/d. Each medication was administered during 5-day outpatient phase, followed by a 3-day inpatient testing phase. The order of medication administration was counterbalanced and separated by at least seven days. Cigarette smoking was assessed during the: 1) outpatient medication induction phase, and 2) inpatient testing phase under an unlimited access condition and using operational choice procedures. During the outpatient phase, a significant negative linear trend was observed between time and number of cigarettes smoked ($p < 0.01$) but no effect of medication was found. During the inpatient phase, when the smoking behavior was monitored during a 4-hour free smoking period, the number of cigarettes smoked was higher during bupropion 7.18 (SD 2.7) and memantine 6.95 (SD 3.0) treatment as compared to placebo 6.09 (2.9) but the effect was not statistically significant ($p = .13$). Following overnight abstinence, participants were given ten opportunities to select between 3 puffs of a cigarette or a \$1.00 alternative, using a progressive ratio schedule with an ITI of 30 minutes. Under these conditions, participants chose cigarettes 4.09 (SD 1.7) times while maintained on memantine compared to 3.18 (SD 2.6) times while on bupropion and 4.82 (SD 1.9) times while on placebo ($p = .16$). These preliminary data suggest that memantine has limited effect on smoking behavior in non-quitting smokers under laboratory conditions.

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77 CHALLENGES AND OUTCOMES IN COMPARING SMOKED MARIJUANA AND ORAL THC

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Controversy remains regarding marijuana as pharmacotherapy. Opponents note that marijuana's primary active constituent, delta(9)-tetrahydrocannabinol (THC), is available as an oral medication, while proponents argue that the plant contains other active constituents, and that smoking allows better dose titration. The controversy might be resolved with empirical comparison of the effects of smoked marijuana and oral THC on therapeutically-relevant outcome measures. However, the design and implementation of such comparisons can be challenging due to issues that include selection of control conditions (e.g., including an "active" placebo and a positive control), timing of drug administration, selection of participant population and therapeutically-relevant measures, and standardization of smoked marijuana dose. Our laboratory planned a study of the relative potency of smoked marijuana and oral THC in healthy, marijuana-experienced volunteers. Six individuals completed this six-condition, within-subject, double-blind, double-dummy, Latin-square ordered study in which they received THC (10 or 20 mg, p.o.), smoked marijuana (3 or 6 puffs from a 3.1% THC cigarette), oxycodone (15 mg, p.o.; positive control) or placebo (capsules and six puffs from 0% THC marijuana cigarettes). Within each session, subjective, physiological, and analgesic response was assessed hourly, and cognitive performance was assessed at only one timepoint. Results suggest that smoked marijuana and oral THC produce similar subjective effects, with a faster onset and greater magnitude associated with smoked marijuana. Oral THC reduced and smoked marijuana increased pain sensation and unpleasantness ratings. This protocol illustrates how the many challenges related to determining the relative potency of smoked marijuana and oral THC on therapeutically-relevant outcome measures can be met. Supported by PHS Grants P50DA005274 and F31DA018447. CORRESPONDING AUTHOR: Melissa Blank, VCU, Box 980205 Richmond, VA 23298-0205 USA.

79 THE CANNABINOID (CB)1 RECEPTOR ANTAGONIST AM251 DOES NOT ALTER IV METHAMPHETAMINE-INDUCED REINSTATEMENT OF LEVER PRESSING IN RATS

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Methamphetamine is abused by humans and self-administered by laboratory animals. The cannabinoid receptor antagonist AM251 decreases i.v. methamphetamine self administration in rats (Vinklerova et al, 2002). The current study examined whether AM251 prevents drug-induced reinstatement of responding in rats that previously self administered methamphetamine. After training to lever press for food, adult male Sprague Dawley rats (n=9) received an indwelling i.v. catheter and self administered methamphetamine (0.1 mg/kg/injection) under a fixed-ratio 2 schedule. Methamphetamine maintained lever pressing in all rats with a significant decrease in responding when saline was substituted for methamphetamine. Thereafter, and on different days, rats received an acute i.v. injection of methamphetamine (0.01-1.78 mg/kg) immediately prior to sessions during which lever pressing resulted in i.v. injection of saline. Self administration was re-established with methamphetamine and, after extinction of responding with saline substitution, the effect of AM251 (0.032-0.32 mg/kg i.v.) on reinstatement by a non-contingent injection of 0.1 mg/kg of methamphetamine was assessed. An inverted U-shaped dose response curve emerged for methamphetamine self administration and for methamphetamine-induced reinstatement. Up to the maximum doses that could be safely studied, AM251 failed to alter methamphetamine-induced reinstatement of responding. Notwithstanding procedural differences between this study and a prior study in which AM251 attenuated methamphetamine self administration, these results fail to support a role for endogenous cannabinoids or cannabinoid (CB) 1 receptors in reinstatement and, therefore, relapse to stimulant abuse. Supported by DA04195 (JLM), Ewing Halsell Foundations (JLM), and Senior Scientist Award DA17918 (CPF)

78 DRUG-USING NETWORK CONTRIBUTIONS TO HIV RISK AMONG SUBSTANCE ABUSERS ENTERING METHADONE TREATMENT

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Objective: To determine if egocentric network factors are associated with injection-related HIV risk in new entrants to methadone treatment. Methods: We recruited new entrants to methadone treatment (either maintenance or 90 -180 day detoxification) and one of their drug-using network partners into a study assessing network impacts on treatment and HIV related outcomes (n=215). Using baseline data, we examined network factors associated with three HIV risk behaviors (receptive and distributive syringe sharing, and sharing cookers). Drug using network characteristics considered were sex with network member, living with network member, network member in drug treatment, and network member either providing or receiving drugs from index case. Results: Demographic characteristics of the overall sample are as follows: 70% male; 40% non-Hispanic white, 40% Hispanic, and 19% African American; 67% with high school or more education; 21% homeless; 3% HIV positive. Controlling for individual characteristics, having sex with a drug using network member ($\beta=0.98$, $p<0.05$) and having a drug-using network member in treatment ($\beta=1.17$, $p<0.05$) predicted receptive syringe sharing in the last 6 months. Having sex with a drug-using network member also predicted distributive syringe sharing ($\beta=1.40$, $p<0.01$). Having a drug using network member in treatment also predicted sharing cookers ($\beta=2.50$, $p<0.01$). Discussion: Injection-related risks among drug users entering methadone treatment were associated with both their behaviors with drug-using network members (sexual partnership) and treatment status of their drug-using partners. Findings suggest that efforts to prevent HIV and perhaps improve treatment outcomes could benefit from the inclusion of strategies aimed at egocentric drug-using networks of drug users.

80 EDUCATION LEVEL: ITS IMPACT ON QUESTIONNAIRE PSYCHOMETRICS AMONG SUBSTANCE ABUSE TREATMENT CLIENTS

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Self-administered client surveys are an important source of information for quality improvement efforts in substance abuse treatment. However, clients' literacy levels vary widely and self-report instruments and instrument items themselves vary in their reading difficulty. Both factors may impact client responses. In this study, 529 substance abuse treatment program clients from a large urban setting completed the Client Evaluation of Self and Treatment (CEST) questionnaire (Joe, Broome, Rowan-Szal, & Simpson, 2002) which has 130 items comprising 17 scales. Approximately 20% of clients reported completing the 9th grade or less and approximately 35% have education beyond high school suggesting that some respondents may have difficulty understanding some items. The reading levels for CEST items range from low elementary grade level through high school and above. Analysis results revealed that CEST items with greater reading difficulty were correlated with the lower variability in responses as measured by the item's standard deviation. Differences were also found in the reliability of the CEST scales across respondents with different educational attainment with lower reliability generally associated with lower educational attainment. Overall, the findings show that client self-reports to paper and pencil questionnaires need to be evaluated carefully depending on clients' literacy levels and survey reading level.

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- 81 MALE-FEMALE CONTRASTS AND OTHER VARIATIONS IN EXPOSURE OPPORTUNITY AND ACTUAL EXTRA-MEDICAL USE OF ANALGESICS IN AN EPIDEMIOLOGICAL STUDY**
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BACKGROUND: Extra-medical use of analgesic drugs is of public health importance. Elsewhere, there is evidence of male-female (M-F) differences in the chance to try heroin, but not in the transition from opportunity to heroin use, but no evidence exists on these transitions for extra-medical use of analgesic medicines. This study probes these M-F differences and other variations. AIM: In epidemiological research, we estimate risk of (a) having a 'chance to try' analgesics for extra-medical reasons by young adulthood, and (b) once this chance occurs, the probability to transition into extra-medical analgesic use. METHODS: Data are from young adult assessments of 2,311 first-graders who started school in 1985-86. Multiple logistic regressions estimate subgroup variation with respect to analgesic transitions. RESULTS: Females were just as likely to have had a chance to try analgesics and also to have used analgesics, as compared to males ($p > 0.05$). Being non-Hispanic white was associated with greater chance to try analgesics (adjusted relative risk, aRR~3.7; $p < 0.05$) and transition from opportunity to use (aRR~2.7; $p < 0.05$). Subsidized lunch at school entry was inversely associated with chance to try (aRR~0.7; $p < 0.02$) and with transition into use (aRR~0.6; $p < 0.05$). DISCUSSION: In relation to extra-medical analgesic drug use, M-F differences in opportunity to use and transition to first use were not observed, but this research has disclosed epidemiological patterns of variation that deserve future scrutiny. SUPPORT: NIDA K05DA015799 and MSU research funds.
- 82 SYNTHESIS OF 4-{2-[BIS(4-FLUOROPHENYL)METHOXY]ETHYL}-1-(2-TRIFLUOROMETHYLBENZYL)PIPERIDINE, AN ALLOSTERIC MODULATOR OF THE SEROTONIN TRANSPORTER**
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Ligands with varying transporter affinity and selectivity can be used to obtain additional information about the properties a compound should have to act as a useful pharmacotherapeutic agent for cocaine addiction, and help unravel pharmacological mechanisms relevant to stimulant abuse. To obtain these ligands, we have synthesized a series of 4-(2-(bis(4-fluorophenyl)methoxy)ethyl) piperidines with substituents at the ortho, meta, and para positions in the aromatic ring of the N-benzyl side-chain. Their affinities and selectivities for the dopamine transporter (DAT), serotonin transporter (SERT), and norepinephrine transporter (NET) were determined. Remarkably, the C2-trifluoromethyl substituted analogue was found to act as an allosteric modulator of hSERT binding and function. It had little affinity for any of the transporters. Several compounds showed affinity for the DAT in the low nanomolar range, and displayed a broad range of SERT/DAT selectivity ratios (up to 56-fold selectivity for the DAT over the SERT and up to 1090-fold selectivity for DAT over NET), providing ligands that might provide leads for future pharmacotherapies for stimulant misuse. This research was supported in part by the Intramural Research Program of the NIH, NIDA and NIDDK.
- 83 INJECTION DRUG-USER CHARACTERISTICS FROM THREE UKRAINE CITIES**
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It is estimated that as many as 500,000 individuals in Ukraine are infected with HIV, or approximately 1% of the adult population, fueled largely by injection drug users (IDUs). What is perhaps most alarming is that up until 1991, or when the Soviet Union collapsed, there were virtually no known cases of HIV in the country. Approximately three years ago, we received a NIDA-funded grant intended to reduce the spread of HIV in three Ukraine cities, Kiev, Odessa and Donesk, using intervention approaches found effective with IDUs in the USA. The findings presented in this study are from the first 900 participants, 300 from each site. Its purpose is to compare demographic and risk behavior differences between IDUs in the three locations. Odessa, and especially Donesk, were and remain much more closely aligned to Russia than Kiev. Kiev, the capital city, is more cosmopolitan than the other two cities although Odessa, located on the Black Sea, is a larger tourist attraction. Donesk, on the other hand, is primarily an industrial, impoverished city. Overall, participants averaged 29 years of age, they had been injecting for approximately 10 years and 22% were female. There were many significant differences between IDUs in the three cities. In Odessa, where the epidemic is believed to have begun, IDUs were 6 to 7 years older on average than those from the other sites and they had been injecting for 6 years longer. Odessa IDUs also were more likely to have tested HIV positive (50% vs. 34% in Kiev and 18% in Donesk). Injection-related risk behaviors were highest in Kiev, while sex-related risks were greatest in Odessa. Across all sites, however, substantial proportions of IDUs were engaged in both high risk sex and injection behaviors. These findings point to the need for interventions targeting drug injectors in Ukraine. Supported by the National Institute on Drug Abuse DA017620.
- 84 BEHAVIORAL FUNCTIONS OF SEXUAL BEHAVIOR ACROSS REGULAR, CASUAL, AND COMMERCIAL PARTNERS AMONG URBAN DRUG USERS WITH A HISTORY OF CHILDHOOD VICTIMIZATION: GENDER AND CONTEXT**
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Risky Sexual Behavior (RSB) and its role in HIV infection is a significant public health concern that is especially relevant for chronic inner-city drug users. A wealth of literature has suggested that childhood trauma is related to later-life RSB, including multiple short-term sexual encounters, exchange of sex for money, drugs, or shelter, unprotected sex, and the contraction of STDs. Despite this consistent and robust association, few studies have explored the reasons behind this phenomenon. As such, the present study utilized a novel method of understanding this association by focusing on the behavioral functions of RSB, with additional analyses testing potential differences across gender and partner type (i.e., casual, commercial, and regular) among a sample of 110 chronic, inner-city drug users. A principal component analysis (PCA) indicated a two-factor solution across regular, casual, and commercial. Specifically, the first function of RSB concerned motives of intimacy, and the second consisted of emotional avoidance (i.e., maladaptive coping) and self-punishment. Reliability for these factors ranged from acceptable to excellent (all alphas were greater than .70). Using the scales derived from the PCA solution for casual and commercial partners, childhood victimization (across sexual, physical, and emotional abuse) was significantly related to avoidance/self-punishment motives, but unrelated to intimacy motives of intimacy. In contrast, childhood victimization was not related to the avoidance/self-punishment motives in sexual acts with a regular partner, but was negatively related to intimacy motives, suggesting an inability to function in an intimate romantic relationship. This latter finding was especially strong among women. The current study is the first to empirically explore the behavioral functions of RSB among victimized individuals, and results are discussed in the context of prevention and treatment.

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85 DRUG USE AND THE DAST-10: DIFFERENCES AMONG COLLEGIATE SEXUAL MINORITY WOMEN

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This exploratory study investigated past year drug use among lesbian, bisexual, unlabeled and heterosexual women in college. In addition, a modified version of the Drug Abuse Screening Test (DAST-10) was administered to assess drug problems. The present study was a Web-based survey, conducted from January through February of 2005 at a large mid-Western university. A random sample of full-time undergraduate students was drawn from the Registrar's Office. The response rate for women was 70%. The final sample for the current investigation was n=2440. Past year drug use was assessed for the following types of drugs: marijuana/hashish, cocaine, LSD, other psychedelics, crystal methamphetamine, heroin, inhalants, ecstasy, as well as the illicit use of four classes of prescription medications. Age, race and living arrangement were entered as control variables. Results from logistic regression analyses revealed that bisexual women were more likely than heterosexual women to report past year marijuana use, as well as any past year drug use. When assessing DAST-10 scores (0-10), the mean for heterosexual women was significantly lower than that of lesbians, bisexual women and unlabeled women. Results from linear regression analyses showed that a non-heterosexual identity significantly predicted DAST-10 scores. These findings suggest important differences in both drug use behaviors as well as drug use problems among sexual minority women. Practice implications include the need for prevention and intervention programs that specifically target sexual minority women. The current study also highlights the need for more research among sexual minority populations to better understand the myriad factors that influence substance use among such groups, and how both antecedents as well as consequences of use may differ. This project was supported by research grants DA07267 (PI: Boyd) and DA018239 (PI: McCabe) from the National Institute on Drug Abuse.

87 DOPAMINE TRANSPORTER CODING VARIANT A559V ASSOCIATED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER CAUSES ALTERATION OF DOPAMINE EFFLUX

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The dopamine (DA) transporter (DAT) is the site of action for psychostimulants such as amphetamine (AMPH), which acts by inducing DAT-mediated DA release. It has been previously shown that AMPH-induced DA efflux is dependent on both voltage and intracellular Na⁺ concentration. Evidence indicates a genetic link between DAT and ADHD, and recent work has identified a nonsynonymous single nucleotide polymorphism in DAT which converts Ala559 to Val (A559V) in two male siblings with ADHD. The functional impact of A559V was examined using transiently transfected COS-7 and SH-SY5Y cells, and it was observed that A559V did not affect DA transport activity, DAT cell surface expression, or the ability of AMPH to inhibit DA uptake. However, these studies were all conducted at resting membrane potential and did not examine the impact of A559V on DA efflux. Thus, we sought to characterize the effect of the A559V variant on DA efflux in response to membrane depolarization. Whole-cell patch clamp technique combined with amperometry was employed on human embryonic kidney cells transiently transfected with the human DAT (hDAT cells) or A559V DAT (hDAT A559V cells). Our preliminary data suggests that at depolarized membrane potentials, hDAT A559V cells display increased DA efflux with respect to hDAT cells. In addition, we observed that the presence of 90 mM intracellular Na⁺ caused higher DA efflux in hDAT A559V cells compared to hDAT cells. Importantly, in resting, nonclamped conditions, hDAT A559V cells exhibited normal [3H]DA uptake but a significantly greater DA efflux with respect to hDAT cells. These data suggest that the A559V variant is associated with a hDAT-mediated DA leak that may underlie the ADHD phenotype in this family, thus offering the potential for new therapeutic approaches for treating ADHD and/or psychostimulant abuse. EAB, MSM, RDB, and AG contributed equally to this paper.

86 CHANGES IN LOCOMOTOR ACTIVITY AND TOLUENE BLOOD CONCENTRATIONS FOLLOWING REPEATED BINGE TOLUENE EXPOSURES IN ADOLESCENT RATS

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In contrast to recent trends in drug abuse, inhalant abuse among adolescents has not declined in recent years. National surveys also indicate that adolescents are particularly susceptible to abuse of toluene-containing products. The relationship between toluene blood concentrations (TBC) and the behavioral effects associated with abuse of toluene-containing products has not been established. This research used a pre-clinical rat model of inhalant abuse to assess the relationship between TBC and changes in locomotor activity both during and following repeated binge toluene exposures typical of abuse. Adolescent male Sprague-Dawley rats were exposed to toluene (0, 8000 ppm or 16,000 ppm) for 15 min/exposure. Exposures occurred twice each day from PN28-PN33 and from PN35-PN40. Locomotor activity was recorded within the exposure chambers during binge toluene exposures. Immediately upon removal from the chambers, blood was drawn from the saphenous vein. Following the blood draw, the animals were placed into separate toluene-free activity monitors for continued assessment of locomotor activity during a 30-min recovery period. Animals exposed to either dose of toluene exhibited more locomotor activity during later exposures than they did during the first day of exposures. Peak TBCs decreased significantly by the last day of exposures in the 16,000-ppm but not the 8,000-ppm dose group. Both groups of toluene-exposed animals recovered more quickly following the final day of exposures (PN40, when hyperactivity peaked by 5 mins) than following the first day of exposures (PN28, when hyperactivity peaked at 20 mins). Changes in peak TBCs over days appear to parallel changes in locomotor activity. Since inhaled concentrations are constant over days, the results imply a metabolic tolerance to toluene. (Supported in part by grants DA15095 and DA015951 to SEB).

88 MEASURING CRIME AROUND METHADONE CLINICS: DOES TYPE OF CRIME DATA MAKE A DIFFERENCE?

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Potential clustering of crime around methadone maintenance clinics (MMCs) has public health and policy implications. There is no agreement on what data provide a valid proxy estimate of crime around MMCs. Treatment providers suggest arrest data inflate crime estimates because arrests depend on police behavior, but police deny increased surveillance around MMCs. Other crime proxies, "incidents" (formal crime complaints) and 911 calls, are not police-dependent, but may not capture important crime categories (e.g., drug crimes). This study compared crime patterns around 11 Baltimore City MMCs using arrest, incident, and 911 call data obtained from the Police Department and geocoded (electronically mapped). (Data on arrests were available for 1996, on 911 calls for 1998, and on incidents for both years.) Four concentric circular "buffers" were defined at 25-meter intervals around each MMC. Crime counts within each buffer were corrected for buffer area. The ratio of counts in the innermost (25-meter) buffer to the average for all 4 buffers was calculated to measure crime clustering around MMCs ("clustering ratio" or "CR"). There was a significant correlation between incidents and 911 calls within 100 meters of MMCs ($r = 0.96, p < 0.04$), but not between incidents and arrests ($r = 0.66, p = 0.34$). The CR for arrests was 1.5, for 911 calls 2.1, and for incidents 2.2 (both years). The significant correlation between incidents and 911 calls suggests that these are similar measures. The non-significant correlation with arrests suggests that incident and arrest data measure different aspects of crime. The CR for arrests appears lower than the other CRs, suggesting that arrest data does not inflate estimates of crime around MMCs. Supported by the Intramural Research Program of the NIH, National Institute on Drug Abuse; the Substance Abuse Policy Research Program, Robert Wood Johnson Foundation; and CSAT, SAMHSA.

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89 KRATOM USE BY ONLINE OPIOID ANALGESIC ABUSERS

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Hypothesis: Persons who self-manage chronic pain with opioid analgesics (OA) may decrease tolerance by taking medication holidays; opioid withdrawal associated with these periods of abstinence may be modulated with kratom, a southeast Asian medicinal herb traditionally used as a substitute for opium. Procedures: We searched forums on www.drugbuyers.com, an important nexus between Internet pharmacies and individuals who use OA to self-manage chronic pain. Drugbuyers has 62,000 members, 68% of whom eschew formal clinical supervision of long-term OA therapy for chronic pain. We identified members' posts between November 2004 and October 2005 that mentioned kratom as a method to decrease opioid withdrawal symptoms during hydro- or oxycodone holidays. Results (month/number kratom mentions): 11/04, 0; 12/04, 1; 1/05, 2; 2/05, 0; 3/05, 5; 4/05, 1; 5/05, 49; 6/05, 168; 7/05, 267; 8/05, 215; 9/05, 435; 10/05, 409. Posts contained information on sources, dose, administration, and effects of kratom. Discussion: These results demonstrate a dramatic increase in the use of kratom to modulate opioid withdrawal by opioid analgesic abusers. Kratom is legally available from Internet businesses selling "ethnobotanical" agents. Biological activity resides in mitragynine, an indole alkaloid that agonizes mu-opiate receptors with high affinity. The increased use of kratom may affect the abuse liability of OA. First, Drugbuyers' members self-treat chronic pain with opioids purchased from Internet pharmacies. Kratom may prolong unsupervised OA therapy and contribute to the striking tolerance described by members of the online community. Second, the ability to manage opioid withdrawal with kratom may prevent contact with medical and addiction professionals. These effects may converge to increase the likelihood of opioid analgesic dependence and addiction in this vulnerable population. Drug treatment and addiction clinicians should consider including assessment of kratom use in evaluations of individuals being treated for OA abuse. Further studies on the effect of kratom on opioid abuse potential and liability are warranted.

91 DEVELOPMENT OF A NOVEL DEPRESSION TREATMENT FOR INNER-CITY DEPRESSED SUBSTANCE USERS CURRENTLY RECEIVING RESIDENTIAL SUBSTANCE ABUSE TREATMENT

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Evidence suggests that substance dependent individuals with co-morbid depression are more susceptible to substance use treatment attrition and subsequent relapse. This is particularly true within inner-city residential substance use programs, where treatment approaches rarely integrate psychosocial treatments for co-morbid conditions. Limited success of integrating cognitive-behavioral treatments (CBT) for depression into standard substance use treatments suggests that the complexity and the time intensive nature of these approaches may limit their effectiveness. Recent evidence indicates that behavioral activation strategies might be equally effective as more elaborate CBT approaches in reducing depressive symptoms while being considerably more brief and less complicated, suggesting the potential for integration into standard substance use treatments. Thus, the objective of the current study was to develop a novel, behavioral approach to substance use treatment for patients with depression that utilizes behavioral activation strategies. A total of 20 patients with major depressive disorder were recruited from an inpatient residential treatment facility in Northeast Washington, DC. In Phase 1, the original manual was piloted with 2 groups of 5 participants. Treatment began at each patient's second week in the center and consisted of 6 sessions across a two week period. Based upon patient feedback and therapist input, necessary modifications to the treatment manual were made. The revised manual was then piloted with an additional 2 groups of 5 participants in Phase 2. Self-reported and interviewer assessed changes in depressive symptoms, quality of life, enjoyment of activities, and activity levels, suggest further evaluation of this program in future randomized clinical trials assessing these outcome variables as well as the mediating role of these changes in substance use outcomes including treatment drop-out and relapse back to substances after leaving the center.

90 TRENDS IN METHAMPHETAMINE DRUG SEIZURES IN CANADA

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Methamphetamine (MA) and its smokeable form 'crystal meth' are gaining increased attention in the media. However the scope of MA use in Canada is not accurately known. The Drug Analysis Service (DAS) of Health Canada analyzes suspected illicit drugs submitted by the police. The DAS operates four laboratories across Canada. All drug seizures that were analyzed by DAS from 1988 to November 2005 were included in this study. Using Stata 8.2, a 2-way table was developed on drug by province and sorted by year of seizure. Compared to cannabis (51.86%) and cocaine (21.96%) the percentage of samples containing MA is very low (1.48%) (range: 0.26% in Nova Scotia and 3.17% in Alberta). Over the 17 year period British Columbia was found to have the highest number of samples of MA analyzed (n=6593), followed by Quebec (n=5473), Ontario (n=5211) and Alberta (n=3521). The number of samples containing MA increased considerably in British Columbia (from 218 in 1995 to 1402 in 2004), Alberta (from 75 in 1997 to 652 in 2003), and Ontario (from 138 in 1998 to 1262 in 2004) and declined in 2005 (to 941 in BC, 496 in Alberta, and 822 in Ontario). In Quebec, the number of samples increased from 43 in 1999 to 134 in 2000 and has continually increased from 2000 to November 2005 with the highest number of samples analyzed in 2005 (1905 cases). Limitations of this study include: only samples that are going through the court system are analyzed (cases in which a guilty plea has been entered are not analyzed) leading to possible under-representation of our sample, and police resource allocation for drug investigations is inconsistent. Overall, the number of MA samples has increased over the past 17 years; however it remains low on the national level when compared with cannabis and cocaine samples. Further discussion on provincial differences will be presented.

92 MORTALITY AND CAUSE OF DEATH OVER 25 YEARS AMONG OPIATE USERS: COMPARISONS BY GENDER AND ETHNICITY

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Hypothesis: Previous studies have shown higher death rates for opiate users than for the general population; however, information is limited on the relative risks for gender and ethnic subgroups. Procedures: This study analyzes mortality statistics and causes of death over a period of 25 years for 914 opiate-dependent individuals who were sampled from methadone maintenance clinics in California in 1979-80. Data were obtained from the National Death Index on date and cause of death information for members of the original study cohort. Analyses: Analyses included years of potential life lost (YPLL) and standardized mortality ratios (SMR). Results: Over the period 1979-2003, 265 deaths (193 males, 72 females) were confirmed in the sample. YPLL (compared to age 75) for those who died averaged 25.8 years per person, about 3 times more than for the U.S. population under 75 years. Most common underlying causes of death were alcohol/drug overdose accounting for 22% of deaths, cancer (16%), liver (13%) and cardiovascular diseases (12%); these causes as well as less prevalent respiratory disease, hepatitis, suicide, and homicide had substantially higher YPLL rates than the U.S. population. Average age at death was 46.7 for females and 50.1 for males (p<.001). Based on SMR, study subjects were 2.6 times more likely to die than individuals of comparable age/gender/ethnicity in the general population, with highest SMR for alcohol/drug abuse, liver and respiratory diseases, and suicide. Most vulnerable demographic subgroups included non-Hispanic white females ages 25-34 (SMR=5.8), 35-44 (SMR=4.6), 45-54 (SMR=5.7); Hispanic females ages 45-54 (SMR=6.5) and 55-64 (4.2); African-American females ages 35-44 (SMR=3.5); and non-Hispanic white males ages 35-44 (SMR=4.2) and 45-54 (SMR=4.4). Conclusion: Opiate users, particularly females, have elevated risk of mortality; public health interventions, within drug treatment and other health services, should be developed to reduce the risks of premature mortality. Supported by National Institute on Drug Abuse (R01-DA015390 and P30-DA016383).

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93 DETERMINANTS OF RACIAL DISCRIMINATION IN ADULTHOOD AND ITS RELATION TO FREQUENCY OF COCAINE AND MARIJUANA DRUG USE

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Background: Studies about the harmful effects of perceived racial discrimination on health have achieved some recognition in public health. Aim: This study (1) investigated which factors during childhood, adolescence and young adulthood are associated with discrimination in young adulthood among African Americans; (2) determined the relation between discrimination and marijuana and cocaine use; and (3) explored gender differences. Methods: Data analyzed come from a cohort of children who started school in Woodlawn – a mostly black and inner city neighborhood located on the south side of Chicago. Measures were collected at three time points: first grade (age 6-7); adolescence (age 15-16); and young adulthood (age 33-34). Results: Seventy percent of the sample reported at least one experience of discrimination among six domains. There were gender differences in perceived discrimination (80% for men and 60% for women). In ordered logistic regression analyses, increased risk of perceived racial discrimination was associated with the following: gender, interpersonal aggression, criminal victimization, U.S. region of the country where one resides, paranoid feelings, and poverty. Using multinomial logistic regression, the results indicated that men who perceived discrimination were more likely to be experimental, former, current moderate, or current heavy marijuana users and current heavy cocaine users. Women who perceived racial discrimination tended to be experimental, former, and current heavy marijuana users, and also experimental and former cocaine users. Conclusion: This investigation explores the association between perceived racial discrimination and drug use over the life course. Future research should continue to explore individuals at high risk of perceiving racial discrimination and to evaluate potential moderators and mediators related to perceived racial discrimination.

95 COMPARING SERVICE DELIVERY STRATEGIES FOR TREATING PSYCHIATRIC COMORBIDITY IN OPIOID-DEPENDENT PATIENTS RECEIVING METHADONE: PRELIMINARY ASSOCIATIONS WITH ONSET OF CARE AND ADHERENCE

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Psychiatric comorbidity is a common problem in drug-dependent patients. Comorbidity is associated with increased severity of baseline drug use, poor psychosocial functioning, and poor drug abuse treatment response. Treating this comorbidity may improve prognosis but delivering specialized psychiatric care is complicated by problematic referral processes and poor patient adherence. Providing specialized psychiatric services in drug abuse treatment settings may help overcome these obstacles. The present study reports preliminary data from a two-group randomized trial comparing on-site (ONS) with off-site (OFS) psychiatric care of opioid-dependent patients with other psychiatric disorders. Both treatment sites offer the same amount and types of psychiatric services. Subjects are administered the SCID by trained interviewers; diagnoses are confirmed via clinical reappraisal by a study investigator. Outcome data compare groups on rates of initiating psychiatric care and adherence to scheduled services for the first 96 randomly assigned subjects (OFS: n=48 vs. ONS: n=48). The sample is 64% female and 52% African-American; mean age is 39 years. The most common current psychiatric diagnoses in the combined sample is major depression (49%). More of the subjects in the ONS versus OFS group initiated psychiatric care (ONS: 96% vs. OFS: 81%, $p=0.03$); the ONS group also had a shorter time delay between referral and onset of services (ONS: 4.9 days vs. OFS: 32.8 days, $p<.001$). Adherence to scheduled psychiatric appointments is favoring the ONS versus OFS group for scheduled appointments with a psychiatrist (ONS: 72% vs. OFS: 49%, $p<.001$) and for scheduled group therapy sessions (11% vs. 3%, $p=0.04$). Early findings continue to support some of the anticipated benefits of offering specialized psychiatric services in drug abuse treatment settings but group therapy attendance in both settings is disappointing. Supported by NIH-NIDA grant R01 DA016375

94 PATIENT COMMITMENT LANGUAGE STRENGTH PREDICTS OUTCOME IN BEHAVIORAL NALTREXONE THERAPY INVOLVING SIGNIFICANT OTHERS

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Analysis of the language produced by patients during motivational interviewing sessions has shown that strength of commitment language (i.e. statements indicating intent to achieve abstinence) is a strong predictor of substance use outcomes. We examined whether commitment language would predict outcome of Behavioral Naltrexone Therapy. BNT is a psychosocial therapy incorporating aspects of network therapy, relapse prevention, motivational interviewing and voucher incentives, with the goal of helping opiate-dependent patients remain on naltrexone and abstinent from opiates. Each week in BNT, patients attend one individual session and one network session with a significant other who monitors naltrexone compliance. Audiotaped individual and network sessions from opiate-dependent patients who participated in an ongoing six-month trial of BNT were coded for strength of commitment language by a blind, independent coder. Mean commitment strength from early individual sessions (Weeks 2-4) did not predict percentage of heroin positive urines, retention in treatment, or compliance with naltrexone ($N = 32$). However, in network sessions ($N = 22$), stronger mean patient commitment language predicted fewer heroin positive urine samples ($r = -0.49$, $p = 0.02$), longer retention in treatment ($r = 0.45$, $p = 0.04$), and showed a trend towards predicting amount of urine-confirmed compliance with naltrexone ($r = 0.38$, $p = 0.08$). Strength of commitment language, a construct shown to be predictive of outcomes in motivational interviewing, is also a strong predictor in a different type of psychosocial therapy. This study points to the importance of a significant other involved in outpatient naltrexone treatment. The study also suggests that commitment statements made in the presence of a significant other may be particularly powerful agents of change in psychosocial treatment.

96 PARTICIPANT FACTORS ASSOCIATED WITH FAILURE TO COMPLETE SUBSTANCE ABUSE TREATMENT IN THE DANE COUNTY DRUG COURT

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A drug court treatment program (DCTP) is provided in over 1000 county, tribal, and territorial jurisdictions in the United States as an alternative to incarceration for drug offenders with substance use disorders. Given their defining use of substance abuse treatment interventions, health-related outcomes during DCTP participation and their correlates have not been adequately examined. Data from the Dane County DCTP during 2001 and 2002 yielded a sample of 160 participants who achieved a final outcome of substance abuse treatment completion or failure. Stepwise logistic regression was undertaken to construct a model of important predictors of treatment failure among these participants. No demographic covariates (e.g. age, gender, socioeconomic status, educational achievement) achieved statistically significant predictive value for treatment failure. Of other collected covariates (e.g. prior arrests, current criminal charges, substance use history, current substance use, treatment history), the only statistically significant predictor of treatment failure, while controlling for age and gender, was presence of an alcohol use disorder [OR 5.89, 95% CI (4.34, 9.09)]. Conclusions include: (1) Substance use factors influenced the probability of treatment completion among drug court participants to a greater degree than demographic/social factors; and (2) alcohol misuse influenced likelihood of treatment completion to a greater degree than illicit substance misuse. This finding is an important one, as alcohol use disorders are often not addressed by drug court treatment programs (Supported by NIH/NIDA K23 Career Development Award 5K23DA017283-02)

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97 LAMOTRIGINE FOR BIPOLAR DISORDER AND STIMULANT DEPENDENCE: A REPLICATION AND EXTENSION STUDY

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Objective: Bipolar disorder (BPD) is strongly associated with substance abuse. We previously reported favorable results with lamotrigine in 30 patients with BPD and cocaine dependence. This report examines lamotrigine in an additional 32 patients to replicate the findings, and extends the previous findings by combining data from both groups, including participants with amphetamine use, examining maintenance phase treatment, and exploring response predictors (n=69 total). Methods: Participants were assessed for up to 36 weeks with the Hamilton Rating Scale for Depression (HRSD17), Young Mania Rating Scale (YMRS), Brief Psychiatric Rating Scale (BPRS18), Cocaine Craving Questionnaire (CCQ), urine drugs screens and self-reported drug use. Results: In the replication sample (n=32), significant improvements were observed in HRSD17, YMRS, BPRS18, CCQ, and dollars/week spent on cocaine. In the extension study, HRSD17, YMRS, BPRS18, CCQ scores, and dollars and days of stimulant use decreased significantly. Conclusion: Lamotrigine was associated with improvements in mood, drug craving and use.

98 GENDER DIFFERENCES IN OLDER HEROIN USERS

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Limited information is available regarding aging drug addicts, yet this population is increasing. As part of a long-term follow-up study of gender differences among older heroin users, 8 gender-specific focus groups were conducted with 38 (19 men, 19 women) older (aged 50+) heroin users. Approximately half of the sample was African American, 29% Caucasian, 8% Hispanic, and 8% other. Almost two-thirds was currently on methadone; 55% reported illegal substance use in the past year. Nearly all (95%) had been incarcerated during their lives. Interviews were analyzed using constant comparative method in ATLAS.ti. Gender differences were apparent in the content and the interactional styles within the groups. Male participants glorified the past, strived to impress one another, and remained fairly abstract in their discussions. They talked extensively about incarceration, including relapse following release. Few were in relationships with significant partners or described ongoing relationships with their children. Some of the male participants stopped using "cold turkey." Quitting was typically precipitated by drug-related deaths of loved ones. Female participants tended to be more introspective and often tried to analyze one another. They described using primarily with their partners, and several had been in long-term marriages. Sixteen women had children, but not all were in contact with them. Several of the women described traumatic childhood experiences, including sexual abuse, and many had used drugs to self-medicate. Female participants spoke about sexual behaviors (e.g., prostitution) in which they engaged in order to maintain their habits. Gender did not differentiate health effects of heroin, in that men and women described similar physical and psychological problems. Aging current and former drug users face many potential long-term health problems, as well as lack of support systems and resources; some of these issues differ by gender. Considering the steady rise in aging individuals seeking treatment, more research needs to address issues specific to male versus female older users. Supported by NIDA 5 R01 DA015390-02 & P30 DA016383.

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

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Considerable discussion continues about ways to achieve desirable healthcare outcomes cost-effectively. Use of an electronic health information system has been the focus of many of these discussions, though generally not in substance abuse treatment settings. Addiction Research and Treatment Corporation (ARTC) is an outpatient opioid treatment program providing onsite primary medical care and HIV-related care for approximately 3,000 predominantly minority adults in Brooklyn and Manhattan in New York City. A large percentage of this economically disenfranchised population is also infected with hepatitis C virus. These patients are subject to significant disparities in healthcare access and quality compared to the general population. ARTC assessed the selection process for implementation of an electronic health information system integrating counseling and social services, medical services, case management, HIV counseling and testing, dispensing information, and administrative and fiscal data. Buy-in by stakeholders (patients, clinicians and managers) was the initial focus of this process. Five specific aims (quality, productivity, satisfaction, financial performance and risk management) with nine related hypotheses were chosen based on needs assessment meetings with stakeholders and literature review of prior published investigations. The final selection of specific health information hardware and software is informed by a number of specific criteria, including the ability to provide relevant data regarding the aims mentioned above, information obtained from stakeholders and literature review, and determination as to whether the system will be developed totally in-house, by an outside vendor or as a hybrid. Presentations by various vendors were evaluated using specific criteria. The results of this detailed program description have the potential to inform continuing discussions about the selection and impact of integrated electronic systems in enhancing healthcare outcomes and agency cost-effectiveness in substance abuse treatment settings for this unique patient population.

100 VICTIMIZATION AND SUBSTANCE USE AMONG ADOLESCENTS ENTERING TREATMENT

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Victimization in childhood has been linked with higher risk of drug use as well as other behavioral, mental and other problems. Identifying these co-occurring disorders, as well as factors that reduce their impact is important for treatment of drug use among victimized youth and the prevention of subsequent disorders. The research question for this study is: For adolescents who are entering substance abuse treatment, does a history of victimization increase the likelihood of: (1) internalizing disorders, (2) externalizing disorders, (3) involvement in and/or arrests due to illegal activities, and (4) HIV risk behaviors? Methods. Data are cross-sectional from 64 adolescent treatment projects located throughout the US (n=5,308). Data were collected through face-to-face interviews, with standardized measurement of internalizing and externalizing disorders, involvement in illegal activity, HIV risk behavior, victimization, drug use problems, and demographic characteristics. Conditional logistic regression models accommodated potential clustering of patients by treatment center and covariates. Results. Victimization is commonly reported among adolescents entering drug use treatment. Adolescents who have experienced some form of abuse are more likely than non-victimized youth to report other mental health problems, involvement in illegal activities and sexual behaviors that put them at risk for contracting HIV/AIDS. Comment. Adolescents who have experienced some form of abuse are more likely than non-victimized youth to report other mental health problems, involvement in illegal activities and sexual behaviors that put them at risk for contracting HIV/AIDS. Acknowledgments. NIDA, grant DA019805-01; analytic runs provided by SAMHSA.

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- 101** EVALUATION FOR SEVERE MENTAL ILLNESS IN BUPRENORPHINE MAINTENANCE THERAPY
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There is growing empirical evidence of buprenorphine's effectiveness in treating opiate dependence across a wide range of patient populations even when compared with the long-standing methadone maintenance approach. However, people with severe mental illness (SMI) are typically excluded from research studies evaluating the effectiveness of buprenorphine. As it becomes more widely available, buprenorphine has the advantage of reaching a larger population of opiate dependent patients because it may be offered in a variety of clinical care settings, including among individuals with SMI. An evaluation of buprenorphine among individuals with SMI is needed. Project BEST is a large, prospective, longitudinal cohort of individuals with opioid dependence with and without SMI, some of whom have HIV and/or hepatitis C. In this abstract, we describe the routine use of structured mental health measures to evaluate for underlying SMI (using a standard SCID by trained staff) prior to starting buprenorphine, a two tier system of drug treatment with buprenorphine based on the severity of mental illness, and the rapid stabilization with acute psychiatric services if required. For those subjects with SMI, one-on-one manualized counseling using cognitive behavioral therapy is conducted weekly in addition to intensive case management support. Preliminary results demonstrate that individuals with SMI can do well in buprenorphine maintenance therapy as in methadone maintenance.
- 102** THE EFFECTS OF NICOTINE CONDITIONED PLACE PREFERENCE IN D2-PRIMED ADOLESCENT RATS: AGE-RELATED AND GENDER EFFECTS
C. L. Bruner, E. L. Cooper, M. K. Perna, C. Estep, K. N. Thompson and R. W. Brown, East Tennessee State University, Johnson City, TN
Past studies from this laboratory have shown that neonatal treatment with the dopamine D2/D3 agonist quinpirole produces long-term priming of the D2 receptor. This study was designed to analyze the associative effects of nicotine in this D2-priming model utilizing the conditioned place preference (CPP) paradigm in adolescent rats. In Experiment 1, male and female Sprague-dawley rats were neonatally treated with quinpirole or saline from postnatal days (P1-21) and raised to adolescence (P30). Beginning on P30, animals were conditioned for eight consecutive days to the non-preferred white compartment in a CPP apparatus through administration of nicotine 15 mins before being placed in this compartment, and administered saline 4 h later before being placed into the black compartment. The control group was administered saline 15 mins before being placed into either compartment. On a post-conditioning test with the divider removed, male rats (P39) administered nicotine demonstrated a stronger preference for the white compartment as compared to controls, whereas female rats did not demonstrate a drug-induced preference. Beginning the next day on P40, animals were trained for eight more consecutive days following the identical procedure, but nicotine did not produce CPP. In Experiment 2, training began on P23 following the identical procedure as Experiment 1, and nicotine induced CPP in both male and female rats at P30, but neonatal quinpirole did not produce any effects. Further training for eight more days only increased nicotine-induced CPP when animals were later tested at P38, again not affected by neonatal quinpirole treatment. This study demonstrates that the associating effects of nicotine are age-related in adolescence and are gender-specific, but do not appear to be affected by D2 receptor priming. Support Contributed By: ETSU honors program
- 103** THE INCREASED ASSOCIATION OF COCAINE USE AND DEPRESSION OVER TIME
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AIM: Previous research has not considered historical effects on the co-morbidity of mental illnesses and drug use. Cocaine provides a particularly useful drug to study in terms of historical effects because of shifts in use and the introduction of crack cocaine in recent decades. The present study seeks to examine historical effects on the co-morbidity of cocaine use and depression. METHODS: Data on mental health as well as drug use behavior was collected from 1981 to 1984 (Wave 1) and 1993 to 1994 (Wave 3) on a cohort of participants in Baltimore, MD as part of the Epidemiologic Catchment Area Program (ECA). 484 individuals between the ages of 27 and 37 during Wave 1 were compared to a different group of 339 individuals between the same ages at Wave 3. Cocaine use was measured as reporting five or more occasions of use ever in one's lifetime. Depression was determined by lifetime DSM-III diagnosis of Major Depressive Disorder (MDD). RESULTS: The association of cocaine use and depression changed over time. The odds ratio (OR) of cocaine use for those who met criteria for MDD compared to those who did not at Wave 1 was 0.62, while the OR of cocaine use for those who met criteria for MDD compared to those who did not at Wave 3 was 3.47. In a multiple logistic regression model, an interaction term of depression and wave resulted in a Beta = 1.73 and $p = .04$, indicating that the change in the association over time was statistically significant. CONCLUSIONS: This study suggests that the shift in the profile of cocaine users between the early 1980's and the early 1990's resulted in a change in the co-morbidity of depression and cocaine use, informing public health policy and intervention strategies for future trends in drug use.
- 104** COMPARISON OF CANNABIS AND NICOTINE WITHDRAWAL FOLLOWING RECENT QUIT ATTEMPTS
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A valid and reliable cannabis withdrawal syndrome has been characterized in both inpatient and outpatient laboratory studies. In order to further judge the clinical importance of this syndrome, we compared cannabis withdrawal with nicotine withdrawal in adults who recently quit daily use of marijuana or tobacco cigarettes. Eighty-nine daily marijuana or tobacco smokers responded to advertisements placed in newspapers in four US cities, and indicated that they had quit marijuana or tobacco use for at least two days during the prior month. A single telephone survey retrospectively assessed withdrawal severity using a symptom checklist, and assessed participant beliefs about the relationship between specific withdrawal symptoms and quit attempt outcomes using a 10-point Likert scale. Generally, the frequency and magnitude of the reported withdrawal symptoms were similar across the two substances. The few differences observed suggest slightly more severe withdrawal among the tobacco smokers; ratings of craving, anxiety, and sweating were significantly higher in the tobacco group. The majority of participants in both groups indicated that withdrawal symptoms had contributed to relapse during past quit attempts. Ratings of the strength of the relationship between relapse and specific withdrawal symptoms suggested similar profiles for both substances. These data from a general population sample of adults who recently quit marijuana or tobacco indicate highly similar withdrawal severity profiles, and thereby support the contention that the cannabis withdrawal has clinical importance. Prospective research is needed to better determine the relation between cannabis withdrawal and relapse, and to explore the efficacy of interventions that target cannabis withdrawal.

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105 SELF-ADMINISTRATION AS AN ASSAY SYSTEM TO MEASURE THE PHARMACOKINETIC AND PHARMACODYNAMIC POTENCIES OF RECEPTOR ANTAGONISTS

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The measurement of drug pharmacokinetics (PK) is an important determinant of clinical efficacy. However, these studies are time-consuming, expensive and typically measure only plasma concentrations. In rats trained to self-administer cocaine and apomorphine, SCH23390 and (-)-eticlopride at doses between 5 and 30 nmol/kg i.v. produced acceleration of self-administration with a concomitant increase in the calculated agonist levels. On an FR1 no time out schedule the level of agonist at the time of each self-administration represents the magnitude of the satiety threshold. After the injection of each antagonist the agonist satiety thresholds rapidly increased and then gradually decreased over time. It was assumed that the increase in the satiety thresholds was proportional to the concentration of antagonist. The calculated absorption and elimination $t_{1/2}$ s for the antagonists were approximately 5 – 7 min and 40 – 50 min, respectively. Both rate constants for each antagonist were independent of the agonist and of the dose of antagonist. The potent, but not centrally active, dopamine receptor antagonist domperidone (100 nmol/kg i.v.) had no effect on the rate of agonist self-administration. It is concluded that the time course of the change in drug satiety thresholds represents an assay system to measure the PK of antagonists of the receptors underlying the satiety response. This assay system is sensitive and requires small quantities of antagonists, no analytical chemistry, reflects antagonist concentrations at the active site in the brain rather than in plasma and is potentially sensitive to active metabolites of the antagonist. In addition, a plot of the agonist dose ratio as a function of the antagonist dose according to the method of Schild should reflect the dose of antagonist that produces 50 % fractional occupancy of the receptors underlying the satiety response (K_{dose}). This measure of the in vivo pharmacodynamic potency of each antagonist should be constant for any response mediated by these same receptors.

106 TWELVE-MONTH RETURN-TO-CUSTODY RATES AMONG PRISON-BASED THERAPEUTIC COMMUNITY PROGRAM PARTICIPANTS COMPARED TO A NO-TREATMENT MATCHED COMPARISON GROUP

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This purpose of this study is to examine differential return-to-custody (RTC) rates among inmates who participated in prison-based therapeutic community (TC) treatment compared to a matched comparison group of inmates who did not receive prison-based TC treatment. Data come from 4 outcome studies conducted by UCLA Integrated Substance Abuse Programs (ISAP) as part of a 5-year evaluation of in-prison TC treatment programs operating in the California state prison system. These studies were conducted at 4 separate prisons where TC treatment programs were operating for drug-involved inmates. The 4 study sites included a pre-release fire camp for male felons, a minimum-security male prison, a maximum-security male prison, and a female prison. At each site, extensive baseline interviews were administered to a sample of inmates enrolled in the local in-prison TC treatment program and a sample of inmates who did not receive TC treatment but who were matched to inmates in the treatment groups on the following factors: age, ethnicity, and drug-related criminal background. Twelve-month post-release RTC data was obtained from the California Department of Corrections and Rehabilitation (CDCR). Preliminary analyses indicated no significant differences in 12-month RTC rates among the treatment and no-treatment matched comparison groups when only in-prison treatment was taken into account. However, when post-prison aftercare was included, inmates in the treatment groups were significantly less likely to be returned-to-custody within 12 months than were inmates in the no-treatment matched comparison groups. The results reinforce the importance of combining aftercare treatment with in-prison TC treatment as a means of maximizing positive treatment outcomes, as measured by 12-month RTC rates, and thus of improving aftercare participation and retention through pre-release assessment of continued treatment needs and matching parolees to the appropriate modality and intensity of aftercare treatment.

107 SLEEP PROBLEMS IN TREATMENT-SEEKING OPIATE-DEPENDENT INDIVIDUALS

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Previous studies have explored the link between the treatment of opiate dependence and sleep problems, but there is virtually no data on sleep function prior to initiating a new treatment episode. We examined the sleep problem: and ASI composite scores for 144 chronic and severe substance users upon admission to opiate agonist treatment. Sleep function in the past 30 days was assessed with the following self report measures: (1) Medical Outcomes Study sleep questionnaire, a measure of perceived sleep quality; (2) Epworth Sleepiness Scale, a measure of daytime sleepiness; (3) Functional Outcomes of Sleep Questionnaire, a measure of the effect of sleepiness on daily functioning; and (4) a set of questions about licit and illicit substance use to increase or decrease sleepiness. This treatment-seeking sample was relatively young (mean 35 years), predominately female (83%), minority (75%), and unemployed (86%). A substantial minority (21%) had transferred from an opiate agonist treatment program for pregnant women. Overall, participants reported significantly poorer sleep quality and more daytime sleepiness prior to enrolling in treatment than non-clinical normative samples, but did not report a high level of subjective dysfunction due to sleepiness. As expected, sleep problems were related to greater recent psychiatric distress and, to a lesser extent, family and social problems. In addition, the majority of participants (83%) reported substance use specifically to increase or decrease sleepiness. Of this group 89% reported the use of illegal drugs for that purpose. Greater substance use to increase or decrease sleepiness was associated with more sleep problems. No overall gender differences were found, but those transferring from a methadone program for pregnant women differed from other participants on ASI composite scores and sleep problems. Results suggest that the assessment of sleep problems endorsed by patients entering treatment is warranted.

108 PREDICTORS OF YOUTH SUBSTANCE USE IN SUBSTANCE-ABUSING FAMILIES

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Children of substance-abusing parents (SAPs) are at greater risk for psychopathology and substance use in adolescence relative to children in the general population. Family functioning may be an important mechanism by which parent psychopathology contributes to youth psychopathology and substance use. However, no studies have examined how this process might differ for substance abusing mothers vs. fathers. Participants included 324 adolescents from 224 families in which at least one parent sought treatment for substance-dependence. We used structural equation modeling (SEM) to test mother and father perceptions of family functioning as mediators of relations between parent psychopathology (Mother Internalizing, Mother Externalizing, Father Internalizing, and Father Externalizing) and youth internalizing, externalizing, and substance use. Family Functioning constructs consisted of mother and father ratings of cohesion, communication, disorganization, and lack of support. The final model fit the data adequately ($\chi^2(81)=176.76$, $p=.00$; $TLI=.81$; $RMSEA=.06$) and indicated that only father externalizing and mother internalizing problems were significantly related to father ($\beta=.46$, $p<.05$) and mother ($\beta=.56$, $p<.05$) family functioning ratings, respectively. Father family functioning ratings were related to youth internalizing and externalizing problems ($\beta=.48$, $p<.05$ and $\beta=.51$, $p<.05$, respectively). These results suggest that family functioning mediates relations between father externalizing problems and youth psychopathology. Father internalizing problems ($\beta=-.23$, $p<.05$) were also direct predictors of fewer youth externalizing problems. Further, family influences on youth substance use were indirect, acting through relations with youth internalizing and externalizing problems. Such findings that pathways to youth problems vary by parent gender can inform prevention and/or treatment with substance-abusing mothers and fathers. Supported by NIDA DA10821 and F31DA017999.

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109 THE K-OPIOID HALLUCINOGEN SALVINORIN A PRODUCES ROBUST NEUROENDOCRINE EFFECTS IN NON-HUMAN PRIMATES

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Salvinorin A is a powerful naturally-occurring hallucinogen, isolated from the leaves of the plant *Salvia divinorum*. Recent *in vitro* studies suggest that salvinorin A is a selective, high efficacy agonist at kappa (κ)-opioid receptors. κ -agonists are known to cause robust dose-dependent increases in serum prolactin levels in many species, including humans and non-human primates. This effect is thought to reflect a κ -agonist-induced reduction in dopaminergic tone in the tuberoinfundibular system in the hypothalamus. Thus, serum prolactin levels may be used as a non-invasive quantitative biomarker for the *in vivo* pharmacological profile of salvinorin A. In these initial studies, the effects of salvinorin A (0.032 mg/kg, s.c.) on serum prolactin levels were studied in gonadally intact, adult female rhesus monkeys ($n=3$). Salvinorin A caused a robust and relatively rapid increase in serum prolactin levels in all subjects. Peak elevations were observable by 15 min after administration, and persisted for at least 90 min. Vehicle administration under identical conditions was essentially without effect. The effect of salvinorin A was almost fully prevented by the opioid antagonist nalmefene (0.1 mg/kg, s.c., 30 min pretreatment). This dose of nalmefene has antagonized *in vivo* effects of selective κ -agonists in this species, in prior studies. Ongoing experiments with *i.v.* salvinorin A (0.0032-0.032 mg/kg) in gonadally intact male subjects are consistent with the above findings. Overall, these studies indicate that the hallucinogen salvinorin A is able to produce robust neuroendocrine effects in non-human primates *in vivo*, consistent with a high efficacy κ -agonist profile. This work was supported by NIH-NIDA grants DA017369 (ERB), DA00049 and DA05130 (MJK).

110 STATISTICAL PROCESS CONTROL METHODS FOR IMPROVED SIGNAL DETECTION IN PRESCRIPTION DRUG ABUSE SURVEILLANCE

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We describe a new approach to prescription drug abuse surveillance that uses statistical process control (SPC) techniques to detect rate changes, and validate this methodology for prescription opioid abuse in Louisiana. This approach focuses on prospective surveillance at statewide, regional, and product-specific levels, enabling earlier and more detailed identification of abuse trends and patterns. SPC was applied to data gathered from January 2002 through September 2003 for 11,068 Louisiana Temporary Assistance for Needy Families applicants. Data were collected via the multimedia version of the Addiction Severity Index (ASI-MV™), a standardized instrument to assess an individual's severity of addiction and need for various treatment components. Data were examined via conventional descriptive statistics and SPC monitoring methods. Statistical control charts were constructed of the opioid abuse rate (percent of applicants who reported using opioids in last 30 days) for each individual region and for the entire state with all regions combined. SPC methods included conventional Shewhart p control charts, standardized Shewhart and EWMA p charts, and new special-purpose charts. Statistical control charts were compared against traditional, retrospective quarterly or semi-annual visual trend analysis. SPC charts detected an increase in the opioid abuse rate in one region of the state approximately 24 weeks before traditional quarterly analysis. Analyses also identified an abuse increase in a second region previously undetected by traditional analysis. Finally, SPC analyses verified a decline in prescription opioid abuse corresponding to the timing of a statewide intervention to reduce abuse. These results demonstrate the responsiveness and potential of this approach for improved real-time prospective surveillance of drug abuse rates beyond standard and more retrospective methods.

111 PHARMACOLOGICAL PROPERTIES OF THE PRIMARY REINFORCING AND REINFORCEMENT-ENHANCING EFFECTS OF NICOTINE

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Nicotine can enhance the incentive value of nonpharmacological stimuli. This effect can be separated from nicotine-seeking with a paradigm that provides concurrent access to drug infusions and a reinforcing visual stimulus (VS). The present studies investigated the pharmacological substrates for each reinforcement-related effect of nicotine in the concurrent-access paradigm. For the critical treatment group (2-Lever), pressing one lever resulted in VS presentation, pressing a second lever produced NIC infusion. Control groups could earn both reinforcers together (NIC+VS group), nicotine infusions (NIC-Only group), or VS presentations (VS-Only group) for responding on one lever, the second lever was designated inactive. Across daily 1 hr self-administration sessions, the 2-Lever and NIC+VS groups responded for the VS at rates that were similar to each other but higher than VS-Only controls. In contrast, the NIC+VS group self-administered more than twice the amount of nicotine taken by the 2-Lever group. This pattern replicates the previously described synergistic increase in responding for the VS induced by NIC when both reinforcers are delivered for making a single operant (NIC+VS) or concurrently available responses (2-Lever group). Pharmacological pretreatment tests were conducted after rats met a response-stability criterion (<30% variability for 3 consecutive days). The competitive metabotropic glutamate 5 receptor antagonist MPEP attenuated the primary reinforcing, but not the reinforcement enhancing effect of nicotine. In an acute challenge test, the non-competitive nicotinic acetylcholine receptor antagonist mecamylamine attenuated the nicotine-induced enhancement of responding for VS but nicotine-seeking was not affected. Repeated challenge with mecamylamine in 7 consecutive tests reduced the primary reinforcing effect of nicotine, suggesting that nicotine's incentive value is mediated by nicotinic systems but is also heavily influenced associative processes.

112 OCCURRENCE OF CANNABIS-RELATED PROBLEMS AMONG FIRST-YEAR COLLEGE STUDENTS

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This report describes initial findings from the College Life Study (CLS) sample of 1253 first-time college freshmen, with respect to cannabis use and related problems, including clinical features of cannabis dependence as well as depression. After sampling, the freshmen completed a face-to-face interview with standardized assessment of cannabis involvement and other characteristics, including DSM-IV criteria for nondependent abuse (NDCA) and cannabis dependence (CDEP). A total of 687 freshmen had smoked cannabis in the year prior to assessment, and comprise the sample for the present analyses. Slightly more than 40% had experienced clinical features of NDCA or CDEP: 14% were assessed as cases of NDCA, while 11% qualified as CDEP cases and roughly 15% were 'diagnostic orphans' with cannabis-related problem profiles that did not match DSM-IV criteria. The most prevalent clinical features among the NDCA problems were (a) regularly driving a car after using marijuana (17% of users), and (b) continuing use despite problems with family or friends (7%). The most prevalent clinical features among the CDEP problems were: (a) spending a great deal of time obtaining or consuming marijuana (23%), and (b) subjectively felt tolerance (19%). Multiple logistic regression revealed that NDCA/CDEP cases differed from non-problematic users with respect to (a) earlier age of cannabis onset, (b) greater frequency of cannabis use, (c) greater number of other illegal drugs used, and (d) greater levels of depressed mood, even with sociodemographic characteristics held constant. Longitudinal follow-up of this cohort is planned to track and understand the progression of clinically significant problems associated with cannabis use.

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113 ARREST HISTORY AS A CRITICAL INDICATOR OF RISK AMONG COCAINE-USING WOMEN

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In 2005, NIDA focused on health disparities among drug users to better understand the impact of health and social problems related to drug use on minorities. Rates of HIV and other consequences of drug use, including incarceration, disproportionately affect minorities. The present analysis aims to shed light on health disparities among cocaine using women enrolled in a peer-delivered HIV prevention study (DA 11622; PI: Cottler) by comparing women referred from the St. Louis Female Drug Court (CT, n=124) to community recruited women, both with any lifetime arrest (COM+, n=232) and without (COM-, n=140). Sociodemographic characteristics of the 496 females who reported using any form of cocaine 6 or more times reveal that they are primarily African-American (86%), never married (61%), undereducated (44% HS+), and living in poverty (90%). CT women were younger (36.3, SD=5.6) than either COM+ (39.3, SD=6.8) or COM- (39.0, SD=7.3). Women with a lifetime arrest history were younger to initiate cocaine use than those with no arrest history (mean age: 24.5 CT, 26.2 COM+, 28.6 COM-). Lifetime polysubstance use was reported across groups, with 91% reporting both alcohol and tobacco use, and 72% reporting cannabis use. CT women were more likely, than others, to report lifetime heroin use (23%; 18% COM+, 4% COM-), and history of injection drug use (32% CT; 23% COM+, 6% COM-). Approximately 60% of the sample met DSM-IV criteria for alcohol, 26% for cannabis, and 81% for cocaine dependence; CT women were more likely to meet criteria for cocaine dependence (96%; 84% COM+, 65% COM-), and opiate dependence (22%; 18% COM+, 3% COM-) than either of the community recruited groups. Surprisingly, COM+ reported more cocaine using days in the prior 30 days than either the CT or COM- women (13.9 COM+, 7.7 days CT, 11.0 COM-), suggesting that women in this less visible, but clearly high-risk, group should be a specific target for future interventions. Interventions aimed at delving below the tip of the iceberg, to alter the trajectory for high-risk women outside the formal criminal justice system, are warranted.

114 SEX UNDER THE INFLUENCE IS COMMON FOR SUBSTANCE ABUSE TREATMENT PATIENTS

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Objectives: In the context of substance abuse treatment, sex under the influence of drugs or alcohol is a risk behavior for HIV/STI transmission. However, normative data concerning sex under the influence is lacking. Methods: All men in NIDA CTN protocol 0018, a gender specific HIV prevention intervention, were administered a structured self report questionnaire at baseline using ACASI methodology focusing on sexual risk behavior in the prior 90 days. This report focuses on the 228 methadone maintenance (MM) and 251 out patient psychosocial (OPS) patients who self report engaging only in heterosexual sexual behavior. Results: The majority of MM (82.8%) and OPS (65.3%) patients reported engaging in sex under the influence in the prior 90 days. OPS patients in long term monogamous relationships (53.3%) were less likely to report sex under the influence than OPS patients with casual partners (76.2%, $\chi^2=13.7$, $p<.001$). During their most recent sexual encounter, more MM patients (52.2%) than OPS patients (36.5%) reported sex under the influence. MM patients compared to OPS patients were more likely to be under the influence of heroin (46.3% vs. 6.1%, $\chi^2=100.4$, $p<.001$), cocaine (42.8% vs. 28.2%, $\chi^2=11.1$, $p<.001$) or benzodiazepines (27.5% vs. 5.7%, $\chi^2=41.3$, $p<.001$) during last sexual event. OPS patients were more likely to be under the influence of alcohol (56.3% vs. 33.2%, $\chi^2=25.6$, $p<.001$). Both MM and OPS patients were more likely to have a casual sexual partner at the last sexual event if they were under the influence. OPS patients under the influence compared to those not under the influence at last sexual event were more likely to engage in anal sex (20.5% vs. 6.6%, $\chi^2=4.7$, $p<.05$) and insertive oral sex (80.9% vs. 68.2%, $\chi^2=4.6$, $p<.05$). Conclusion: Sex under the influence is common for MM and OPS patients and is associated with riskier sexual behaviors.

115 PREVALENCE AND RISK FACTORS FOR HEPATITIS AND HIV IN SUBSTANCE ABUSE PATIENTS IN WEST CENTRAL MEXICO: GUADALAJARA REPORT

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L. Diaz-Barriga(2), M. C. Balanzario(2) and E. Aceves(2), (1) CUCS, Universidad de Guadalajara, (2) Centros de Integración Juvenil, AC, (3) Prevalence of viral hepatitis and HIV infections in the general substance abuse population in Mexico seems to be low. Prevalence of hepatitis C virus in the general population is 1.2 % whereas HIV prevalence (15-49 yr old age group) is 0.3 %. We found previously a 0.9 % prevalence of hepatitis and 12 % of HIV in a sample of 322 drug addicts where 2.5 % were injection drug users (IDU). No other similar study has been reported in the last 5 years. METHODOLOGY.- We sampled patients attending actively a treatment program at Youth Integration Centers (Centros de Integración Juvenil, CIJ) from all 5 treatment centers of Guadalajara who voluntarily participated. We investigated the pattern of drug use and presence of risk factors. Blood sampling started in December 2005. RESULTS We have included 50 patients (42 male, 8 female), with a mean age of 27.4 years \pm 9.6; 52 % of the patients had used some kind of substance for over 5 years, 18 % had used between 1-2 years and 14 % had been active users for 2-3 years and 3-5 years each. First substance used was alcohol (34 %), tobacco (28%), marihuana (20 %), and cocaine (10%). Latest drug use was: cocaine (48 %), marihuana (20 %), alcohol (18 %). Among the risk factors for infections there were: piercing (30 %), promiscuity (26 %), surgery (24%), tattoos (36%), STD (6%), hepatitis (4%), travel to USA (12%), bisexual activity (4%). Only three patients reported injection drug use. There was only one patient positive to HIV who did not have known risk factors for infections. The rest of the serological markers were negative. CONCLUSIONS.- prevalence of hepatitis and HIV infections among substance and drug users attending CIJ clinics remains low. So far intravenous drug use is not very common and thus does not seem to be a risk factor among these patients.

116 ILLICIT DRUG USE INITIATION IN PRISON

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Although many inmates in the US prison systems have a history of drug use, little is known about initiation of drug use in prison and its correlates. Data from our survey of drug use in the Puerto Rico prison system reveals that 5.5 % of inmates reporting lifetime use of illicit drugs initiated use during this incarceration. We report type of drug used by initiators and compare initiators to inmates who deny ever using drugs (non-users) to determine if they differ in socio-demographic, mental health variables, and incarceration history. We surveyed a representative sample of the inmate population in the PR prison system in 2005 to assess drug treatment needs. Data was obtained on 1,179 respondents (89.7% response rate) using structured questionnaires administered through two interview modalities: Computer Assisted Personal Interview (CAPI) for social and health variables; Audio Computer Assisted Self Interview (ACASI) for sensitive information related to lifetime use of illicit drugs and alcohol and drug and alcohol use in prison. Two groups of inmates were compared: initiators in prison vs. non-users. Multivariate logistic regression was performed to explore differences between these two groups, controlling for years since admission. Heroin (48%) and Cocaine (36%) were the most used drugs. Over half of heroin users (58%) inject. Initiators were more likely than non-users to have completed 2 or more years of their sentence (OR=3.5, 95% CI=1.13-9.4), to have significant symptoms of adult Attention Deficit Disorder (OR=3.53, 95% CI=1.55-8.04), and to report use of alcohol prior to incarceration (OR=4.36, 95% CI=2.00-9.50). Other socio-demographic variables in the model did not reach significance. Our results suggest that it is possible to identify factors associated with illicit drug use initiation in prison that are amenable to interventions. Given that in this context initiation involves injecting drugs, efforts to reduce the likelihood of adverse health outcomes associated with injection should be implemented in the correctional setting.

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117 CHILE-USA COMPARISONS: STUDENT DRUG USE TRENDS, 1995-2001

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AIM: Our research group conducted national sample school surveys of drug use in Chile from 1995-2001, in parallel with USA Monitoring the Future studies. These trend data are compared and contrasted to shed light on the public health significance of student drug use. METHODS: A comparable research approach was used, with nationwide probability sample surveys of school-attending youths, and standardized self-report questionnaires. RESULTS: Markedly greater tobacco smoking prevalence is seen in Chile as compared to USA at all grade levels under study, with sharply increased prevalence between 1999 and 2001. Before 2001, striking prevalence differences emerged after Grade 8, but in 2001, the situation changed, and in that year smoking affected 63% of 8th graders in Chile vs. 37% in the US. Underage drinking also is more common in Chile even in 12th grade. As for cannabis and cocaine, the situation generally is reversed, with comparable or larger prevalence values for the USA as compared to Chile, except perhaps for 12th graders in 2001. CONCLUSION: Though Chile is nearer to coca-producing areas and cocaine use may become a more prominent issue in the future, the central public health priority for Chile must to reverse increased occurrence of tobacco smoking, with preventive interventions put into place well before Grade 8. SUPPORT: Government of Chile, NIDA R01DA09897 & K05DA015799; NIH Fogarty Center TW005692.

118 DOES CUE-REACTIVITY EXTINGUISH WITH REPEATED LABORATORY SESSIONS?

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In laboratory-based investigations of cue reactivity, nicotine-dependent individuals generally report high levels of craving in response to cues associated with tobacco. It is unclear to what extent, if at all, individuals' response to cues extinguish as cues are presented through repeated presentations over an extended period. The present study investigated whether craving in response to smoking-related cues extinguishes over multiple sessions. Over 4 experimental sessions held one week apart, 19 non treatment-seeking nicotine-dependent males participated in cue presentations that involved handling either smoking-related paraphernalia (i.e. cigarettes) or neutral paraphernalia (i.e. pencils). Ratings of craving, as measured by the Questionnaire for Smoking Urges - Brief form (QSU-B), were collected before (baseline ratings) and after each cue presentation. As expected, smoking related cues evoked higher craving relative to neutral cues, $F(1, 18) = 10.00, p < .01$. While there was some evidence for reduced craving over sessions, $F(3,54) = 3.44, p < .05$, this effect was attributable to a decline in baseline craving ratings; when baseline was subtracted from post-cue ratings, the resulting change scores showed no evidence of effects of session. Moreover, there was no significant Session x Cue Type interaction. The significant effect for cue type (smoking vs. neutral cues) held across Sessions 1, 2 and 4 ($p < .05$), and as a trend for Session 3 ($p < .07$). Thus, these results suggest that although there may be a reduction in baseline craving during repeated laboratory sessions, cue-reactivity (craving evoked by smoking cues vs. neutral cues) may not extinguish over multiple sessions in non-treatment seeking nicotine-dependent individuals. This study was supported by National Institute of Drug Abuse (NIDA) Training Grant T32DA007288 (MJC), Component #3 (HPU) of NIDA P50DA016511 (KTB), and M01 RR0107 from the MUSC General Clinical Research Center *Correspondence: Matthew Carpenter, PhD: (843) 792-3974; carpente@muscd.edu.

119 GENDER DIFFERENCES IN COCAINE WITHDRAWAL-ASSOCIATED 5-HT_{2A} SEROTONIN RECEPTOR SIGNALING IN AMYGDALA

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We have previously reported that in hypothalamus of male rats, withdrawal from cocaine: (1) increases 5-HT_{2A} receptor-mediated function, and (2) increases the levels of 5-HT_{2A} receptor-associated Gαq and Gα11 G-proteins (EJP 221:121,1992 & JPET 307:1012,2003). These effects were not observed in female rats after a comparable cocaine treatment and withdrawal paradigm. The present study investigated the effects of cocaine withdrawal in male and female rats on: (1) 5-HT_{2A} receptor function in amygdala and (2) Gαq and Gα11 protein levels in basolateral (BL) and central (Ce) amygdala. Adult male and female ovariectomized rats received saline or cocaine (15 mg/kg, ip, bid) for 5 days and withdrawn for 48 h. Changes in G-protein activation of phospholipase C (PLC) and 5HT_{2A} receptor-stimulated PLC activities in amygdala were determined by GTPγS-increases in PLC activity and serotonin (5-HT)-stimulated activity above GTPγS-stimulated PLC activity, respectively. In male rats, cocaine withdrawal produced increases in: (1) 5-HT_{2A}- and G protein-stimulated PLC activities (80 and 110 pmol/mg protein/min over control, respectively) and (2) levels of membrane-associated Gαq and Gα11 G-proteins in BL amygdala (52-60% for Gα11 and Gαq) and Ce amygdala (≈ 48% for Gαq and Gα11). We detected comparable increases in membrane-associated Gαq and Gα11 G-proteins in BL and Ce amygdala of male rats that exhibited conditioned place preference for cocaine. In contrast, female rats withdrawn from cocaine exhibited neither enhanced function of 5-HT_{2A} receptors in amygdala nor increased levels of membrane-associated Gαq and Gα11 G-proteins in BL and Ce amygdala. In summary, our results in BL and Ce amygdala reveal unique gender differences in withdrawal-induced adaptive changes in 5-HT_{2A} receptor signaling. These findings may be relevant to some of the gender different responses to drugs of abuse. Supported by USPHS DA13669 & DA07741

120 EFFECTS OF GHB AND TRIAZOLAM ON COGNITIVE TASKS IN HUMAN VOLUNTEERS

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Gamma-hydroxybutyrate (GHB) is a drug that has received notoriety for its use in drug-facilitated sexual assault ("date-rape"). Like other drugs that are used for drug-facilitated assault (e.g., ethanol, flunitrazepam), GHB has been reported to produce robust anterograde amnesia. However, unlike ethanol and flunitrazepam, the effects of GHB on memory and cognitive processes in healthy volunteers have not been examined. The aim of this study was to examine the effects of GHB and triazolam on cognitive tasks designed to measure distinct memory processes. Single, acute doses of GHB (1.125, 2.25, 4.5 g/70 kg; oral solution), triazolam (0.125, 0.25, 0.5 mg/70 kg; capsules), and placebo were administered to healthy volunteers under counterbalanced, double-blind, double-dummy conditions across seven sessions. The time course and peak physiological (heart rate, blood pressure), psychomotor (circular lights, digit-symbol-substitution), subjective (visual analog scales), and cognitive effects were examined in an outpatient laboratory setting. Cognitive tasks included word recognition, word recall (episodic memory), and modified Sternberg memory tasks (working memory). GHB and triazolam produced dose- and time-dependent decreases in psychomotor performance measures. Both drugs increased participants' ratings of "depressant or sedating," "sleepy," and "tired or lazy" and decreased ratings of "energetic" and "alert." Preliminary analyses indicated that impairment of working memory was dose- and time-dependent. Deficits in word recall and word recognition were observed when words were studied during, but not before, the period of drug effect. Together, these data suggest that doses of GHB and triazolam that impair psychomotor performance and produce sedative subjective effects can also impair some memory processes. The finding of deficits in episodic memory when words were studied during, but not before, the period of drug effect suggests that triazolam and GHB impair the encoding of new information. This work is supported by USPHS Grant DA003889

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- 121** A METHOD TO STUDY PAIN AND FACTORS INFLUENCING PAIN SENSITIVITY IN AGED RATS
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The population is getting older, and a common problem in the elderly is chronic pain, due to age-related conditions such as osteoporosis, arthritis and cancer. Use of chronic opioids is underutilized in the aged due, in part, to a belief among physicians and patients of the potential for dependence or addiction. Literature regarding pain sensitivity and differential responsiveness to opiates as a function of age is inconsistent. This confusion may arise from the widespread use of reflex-based outcome measures in the assessment of animal models of pain. This presentation will describe a strategy of pain assessment using an operant escape-based method, and its adaptation for use in older animals. The method involves escape from a "hot-plate" onto a brightly lit platform (an aversive stimulus condition). Latency to escape from the plate, time of session spent on the platform, and an analysis of response patterns can be determined. Results from this pilot study suggest that the procedure results in temperature-dependent increases in escape duration. Baseline levels of escape do not differ as a function of age (12, 20 and 30 months of age). Parallel studies examining physical performance measures that assess muscle strength and stamina show age-dependent decreases. These data suggest that older animals can be studied using operant pain procedures and that physical performance decrements observed with increasing age do not confound performance in this task. Implications of the development of this model for the study of pain in older animals include the study of initial sensitivity to and the effects of chronic administration of opioids, increases in pain sensitivity due to experimental manipulations, the physiological mechanisms underlying differential sensitivity as a function of age, and the sensitivity to the abuse-related effects following a history of chronic opioid administration.
- 122** INTEGRATION OF BUPRENORPHINE INTO A VA NARCOTIC TREATMENT PROGRAM IN NEW YORK CITY: TWO YEARS LATER
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The introduction of buprenorphine in to office-based medical practice is expected to expand treatment options for opiate addicts in the United States. Patients who could only be legitimately treated in the structured and highly regulated methadone programs now have the option of private office or primary care treatment. One of the limitations of the new law has been the 30 patient limit for practitioners other than those in group practices. Narcotic treatment programs have not had this limit imposed, but are required to provide buprenorphine subject to the regulations of the methadone clinics. The NY Harbor Health Care System Clinic began using buprenorphine in November 2003. We participated in a recent NIDA sponsored Trial (CTN 0003) evaluating buprenorphine detoxification with assignment to either a 7 day or 30 day taper schedule. As a result staff were trained in management of buprenorphine patients. We chose to offer this medication option in spite of the restrictions and complexities in order to provide state-of-the-art treatment to our patient population. Many of our patients were being treated with the soon-to-be-discontinued LAAM, were on reduced visits and did not want to return to methadone. We also wanted to assess the viability of using buprenorphine in a methadone clinic. This presentation will review Clinic admissions from December 2003-2005, patient self-assignment either to methadone or buprenorphine, retention, compliance, therapeutic response and the challenges of using a medication with a pharmacologic profile that challenges the practicality of use in a highly regulated methadone setting.
- 123** ADOLESCENTS SENSITIZE MORE THAN ADULTS TO A SINGLE HIGH DOSE OF COCAINE
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Adolescence is a critical period for drug addiction. Most life-long addiction begins during this time and clinical data suggests that adolescents may progress to drug dependence faster than adults. Many species are known to sensitize to the behavioral effects of psychostimulants even after a single dose and this augmentation is believed to provide an animal model for the neuroadaptations underlying the transition to human addiction. Sensitization becomes more robust between infancy and adulthood. However, direct comparisons of sensitization between adolescents and adults are few. Our lab has previously shown that adolescents have exaggerated behavioral responses to a single acute dose of cocaine. In the present study we tested the hypothesis that adolescents would also show a more enhanced single dose sensitization. We investigated the acute behavioral responses of male rats post natal day (PN) 28 (young adolescent), 42 (mid-adolescent), and 65 (young adult) to a single injection of saline or cocaine (40 mg/kg; ip) and their responses to a challenge dose of cocaine (10 mg/kg) 24 hours later. The high dose of cocaine acutely stimulated significantly more locomotor activity in the youngest adolescents. It induced a similar frequency of stereotyped behaviors in animals of all ages. However, when all of the animals were challenged with cocaine 24 hours later, cocaine pretreatment enhanced the locomotor responses in both adolescent groups. In the mid-adolescent animals, cocaine pretreatment also enhanced the frequency of stereotypies induced by the challenge dose. In contrast, adults did not sensitize to the cocaine-induced locomotor activation or stereotypies. These data suggest that a single dose of cocaine activates the neural circuits that mediate the acute behavioral responses more in adolescents. It also induces changes to these circuits that are necessary for behavioral sensitization more in adolescents than adults. These results suggest a possible biological mechanism to explain why adolescents progress to addiction faster than adults. This work is supported by NIDA grant DA019114.
- 124** THE HELPING ALLIANCE IN A MOTIVATIONAL INTERVENTION TO REDUCE COCAINE USE AND INCREASE HIV MEDICATION ADHERENCE
S. D. Ceperich(1), K. S. Ingersoll(1) and C. C. Wagner(2), (1) University of Virginia, Charlottesville, and (2) Virginia Commonwealth University, Richmond, VA
As part of a behavioral therapy development project, we developed CART (Cocaine and Adherence Readiness Treatment), based on motivational interviewing, to address cocaine use and poor medication adherence among patients with HIV. Preliminary outcomes are promising, and in this paper, we will assess the helping alliance between patient and therapist across the six sessions and examine its relationship to outcomes. Eighteen mostly female (61% African-American (78%) people with HIV or AIDS (28%) who were less than 85% adherent to antiretroviral therapy participated. All were cocaine dependent, 44% screened positive for cocaine, and had used cocaine an average of 29% of days during the past month. Most had additional DSM-IV diagnoses including Major Depression, anxiety disorders, and alcohol use disorders. Patients and therapists completed the Helping Alliance Questionnaire-II after each treatment session. The HAQ showed excellent internal consistency reliability, with standardized Cronbach's alpha ranging from .77 to .94 across sessions for patients, and ranging from .59 to .86 across sessions for therapists. Mean HAQ total scores after session 1 were 95.5 (sd 11.6) among patients and 86.07 (sd 9.3) among therapists and increased to 97 (sd 5.1) for patients and 87.8 (sd 7.7) for therapists after session 2, indicating strong therapeutic alliances had formed early in treatment. Patient and therapist alliance at session 1 was strongly correlated ($r=.83, p<.04$). Ratings fluctuated across sessions with the lowest helping alliance ratings for session 3, which focused on exploring ambivalence, and the highest for session 6, which focused on moving forward with goals or change plans. We will examine the relationships among the helping alliance and treatment outcomes. We will also examine ratings of interpersonal behaviors and their relationship to the treatment alliance and outcomes.

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125 SOCIAL AND PSYCHOLOGICAL DAILY CONTEXTS OF REGULAR ALCOHOL USE

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The goal of this program of research is to determine social and psychological contexts of alcohol users without substance use disorders in their daily life. Data will be collected from an initial sample of 1,500 students from diverse disciplines (human and social sciences, hard sciences, languages, arts and literature...) at the University of Clermont-Ferrand, France. Using self-report measures, we will collect data on sociodemographic status and alcohol use in the last month and in life time. This first stage will serve to select about 200 participants representative of regular alcohol users and non users in the last month. The average age of this sample will be approximately 19 years. Participation will be voluntarily, with answers being anonymous and confidential. In the second stage, personality and psychopathological disorders will be assessed with standardized questionnaires and structured interviews. The final stage will take place immediately afterwards. In this stage, we will collect repeated data on context of alcohol use, mood and behavior in the daily life of the participants. We will use the Experience Sampling Method: participants will receive a Palm or Pocket PC, an auditory signal will alert them five times per day, over a period of 7 days, to fill out an electronic questionnaire. This study addresses the following main objectives: 1. Determine social contexts (place of use, presence of friends, time of use...) of alcohol use in daily life; 2. Understand the role of some psychopathological disorders (depression, mania...) in daily life associated with alcohol use; 3. Identify differences between alcohol users and alcohol abusers/dependent with regard to psychopathological disorders and contexts of consumption (for example, festive consumption for users and consumption alone for abusers or dependent). This program of research will be supported by the "Institut de Recherche et d'Etude sur la boisson" (IREB; English : "Institute of Research and Study on Drinking"), Paris, France.

126 GENDER DIFFERENCES IN PSYCHIATRIC MULTIMORBIDITY AMONG ADOLESCENT SUBSTANCE USERS ADMITTED TO TREATMENT

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Background: Substance users often reported suffering from multiple psychiatric disorders and were required sufficient mental health treatment in addition to their substance use problems. The purpose of this study is to investigate gender differences in prevalence and patterns of psychiatric multimorbidity among adolescent substance users in treatment. Methods: Study sample consisted of 1526 females and 4105 males, aged 12-18, who were treated in 101 substance abuse treatment programs in the United States. Measures assessing past 12-month psychiatric disorders via standardized interview with the Global Appraisal of Individual Needs (GAIN) were gathered at the entry of treatment. Multimorbidity was defined as an individual with two or more of the following co-occurring psychiatric disorders in the past 12 months: substance use disorders (SUD), internal mental distress disorders (major depressive disorder MDD, generalized anxiety disorder GAD, and traumatic distress disorder TSD), and external behavior disorders (attention deficit hyperactivity disorder ADHD and conduct disorder CD). Results: Female drug users were significantly more likely than male drug users to have MDD (Odds ratio OR=3.0, 95% CI=2.7-3.4), GAD (OR=2.2, 95% CI=1.9-2.5), TSD (OR=2.9, 95% CI=2.6-3.3), ADHD (OR=1.6, 95% CI=1.4-1.8), CD (OR=1.3, 95% CI=1.2-1.5) and to be diagnosed with substance dependence (OR=1.4, 95% CI=1.2-1.6). Females had significantly more diagnoses than males (3.3 vs. 2.5, t-test $p < .001$) and were significantly more likely to have multimorbidity (78% vs. 65%, $p < .001$) and to have diagnoses in each of the three areas of substance, internal and external disorders (50% vs. 31%, $p < .001$). Cluster analysis identified four distinctive patterns of psychiatric disorders, with the percent of females in these groups varying significantly from 18% to 43%. Conclusion: Adolescents presenting to substance abuse treatment have a wide range of psychiatric disorders and the multimorbidity is the norm. Female drug users have different patterns of presenting diagnoses and multimorbidity as compared to male drug users.

127 DISCLOSURE OF SENSITIVE INFORMATION IN NON-TREATMENT-SEEKING POST-PARTUM WOMEN: A RANDOMIZED TRIAL OF FOUR APPROACHES TO PARTICIPANT PROTECTION

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Participant protection-both actual and perceived-is crucial in research involving stigmatized behaviors such as illicit drug use, particularly with non-treatment seeking and/or vulnerable individuals. Nearly all sensitive longitudinal research utilizes a single secure table linking identifying information and data, often with the addition of a Federal Certificate of Confidentiality (COC); quasi-anonymous approaches, in which there is no link between name and data, have also been proposed. However, the relative effect of these procedures on disclosure is largely unknown. This study compared disclosure of sensitive information under four different consent conditions: secure linking table only, secure linking table plus COC, quasi-anonymous, and fully anonymous. A total of 200 urban post-partum women were randomly assigned to each condition and completed a battery of questions tapping sensitive content areas such as illicit drug use, sexual behavior, child abuse, and intimate partner violence. The primary outcomes were a summary score representing frequency of endorsement across all sensitive items, and a single visual analogue scale item measuring the extent to which participants believed their answers could be traced to them. Analyses showed that (a) the COC and both anonymous conditions yielded more disclosure than the linking table only condition (overall $F [3, 194] = 7.8, p < .001$), and (b) participants perceived the anonymous conditions as providing greater protection from name-data connection than the confidential conditions (overall $F [3, 194] = 32.6, p < .001$). These results suggest that anonymous approaches should be considered first in cross-sectional studies of stigmatized behavior. For longitudinal studies, these results suggest that while COC's do facilitate disclosure of some sensitive information, quasi-anonymous approaches perform at least as well in that regard. Given the greater actual and perceived protection provided by the quasi-anonymous approach, further research into its use and relative advantages/disadvantages appears warranted.

128 BUPRENORPHINE TREATMENT AS AN ALTERNATIVE TO ORTHOPEDIC SURGERY IN OPIOID-TOLERANT PATIENTS TAKING PRESCRIPTION OPIATES FOR SEVERE PAIN

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Buprenorphine's analgesic properties are well known, but using the sublingual tablet (Subutex/Suboxone) preoperatively to stabilize pain in opiate dependent chronic pain patients awaiting orthopedic surgery is unique and novel. Worsening pain in these patients may be due to opioid induced hyperalgesia and mistaken as a signal to proceed with surgery. Buprenorphine's anti-hyperalgesic effects may benefit these patients by reducing pain and enabling surgery to be postponed or cancelled. This report describes results with 18 opioid tolerant patients taking prescription opiates for severe pain due to lumbosacral (n=16) or cervical spine (n=2) disc disease. All patients were preoperative and referred before scheduling surgery by orthopedic and neurosurgeons to The P.A.I.N. Institute for buprenorphine treatment. Patients (11 male; 7 female) averaged 48 years old (range 33-69) and were mostly white (89%), insured (100%), working (95%) and college educated (95%). Patients had been maintained on prescription opiates for a mean of 4.9 years (range 1-15), 12 had none and 6 had between 1 and 5 prior surgeries. After treatment with Subutex (n=13) or Suboxone (n=5), 89% (16/18) no longer required surgery. Surgery is being considered for 1 patient after 13 months on Subutex and another had surgery and has since returned to Subutex. To date, 89% (16/18) have continued buprenorphine maintenance at a mean daily dose of 19.1 mg (range 1-32) for a mean of 16.7 months (range 2-31). No patient has become tolerant to buprenorphine, nor has there been any medication misuse, diversion or safety issues. Pain ratings on a 10-pt scale averaged 6.9 before and decreased to 2.7 during treatment. These clinical findings support using Subutex/Suboxone for pain reduction in preoperative, opiate dependent chronic pain patients. The potential medical and economic benefits of buprenorphine treatment for avoiding surgical complications, time and work lost, and monetary costs to society are tremendous.

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129 COGNITIVE DEFICITS OF OPIATE-DEPENDENT INDIVIDUALS ENTERING METHADONE MAINTENANCE AND BRIEF COGNITIVE-BEHAVIORAL TREATMENT

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Cognitive impairments can affect patients' response to drug counseling but may be amenable to specific cognitive remediation techniques or require modifications of treatment. We evaluated cognitive and executive functions in methadone maintained patients (N=16) with persistent depressive symptoms, and therefore poor prognosis, entering a clinical trial comparing the efficacy of brief cognitive behavioral treatment with standard methadone drug counseling. Assessments included the Rey Osterrieth Complex Figure (ROCF) test of visual memory, a computerized short term memory priming task, the Balloon Analogue Risk Task, attention-deficit/hyperactivity disorder self-report symptom checklist (ASRS-v1.1), and the Barratt Impulsiveness Scale. Distinct and identifiable cognitive impairments, primarily in memory tasks, were identified in 10/16 patients. These patients showed multiple errors on the ROCF task and were either unable to successfully complete the priming task (n=7) or showed no gains in speed or accuracy from priming (n=3). The other 6 patients showed only moderate memory impairments on the ROCF task and all successfully completed the priming task, averaging 80 ms improvement in reaction time and 34% improvement in response accuracy in primed trials vs. unprimed trials. Patients with identifiable cognitive impairments were comparable in age (49 vs. 42 years) but reported longer histories of heroin dependence (17 vs. 8 years) compared to patients with less overt impairments. Measures of ADHD and impulsivity also showed substantial range of performance difficulties, but impairments in these areas were less clearly differentiated among the subjects. The potential impact of cognitive impairments on treatment response and comparisons between patients with and without persistent depressive symptoms are currently being investigated. Supported by R01 DA013108, K24DA000445

130 CANNABIS CLINICS: PART OF THE FRENCH CANNABIS POLICY

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Cannabis clinics network is one of the four components of the French Cannabis Policy launched at the beginning of 2005 to tackle cannabis abuse among youth. It is part of the "2004-2008 French Government Plan for the Fight against illicit drugs, tobacco and alcohol". A range of medical and social settings (alcohol services, drug dependence clinics, youth centres, primary care services) were selected across the country to offer counselling services to adolescents and young adults as well as to their parents or relatives, according to specific guidelines (opening hours, no mixing with alcohol or hard drugs dependent clients, no waiting list, free and anonymous service). Cannabis clinics offer assessment of cannabis abuse based on standardized questionnaires (e.g. CRAFFT, ALAC), information, counselling, brief therapy (5 visits max.), referral to drug dependence clinics, to psychiatric care or to social services for young people with multiple problems. Evaluation is based 1) on monthly monitoring of activity (number of new clients, total number of sessions, waiting time prior to the first interview) 2) a one-month survey documenting detailed information of clients. In November 2005, 266 medical care structures had been set up. The global cost is around 4 500 000 \$. The target population is about 50 000 young people. From March to November 2005, 30 057 visits were registered including for 21 449 cannabis users (71%), 47% being new clients and around 25% parents. The average waiting time is 8 days. Two hundred and fifty-two structures (95%) answered to the one-month survey. Around 4 200 persons were included: 80.4% were males; half were 16 to 20 and 7.4% 30 or older. Among 18 years old users, school education is less frequent than in the general same age group (53% vs 84%). Sources of requests: one third of requests coming from the relatives with the majority being female (69%), one third spontaneous and 40% after a judiciary order. Further data analysis is on progress.

131 POTENTIAL ROLE OF 14-3-3 PROTEINS IN THC-MEDIATED NEUROPROTECTION

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To identify the molecular mechanisms of NMDA-induced cell death and the neuroprotective effect of Delta 9-tetrahydrocannabinol (THC), cDNA microarray analysis was used to examine the transcriptional profile of AF5 cells treated with toxic concentrations of NMDA, as compared to NMDA plus cannabinoids or capsaicin. Approximately 5.1% of a total of 15K transcripts were changed in response to NMDA treatment, and of these 12%, or 95 transcriptional changes, seen after NMDA alone were reversed by THC treatment, including 14-3-3 η (YWHAH). As measured by microarrays and quantitative PCR, 14-3-3 η expression was significantly down-regulated by NMDA toxicity and up-regulated by THC treatment prior to NMDA exposure. There were no changes in message levels for four other 14-3-3 isoforms 14-3-3 θ (YWHAQ), 14-3-3 γ (YWHAG), 14-3-3 ϵ (YWHAE), and 14-3-3 β (YWHAB) represented in the microarray. In addition 14-3-3 ξ (YWHAZ) was also found to be down-regulated by NMDA and up-regulated after NMDA plus THC treatment by quantitative PCR. While up-regulation of 14-3-3 ξ expression was observed 30 min after treatment with THC plus NMDA, down-regulation by NMDA alone was not seen until 16 hr after treatment. 14-3-3 proteins were detectable in AF5 cells by Western blotting, and up-regulation of the protein after exposure to THC plus NMDA, as compared to NMDA alone, was found. Transient transfection of plasmids expressing 14-3-3 η or 14-3-3 ξ in AF5 cells decreased NMDA-induced cell death, while control plasmids had no effect. Therefore, changes in the expression of 14-3-3 η and 14-3-3 ξ can influence the initiation of NMDA-induced apoptosis, and may play an important role in the neuroprotective effect of THC in AF5 cells. This research was supported by the IRP of NIDA, NIH, DHHS.

132 CONTEXTUAL DIFFERENCES IN THE TRANSITION FROM ALCOHOL TO TOBACCO AND ILLEGAL DRUG USE

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Aim: To examine whether adolescent drinking patterns and the transition from alcohol into the use of tobacco and other illegal drugs differ by first drinking context. Methods: Over 19,000 school-attending youths aged 12-18 were identified from the 2004 National Survey of Illegal Drug Use among Adolescents (NSIDA) in Taiwan. Questions about sociodemographic characteristics, drug use, and other developmentally problem behaviors were assessed using web-based self-administered questionnaires. Lifetime drug-using experiences were further assessed for ever users, including age and context at first use, cumulative frequency, and recency of use. Logistic and Cox's proportional hazards regression models were used to estimate the association linking first drinking context with subsequent drinking patterns and other drug involvement. Results: Adolescents who had first alcoholic beverages at friends' home or entertainment settings (e.g., pub, KTV) were more likely to experience tobacco and illegal drugs, compared with those having the first drink at home; however, no differences were found in relation to recent use and cumulative occasions of alcohol drinking. After statistical adjustment for socioeconomic background, first drinking in the context of friends' home or entertainment settings was associated with an elevated risk to start use of tobacco or other illegal drugs (adjusted hazard ratio=1.4-1.7). Discussion: The transition from alcohol to tobacco and other illegal drug use seems varied by the first drinking context. Intervention programs targeted at high-risk locations may be appropriate to reduce the involvement of psychoactive drug in adolescence.

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- 133** A MULTI-COUNTRY STUDY OF 'NON-DEPENDENT ALCOHOL ABUSE: MALE-FEMALE DIFFERENCES AND OTHER EPIDEMIOLOGICAL PATTERNS
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AIMS: This report presents original estimates from multiple countries now participating in the World Health Organization World Mental Health 2000 survey initiative (WMH2000) with respect to male-female differences and other epidemiological patterns of variation in the occurrence of 4 clinical features of nondependent alcohol abuse. In male-female contrasts, frequency of drinking is taken into account. METHODS: The estimates are from large-sample epidemiological data, all based upon a standardized multi-site sampling, assessment, and analysis protocol for epidemiological survey research. To date, the 14 countries reporting data are: United States, Mexico, Colombia, Netherlands, Belgium, France, Spain, Italy, Germany, Ukraine, Japan, Lebanon, Nigeria, and China (Beijing and Shanghai). Analysis methods are used to take sampling weights and complex survey design into account. RESULTS: Clinical features of nondependent alcohol abuse were more prevalent among men as compared to women in all countries under study, irrespective of drinking level, although some of these comparisons are not statistically robust due to smaller numbers of female drinkers. In many (but not all) countries, taking risky actions right after drinking (driving a car, operating a machine, riding a bicycle) was most prevalent among these clinical features. In other countries, the more prominent clinical feature was job difficulty due to drinking. As expected, occurrence of these clinical features of nondependent alcohol abuse was greater at higher frequencies of drinking. CONCLUSIONS: On the strength of the standardized multi-site protocol, the WMH estimates extend prior evidence based upon cross-national comparisons of per capita beverage alcohol sales and other indirect indicators of alcohol problems. Notwithstanding limitations, these epidemiological estimates help confirm the general pattern of male excess in the occurrence of these drinking problems. SUPPORT: NIDA K05DA015799, R01DA016558, U01MH060220, & an MSU research award.
- 134** GENDER DIFFERENCES IN MOTIVATIONAL AND VALUATIONAL PROCESSING OF VISUAL-REWARDING STIMULI: IMPLICATIONS FOR INCREASED PROPENSITY TO DRUG DEPENDENCE
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Incentive motivation theory posits that craving is mediated by drug-induced changes in mesolimbic dopaminergic circuitry underlying motivational, rather than valuational aspects of reward. Given earlier reports of significantly heightened levels of craving in drug dependent females, it is plausible that neural systems subserving incentive/motivational function could be sexually dimorphic. To address this question, healthy male (N=17; age: 28.7±8.7) and female (N=16; age: 24.9±3.4) participants were administered two tasks assessing motivational and valuational reward functions, respectively, including: (a) key pressing to change the viewing time of average or beautiful female or male facial images, and (b) rating the attractiveness of these images. The results for the keypress task showed a significant effect of face type ($p<0.01$) along with significant face type by group (i.e., males and females) interaction ($p<0.01$). No significant group effect was detected indicating that total number of keypresses did not differ between the groups. The results of the rating task qualitatively parallel those for the keypresses. Post-hoc analyses revealed that females expended effort to increase the duration of viewing of both attractive males' (53.3±179.9) and attractive females' (36.8±146.6) images. Males expended more effort to extend the viewing time of the beautiful female faces only ($P<0.01$); the magnitude of this effort significantly exceeded that of females. Keypress responses correlated with the attractiveness rating in the male ($p=0.02$), but not in the female group ($p=0.2$). These data suggest gender-related difference within and across the categories of the facial stimuli as well as potential dissociability of motivational and valuational reward processes in females. As female sex hormones are purported to modulate mesolimbic dopaminergic systems, further studies will be needed to investigate possible mechanisms of the observed differences, and their role in the propensity to develop drug dependence.
- 135** IS PRETREATMENT ASSESSMENT THERAPEUTIC? CHANGE IN MARIJUANA USE AMONG CANNABIS-DEPENDENT TREATMENT SEEKERS DURING THE CLINICAL TRIAL EVALUATION PERIOD
M. Chicurel(1), D. J. Brooks(1) and F. R. Levin(1,2), (1) New York State Psychiatric Institute and (2) Columbia University, New York, NY
Participants in drug treatment studies usually undergo extensive assessments prior to treatment initiation in order to determine protocol eligibility. The impact of assessment on baseline drug use has typically not been studied. The current study examined the pattern of marijuana use during the pretreatment (preTx) phase of 2 clinical trials for cannabis dependence. Secondary analysis compared the change in pattern of marijuana use between patients screening for a shorter vs. longer period of time. Participants' marijuana use was assessed prior to treatment initiation: 1) at an initial screening evaluation (ISE) and 2) a subsequent 4-hour baseline interview. The sample consisted of 36 participants who were predominately male (83%) and 58% Caucasian, 17% Hispanic, and 25% African American. The average age was 37 ± 11 years. All participants met DSM-IV criteria for cannabis dependence. The average time-span between ISE and baseline was 17 ± 10 days. There was no change in the frequency of marijuana use (days/week) between the ISE and baseline (6.5 ± 1.2 vs. 6.5 ± 1.2; $t=-.13$, $p=.90$). However, there was a significant change in the amount of use per using day (joints/day) between ISE and baseline (8.0 ± 11.0 vs. 4.3 ± 5.3; $t= 2.85$, $p=.01$). Based on the median days of screening, a short screen was 15 days. There were no differences in the frequency or in the amount of marijuana use over the preTx phase between these groups. Contrary to what has been reported prior to alcohol treatment studies, marijuana users do not appear to lessen their frequency of use, however, the amount of marijuana used on using days significantly decreases once the assessment period has been initiated. Such findings should be considered since they can have an impact on how outcome from clinical trials is interpreted. Supported by NIDA Grants: P50DA09236, R01DA15451 and K02 00465
- 136** LIMBIC ACTIVATION BY COCAINE CUES PRESENTED OUTSIDE AWARENESS IN COCAINE PATIENTS: PRELUDE TO CRAVING?
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Drug cues trigger appetitive craving and activate the limbic (e.g., amygdala) brain circuitry implicated in drug motivation/cued-relapse. Cue studies typically use visually recognizable stimuli ranging from several seconds to several minutes in length. Whether exceedingly brief (33 msec) drug cues presented outside awareness can activate limbic motivational circuits is not yet known. We used event-related BOLD fMRI at 3 Tesla and backward masking to determine whether cocaine cues presented outside conscious awareness would produce limbic activation in treatment-seeking cocaine patients (n=18). Target stimuli were randomly-presented cocaine-related, appetitive (sexual), aversive, and neutral cues of 33 msec duration. Each target was followed by a neutral "mask" of 467 msec duration. 120 unique visual stimuli (24 in each of the 4 target categories, plus 24 null events) were presented without replacement, and then repeated. Average ("jittered") inter-stimulus interval (TR) was 2 seconds. Data from the first 120 target presentations were the focus of the initial analysis. Data were analyzed within SPM2 with HRF as the basis function. Cocaine cues presented outside awareness indeed produced differential activation of the amygdala and interconnected limbic regions (ventral prefrontal cortex, ventral striatum, and anterior insula) in cocaine patients ($t > 3.0$). Sexual and aversive cues produced less pronounced activation than the cocaine cues in this population. These data provide the first evidence that drug cues presented outside awareness can activate limbic motivational circuitry. The rapid limbic response to "unseen" drug cues may be a precursor to (conscious) drug craving, and may have utility as a novel predictor of relapse vulnerability and/or the efficacy of candidate treatment interventions. NIDA (R01 10241, 14316, P60-DA-05186, NIDA P-50-DA-12756), Research Division, Department of Veteran's Affairs Medical Center, VA VISN 4 MIRECC, and the Alexander Foundation.

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- 137** **PHYSIOLOGICAL, SUBJECTIVE AND HORMONAL RESPONSES TO ACUTE PSYCHOLOGICAL STRESS: EFFECTS OF SEX AND SMOKING STATUS**
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Psychological stress plays an important role in the development of psychopathologies, including substance dependence. One way that acute stress can affect drug-taking behaviour is by directly altering physiological and/or subjective effects of drugs. This study was designed to characterize the time-course of responses to acute stress in men and women and in smokers and non-smokers. We measured physiological, psychological and hormonal responses to the Trier Social Stress Test in male smokers and non-smokers, and in female non-smokers in two phases of the menstrual cycle. Volunteers (N=66) participated in two sessions, one with stress and the other without stress. Heart rate, blood pressure, subjective ratings and plasma hormones were measured before and at repeated times during each condition. In all participants, stress increased heart rate, cortisol, progesterone, and ratings of negative mood (e.g. anxiety, jitteriness), and decreased ratings of positive mood (e.g. calm, relaxed, positive mood). The effects of stress were similar between male smokers and non-smokers, except that smokers exhibited prolonged heart rate responses and blunted cortisol responses. Male and female non-smokers differed in their physiological responses to stress. Male participants showed greater cardiovascular reactivity (heart rate, systolic blood pressure) and higher levels of cortisol after the stress and no stress conditions than females in either phase. These findings indicate that the effects of acute stress depend on the smoking status and sex of the individual, and suggest that stress-drug interactions may also depend on individual characteristics. Levels of other plasma hormones (ACTH, allopregnanolone, testosterone, catecholamines) will be examined and correlated with alterations in mood. This research was supported by DA02812 and M01RR00055.
- 138** **MODELING THE EFFECTS OF BRIEF SMOKING LAPSES DURING THE INITIAL WEEKS OF SMOKING CESSATION**
L. Chivers, S. T. Higgins, R. M. White, G. J. Badger and S. H. Heil, University of Vermont, Burlington, VT
Evidence from clinical research shows that any smoking, even a few puffs, during the first two weeks of a quit attempt greatly increases relapse risk. The goal of the present study was to use contingency management to bring abstinence under experimental control and to examine the influence of brief smoking lapses on measures associated with relapse risk. Subjects were 59 adult smokers not currently trying to quit. Subjects were randomized into one of four conditions, three of which received abstinence-contingent payments for 14 consecutive days (14C), and one of which had abstinence-contingent payments on Day 14 only (1C). Within 14C, people were randomized to receive no puffs, 1 puff, or 8 puffs on a cigarette on five evenings. Smoking status was assessed 3x/day, with abstinence operationalized as breath CO \leq 4ppm. Participants completed questionnaires each evening. On Day 14, all subjects completed a 3-hr lab session wherein they made a maximum of 20 exclusive choices between receiving two puffs on a cigarette or money (\$.25/choice). Analyses were broken into two phases: Days 1-13 and Day 14. Abstinence was successfully manipulated, as 59% of 14C participants abstained over days 1-13, vs. 0% in 1C. For Day 14, more in the 14C than 1C abstained from smoking (86% vs 53%). No significant effects of experimenter-administered puffs were noted on abstinence or self-reported withdrawal or other measures. For Days 1-13, 14C participants reported significantly more withdrawal and desire to smoke, but those differences decreased across time. Ratings of ease of abstaining and confidence increased significantly across time in 14C but not the 1C condition, with differences still discernible on Day 14. Despite differences in ratings of ease of abstaining, no differences between conditions were noted in the 3-hr choice session. Overall, these results suggest that experimenter-delivered puffs may have little effect on factors affecting abstinence, and provide further but limited evidence that a period of sustained abstinence may directly facilitate further abstinence.
- 139** **TREATING DRUG-OFFENDERS: OUTCOMES OF CALIFORNIA'S PROPOSITION 36**
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Background: The aim of California's Proposition 36 is to reduce criminal activities, re-incarcerations, and substance use. Despite the increased attention, only a few studies about the effectiveness of Proposition 36 have been published, particularly in terms of its treatment outcomes. This study evaluates Proposition 36's impact on reductions in criminal recidivism as well as its effect on substance use in a therapeutic community. Methods: Participants were opioid-dependent men and women admitted to a residential treatment program in San Francisco. Using mixed effects regression and generalized estimating equation (GEE), we compared treatment outcomes between those mandated to treatment under Proposition 36 (n = 24) and those on probation but not involved in Proposition 36 (n = 61) at admission, at 6 and 12 month follow-ups, using partial 12 month follow up data. Outcomes included Addiction Severity Index (ASI) composite scores, treatment retention, incarceration, arrest, employment, job training, and drug use treatment. Participants had a mean age of 38.5 years (SD = 9.2). Approximately 36% were women and most (75%) had completed high school. The participants were mostly White (54%) and African American (27%). Results: Results showed significant improvement over time on ASI employment composite scores in both groups. Participants in both groups also were, over time, more likely to be arrested and be engaged in work, but less likely to be engaged in job training. Using survival analysis, the mean number of days in the treatment among probation clients (153 days, SE=15.35) was not significantly different from that of Proposition 36 clients (147 days, SE=19.92). Conclusion: In this sample of persons meeting Proposition 36 eligibility criteria, who were mandated to treatment in lieu of incarceration, outcomes were similar to those seen in a non-Proposition 36, criminal justice comparison group.
- 140** **CHARACTERIZATION OF INDIVIDUALS WHO ABUSE PRESCRIPTION OPIOID ANALGESICS OR HEROIN**
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In prior risk-management programs for prescription opioid analgesic abuse, we provided evidence of a substantial increase in the abuse of nearly all prescribed opioid analgesics, notably extended release (ER) oxycodone and hydrocodone products, over the past decade. While abuse is prevalent nationwide, it seems to be heavily localized in rural, suburban and small urban areas. The purpose of the present studies was to take the next step following abuse detection and localization: identifying the characteristics of the expanding pool of prescription drug abusers so that intervention strategies can be developed to reduce or "manage" the risk of abuse. Detailed questionnaires were filled out by a sample of over 1,000 subjects drawn from regions where prescription opioid analgesic abuse was disproportionately represented. The results revealed the following: first, the age distributions suggest overall that both male and female prescription opioid abusers are much older than those who use illicit drugs; second, within the subject pool there are gender differences in age (females > males) and other patterns of use/abuse, such as source of drugs (use of doctor prescriptions: females > males); third, 78% of the total sample was white, relatively well educated and employed; fourth, 40% of the subjects reported that they receive their drugs from a physician, suggesting either a legitimate prescription for pain, doctor-shopping, scamming or ill-informed doctors; fifth, we have strong evidence that pain may be an important co-morbid factor in prescription opioid abuse; sixth, iatrogenic (i.e., therapeutically induced) dependence may be a major factor in the abuse of prescription drugs; and finally, prescription drug abuse may serve as a "gateway" leading to abuse of heroin.

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- 141** TRANSFERRING FROM HIGH DOSES OF METHADONE TO BUPRENORPHINE: A RANDOMISED TRIAL OF THREE DIFFERENT BUPRENORPHINE SCHEDULES
N. Clark(1,2,3), N. Lintzeris(5), D. Jolley(4), G. Whelan(3), J. Bell(6), A. Ritter (1) and A. Dunlop(1), (1) Turning Point Alcohol & Drug Centre, (2) Addiction Medicine Unit, Southern Health, (3) Department of Medicine, U. of Melbourne, and (4) Services Research, Monash U., Melbourne, Victoria, Australia; and (5) Transferring from high doses of methadone to buprenorphine can precipitate severe opiate withdrawal symptoms, posing a dilemma for people on high doses of methadone considering alternative treatment options. We examined the severity of opiate withdrawal associated with three approaches to transferring from methadone doses between 40 and 100mg commencing with either 0.8mg, 4mg or 32mg buprenorphine and increasing to 32mg daily. Thirty participants were admitted to a residential detoxification unit and randomly allocated to one of the three different treatment approaches. All participants waited at least 2 days before commencing buprenorphine. Overall withdrawal symptoms were mild and only three patients did not complete the transfer. Higher methadone doses, a shorter time period between methadone and buprenorphine and female sex were associated with more severe withdrawal. The low and high buprenorphine dose schedules resulted in less opiate withdrawal. There were also differences in the pattern of opiate withdrawal following buprenorphine with the low dose group having less withdrawal following the first dose of buprenorphine and the high dose group having the shortest duration of opiate withdrawal. When taking withdrawal features, medication use and drop out into consideration, low doses and high doses appear to result in better outcomes than doses in between. Participants were followed up for three months post transfer, at which time 18 patients were still taking buprenorphine. Overall, heroin use reduced and quality of life improved significantly as a result of the transfer particularly in those who chose to remain on buprenorphine or cease opioid substitution treatment completely.
- 142** CLINICIAN REFERRAL AND TREATMENT PRACTICES TO PROMOTE SELF-HELP ATTENDANCE FOR CLIENTS WITH CO-OCCURRING DISORDERS
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Introduction. Affiliation with 12-Step self-help groups (e.g., Alcoholics Anonymous) and specialized self-help groups (e.g., Double Trouble in Recovery) is associated with favorable outcomes for individuals with co-occurring substance use and mental health disorders (COD). Mental health and addiction treatment providers can play a major role in clients' engagement in self-help groups, yet clinical practices and professional opinions toward self-help networks vary widely. Method. As part of a SAMHSA-funded Co-occurring Disorders State Incentive Grant (COSIG), we surveyed clinical staff at 5 addiction and 4 mental health treatment agencies regarding referral practices, attitudes and beliefs about self-help networks, and the perceived utility of self-help groups for clients with substance use disorders or COD. We also explored the use of treatment practices that incorporate 12 Step principles. Results. Staff (n=74) reported high familiarity with and believe 12-step groups play an important role in treatment and recovery, but were less familiar with specialized self-help for COD. Staff referred 75% of clients with substance use disorders and 68% of clients with COD to 12-step groups. Clinicians at addiction agencies, certified as addiction counselors, or who regularly attend 12-step meetings referred higher proportions of clients to 12-step groups, while staff with graduate degrees referred fewer clients. Similarly, practices to promote 12-step affiliation were conducted more frequently by staff at addiction agencies and by certified clinicians. Discussion. Surprisingly, clients with COD were nearly as likely to be referred to self-help groups as those with substance abuse only. Despite similar beliefs about the utility of 12-step groups, clinicians at mental health agencies or with graduate degrees referred fewer clients than other staff. The implications of professional-centrism on treatment practices and staff training are discussed.
- 143** RACE DIFFERENCES IN HEALTH SERVICE UTILIZATION ASSOCIATED WITH ALCOHOL/TOBACCO USE IN BALTIMORE, MARYLAND
P. Clubb(2,3), F. A. Wagner(1,2,3), D. C. Browne(1,2,3) and S. Zhu(2,3), (1) DARP & School of Public Health, (2) Drug Abuse Research Program & Center for Health Disparities Solutions, and (3) Morgan-Hopkins Center for Health Disparities Solutions, Morgan State University, and Johns Hopkins University, Socio-environmental characteristics often confound the association between race and drug involvement. The research questions for the study were: Are there differences in health care utilization among African Americans and whites with similar socioeconomic and environment characteristics? Are these differences associated with alcohol and tobacco utilization? And, finally, do differences persist after adjusting for other potential confounders? Methods. 1427 participants from two adjacent communities, with similar representation of Blacks and whites socioeconomic indicators (i.e., income and educational attainment), were interviewed using a standardized questionnaire. Past month alcohol and tobacco use data were collected; race was self-identified. Health service utilization was measured by asking the number of visits to a doctor or medical clinic for any reason in the past two years. Other potential confounders included age, sex, income, health insurance, as well as depression symptoms. Negative binomial models with random effects used to accommodate clustering of respondents by household. Results. Participant who used alcohol were estimated to have lower rates of health service utilization (unadjusted Incidence Rate, IR_a=0.5; 95% CI= 0.3, 0.8 for Blacks, and IR_a=0.6; 95% CI=0.4, 1.0 for whites). Adjusting for potential confounders affected the IR for whites (adjusted IR_a=1.0, 95% CI=0.5, 1.7) but not for Blacks, substantially (aIR=0.6; 95% CI= 0.4, 1.0). Comments. Results may be indicative of actual differences within groups of African Americans in the association between drug use and health care utilization. Further research and interventions are needed to address nicotine and problematic alcohol use in this population. Acknowledgements. NIDA, grant DA12390 & CMHHD, grant MD002217.
- 144** IMPULSIVITY AND RAPID DISCOUNTING OF DELAYED HYPOTHETICAL REWARDS IN BORDERLINE PERSONALITY DISORDER WITH AND WITHOUT A SUBSTANCE USE DISORDER
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Impulsivity is one psychological construct thought to underlie both borderline personality disorder (BPD) and substance use disorders (SUD); psychiatric conditions that often co-occur. In an effort to measure impulsivity in humans, investigators have studied the value of delayed rewards by presenting hypothetical choices to subjects: a large reward received after some delay vs. smaller rewards available immediately. For any specified delay, the point at which the smaller immediate reward is equivalent to the larger delayed reward is the point of indifference. If a variety of time delays are presented, the points may be plotted as an indifference curve to gain information about the rate at which the subjective value of a reward decreases with increasing delays to reward delivery. This approach to understanding impulsivity has been termed delay discounting. In an ongoing study, we test the hypothesis that BPD-SUD individuals (n=8) represent a more severe subsample of BPD patients (n=7) using a computerized version of the delay discounting paradigm. Both the BPD and BPD-SUD groups are compared to a healthy control group (n=13). All subjects are presented with hypothetical immediate and delayed rewards with the 8 delay conditions ranging from 6 hours to 25 yrs. Subjects are presented with hypothetical monetary rewards with objective values ranging from \$1 to \$1000. Consistent with previous research, preliminary data suggests that a hyperbolic discounting function provides a good fit of the data. As hypothesized, the BPD and BPD-SUD subjects discount monetary rewards at a higher rate than the control subjects. However, contrary to our hypothesis the two BPD groups do not differ on the delay discounting task or on self-report measures of impulsivity. These data provide laboratory-based evidence that BPD individuals are more impulsive than healthy controls. Supported by NIMH grant MH069627.

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145 RELATIONSHIPS BETWEEN RELIGIOUS COPING, PERCEIVED HEALTH, AND METHADONE MAINTENANCE TREATMENT OUTCOMES

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Background: Religious was found to be associated with success of drug abuse withdrawal. However, most studies evaluated religious coping using a one-dimensional measure only, and only few studies evaluated MMT patients. Aims: to determine whether religious coping (RCOPE) is associated with sense of coherence (SOC), perceived health, and success in MMT. Methods: A cross sectional study included 118 MMT patients who filled the SF36 for perceived health, the RCOPE questionnaire (defined as strategies through which religion is involved in the process of coping(and SOC (defined as "a global orientation that expresses the extent of the person's confidence and ability to cope with pressures in life"). Drug abuse for cocaine, amphetamine, THC, benzodiazepines and opiates during the 3 months preceding questionnaire completion was defined as positive if at least one urine sample of any drug was positive. Results: Of 118 MMT patients, 70(59.3%) abused any drug and 48 (40.7%) did not. Mean duration in treatment was $5\pm 3.3y$ (range 0.2-11.6y). Inverse correlations were found between positive and negative religious coping strategies and SOC (e.g., seeking spiritual support, $r=-0.28$, $p=0.002$), SF36, and duration in treatment. SOC was higher in non-abusers compared with abusers (4.7 ± 0.9 vs. 4.2 ± 1 , $F=8.8$, $p=0.004$) and was associated with duration in treatment ($r=0.27$, $p=0.004$) and with SF36 ($r=0.43$, $p<0.0005$). Conclusions: We found that patients with shorter time in treatment had worse health and lower SOC, and used more religious coping. This finding is in contrast with previous studies showing associations between religion and positive outcomes in MMT. It might be that MMT patients, known to have hyper-responsiveness to stress, may utilize religious coping.

146 SELF-REPORT AND BEHAVIORAL MEASURES OF IMPULSIVITY IN LIGHT AND MODERATE FEMALE DRINKERS

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Alcohol use disorders among women are a significant problem in the U.S. Impulsivity is a factor shown to be involved in alcohol abuse in men, but there is little research to date examining the role of impulsivity in alcohol use in women. Thus, the present study examined light and moderate female drinkers on various self-report and behavioral measures of impulsivity. To date, 15 light drinkers (mean of 2 drinks/week) and 22 moderate drinkers (mean of 15 drinks/week) have completed the study. None of these women met criteria for alcohol abuse or dependence. Participants completed three self-report measures of impulsivity, and were then given 14 days of daily rating forms. The daily rating forms allowed us to assess various aspects of mood and prospectively measured alcohol consumption. Three weeks after the initial visit, participants returned to the laboratory and completed three behavioral measures of impulsivity. Moderate drinkers scored significantly higher on several self-report measures of impulsivity, including the Non-Planning subscale of the Barratt Impulsiveness Scale, the Impulsiveness subscale of Eysenck Impulsivity Questionnaire, and both the Disinhibition and General subscales of the Zuckerman Sensation-Seeking Scale. Moderate drinkers scored significantly higher on a behavioral measure of impulsivity, the Delay Discounting Task, than light drinkers: moderate drinkers chose smaller immediate rewards more than larger delayed rewards compared to light drinkers. There were no significant differences between moderate drinkers and light drinkers on two other behavioral measures of impulsivity (the Immediate/Delayed Memory Task and the Go Stop Task). Together, the results suggest that female moderate drinkers are more impulsive than female light drinkers. Ultimately, these data could contribute to a greater understanding of factors that are associated with, and perhaps predict, increased risk for drug or alcohol abuse in women. Supported by NIDA grant DA009114.

147 REINFORCEMENT HISTORY DETERMINES THE REINFORCING EFFECTS OF QUINPIROLE IN THE RAT

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These experiments were aimed at defining the reinforcing properties associated with D3 receptor stimulation using several self-administration paradigms in the rat ($n=6$ per group). In one set of studies, rats were trained to self-administer cocaine (COC) (0.56 mg/kg/inf) under a FR 1 schedule, and the ability of the D3 agonist quinpirole (QPR) (0.01, 0.032, and 0.1 mg/kg/inf) to function as a reinforcer was assessed by substitution of QPR for a period of 7 days. QPR dose-dependently functioned as a reinforcer, resulting in an inverted U-shaped dose-response curve, with peak responding maintained by 0.032 mg/kg/inf QPR. In a second set of studies, the influence of drug history on QPR's reinforcing effects was addressed using a multiple 7 day substitution procedure in which rats were trained to respond for food under an FR 1 schedule. During the first substitution, food was replaced with an infusion of either saline, 0.56 mg/kg/inf COC or 0.032 mg/kg/inf QPR. Upon reacquisition of food responding, 0.032 mg/kg/inf QPR was substituted for all rats. Significant drug history effects were observed as QPR failed to function as a reinforcer during the initial substitution, however during the second substitution responding for QPR was observed in rats previously exposed to COC, and this responding was significantly greater than when rats were exposed to either saline or QPR in which responding remained low. These studies show that QPR was an effective reinforcer only if rats had a reinforcement history of cocaine; simple exposure to QPR is not sufficient. It will be interesting to determine the amount and type of drug history that induces the reinforcing effects of QPR. Furthermore, further analysis of QPR's reinforcing effects may provide valuable insight into the roles of the D3 and/or D2 receptors in COC abuse. Research supported by USPHS grants DA00254 and F013771 through NIDA

148 CONCURRENT USE OF HEROIN WITH OTHER DRUGS AMONG YOUNG NEVER-INJECTING HEROIN USERS IN PUERTO RICO

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Introduction. The concurrent use of heroin with other drugs has been documented in several studies. However, the range of drug combinations in use and its effects on heroin use and dependence are not well known. In this study we examined patterns of concurrent use of heroin with other drugs among a sample of never-injecting heroin users in Puerto Rico. Methods. Subjects were recruited in street settings ($n = 411$), screened for eligibility and asked to consent to participate. Eligible subjects were 18 to 25 years old, current heroin users with no history of injecting drugs. Measures included the drugs used concurrently with heroin (mixed or taken together), the amount of heroin consumed per day (heroin bags), and heroin dependence (meeting DSM-IV criteria). Results. Of the 411 heroin users, 22.1% reported not using any other drug concurrently with heroin. Concurrent use of tobacco was reported by 30.2%, alcohol 7.8%, marijuana 52.3%, powder cocaine 25.8%, crack cocaine 25.8%, and xanax 3.4%. Participants not using heroin concurrently with any other drug consumed, on average, 3 heroin bags per day. Amount of daily heroin bags was regressed against drugs used concurrently with heroin. Concurrent use with tobacco increased daily heroin bags by 0.78 ($p=.041$), concurrent use with marijuana decreased heroin bags by 0.74 ($p=.038$), concurrent use with cocaine increased the amount by 1.25 ($p=.002$). Close to half (47.6%) of heroin users not using any other drug concurrently met DSM-IV criteria for heroin dependence. Heroin dependence was regressed against types of drugs used concurrently with heroin. Concurrent use with cocaine significantly increased the odds of heroin dependence ($OR = 2.3$, $p = .002$). Conclusions. The great majority of heroin users in this study used other drugs concurrently with heroin. Concurrent use of cocaine seemed to increase the amount of heroin consumed and the risk of heroin dependence. Concurrent use of drugs merit more research to understand its pharmacological basis, clinical implications, and public health impact.

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- 149** EFFICACY OF DEXTROMETHORPHAN ON OPIOID-INDUCED HYPERALGESIA IN METHADONE PATIENTS
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Accumulating evidence indicates that patients on opioid maintenance (i.e., methadone) for the treatment of opioid addiction are significantly less tolerant of experimental pain in comparison to matched normal controls or drug-free ex-opioid addicts, a phenomenon theorized to reflect opioid-induced hyperalgesia (OIH). Agonist activity at the excitatory ionotropic N-methyl-D-aspartate (NMDA) receptor on dorsal horn neurons is implicated in the development of both OIH and its putative expression at the clinical level, opioid tolerance. The aim of this ongoing study is to evaluate the potential utility of the NMDA-receptor antagonist, dextromethorphan (DEX), to reverse or treat OIH in methadone-maintenance (MM) patients. Utilizing a clinical trial design and double blind conditions, improvement in pain tolerance following a six-week trial of DEX in comparison to placebo was evaluated in a well-characterized sample of MM patients. Subjects were titrated to DEX 480mg/day dose, and pain responses to both thermal (cold-pressor) and electrical pain stimuli evaluated. The sample (n = 23) was 56% male, and ethnically diverse (40% Latino, 40% African-American, 16% white, 4% other), with a mean age of 44 (SD=4.7) years. Paired t-test analyses found no difference between cold-pressor pain threshold (t = 0.931, n.s.), cold-pressor pain tolerance (t = 1.142, n.s.), or electrical pain tolerance (t = .828, n.s.). These results suggest that chronic high-dose DEX therapy does not alter the relative pain intolerance noted in MM patients, and provide preliminary information on the clinical efficacy of a hypothesized pharmacotherapy to treat OIH.
- 150** REDUCTIONS IN SUBSTANCE ABUSE AMONG YOUNG PEOPLE LIVING WITH HIV
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Hypothesis: Reductions in substance use will occur among young people living with HIV (YPLH) when a case-management cognitive-behavioral intervention is delivered. However, these reductions will be difficult to document when there is a high rate of no substance abuse. Procedures: YPLH aged 16 to 29 years (n = 175; 26% Black & 42% Latino; 69% gay males) in Los Angeles, San Francisco, and New York were randomly assigned to a 3-module immediate preventive intervention totaling 18 sessions or a delayed-intervention condition. The frequency of use was reported across several substances over 15 months. Statistical Analyses: At least half of the YPLH were reported non-users for each illicit substance (a zero count) across all observed follow-up assessments. We fit longitudinal zero-inflated Poisson models to each substance use count measure to examine the intervention effect on substance use in the presence of zero inflation. A zero is allowed to come from two processes; with probability p, one process, the "non-user" state, has zeros as the only possibility and with probability 1-p, the other process has Poisson distributed counts. Results: Intention-to-treat analyses found that the immediate intervention resulted in a significant reduction in the frequency of cocaine and methamphetamine use whether YPLH were likely to be using substances or not in the non-user state. Conclusions: Cognitive-behavioral interventions reduce substance use among HIV+ young people. Accounting for the high frequency of non-use is important when examining intervention effects on substance use measures.
- 151** SUICIDE ATTEMPTS AMONG INDIVIDUALS WITH OPIOID DEPENDENCE: THE CRITICAL ROLE OF FELT BELONGING
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Introduction: Individuals who seek treatment for opioid dependence are at elevated risk for suicidal behavior and prevention efforts may be enhanced by improved understanding of risk factors for suicide attempts in this population. Methods: Subjects were recruited by poster advertisements from a methadone maintenance program at an urban university hospital and completed a standardized interview including self-report measures of perceived 1) belonging 2) burdensomeness, and 3) loneliness. Individuals with a history of attempted suicide were compared to non-attempters using multivariate logistic regression. Results: One hundred thirty-one subjects, with a mean (SD) age of 42(9.6) years, completed at least one interview. The sample was 53% women, 23% black, and 21% Hispanic. Most individuals (70%) had been enrolled in the program for at least one year and 82% reported a history of intravenous drug use. Forty-nine (37%) subjects reported a lifetime history of attempted suicide. Among suicide attempting individuals, 67% had made two or more attempts, 14% had made an attempt within the past year, and 69% received emergency treatment within 24 hours of an attempt. The most common methods were intentional overdose (59%), cutting (18%), and hanging (10%). Seventy-eight (60%) subjects reported a history of unintentional overdose. As hypothesized, low belonging distinguished suicide attempters, after accounting for covariates including age, sex, race, drug use severity, aggression, depression, and hopelessness. Belonging was unrelated to unintentional overdose signifying results were not attributable to endorsing difficulties. Burdensomeness findings were suggestive but not definitive. Results did not suggest a role of loneliness. Conclusions: Findings underscore the relevance of a sense of belonging to vulnerability to suicidal behavior. Supported by NIH grants AA00318 and DA00455
- 152** PRENATAL EXPOSURE TO TOLUENE ALTERS ATTENTION AND IMPULSIVE BEHAVIOR IN RATS IN A "WAITING-FOR-REWARD" TASK
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Toluene is one of the most abused inhalants in the world and its abuse during pregnancy is a rapidly growing world-wide public health concern. However, the neurobehavioral teratogenic effects of toluene at the high concentrations and binge-like exposure patterns typical of abuse remain understudied. We assessed the effects of binge prenatal toluene exposure on behavioral impulse control in the rat using a "waiting-for-reward" operant task. Timed-pregnant Sprague-Dawley rats were exposed for 15 min, twice daily, from gestational day (GD) 8 through GD20 to either air, 8000, 12,000 or 16,000 ppm toluene in a static exposure system. At postnatal day 60, male and female offspring were trained to lever press in a standard fixed-ratio 15 (FR15) paradigm. After responding had stabilized, a wait requirement was introduced such that after each FR15 completion, a "free" pellet was delivered at increasing time intervals (2 s, 4 s, 6 s, etc.). The animal would continue to receive "free" pellets until it pressed another signaled lever which would then reinstate the FR component (FR reset). After a period of stabilization, the FR15 component was slowly increased to (and remained at) FR50. Repeated binge prenatal toluene exposure increased response rates and the number of FR resets, decreased mean waiting time, and resulted in a higher response to reinforcer ratio than exhibited by controls. These results suggest that acute prenatal toluene exposure significantly impacts neurobehavioral development, in general, and behavioral inhibition and/or response to reward, in particular. The lack of significant improvement in these deficits also suggests that these may be long-term behavioral decrements. Supported by grants DA15095 and DA15951 to SEB.

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153 ETHICAL ISSUES IN SUBSTANCE USE DISORDER GENETICS: RESEARCHERS' PERSPECTIVES

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Hypotheses:(1)Regarding the ethical and social implications of genomic research in substance use disorders (SUD), researchers will articulate different issues from those published in the bioethics literature; (2)NIH funding for ethics research in SUD comprises a small percentage of the number of grants awarded. Procedures:(1)This is a qualitative study designed to analyze the contents from a scripted focus group with 19 principal investigators at a NIDA-sponsored meeting. The discussion included the meaning of ethics, ethical implications of their work, and potential future applications. (2)A survey of the CRISP database identified current NIH grants awarded in behavioral genetics, ethics, alcohol, nicotine, drugs, and addiction. Analyses:Analysis was done using NVivo, software for qualitative analysis, to interpret and relate salient themes that emerged. Results:(1)Common ethical themes expressed by researchers and the bioethics literature were: privacy, confidentiality, genetic discrimination, stigmatization, psychiatric genetic exceptionalism, freedom, responsibility, integrity, and eugenics. The researchers focused on different scientific implications: expressivity, probabilistic, common alleles, complex traits, medicalization, scientific uncertainty, early detection/no intervention, education, and unintended consequences. They showed greater concern about commercial and legal issues: maldistribution of financial gains, misuse of public databanks, and legal applications of repositories. (2)The number of grants awarded that addressed the ethics of genomics research in SUD by NIDA, NIAAA, NHGRI, NIMH were less than 1% of the total grants funded. Implications:Different issues from a bioethics literature search included informed consent, justice, pleiotropy, fear, parental guilt, exploitation of ethnic groups, inequality, and broad temporal range of genetic information. Although both groups articulate common themes, our results support the hypotheses that researchers articulate different concerns than bioethicists, and grant funding for SUD ethics is comparatively low.

154 READY TO DRINKS: ALCOHOL TASTE PERCEPTION AND YOUNG PEOPLE

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Early age of initiation and regular alcohol use have been identified as risk factors for the development of alcohol dependence. One of the new and increasingly popular beverages are 'ready to drink' (RTD) preparations, particularly among adolescent drinkers. This study aimed to:(1) determine which beverages are most palatable to the adolescents and young adults;(2)if this pattern changes with age and gender; and(3)the extent to which packaging affects the palatability ratings. A convenience sample of 350 participants was recruited, 70 in each of five age groups. Participants were grouped:12-13yrs, 14-15yrs, 16-17yrs, younger adults of 18-23yrs, and older adults of 24-30yrs. The experimental drinks included three sets of RTDs and their components, beer, wine and a novel beverage control. There were blind and non-blind testing phases of the study.A number of univariate and multivariate tests of significance were conducted.These revealed that the palatability of alcohol and the appeal of its packaging increased with age; however, a chocolate milk and vodka RTD, and to a lesser extent a watermelon flavoured white rum RTD, were judged to be more like their their soft drink base than their alcohol component in blind testing. There were no gender differences in palatability of alcohol types in the adolescent sample. Overall, packaging was found to positively influence palatability for alcohol. This suggests that great caution should be exercised when using milk as a base for an RTD, particularly with an alcoholic base that is less readily detected by adolescents, such as vodka. Given that a large proportion of very young adolescents felt that RTDs were packaged to appeal to them, awareness should be drawn to the way these products are being marketed.

155 SMOKING OUTCOME EXPECTANCIES PREDICT NICOTINE WITHDRAWAL SYMPTOMS IN MILDLY AND MODERATELY DEPRESSED COLLEGE WOMEN SMOKERS

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Twenty-one female college student smokers participated in the present study, which was conducted to examine the relation among nicotine withdrawal symptoms, depression, and smoking outcome expectancies in smokers. Participants were assessed at baseline for carbon monoxide (CO) level and salivary cotinine (ng/ml) to verify self-reported smoking status. They then completed a smoking history form, the Fagerström Test for Nicotine Dependence (FTND), the Smoking Consequences Questionnaire (SCQ), and the Beck Depression Inventory-II (BDI-II). Participants monitored nicotine withdrawal symptoms using the Smoking Withdrawal Questionnaire (SWQ) over the subsequent week as they attempted to abstain from smoking and returned to the lab each day for CO readings. Participant characteristics were: age (m = 21 years), smoking rate (m = 20 cigs/day), years smoking (m = 5.3), FTND (m = 4.3). Twelve participants' BDI-II scores were > 10, indicating at least half of the sample was mildly depressed. Five participants' BDI-II scores were > 23, indicating moderate to severe depression. Baseline Negative Reinforcement/Negative Affect Reduction outcome expectancies were associated with nicotine withdrawal symptoms related to mood and alertness/fatigue among those women meeting diagnostic criteria for mild or moderate depression. Possible mechanisms and the implications of these findings for cessation treatment strategies will be discussed.

156 EXAMINING THE POTENCY OF A COMMUNITY-FRIENDLY HIV RISK-REDUCTION INTERVENTION

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Few evidence-based HIV risk reduction interventions have been designed for use within drug treatment CBOs such as methadone maintenance programs. Those that are potentially applicable to drug treatment CBOs are not "community-friendly" and are not likely to be implemented as intended in such clinical settings. In response, we have conducted formative research resulting in a substantially shortened, "community-friendly" version of the comprehensive evidence-based Holistic Health Recovery Program (HHRP; Avants et al., 2004; Margolin et al., 2003). Our shortened version, the Community-friendly Health Recovery Program (CHRP; Copenhaver et al., under review) has demonstrated feasibility and preliminary evidence of effectiveness among 226 injection drug users participating in a methadone maintenance program. As a follow-up analysis, the current study examines (1) the extent to which significant intervention effects - including improvements in HIV-related knowledge, motivation, behavioral skills, and drug- and sex-risk reduction behavior - decayed over time and (2) whether repeated exposure to the CHRP intervention provided additional benefit to participants in terms of HIV risk reduction. Immediately prior to repeating the intervention, 62 participants were re-assessed on HIV-related knowledge, motivation, behavioral skills, and drug- and sex-risk reduction behaviors. Correlations were used to examine the strength of association between the lapse of time from the original intervention exposure and changes in participants' risk reduction scores. After an average of 10 months from the end of the original intervention, no evidence of decay was found. Immediately following their second exposure to the intervention, participants were re-assessed. No additional improvement was found in HIV risk reduction scores after participants repeated the intervention. This was no surprise given that we found no decay in participants' HIV risk reduction outcomes following their initial participation. Results suggest that the CHRP intervention may be potent as well as community-friendly.

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157 GENDER DIFFERENCES IN THE EXPERIENCE OF SPONTANEOUS CANNABIS QUITTING

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Cannabis is the most widely used illicit drug in the world. Epidemiologic evidence suggests that many cannabis users attempt to stop use without formal treatment. There are few data on the experience of spontaneous quitting in adults, especially regarding the effect of gender, which has been shown to influence the acute effects of cannabis. This study examined gender differences in retrospectively self-reported characteristics of spontaneous cannabis quitting among 81 male and 23 female, non-treatment-seeking, adult cannabis smokers (52% white, 40% African-American, mean [SD] age 35 [11.3] years, 19 [10.1] years of cannabis use, 16.6 [3.9] years old at first cannabis use, 3.9 [10.2] lifetime quit attempts) who reported at least one "serious quit attempt" (self-defined). There were no significant gender differences in sociodemographic characteristics, cannabis use history, or quitting strategies. Women were significantly more likely than men to quit cannabis use due to concerns about health (78% v. 54%), productivity (78% v. 48%), energy level (78% v. 51%) and a desire to not burn holes in clothes or furniture (30% v. 11%); to resume use to relieve dysphoria (26% v. 9%), or due to the ending of a constraint against use (26% v. 6%); and to report upset stomach as a withdrawal symptom (17% v. 2%). Men were significantly more likely to quit due to displeasure from another (27% v. 0%); and to report marijuana craving (72% v. 48%) and an increased sex drive (23% v. 4%) as withdrawal symptoms. Both men and women initiated or increased use of legal substances during their quit attempt but did not initiate new illegal drug use. These findings highlight important gender differences in spontaneous quitting of cannabis use that suggest the need for differential treatment approaches. Supported by the Intramural Research Program of the National Institutes of Health, National Institute on Drug Abuse and NIH grant RO-1 DA03018.

158 ALCOHOL USE BUT NOT CANNABIS USE REPORTED TO CONTRIBUTE TO DEPRESSION IN TREATMENT TRIAL OF COMORBID ADOLESCENTS

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The authors are currently conducting a first double-blind, placebo-controlled trial of fluoxetine (20 mg) in adolescents with a cannabis use disorder and major depression, most of whom also used alcohol. All subjects also receive motivational and cognitive behavioral psychotherapy. That NIDA-funded study remains ongoing. However, certain preliminary data are available, mostly involving data from the baseline assessments, based on data from the first 48 subjects. Study methods will also be described. Subjects were asked at baseline whether cannabis use contributed to their depressive symptoms, or whether on the other hand their depressive symptoms contributed to their cannabis use. A similar pair of questions was also asked regarding whether alcohol use contributed to their depressive symptoms, and vice versa. We evaluated these of these four questions in four separate chi-square analyses. Subjects participating in the treatment study did not report that cannabis use contributed to their depressive symptoms (chi-square=1.09, p=0.300), but depressive symptoms were reported to strongly contribute to cannabis use (chi-square=8.80, p=.003). In contrast, alcohol use was reported to contribute to depressive symptoms (chi-square=5.00, p=0.025), and depressive symptoms reportedly contributed to alcohol use (chi-square=7.05, p=0.008). No subject to date has complained of serious or persistent medication side effects, and none has been discontinued from medications because of side effects. These findings provide preliminary evidence that alcohol use but not cannabis use contribute to the depressive symptoms of comorbid adolescents. These preliminary findings also suggest that depressive symptoms contribute to both the cannabis use and the alcohol use of comorbid adolescents. ACKNOWLEDGEMENTS: Supported by NIDA grants R01 DA019142, 2P50 05605, R01 DA14635, and R01 DA019992; by NIAAA grants R01 AA13370, R01 AA015173, K24 AA15320, and K02 AA00291; and by a VA MIRECC grant.

159 NICOTINE SENSITIZATION IN ADOLESCENT BETA ARRESTIN-2 KNOCKOUT MICE

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This study was designed to sensitize adolescent Beta Arrestin-2 knockout (BA-2 KO) mice to the psychostimulant nicotine. Beta Arrestin-2 is a protein that is involved in signaling of the metabotropic D2 receptor, and has been shown to play a mediating role in dopamine signaling and sensitization to psychostimulants such as cocaine, as well as the opiate morphine. In this study, 3-4 week old adolescent BA-2 KO and wild type C57 black mice were habituated to a square locomotor arena for one 30 min session. The following day, animals were administered either nicotine tartarate (s.c. 0.5 mg/kg free base) or saline 10 min before being placed into the locomotor arena for seven consecutive days. An drug-free abstinence period of seven days followed, at the end of which animals received a nicotine challenge (0.5 mg/kg free base). Results showed that although BA2 KO mice demonstrated equivalent levels of activity to wild types during habituation and initial hypoactivity to nicotine, BA2 KOs remained in a hypoactive state throughout the first 6 days of sensitization training compared to saline-treated BA2 KO mice as well as wild types. However, nicotine treated BA2 KO mice were also hypoactive compared to BA2 KO mice given saline on the challenge day. Additionally, wild types demonstrated normal sensitization to nicotine, with an initial hypoactive response as compared to controls, but significantly increased locomotor activity as compared to control wild types given saline as training continued. These animals also demonstrated sensitization to nicotine on the challenge compared to all other groups. These results appear to indicate the importance of the BA-2 protein in locomotor sensitization to nicotine in adolescence.

160 METHAMPHETAMINE INJECTORS COMPARED TO OTHER IDUS IN DENVER, CO

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This study compared demographics and HIV/HCV injection risk behaviors among injection drug users (IDUs) who use methamphetamine (meth) and IDUs who don't inject meth in Denver, Colorado. Between May 2004 and November 2005, we recruited 287 participants (69 meth IDUs and 218 non-meth IDUs) through street outreach and conducted structured interviews examining these variables. The average age of meth IDU participants was 36 years old and 25% were female. Additionally, 80% were Caucasian, 15% Latino, less than 2% African-American, and 4% of another ethnicity. Seventy-one percent reported being heterosexual. Nearly 80% had a high-school diploma or GED and over half of these had some post high-school education. Despite this relatively high level of education, over half considered themselves to be homeless. Nearly 8% had been told that they have HIV (past studies of HIV among IDU in Denver typically range between 4-5% positive) and 49% had been told they have HCV. In regard to risk behaviors, these meth users reported an average of 113 injections in the past month. Sixty-four percent had used a dirty needle in the past month, 72% had shared other drug paraphernalia and 69% had shared the drug solution with another injector. We also ran preliminary analyses to compare meth injectors with non-meth injectors. The meth IDUs were significantly more likely to be white, to have some post high-school education, to not be heterosexual and they averaged about 8 years younger in age than non-meth IDU. One of the most striking findings was that they were significantly more likely to have used a used needle in the past month (64% vs. 40% for non-meth IDU). They were also significantly less likely to have HCV (by self-report: 49% vs. 73% for non-meth IDU). The younger age and the lower HCV positive rate of meth IDUs, coupled with the dramatically higher rate of risky behaviors (needle sharing), lends an urgency to the need for effective risk reduction interventions targeting this population. Supported by the National Institute on Drug Abuse DA016994.

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161 SPECT IMAGING OF BETA2 NICOTINIC ACETYLCHOLINE RECEPTORS IN TOBACCO SMOKERS DURING ACUTE AND PROLONGED WITHDRAWAL

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Nicotine initiates its actions in brain through nicotinic acetylcholine receptors (nAChRs). Preclinical and clinical studies demonstrate a nicotine-induced upregulation of nAChRs, which is reversible; however, the exact time course of the normalization is unknown. We recently demonstrated that in human tobacco smokers, beta2-nAChRs were significantly elevated throughout the brain (25-35% in cortical and 9-26% in subcortical regions) compared to nonsmokers as measured with the high affinity nicotinic agonist [123I]5-IA-85380 (5-IA) and SPECT. The purpose of the present study is to image human tobacco smokers during acute and prolonged withdrawal using 5-IA SPECT to examine the time course of normalization of beta2-nAChRs during tobacco cessation. To date, 6 subjects have been studied. At the time of admission, tobacco smokers smoked 19.8 + 3.2 cigarettes/day and had a mean FTND score of 6.6 + 2.0. Smokers abstained from smoking for an average of 7-9 days prior to the first scan to allow time for residual nicotine to clear from the brain. At 22-30 days of smoking abstinence they participated in a second scan. They were assisted in their efforts to quit smoking with contingency management techniques. Urinary cotinine levels <100 ng/mL and carbon monoxide levels <10 ppm on both scan days confirmed abstinence. 5-IA was administered I.V. as a bolus to constant infusion for 8 h and subjects were scanned between 6-8 h. Results demonstrate that 5-IA uptake decreased throughout cortical and subcortical regions over time. These findings confirm that the high affinity nicotinic agonist binding site is upregulated in recently abstinent smokers, compared to a previously acquired group of control nonsmokers, and that approximately 30 days of abstinence may be required to detect the normalization of beta2-nAChRs. Funding: RO1DA015577, P50AA15632, P50DA1334

162 SEX (TRADING) IN THE CITY: PRACTICES AND BELIEFS AMONG FEMALE CRACK/COCAINE SEX TRADERS

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Although detailed histories of sexual behaviors have been collected in prevention studies, they are not usually examined thoroughly. A NIDA-funded study to reduce HIV behaviors among 445 crack/cocaine using women in St. Louis obtained detailed sexual histories, including types and number of sex acts, with and without protection. Overall, women averaged 54 acts over a 4 month period with 26% protected. Vaginal sex was the most commonly reported (mean=33), comprising 69% of all sex with 31% protected. Performed oral sex was reported 9 times in the 4 month period (12% of total) while received oral sex averaged 12 times (17% of total). Performed oral sex was protected 12% of the time, but only 4% for received oral sex. Anal sex was rare (1%). 87% of women who reported having all 3 types of sex were sex traders. Sex traders also reported a higher number of sex acts than non-sex traders (62 vs 43). Vaginal sex, in relation to all sex, was reported less among sex traders than non-sex traders (62% vs 80%); traders used more protection than non-traders for vaginal sex (35% vs 25%). Sex traders performed oral sex more often than non-sex traders (13 vs 3 sex acts); in contrast to vaginal sex, oral sex was performed proportionally more among sex traders compared to non-sex traders (17% vs 5% of all sex). Sex traders were more likely to report protection when performing oral sex compared to non-sex traders (16% vs 5%). There were no differences in the amount of oral sex received or anal sex between the two groups. While sex traders may report higher rates of protection, the rates are abysmal. Additionally, traders compared to non-traders have faulty health perceptions in that they report washing their own or their partners' genitals before sex with soap and alcohol, substituting oral for vaginal sex, using earwax to determine presence of STDs, and having sex "only with healthy looking people". Finally, they report that they have no sex behaviors to change. What can we, as prevention specialists, do to improve our prevention messages? These, and other issues, will be discussed.

163 PREVALENCE OF ERECTILE DYSFUNCTION MEDICATION USE BY VETERANS APPLYING FOR SUBSTANCE ABUSE TREATMENT

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Objectives: Erectile dysfunction (ED) is a common complaint among men seeking substance abuse treatment. Prevalence data on use and misuse of ED medications by these men is needed. Methods: Male veterans (n=225) applying for substance abuse treatment voluntarily completed an anonymous questionnaire regarding their use of ED medications. Their primary drugs of abuse were alcohol (56.7%), cocaine (24.7%), methamphetamine (5.2%), cannabis (2.6%), opioids (9.8%). Mean age was 52.5 years (sd=15.6). Results: Lifetime use of ED medications was reported by 32.5%. All of these reported using sildenafil. Use of vardenafil (n=3) and tadalafil (n=7) was also reported. Use in the last 90 days was reported by 33.3% of lifetime users. The majority (65%) obtained their ED medications by prescription most of the time. However, obtaining ED medication from the street or internet (11.6%) and friends (22.2%) was common. How ED medications were obtained did not differ as a function of primary drug of abuse. Using ED medications to enhance one's sexual experience rather than for ED was reported by 61.6% of ED medication users suggesting some medication misuse. The following effects or sexual functioning were endorsed by ED medication users: firmer erections (68.3%), longer lasting erections (70%), increased sensation (36.7%), increased sexual desire (36.7%), more intense orgasm/ejaculation (30%), ability to have sex multiple times in one session (40%), ability to delay orgasm (35%). Conclusion: About a third of substance abuse treatment applicants had used ED medications previously. Although the majority obtained ED medications by prescription, non-prescribed use was common. Use of ED medications to enhance sexual experience rather than to treat ED was also common. Most ED medication users experienced an improvement in erectile function and about a third endorsed other sexual enhancements associated with ED medication use.

164 WOMEN'S ALCOHOL CRAVING AND SYMPTOMS IN EARLY RECOVERY

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Objective: This descriptive longitudinal study examined the relationship between physical and psychological symptoms and alcohol craving reported by women during their 2nd, 3rd and 4th months of recovery. Method: Alcohol-dependent women (n=16) with a goal of abstinence from drugs and alcohol were recruited from the community. They reported craving, depression and symptoms of psychophysiological activation weekly for 12 weeks based on obsession items from the Obsessive Compulsive Drinking Scale (OCDS), the Beck Depression Inventory (BDI) and the Symptoms of Stress Inventory (SOS) respectively. Women also reported weekly use of alcohol, nicotine, psychoactive drugs and prescription medications. In the analysis, two groups emerged: Abstainers (n=10) who used no alcohol or drugs across time and Relapsers (n=5) who used substances intermittently. The analysis focused on 1) the association of craving and depression using correlations 2) differences in craving pre and post relapse using t-tests and 3) patterns of symptoms and craving across time using intercept, slope and R2. Results: OCDS scores ranged from 0 to 24 and BDI scores from 0 to 38. Significant correlations were observed between the BDI and OCDS scores averaged across weeks 10-12 (r=.56), but not across weeks 1-3. The OCDS scores for the relapse week and the week following relapse (M=8.50, SD=3.08) were significantly higher than those 2 weeks prior to relapse (M=5.63, SD=3.42) (t=5.19, p=.014). The pattern of change revealed a linear decrease in SOS scores for Abstainers (R2=.45), but not for Relapsers (R2=.12). Four of the 5 Relapsers used prescribed medications (narcotics, tranquilizers or sedatives) immediately prior to relapse. Conclusions: The significant association between depression and craving and the rise in craving with relapse are consistent with literature linking depression and craving to CNS dysregulation from substance abuse. They highlight the importance of managing depression and promoting abstinence in alcohol-dependent women in early recovery. This study was supported in part by NIDA grant T32 DA07257, Sigma Theta Tau and the Hester McLaws fund.

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- 165** COMPARISON OF THE EFFECTS OF (±)3,4-METHYLENEDIOXYMETHAMPHETAMINE, (±)3,4-METHYLENEDIOXYAMPHETAMINE AND D-METHAMPHETAMINE ON R. D. Crean, S. A. Davis, S. N. Von Huben, C. C. Lay, S. N. Katner and M. A. Taffe, The Scripps Research Institute, La Jolla, CA

Rationale: Recreational "Ecstasy" pills thought to contain (±)3,4-methylenedioxyamphetamine (MDMA) frequently include other substituted amphetamines such as (±)3,4-methylenedioxyamphetamine (MDA) and d-methamphetamine (METH). Hyperthermia is a critical factor in Ecstasy-related Emergency Department visits and fatalities, and the degree of hyperthermia is related to the severity of MDMA-induced neurotoxicity in animal studies. Given that the majority of Ecstasy pills are contaminated with other amphetamines, the etiology of thermoregulation is unclear. Objective: To determine the relative thermoregulatory disruption produced by recreational doses of MDMA, MDA and METH in nonhuman primates. Methods: Body temperature and spontaneous home cage activity were monitored continuously in six male rhesus monkeys via radiotelemetric devices. The subjects were challenged intramuscularly with 0-2.4 mg/kg (±)MDMA, 0-2.4 mg/kg (±)MDA and 0-1.0 mg/kg METH in a randomized order. Results: Temperature was significantly elevated by all three substituted amphetamines, and the increase was not dose dependent. A disruption of nighttime circadian cooling was observed as long as 18 hours after 1.0 mg/kg METH and 1.78-2.4 mg/kg MDA, but not after MDMA. With the exception of 0.32 mg/kg METH, activity levels were not increased. Conclusions: All three substituted amphetamines produce hyperthermia in rhesus monkeys and these effects do not depend on elevated locomotor activity. These studies establish a novel model of thermoregulatory disruption associated with substituted amphetamines. The results further our understanding of the risks posed by recreational Ecstasy exposure, clinical MDMA use, and help to refine preclinical models of exposure to substituted amphetamines.

- 167** SALIENCE OF FOLLOW-UP RESEARCH INCENTIVES AS A FUNCTION OF MAGNITUDE AND MODE OF PAYMENT: GENERALIZABILITY TO HIGHER PAYMENT MAGNITUDES

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Research participants are typically promised monetary compensation for completing follow-up assessments. However, it is unclear how well this compensation is retained. If the compensation is not remembered, it is unlikely to serve as an effective incentive. Our previous research randomly assigned outpatient drug treatment clients to receive \$10, \$40, or \$70 in either cash or gift certificate to examine whether the amount and/or mode of compensation affected their ability to recall the compensation and whether their recall reduced the effort required to contact them for their follow-up assessments. Results suggested that offering participants higher value and cash compensation increased the salience of the compensation at 6 months following admission, leading to higher follow-up rates. The current study attempts to extend the previous findings to larger magnitude incentives (\$70, \$100, \$130, or \$160 in either cash or gift certificate). We randomly assigned 250 outpatient drug treatment clients to one of these conditions and contacted them 2 weeks prior to their scheduled 6-month follow-up to remind them of their appointments and to ask if they recalled the amount and type of compensation they were scheduled to receive. We were able to contact 160 (64%) of the participants. Similar to previous findings, results indicated that participants promised cash compensation were more likely to recall the amount (78% vs. 63%; $p < .05$) and type of compensation (89% vs. 63%; $p < .01$). Those who correctly recalled the type of compensation also required significantly fewer calls to be contacted (4.5 vs. 6.5; $p < .05$). Contrary to previous findings, magnitude of incentives was not significantly associated with better recall or a reduced number of calls. These results suggest that at compensation amounts over \$70, the type rather than the amount of compensation increases the salience of the promised compensation and that this salience may lead to higher follow-up rates. Supported by NIDA grant #R01-DA-13408

- 166** IS METHAMPHETAMINE ADDICTION TOO DIFFICULT TO TREAT?

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Over the past five years, Los Angeles has seen an increase in the number and percentage of treatment participants who report methamphetamine as their primary drug for all race/ethnic groups except African-Americans. Historically, cocaine and alcohol were the two most commonly reported primary drugs. Starting in 2004, methamphetamine supplanted both of these substances as the most commonly reported primary drug for many race/ethnic groups. In the county of Los Angeles, treatment is defined as either residential or non-residential (e.g., outpatient). Treatment outcomes differ depending on the type of treatment, the route of administration for the drug, and the demographics of those being treated. There is growing concern that methamphetamine addiction is more difficult to treat versus other stimulants, such as cocaine. Although analyses show specific treatment outcomes differ, primary methamphetamine users do produce reductions in their primary drug use that are comparable to primary cocaine users. Furthermore, other areas of functioning such as reported physical and mental health problems also decrease at levels similar to those who report primary cocaine use. The differences appear when comparing the type of treatment (residential and outpatient). Primary cocaine users remain in treatment longer when in residential treatment when compared to primary methamphetamine users who are also in residential treatment. In addition, primary cocaine users in residential treatment have better admission to discharge reductions in drug use when compared to methamphetamine users also in residential treatment. When examining outpatient treatment, the opposite is true, methamphetamine users remain in treatment longer and have better outcomes than compared to primary cocaine users in outpatient treatment. These results will be considered given the state of the treatment system in Los Angeles County and the dynamics of treating an ever increasing number of methamphetamine users.

- 168** WEIGHT GAIN FOLLOWING SMOKING CESSATION AMONG FEMALE PRISONERS

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Concerns of weight gain among female smokers are high and some women use smoking to control weight. The impact of weight on smoking cessation has not been investigated with female inmates during a smoking cessation intervention, even though it is estimated that 80% of women smoke in prison. This study was a randomized controlled trial to determine changes in weight during a group smoking cessation intervention with female prisoners (10-week group intervention combined with NicoDerm CQ). 147 participants signed informed consent and had complete weight data at 3 month follow-up; 113 intervention and 94 controls were compared for weight change over three and six months. The sample was evenly split between Caucasians (47.2%) and African Americans (43.8%) with most women having a high school degree/GED or higher education (70.6%). The average age was 33.1 years (SD = 8.6) and most participants had never been married (45.8%) or were divorced (30.6%). Both groups lost weight over three and six months, however controls had lost significantly more weight compared to intervention participants at 3 months (-4.1 lbs vs. -1.1 lbs; $p = .014$) and 6 months (-6.7 lbs vs. -2.7 lbs; $p = .067$). At 3 months, 30% of participants in the intervention group had quit smoking. Participants who completed the intervention and quit smoking were compared to participants who continued smoking for weight change at 3 months. Participants who continued to smoke had lost weight while participants who quit smoking had gained weight (-2.0 lbs vs. 0.8 lbs; $p = .058$). By six months, 18% of participants had quit smoking. Participants who continued smoking had lost weight while participants who quit smoking had gained (-4.8 lbs vs. 5.4 lbs; $p = .011$). These findings support previous studies from smokers in the general population that indicate modest weight gain following smoking cessation. Future studies should focus on combining weight control strategies with smoking cessation in a female prisoner population for optimal health benefits.

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- 169** A PAPER-PENCIL ABUSE-NEGLECT ASSESSMENT FOR YOUNG ADULTS WITH SERIOUS SUBSTANCE AND CONDUCT PROBLEMS: VALIDITY
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Abuse-neglect experiences are significantly associated with adolescent substance and conduct problems (SCP). Quantitative measures of such experiences could comprise "measured environmental influences" in genetic epidemiologic studies, but our Colorado Adolescent Rearing Inventory (CARI), an interview assessing abuse-neglect experiences, is too lengthy for large-scale studies. HYPOTHESIS: Scores on the CARI will correlate favorably with scores on a briefer CARI-Questionnaire (CARI-Q). METHODS: Subjects: 1 current and 59 former patients (23 females) treated for serious adolescent SCP, now 18-23 yrs old. During treatment all had completed the 20-45 min CARI interview (51 items with additional probe questions). A mean of 4.9 yrs later all again completed CARI and the CARI-Q, a 10-20 min, paper/pencil CARI-based assessment with 20 stem questions. RESULTS: Spearman correlations: 1st CARI vs. 2nd CARI, 0.76 ; 1st CARI vs. CARI-Q, 0.72 ; 2nd CARI vs. CARI-Q, 0.71 (each $p < 0.0005$). Within subjects differences were small between 2nd CARI score and CARI-Q score (mean 0.78 items; SD 1.2). Individuals' endorsements of most CARI-Q items agreed well with their endorsements of corresponding 2nd CARI items (for 18 of 20 CARI-Q items, kappa's 0.4-1.0, p 's < 0.0005). CONCLUSIONS: Strong correlations with the CARI, previously demonstrated to have discriminative validity, support the validity of CARI-Q in young adults previously treated for SCP. CARI itself shows strong long-term test-retest reliability in that group. Grant Support: NIDA DA-009842, 011015, 012845; NIMH MH-01865
- 170** TOLUENE PRODUCES ANTIDEPRESSANT-LIKE EFFECTS IN THE FORCED SWIMMING TEST
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It has been reported that adolescents with inhalant abuse or dependence are significantly more likely to have major depression episodes and suicide attempts, than adolescents who have never used inhalants. In spite of this, to our knowledge, there are no studies addressing the actions of inhalants in animal models of depression. The purpose of this work was to provide a first screening of the action of toluene inhalation in an animal model of depression, the forced swim test (FST). To this aim, two experiments were done. In the first one, male mice were exposed to toluene (0, 1000, 2000, 4000 parts per million (ppm)) in a static exposure chamber for 30 min, and immediately after evaluated in the FST for 10 min. The results were compared with those obtained from mice treated with the antidepressants chloripramine and desipramine (0-20 mg/kg i.p.). Toluene produced antidepressant-like effects manifested as a significant decrease in the total time of immobility in a concentration-dependent manner similarly to that produced by the antidepressants used as control. In the second experiment, the long-term effects of toluene (8000 ppm) in the male offspring of pregnant rats were evaluated. Dams were exposed to air or toluene for 30 min, twice daily, from gestational day 8 (GD8) through GD20. The male offspring was tested on postnatal day 30 (PN30) and PN90 in the FST. Results showed that mice prenatally exposed to toluene presented significantly less immobility on PN30 than those exposed only to air. This effect cannot be attributed to a general increase in locomotor activity because toluene prenatal exposure decreased, rather than increased this behavior in the open field test. It is concluded that toluene produces antidepressant-like effects, which should be further characterized both pharmacologically and behaviorally. This research was partially supported by grants No. 43604-M (to S.L.C.) and 40895-M (to C. L-R) from Conacyt.
- 171** EFFECTS OF HIGH-DOSE METHADONE MAINTENANCE ON BEHAVIORS MOTIVATED BY COCAINE, RECEPTIVE FEMALES AND PALATABLE FOOD IN MALE RATS
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It has been demonstrated that high-dose methadone maintenance is efficacious in reducing cocaine abuse in opioid-dependent individuals, but it is not clear whether this is caused by an action of methadone on the direct reinforcing properties of cocaine. In rats, high-dose methadone maintenance via osmotic mini-pups (30-55 mg/kg/day, sc) blocks cocaine seeking behavior without altering intravenous cocaine self-administration on a continuous schedule of reinforcement. Furthermore, recent in-vivo microdialysis studies showed that methadone maintenance does not reduce, and even enhances, cocaine-induced elevations in dopamine concentration in the nucleus accumbens. However, when response requirements for intravenous cocaine infusions are higher (progressive ratio schedule), animals maintained on methadone show significant reductions in cocaine self-administration. Additionally, the same doses of methadone maintenance also reduce sexual behaviors directed toward receptive females in bilevel chambers that force males to chase the females, but not consumption of easily obtainable palatable food. Taken together these results suggest that high-dose methadone maintenance does not interfere with the direct reinforcing effects of cocaine, but effectively reduces the intensity of behaviors motivated by cocaine, cocaine conditioned stimuli and other natural incentives, especially when these stimuli are not readily accessible.
- 172** DECISION-MAKING DEFICITS AND SOCIAL ADJUSTMENT IMPAIRMENTS IN BRAZILIAN CRACK COCAINE USERS
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Background: the orbitofrontal cortex (OFC) is a part of the prefrontal cortex (PFC) that is associated to executive cognitive functions (ECF), decision-making and social behavior. Neurological patients with OFC lesions show deficits in social adjustment and personality changes. Recent studies have shown that cocaine-dependent patients present OFC abnormalities in the brain. However, few studies have examined the association between cognitive deficits and social functioning in drug users. The aim of our study was to investigate the neuropsychological deficits and social adjustment in crack cocaine users. Methods: we used the Brazilian version of the Social Adjustment Scale (SAS) and two neuropsychological instruments: Wisconsin Card Sorting Test (WCST) and Iowa Gambling Task (IGT). The COC group was composed by twelve crack cocaine dependent patients diagnosed by DSM-IV criteria (APA, 1994), abstinent for two weeks. The cognitive performance of the COC group was compared to a control group (CON) which included 12 paid volunteers without substance dependence, psychiatric illnesses and neurological disorders. Results: there were no statistically significant differences between COC and CON in age, ethnicity, socioeconomic background, intelligence and education ($p > .05$). Neuropsychological performance in the WCST did not reveal any statistically significant difference when comparing the groups. Nevertheless, COC performed more poorly than CON in the SAS ($p = .0001$) and IGT ($p = .0375$). We also found some evidence of correlation between SAS and IGT ($rS = -0.59$; $p = .0518$). Conclusion: these data provide evidence that Brazilian crack cocaine users show not only marked decision-making deficits when compared to a control group but also social adjustment impairments that could be related to OFC dysfunction, a possible consequence of the long-term effects of substance abuse. We believe that these findings have some implications to real-life situations, clinical decisions and to addiction research.

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173 SMOKING CUE-INDUCED BRAIN ACTIVITY SHORTLY AFTER QUITTING

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Background: We investigated smoking cue-induced brain activities in recently abstinent smokers recruited from a smoking cessation program. **Number of subjects:** A total of 20 subjects were included in the study. Six subjects had to be excluded due to technical problems or subjects' violations of the protocol. **Procedures:** At the time of testing, subjects were abstinent for ten days on average. Participants were shown pictures with smoking-related, neutral or control stimuli, each for 4 sec (plus 10 sec resting period). Current level of nicotine craving (scale 0-6) was assessed immediately before and after scanning. During the experiment a total of 504 gradient echo EPI-volumes (TR=2500 ms, TE=50 ms, flip angle=90, 24 transversal slices parallel to AC-PC-line, FOV=220x220, in-plane resolution=64x64, 5mm thickness, gap 0.5 mm) were acquired on a 1.5T Siemens MR scanner. **Statistical Analyses:** Spatial preprocessing and statistical data analyses were conducted using SPM2. **Smoke, neutral and control picture onsets** were modelled as HRF regressors in an event-related design, including additional regressors for temporal derivatives and realignment parameters. Contrast images for the comparison "smoking minus neutral" were computed on single subject level, and entered into a "random-effects" correlational analysis, with craving level as covariate. **Results:** Craving levels were positively correlated with higher activation levels (voxelwise p10 voxels) in a large region of the posterior cingulate. Further activations were seen in the dorsal anterior cingulate, anterior insula, and motor-related areas. **Conclusions:** These data extend previous reports of cue-induced brain activity in smokers, which mostly studied active smokers with abstinence durations <24h. The correlational relationship to experienced craving level emphasizes the role of the affective/ withdrawal status in cue reactivity.

174 SYSTEMIC DISEASE AMONG CASES OF FATAL OPIOID TOXICITY

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Aims: Determine levels of systemic disease among cases of death due to opioid toxicity; and compare these to a comparison group of non-drug related deaths. **Design:** Case control of 841 cases of death due to opioid toxicity, and a comparison group of 360 cases of death due to hanging. **Findings:** Ventricular hypertrophy was present in 5.9% of opioid cases and severe coronary artery atherosclerosis in 5.7%. Opioid cases were more likely than controls to have ventricular hypertrophy and severe atherosclerosis. Severe coronary pathology was more pronounced amongst older opioid cases. Pre-existing bronchopneumonia was present in 13.2% of opioid cases, who were more likely than controls to be diagnosed with bronchopneumonia, bronchitis, and pulmonary fibrosis. Liver pathology was particularly common among opioid cases, who had a higher likelihood of lymphocytic infiltrate (43.0 v 4.7%), steatosis (37.3 v 24.2%), fibrosis (10.6 v 1.9%), cirrhosis (7.4 v 0.8%), hepatomegaly (5.2 v 1.7%) and hepatic necrosis (5.0 v 0.3%). Hepatic pathology was more marked amongst older cases. Cirrhosis was present in 7.4% of opioid cases, including 25.3% of those aged >44yrs. Levels of renal pathology were comparatively low, but opioid cases were more likely to be diagnosed with nephrosclerosis. The only pathology for which gender was an independent predictor among opioid cases was ventricular hypertrophy, more common in males. **Conclusions:** Systemic disease, most prominently liver disease, is common among fatal opioid toxicity cases, and would appear to be a factor in understanding the dynamics and age demographics of opioid-related death.

175 ADOLESCENT PRESCRIPTION OPIOID ABUSE AND MISUSE: SURVEILLANCE BY POISON CENTERS

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Objective: As prescription drug abuse and misuse continues to rise, there is growing concern about the abuse of prescription opioids by adolescents. Our objective was to describe the adolescent exposures to prescription opioids reported by poison centers (PCCs). **Methods:** PCCs use a standardized electronic data collection system to manage and record spontaneous calls from the public and health professionals throughout their service areas (urban, suburban, rural). 15 geographically dispersed PCCs serving 102 million US residents participated in the study. Calls during 2004 involving intentional exposure to one or more of 7 opioid analgesics (i.e., buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone) by individuals aged 12-17 years. A rate was formed by dividing the number of exposure calls to PCC for each drug using two alternative denominators: 1) Population (2000 Census), 2) Unique Recipients of Dispensed Drugs (URDDs), which is the number of individuals that actually filled a prescription for the drug of interest during a given calendar quarter. **Results:** Of 12,310 exposures reported to PCCs, 8% involved patients aged 12-17 years. The call rates by type of exposure were: 1) suicide: 3.84 per million population; 2) abuse: 2.81; and, 3) "intentional unknown:" 1.45. The population-based rate of exposure calls per drug was: hydrocodone 5.59 per million; oxycodone 2.05; methadone 0.55; morphine 0.43; fentanyl 0.15; hydromorphone 0.07; and buprenorphine 0.06. The URDD-based rate per drug was: buprenorphine:12.95 per thousand URDDs; methadone: 11.30; morphine 5.88; hydromorphone 3.44; oxycodone 3.16; hydrocodone 2.96; and fentanyl 1.97. **Conclusion:** Suicide and abuse are the most frequent exposures associated with prescription opioids in the 12-17 year age group. The exposure rate per million population was highest for hydrocodone and oxycodone; in contrast, the exposure rate per million URDDs was highest for buprenorphine and methadone.

176 DISTRESS TOLERANCE AS A PREDICTOR OF ADOLESCENT SUBSTANCE USE

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The problem of substance use among adolescents continues to grow despite large-scale public health efforts to reduce both its incidence and prevalence. Current evidence indicates that early adolescents high in negative emotionality who exhibit avoidant coping techniques are at an especially high risk for using substances in times of emotional distress. Relatedly, researchers in the adult substance use literature have begun to utilize behavioral measures of distress tolerance to assess one's ability to effectively cope with emotional distress. Indeed, distress intolerance has consistently been associated with substance use among adults. Hypothesizing that similar processes are occurring among early adolescents, we measured levels of distress tolerance among a community sample of 66 10-11 year olds as an indicator of self-reported past year alcohol and illicit drug use. Briefly, participants engaged in a challenging task that increased in difficulty until success on the task was virtually impossible. Participants were given a 'quit option' on the last level of the task yet instructed that their performance would determine their reward at the end of the session. The sample was 65.2% male with a mean age 10.9 (SD = 0.9). In addition, the sample was diverse and representative of the Washington, DC community with over 50% indicating minority status. Twenty one percent (n = 16) of the sample reported any past year alcohol use (<1% of the participants indicated past year illicit drug use). As expected, 68.8% of participants who reported alcohol use terminated the task early (i.e., distress intolerance), compared with only 31.2% of participants who did not use alcohol (p < .05). Further, these findings persisted after controlling for demographic and mood related variables. Future directions and treatment implications will be discussed.

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- 177 DRUG PREEXPOSURE IN FISCHER (F344) AND LEWIS (LEW) RATS: EFFECTS ON PLACE AND TASTE CONDITIONING**
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Although the LEW and F344 rat strains differ in their reactivity to a number of drugs, these assessments are generally in acute preparations. Little is known if these strains differ following chronic exposure or if they differ from outbred rats under such conditions. To address this, rats from both strains were preexposed to either morphine or cocaine and the ability of each of these two drugs was assessed for its ability to condition a taste aversion and place preference using a combined CTA/CPP procedure. Specifically, 57 F344 and 59 LEW rats were preexposed to cocaine (32 mg/kg, ip), morphine (5 mg/kg sc) or vehicle every other day for 10 days. They were then given a saccharin solution, injected with cocaine, morphine or vehicle and placed on the smooth side of a conditioning apparatus. On the next day, they received access to water, injected with vehicle and placed on the textured side of the apparatus. After four trials, they were given a CPP and a CTA test. A 5 (Trial) X 2 (Strain) X 2 (Preexposure) repeated measures ANOVA revealed a significant three-way interaction [$F(3,60) = 16.587, p = .001$] with only the F344 rats acquiring a morphine-induced CTA; the CTA was significantly attenuated by morphine preexposure. Both LEW and F344 rats acquired a morphine-induced CPP that was unaffected by morphine preexposure. Both strains acquired a cocaine-induced CTA that was significantly attenuated by cocaine preexposure, $F(3, 84) = 84.565, p = .000$. Neither group displayed a cocaine-induced CPP at this dose, and the preference for the cocaine-associated side was unaffected by drug preexposure. Drug history impacted aversion learning in a manner similar to that of outbred rats (i.e., attenuation) with no differential pattern for the two strains. Drug preexposure did not impact CPPs in either strain, a result inconsistent with that in outbred rats that show a potentiated preference. Such findings may have implications for the use of the F344 and LEW strains as animal models of drug use and abuse.

- 179 CLINICAL EVALUATION OF MDMA-INDUCED NEUROTOXICITY**

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A number of animal studies suggest that MDMA may be neurotoxic in humans. Results from clinical studies show mainly mild disorders in neurocognitive performance. A three years follow-up study was undertaken to evaluate mid-longterm toxicity induced by MDMA. Population: 117 subjects, mean age 22.7 years (18-34 years), 41% males and 59% females. Distribution among study groups: MDMA (moderate consumption of alcohol, cannabis, cocaine and methamphetamine tolerated and controlled because difficulties in finding MDMA only users) $n = 39$, Cannabis (only) $n = 24$, Control (drug free) $n = 34$. Evaluations: All participants were subjected to a medical examination, EEG, routine biochemical tests and passed a questionnaire on their toxic habits (verified by drugs of abuse testing in urine and hair), diagnosed for psychopathology and substance abuse disorders following DSM IV (PRISM) criteria. Neurocognitive performance (battery of tests), immune system functionality (cytokines, immune cells sub-populations and functionality) were also evaluated. Controls were performed at 0, 6, 12, 24 and 40 months Results: MDMA are polydrug users, and are the only ones were new diagnoses of abuse and dependence are made along the study. The largest prevalence of psychopathology (affective, anxiety and nutrition disorders) is observed among MDMA users (19/37) and new diagnoses are only performed in this study group. Their neurocognitive performance is within the distribution of the normal population but poorer than the observed in the other study groups. Conclusions: MDMA induces sub-clinical alterations in cognitive performance, a higher prevalence of psychopathology is observed. Acknowledgements: This study was supported in part by "Neurotossicità a Lungo Termine dell'Ecstasy" project from Istituto Superiore di Sanità, Rome, Italy; Generalitat de Catalunya (2001SGR00407); Fondo de Investigaciones Sanitarias (FIS-00/00777); and Plan Nacional Sobre Drogas (INT/2012/2002), Spain

- 178 INDIVIDUAL VARIABILITY IN ADDICTION PROFILES: IMPORTANCE FOR MEDICATIONS DEVELOPMENT**

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The most common theories of addiction include Negative Reinforcement/Opponent Process (NROP), Pleasure Seeking (PS), Incentive Salience (IS), Habit/Stimulus-Response Learning (HSRL), and Impaired Neurocognition (NC). For the NROP theory, we assessed depression ratings in 10 methamphetamine (MA)-dependent volunteers. >70% of participants exhibited significant remission of symptoms ($p=0.025$) within 3 days of initiation of abstinence (in the absence of any treatment). For the PS theory, we examined responses of 20 MA-dependent volunteers to placebo or MA (30 mg, IV). Group means reveal extremely low or absent rankings for "High" (reflecting reward value) at baseline, no change after placebo, and significant increases ($p<0.005$) following MA. Individual data revealed a wide range in ratings of High, raising doubts for PS as a cause for ongoing use in a majority of dependent volunteers. For the IS theory, "Desire" subjective responses were examined in volunteers ($N=20$) after placebo or MA (30 mg, IV). Group means reveal that only 1/3 of participants reported craving at baseline (despite knowledge of impending access to the MA in the session), no change after placebo, and significant increases following MA ($p<0.005$). Individual data revealed a wide range of responses to craving after MA raising doubts for IS as a cause for ongoing use in a majority of dependent volunteers. HSRL and NC theories of addiction were assessed in MA-dependent volunteers ($N=15$) using an IV self-administration paradigm. A subset of individuals did not choose a single dose of MA (3 mg, IV) despite access to 10 infusions during a 2.5h session. These data raise questions regarding HSRL and NC as causes for ongoing use in MA-dependent volunteers. Overall, the data indicate that these theories of addiction do not fully explain the persistence of addiction in non-treatment seeking MA-dependent volunteers. We recommend research into the potential of targeting treatments for patients on the basis of their individual addiction profile. Supported by NIDA: DA-14593, DA-18185, DA-17754.

- 180 HALLUCINOGEN DEPENDENCE CLINICAL FEATURES SOON AFTER ONSET OF HALLUCINOGEN USE: U.S., 2003**

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AIM: To shed new light on hallucinogen (HA) user experiences, this study takes an 'analyze, then summarize' approach to data on individual clinical features of HA dependence soon after onset of use. This 'analyze, then summarize' approach differs from a prior 'summarize, then analyze' approach involving use of either latent structure methods or DSM-like algorithms. Here, we summarize experiences of recent-onset users as individual clinical features with multivariate methods used to take into account statistical interdependencies. METHODS: Data are from the 2003 National Household Survey on Drug Use and Health's 923 recent-onset HA users found within a nationally representative sample of 55,230 community residents. Users were asked about 9 clinical features of HA dependence (HDCF). Cumulative occurrence of HDCF was estimated with due attention to procedures appropriate for complex sample designs. RESULTS: Among 923 recent-onset users, the 2 most commonly occurring HDCF were (a) tolerance (same amount less effect), 4.5%, and (b) salience (spent a lot of time getting, using, getting over the effects of drug), 3.6%. Least common HDCF were: (c) physical problems (0.3%), and (d) unable to cut down (0.6%). CONCLUSIONS: This study's 'analyze, then summarize' approach is not elegant, but it provides a fine-grained view of the individual clinical features experienced by drug users in the first weeks and months after onset of drug use, while taking into account the statistical interdependencies among these HDCF. Subject to confirmation in later research, the earliest manifestations of incipient hallucinogen dependence may be seen in the development of tolerance and salience within months of first hallucinogen use. Whereas these clinical features are somewhat subjective and may be more difficult to detect than hallucinogen-associated psychiatric distress or socially maladaptive behavior, they might serve as 'canaries in the coal mine' and a guide during early public health outreach or intervention. SUPPORT: D43TW005819, K05DA015799, T32DA007292

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181 SUBSTANCE USE DURING PREGNANCY IN WEST CENTRAL MEXICO

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Substance use has increased among women in Mexico. However there is no reliable data about substance use and abuse during pregnancy, which comprises a very high interest group of patients (mother and child). As a first approach we looked at the hospital records of the largest General Hospital in the state and region (Hospital Civil de Guadalajara) and reviewed the statistics for 15,789 pregnant women who gave birth during the year 2004. Only 432 out of 15789 pregnant women reported to have used any kind of substance of abuse: 83 % smoked tobacco, 26 % used alcohol and 16.9 % used illegal drugs. Mean age was 25 years and the majority who were using some kind of substance were from low educational and economic status. Among the latter highest frequency was seen among single mothers. Alcohol use was highest among housewives with low or no education. We assume there is much under-registered information about substance use in our records. We hypothesize that mothers with low educational level do not worry much about the use of substances as they ignore the harm those produce, particularly in the fetus. Our second hypothesis is that pregnant women who continue using a substance during pregnancy may have a strong dependence limiting their abstinence. There should be preventive campaigns aiming to target the group depicted here. We plan to conduct a prospective survey with cohorts of unpregnant women with substance use with high chances to conceive and get pregnant.

182 HOSPITAL STAYS FOR DRUG-RELATED PSYCHOTIC EPISODES IN AUSTRALIA, 1993-2004

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Background: There has been increasing public attention focused upon cannabis use among young people, and associations with psychosis. Some have implied that cannabis use is increasing and that concomitant mental health problems may also be on the rise. However, heavy use of methamphetamine has increased in Australia and has also been related to drug induced psychosis. Aim: To examine trends in hospital stays due to "drug induced" and "alcohol induced" psychotic episodes (as diagnosed by clinicians). Data on illicit drug induced psychotic episodes were considered in the light of data on the patterns of cannabis and methamphetamine use in Australia. Method: Data from the National Hospital Morbidity Database (NHMD) were analysed from 1993 to 2004. Data on cannabis and methamphetamine use were obtained from the 2004 Australian National Drug Strategy Household Survey (NDSHS), a stratified random sample of Australians aged 12 years and over (n = 29,445). Results: There have been notable increases in hospital stays thought by clinicians to have been due to "drug-induced" psychosis. These increases appear to have been driven by increases in methamphetamine related episodes rather than cannabis. The rate of hospital stays was higher for amphetamine users than it was for cannabis users in all age groups, and the rate increased among older amphetamine users. Higher rates among younger cannabis users than older cannabis users might be related to patterns of use, with younger users more likely to report using large amounts per occasion of use. The rate of hospital stays for alcohol induced psychosis was higher among older groups and a more common cause of hospital stays among these older groups than illicit drug induced psychotic episodes. Implications: At present, although it is understandable that there is community concern about the potential for cannabis to induce psychotic symptoms among young people, it would seem that the risks associated with amphetamine use are greater and represent a greater issue for users in all age groups. Research is needed to examine these differences in greater depth.

183 CHARACTERISTICS OF PROBLEMATIC OPIATE USERS IN BORDEAUX (FRANCE). ROSE PROJECT

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Scarce data is available about the characteristics of problematic opiate users (POU) who are out-of-treatment or fail treatment. ROSE (Risk Opiate Study in Europe) was a European multi-centre study conducted in 10 European cities, to address this issue. Objective: To produce epidemiological data on POU and to describe samples of POU in Bordeaux, France. Methods: Review of collected data from local reports and standardized interviews of key informant (clinicians, administrators). POU were interviewed from in-treatment POU and out-of-treatment POU. Participants were recruited from outpatient drug treatment services and low-threshold programs. They were interviewed through a questionnaire derived from the Addiction Severity Index (ASI). Results: In Bordeaux, 2,800 inhabitants were estimated POU. 65% were currently in drug treatment. 92 % of these were in pharmacological maintenance treatments, and a minority (8 %) was in drug-free abstinence treatment. About 1,000 POU were out-of-treatment but 45 % had some contacts with health programs. 89 POU were interviewed (61 in-treatment, 28 out-of-treatment). In-treatment POU were significantly older and had received more previous treatments. Out-of-treatment participants used heroin, cocaine, hallucinogens and amphetamine more often. There was no difference between groups regarding lifetime substance use, age of first use or first substance used except for cocaine. ASI Drug composite scores, that reflected substance use impairment, were significantly higher for out-of-treatment participants. Compared to others European cities involved in ROSE, Bordeaux one of the cities where POU were most reached by treatment. Conclusion: POU in-treatment although treatment non-responder did better than POU out-of-treatment. However the design does not permit to say whether this was related to treatment. Some shortcomings in current treatment approaches might help to develop guidelines and standards in order to adapt drug services to the needs of POU in-treatment and help out-of-treatment POU to access treatment services.

184 EPIDEMIOLOGICAL EVIDENCE FOR A LINK BETWEEN PAIN AND OPIOID ABUSE

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Background: An increase in abuse of semi-synthetic opioids has been detected by numerous national epidemiologic studies. This is temporally related to an increase in the prescription of these drugs for chronic pain conditions. This study was performed to evaluate the association between pain and prescription opioid abuse or addiction. Methods: Data analyzed were from the National Epidemiological Study of Alcohol and Related Conditions (NESARC), 2002, a nationally representative study of the U.S. household population ages 18 and older (N = 43,093). The NESARC study defines functional impairment by four categorical levels. Rates of functional impairment due to pain (FIP) were calculated for the population as a whole and according to socio-demographic and DSM-IV disorder subgroups of personality, mood, and anxiety. The association of pain to each of the possible risk factors was estimated by adjusted odds ratios. Results: FIP was found in 71.2 million (35%) of adults in the U.S. population. The two highest, of 4, levels of FIP due to pain was found in 25 million (12%). FIP was more common in women and older age groups. African Americans and Hispanics were slightly more likely to report FIP than whites. Mood, anxiety, and personality disorders were associated with FIP. Opioid misuse and opioid disorders, and tobacco use and tobacco dependence were also significantly associated with FIP. However, use of (and disorders due to) alcohol and other illicit substances were not found to be associated with FIP. Discussion: This is the largest epidemiological study of the U.S. population to address the association of pain to DSM-IV psychiatric disorders, including substance use disorders. In this study, FIP was found to be positively associated with opioid misuse and opioid disorders, tobacco use and tobacco dependence. Therefore the presence of pain does not protect from opioid disorders, but may be a risk factor. Personality, mood, and anxiety disorders were also significantly associated with FIP possibly indicating a common etiology or correlates for these disparate conditions.

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185 CORRELATES OF LONG-TERM RECOVERY AFTER TREATMENT

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Clients often relapse and require multiple episodes of care before sustaining recovery. This study examines the correlates of long term recovery after treatment. Data are from 836 adults recruited between 1996 and 1998 from sequential admissions to a central intake and 12 treatment units on the west side of Chicago who were then interviewed annually for 7 years after intake (94% or more follow-up per wave). Participants were predominantly African American (90%), females (62%) treated for cocaine, alcohol, opioids, and marijuana. At year 7, they were classified into four groups using self report and urine tests: (a) still using, (b) using but less frequently than at 2-year, (c) short-term abstinence [1-11 months], and (d) long-term abstinence [1+ years]. Compared to those that continued to use, participants in long-term abstinence showed greater improvements in employment, income, health, and mental health outcomes, and virtually no illegal activity. Participants who achieved abstinence also report at the end of the study more support from family, friends, and from other sources more support and involvement in religious and spiritual activities; and greater belief in their ability to deal with their substance use problems. The findings indicate that achieving sustained abstinence accrues with it other positive benefits that improves the person life-functioning and supports the recovery process. (Supported by NIDA DA15523.)

186 HIV RISK REDUCTION FOR MIGRANT DRUG USERS: MMTP CLIENTS CONDUCTING PEER OUTREACH

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Hypothesis: Migrant drug users from Puerto Rico (PR) to NY are at higher risk of HIV than other users. An intervention in MMTPs trained clients to conduct peer outreach to PR migrant drug users, & trained staff about their HIV risks. Hypotheses: in intervention clinics, staff knowledge about risks of migrants would be greater; clients trained as peers and migrants (in communities where outreach was conducted) would reduce HIV risks and increase service use. # of Ss: 4 pairs of MMTP clients will participate in the study (4 intervention [I] and 4 comparison [C] clinics). This report is based on results for the 1st pair of clinics: 40 peers (20 I, 20 C) 33 MMTP staff (18 I, 15 C), and 69 street-recruited migrants (29 I, 40 C). Procedures: MMTPs in NY were randomly assigned to I or C conditions. In each MMTP, 20 clients were recruited who were bilingual & had used drugs in PR. Baseline intvs were conducted with staff & clients. In the I clinic: staff received a 10-hr training on risks of migrant drug users and advantages of using peers for HIV prevention; peers received a 35 hr training on outreach among migrant drug users and conducted outreach to community migrants for 3 mos. Follow-ups occurred after the 3-mo outreach and 3 & 6 mos post intervention. Focus groups and individual intvs were held in I clinic. Results: 78% of participants were male. Peers were less likely to be homeless (10% vs 23% of migrants), more likely to be HS grad (52% vs 30%). Migrants were more likely to be injecting (54% vs 10% of peers) & to report multiple sex partners (29% vs 8%). Preliminary analysis of follow-up: staff in the I clinic increased HIV knowledge. Qualitative findings: peers increased self-esteem and some were motivated to seek employment as outreach workers. Outcomes for risk behaviors and service use will be presented using multivariate analyses. Conclusions: MMTP clients can be trained as peer outreach workers for migrant drug users and staff training can increase knowledge about HIV risks of migrants. Peers can reach high-risk drug users and conducting outreach enhanced their self-esteem and motivation.

187 SPIRITUAL ORIENTATION AND ENGAGEMENT IN THERAPEUTIC COMMUNITY TREATMENT

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Spirituality has received increasing attention as a characteristic which may influence response to substance abuse treatment. The purpose of this study was to determine the extent to which personal spiritual orientation was associated with engagement in Therapeutic Community (TC) treatment. One hundred eighty-seven patients in residential TC treatment completed a survey assessing spiritual orientation to life, attitudes towards Twelve-Step approaches and engagement in TC treatment. Personal spiritual orientation was significantly associated with positive attitudes towards Twelve-Step meeting involvement including perceived benefit of AA and NA and endorsement of spirituality/Twelve-Step interventions in TC treatment. Personal spiritual orientation was significantly correlated with multiple indicators of engagement in TC treatment including acceptance of TC principles and work role status. The results of a multiple linear regression analysis indicated that spiritual orientation was the strongest predictor of TC clinical progress. These findings highlight the importance of integrating treatment approaches which address the spiritual needs of TC residents.

188 CONVERGENCE OF HIV SEROPREVALENCE AMONG INJECTING AND NON-INJECTING DRUG USERS IN NEW YORK CITY: A NEW STAGE IN A VERY LARGE HIV EPIDEMIC

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Objective: To compare levels of HIV infection among injecting and non-injecting heroin and cocaine users in New York City. As HIV is readily transmitted through the sharing of drug injecting equipment, HIV infection would normally be much more common among injecting drug users. Study Design: Two separate cross-sectional surveys, both with HIV counseling and testing and drug use and HIV risk behavior questionnaires. Settings: Drug abuse treatment programs and a storefront research office, all in New York City. Participants: Injecting and non-injecting heroin and cocaine users entering detoxification and methadone maintenance treatment from 2000-04 (N = 2121) and recruited through respondent driven sampling from a research storefront in 2004 (N = 448). Results: In both studies, HIV prevalence was nearly identical among current injectors (injected in the last 6 months) and heroin and cocaine users who had never injected: 13% (95% CI 12% to 15%) among current injectors and 12% (95% CI 9% to 16%) among never-injectors in the drug treatment program study, and 15% (95% CI 11% to 19%) among current injectors and 17% (95% CI 12% to 21%) among never injectors in the respondent driven sampling storefront study. There were overlaps in the 95% CIs in all gender and race/ethnicity subgroup comparisons in both studies. Conclusions: The very large HIV epidemic among drug users in New York City appears to be entering a new phase, in which sexual transmission may be equally or more important than injecting related transmission. New prevention programs are needed to address this transition.

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- 189 RISK FOR OPIOID ABUSE/DEPENDENCE IN NON-MEDICAL PRESCRIPTION OPIOID USERS: EVALUATING THE ROLE OF GENDER**
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The transition to prescription opioid abuse/dependence (POD) in non-medical users of prescription opioids is relevant to prevention and treatment. We analyzed the 2003 National Survey on Drug Use and Health, restricting our analysis to those reporting past year non-medical use of prescription opioids (NMUPO). We determined the association of specific demographic and clinical characteristics with POD using a multivariable logistic regression model and then stratified the model by gender. 4136/55230 (7.5%) of the respondents reported past year NMUPO; age range 12-80, 48% women, 73% white, 66% had > 12th grade education, 50% consistent past year employed, 32% consistent past year insured, 18% reported mental illness. Past year prevalences: 61% cigarette use, 57% alcohol use, 28% alcohol abuse/dependence, 53% illicit drug use/abuse/dependence, 28% sedative use/abuse/dependence, and 13% stimulant use/abuse/dependence; and lifetime prevalences of use: 60% hydrocodone, 38% oxycodone, and 15% oxycontin. On multivariable analysis, characteristics associated with POD: younger age (12-17 years) (OR 2.26; 1.36-3.75), uninsured in the past year (OR 1.86; 1.14-3.02), mental illness (OR 1.90; 1.30-2.78), past year sedative use/abuse/dependence (OR 1.75; 1.18-2.61), ever used oxycodone (OR 1.67; 1.14-2.46), ever used oxycontin (OR 2.62; 1.73-3.96), and no past year alcohol use (OR 4.51; 2.38-8.55). By gender, the risk for past year POD was present in women, but not in men, with mental illness (OR 2.32; 1.33-4.08), past year sedative use/abuse/dependence (OR 2.22; 1.27-3.88), and early age (1-11 years) initiation of illicit drugs (OR 4.48; 1.51-13.27). Among those with past year NMUPO, the risk for POD is greatest in those who are younger, without consistent insurance, with mental illness, with past year sedative use/abuse/dependence, ever used oxycodone products, and without past year alcohol use. In women, there is increased risk with early initiation of illicit drugs. These factors should influence screening, prescribing and treatment efforts designed to decrease the impact of POD.
- 190 PHARMACOPHORE FOR METHYLPHENIDATE AT THE DOPAMINE TRANSPORTER**
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A series of threo-1-aza-3 or 4-substituted-5-phenyl[4.4.0]decanes (quinolizidines), which we envisioned as restricted rotational analogs of methylphenidate (Ritalin), was synthesized and tested for inhibitory potency using [3H]WIN 35,428 (WIN) binding at the dopamine transporter(DAT), [3H] citalopram (CIT) binding at the serotonin transporter (5-HTT), [3H]nisoxetine (NIS) binding at the norepinephrine transporter (NET), and in some case the inhibition of [3H]dopamine uptake. The unsubstituted compound threo(trans)-1-aza-5-phenyl[4.4.0]decane shows the same potency ($K_i = 76.2$ nM) as threo-methylphenidate ($K_i = 74.6$ nM) in the WIN binding assay. Generally the restricted rotational analogs showed similar relative potencies to the corresponding methylphenidate derivatives in all of the binding assays; thus as compared to DAT, they have similar potency for the NET and low potency for the 5-HTT. The extra ring in these analogs, which reduces the conformational freedom, is of critical importance to the biological activity. Both the "broken ring" analog and the "no ring" analog had very low potency at the all the transporters. Analogs with substituents at the 4-beta position of the restricted rotational analog generally had higher potency than those with 4-alpha substituents. Compounds with non-polar substituents at the 4-positions were much more potent than those with polar substituents. In addition, a quantitative explanation of the "3,4-dichloro" effect is offered. All of these observations allow for a fairly detailed description of the pharmacophore.
- 191 S-(+)-GAMMA VINYL-GABA (S-GVG) BLOCKS THE RESPONSE TO METHAMPHETAMINE (METH) IN ADOLESCENT AND ADULT ANIMALS TREATED WITH METH AND S-GVG DURING ADOLESCENCE**
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Racemic GVG dose-dependently blocked the biochemical and behavioral effects of cocaine, methamphetamine (METH), amphetamine, heroin, morphine, alcohol, nicotine and their combinations in adult male Sprague-Dawley rats (Schiffer, et al., 2004). In addition, we completed two small open-label clinical trials using racemic GVG in cocaine and METH abusers (Brodie, et al., 2003; 2004). These studies suggested clinical efficacy and demonstrated visual safety (Fechtnr, et al., In Press). Here, we used small animal imaging in combination with 11C-raclopride (11C-rac) and 18FDG to examine the effects of S-GVG on METH-induced increases in brain dopamine and metabolism, respectively. Adolescent animals (30 days old) received baseline microPET scans (R4, CTI, USA) using 11C-rac and 18FDG. Then animals received a METH challenge (1.0 mg/kg, iv) followed by another set of 11C-rac and 18FDG scans. METH significantly reduced the striatal BP of 11C-rac (increase in dopamine) by approximately 22% and increased 18FDG uptake cortically, subcortically, and in the cerebellum. There were no effects of METH on occipital 18FDG uptake. However, an acute dose of S-GVG (150 mg/kg; 2.5 hrs prior to a METH challenge) completely abolished these increases just as it blocked the expression of METH-induced conditioned place preference (CPP). These adolescent animals were then placed on S-GVG (150 mg/kg/day) for 5 days which blocked METH-triggered reinstatement of this expression. As adults (> 90 days old), these animals received another METH challenge during 18FDG uptake. Adolescent exposure to S-GVG attenuated METH-induced changes in 18FDG uptake in these adult animals and suggests that it may be an effective strategy for blocking the biochemical and behavioral effects associated with METH abuse. USDOE/OBER DE-AC02-98CH10886 and NIH DA15041, DA16025, DA15082
- 192 IMPULSIVITY AND AGE OF FIRST ALCOHOL CONSUMPTION AS RISK FOR DRUG AND ALCOHOL ABUSE IN MALE ADOLESCENTS**
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Background: Impulsivity and age of first drink have been independently associated with drug and alcohol dependence in clinical samples. However, few studies have investigated these factors in non-clinical samples, particularly adolescents. Objective: To evaluate the association between impulsivity and age of first drink with drug or alcohol abuse. Method: A case-control study of male adolescents between 15 and 20 years nested in a community survey of a low income population from southern Brazil was conducted. Drug or alcohol abusers were selected as cases (n=60) and compared to 404 non-abusers that served as controls. Cases and controls were defined according to DSM-IV abuse criteria. Impulsivity was measured by the Barratt Impulsivity Scale (BIS). Odds ratio (OR) were estimated through logistic regression in a hierarchical model. Results: The mean age was 17.3 ± 1.7 years, 8.7 ± 2.2 years of schooling, with a median family income of US\$348, and 69% were white. The final model after logistic regression included the following variables, in the first level: years of schooling of the father; second level: impulsivity scores categorized in tertiles; third level: number of school failures and age; fourth level: age of first drink categorized in tertiles. Impulsive subjects (BIS>66) had an OR of 3.3 (1.4-7.6) and age of first drink 13 or less OR of 4.7 (1.5-14.8). Conclusion: Though limited by the cross-sectional nature of the design, the findings suggest that impulsivity and precocity of first drink are strongly associated with a greater odds for alcohol and drug problems. Temporality and dose-response of the association should be checked in a longitudinal design.

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- 193 PREDICTIVE VALIDITY OF FOUR NICOTINE-DEPENDENCE MEASURES IN A COLLEGE SAMPLE**
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Objective: The present study compared the predictive and incremental validity of four commonly used dependence measures (Diagnostic and Statistical Manual-IV [DSM-IV] nicotine dependence criteria, Fagerstrom Test for Nicotine Dependence [FTND], Hooked On Nicotine Checklist [HONC], Nicotine Dependence Syndrome Scale [NDSS]) in a first year college sample reporting relatively light smoking patterns. Method: Participants who reported smoking during the past week completed the nicotine dependence measures at the end of the first semester. The present analyses included 95 participants who completed the web-based surveys at the end of their first semester and at the end of their first year and 55 participants who completed the follow-up survey at the end of the second college year. Logistic and linear regression analyses were conducted to examine the ability of each nicotine dependence measure to predict continued smoking, quantity, frequency, and length of smoking abstinence at each follow-up. Results: Higher levels of dependence as measured by the HONC and DSM-IV symptoms and diagnosis significantly predicted continued smoking at the end of the first academic year. The DSM-IV measure continued to predict second year smoking status. In addition, the HONC and DSM-IV measures significantly predicted smoking quantity and frequency at the end of the first and second year. Higher scores on the NDSS-Total, NDSS drive, and NDSS-tolerance factors predicted higher smoking quantity and frequency during follow-up assessments. Higher dependence scores on all four measures were related to shorter lengths of smoking abstinence. DSM-IV measures and NDSS-priority and tolerance scores continued to predict follow-up smoking behavior after controlling for initial smoking quantity. Conclusions: These findings suggest that some nicotine dependence measures successfully predict future smoking among light smokers.
- 194 CONSUMPTION OF BENZODIAZEPINES AMONG DRUG ADDICTS IN ÎLE DE FRANCE AREA: COURSE OVER 5 YEARS**
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The Centers of Evaluation and Information on Pharmacodependance (CEIP national network in drug dependence monitoring) developed tools allowing the monitoring of the psycho-active substances misuse. One of them, OPPIDUM program (Observation of Illegal drugs and misuse psychotropic medications) is an annual, national and multicentric pharmacoepidemiological study describing consumption profile of substances. Based on OPPIDUM results, we looked at the course of the consumption of benzodiazepines and related (BZD) among the patients consulting in structures of care specialized between 2000 and 2004. 32% of outpatients reported to consume at least one BZD. They were mostly men (72%) and their mean age was 37.4 years. 61% of them lived under unfavourable socio-economic conditions. Polydrug use was noted in 96 % of the cases with an average number of products of 3.3. The BZD were consumed orally in 98%, in a daily way in 82% and since more than one year in 55% of the cases. The BZD were got through illicit way in 15%. Whereas flunitrazepam was the BZD of choice for the drug addicts during the Nineties, its consumption decreased, presumably due to the new health regulator limiting its prescription and its delivery, and seemed to be replaced by other BZD such as bromazepam. Consumption of clonazepam and zopiclone also seems to increase gradually. This trend is confirmed by the Nots data (data from spontaneous notification).
- 195 THE LONG-TERM INFLUENCE OF ANTISOCIAL BEHAVIOR ON DRUG USE PATTERNS**
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Although prior research shows a relationship between antisocial behavior and early onset of drug use and dependence, little is known about its influence on these outcomes through mid-adulthood. A community cohort of African-American inner-city males and females has been followed from childhood through adulthood (first grade, age 16, age 32, and age 42). Nonparametric survival analyses and log-rank tests of significance were used to estimate the age of first use of marijuana, cocaine, and heroin, and the first symptom of drug dependence for any illegal drug. Survival curves were compared for those in the top and bottom 20 percent of the distribution of a 23-item scale of self-reported adolescent antisocial behavior (N=584). Results indicated that antisocial behavior is linked to onset of each drug throughout the life span. For example, on average, those in the top 20 percent of the delinquency distribution first used cocaine at age 23 while those in the bottom 20 percent first used cocaine at age 26. Log-rank tests indicated that the survival curves for cocaine incidence were statistically different through age 42 ($\chi^2 = 25.59$, $p = .000$). Also, while incidence accumulates for all levels of antisocial behavior, it is considerably higher for those who were most delinquent in adolescence as opposed to least delinquent (42.3% vs.11.8%, respectively). Similar results emerged for marijuana ($\chi^2 = 39.11$, $p = .000$; 69.5% vs. 34.5%) and heroin use ($\chi^2 = 17.70$, $p = .000$; 17.5% vs. 2.7%). Similar differences in cumulative incidence of drug dependence emerged (31.2% vs. 7.5%) yet the difference in the curves were only statistically significant for females ($\chi^2 = 15.05$, $p = .001$). Overall, these results suggest that antisocial behavior in adolescence continues to play a role in predicting onset into substance use and dependence throughout adulthood. Further investigation into whether antisocial behavior continues to predict patterns of substance use and dependence in a multivariate framework and an examination of whether antisocial behavior predicts time from first use to dependence are needed.
- 196 PERFORMANCE OF STROOP TASKS BY SMOKERS AND NON-SMOKERS: DO CIGARETTE SMOKING AND WITHDRAWAL AFFECT SELECTIVE ATTENTION?**
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Although difficulty in concentrating is a diagnostic feature of nicotine withdrawal, laboratory findings on this point have been inconsistent. We therefore tested the effects of overnight abstinence from smoking (as well as acute smoking and smoking history) on selective attention, using Stroop tasks. Our goal was to determine whether smokers and non-smokers differ in selective attention, whether overnight abstinence from smoking impairs performance by smokers, and whether smoking a cigarette improves performance by smokers. Smokers and non-smokers were tested with Color-Word Stroop (n's = 31 and 43 for smokers and non-smokers, respectively), and Smoking Stroop (n's = 37 and 51) Tasks. Smokers were tested in two blocks each following overnight abstinence (> 13 h) or only brief abstinence (< 13 h abstinence, the effect of smoking one cigarette was a reduction of the Stroop effect on the Color-Word Stroop Task. In both brief and overnight abstinence, smoking a cigarette reduced latencies on the Smoking Stroop Task. Neither craving nor withdrawal was correlated with these effects. The data support subjective reports by smokers and objective laboratory research that abstinence from cigarettes impairs the ability of smokers to focus attention and that resuming smoking alleviates this impairment.[RO1DA014093(EL), TRDRP 10RT-0091(EL), Philip Morris 02066286(EL)]

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197 A QUASI-EXPERIMENTAL EVALUATION OF EMPLOYMENT-BASED REINFORCEMENT OF COCAINE AND OPIATE ABSTINENCE IN UNEMPLOYED COMMUNITY METHADONE PATIENTS

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Employment-based reinforcement has been effective in promoting cocaine abstinence in unemployed community methadone patients. An ongoing study seeks to evaluate the efficacy of employment-based reinforcement in sequentially promoting abstinence from cocaine and then opiates in a similar population using a quasi multiple-baseline design. Welfare recipients enrolled in community methadone treatment and using cocaine (N=83) were invited to attend a therapeutic workplace for 6 months. Urine samples were tested three days per week for opiates and cocaine. Participants could earn a base pay of \$8 per hour in vouchers for attendance and additional productivity pay. Initially, there were no abstinence contingencies. Once attending work for at least 15 days over 4 weeks, the participant was required to show evidence of recent cocaine abstinence (urinary metabolite concentration $\leq 300\text{ng/mL}$ or 20% per day decrease since last sample) to work each day and to maintain maximum base pay. After 3 weeks of cocaine-negative urine samples, participants were also required to show evidence of recent opiate abstinence to work and maintain maximum pay. The percent of cocaine negative urine samples increased significantly and abruptly after implementation of the cocaine abstinence contingency (mean of 24% negative in 10 samples before compared to 51% negative in 10 samples after; $p < 0.001$). Of the original 83 participants, 50 initiated cocaine abstinence and were exposed to the opiate contingency. For this subset of participants, the percent of opiate negative urine samples did not change when the cocaine contingency was arranged, but it did increase significantly after the opiate contingency was introduced (mean of 92% negative in 10 samples before compared to 97% negative in the 10 samples after; $p < 0.05$). The results show that sequential implementation of employment-based reinforcement can be effective in promoting cocaine and opiate abstinence in unemployed community methadone patients.

198 DATA MINING FDA'S POST-MARKETING ADVERSE-EVENT-REPORTS DATA TO EXAMINE DRUG-DEPENDENCE REPORTING

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Prescription opioid drug misuse and dependence have emerged as serious public health issues. The Adverse Event Reporting System (AERS) database maintained by the Food and Drug Administration (FDA) contains adverse event data reported for marketed drugs. We examined reporting patterns of misuse and dependence between selected opioid analgesics reported in AERS from 1968-2005. The aim of this study is to estimate the adjusted reporting ratios of drug dependence terms listed in AERS associated with hydrocodone, oxycodone, propoxyphene, and codeine. We calculated adjusted reporting ratios of two adverse event terms ("drug dependence" and "intentional misuse") for the selected opioids. We applied the Multi-item Gamma Poisson Shrinker data-mining algorithm to the entire database to calculate adjusted observed/expected ratios of drug-event associations (Empirical Bayes Geometric Means or EBGM values). Higher EBGM scores for a drug-event combination indicate stronger statistical associations between drug and event reports in the AERS database. All four drugs showed signals ($EB05 > 2$) for drug dependence and intentional misuse. For drug dependence, the EBGM scores were: oxycodone 13.1 (90% CI=12.7, 13.6); propoxyphene 10.5 (90% CI=9.6, 11.4) hydrocodone 5.3 (90% CI=4.7, 5.9) and codeine 2.7 (90% CI=2.2, 3.2); for intentional misuse: propoxyphene 5.4 (CI=5.0, 5.8), codeine 5.1 (CI=4.6, 5.7); oxycodone 3.7 (CI=3.5, 3.9); and hydrocodone 2.5 (CI=2.3, 2.7). In AERS, EBGM values for drug dependence and intentional misuse were higher for oxycodone and propoxyphene than for hydrocodone suggesting that AERS reports of oxycodone and propoxyphene are more likely to describe dependence/misuse events than for hydrocodone. However, EBGM values do not necessarily indicate causality or relative risk. The public health importance of these findings should be interpreted in conjunction with other analyses. Limitations include the voluntary nature of AERS reports, reporting bias, and AERS lack of exposure data.

199 EARLY ADOLESCENT THC ALTERS BEHAVIOR IN AVOIDANCE PARADIGMS IN SEX-SPECIFIC WAYS

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Marijuana is the most widely used abuse drug in the US today. Tetrahydrocannabinol (THC), the major active constituent of marijuana, has been found to alter several types of behaviors including cognitive behaviors. We hypothesized that THC administered during a time when the brain was developing would produce long-term alterations in behaviors which rely on the hippocampus, a brain region known to contain cannabinoid receptors. Therefore, we dosed Sprague-Dawley rats with 0, 1 or 5 mg/kg THC during postnatal days 22-40, a time equivalent to early adolescence and tested behavior in adulthood. At 60+ days, we conducted Active Place Avoidance testing, at 132+ days, passive avoidance testing and at 140+ days, active avoidance testing. Results show that at 60 days, while both doses of THC improved performance in the active place avoidance paradigm, the learning curves were different for male and female rats. There were no effects of THC on latency to cross to dark compartment on test day for passive avoidance. However in active avoidance, control females showed a greater percentage of avoidances compared to THC-treated females while in males, the high dose THC group performed better than the other groups. These data suggest that a brief exposure to THC during early adolescence has lasting effects on avoidance learning that vary depending on the sex of the subject and the testing modality utilized. Supported by NIDA grant DA 019348

200 SUBSTANCE ABUSE TREATMENT AMONG ADULTS WITH SEVERE MENTAL ILLNESS

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AIM: Individuals with severe mental illnesses (SMI) are at increased risk of substance abuse (SA) and would be expected to benefit from treatment. In a cohort of Medicaid enrolled SMI adults, lifetime and point prevalence of substance abuse problems as well as formal and informal sources of treatment received is examined. METHODS: We used the 1994, 1998, and 2000 waves of the Maryland Mental Health Outcomes Survey. The initial study population represented a 15% sample of adult Medicaid enrollees with probable or highly probable SMI; 315 study participants completed all three waves of data. Descriptive analyses were performed to estimate the prevalence of any alcohol and drug-related problems among adults with SMI. We further investigated their past year use of self-help and formal SA treatment at three time points. RESULTS: Approximately 33% of adults with SMI reported ever experiencing alcohol and/or drug problems. These individuals were more likely to be younger than 45, male, and reside in an urban environment. At the beginning of the study, over 15% of adults with SMI had substance-related problems with almost 6% reporting problems with both substances. A decrease was found among adults with SMI during the following waves; however, the occurrence of problems rebounded for alcohol (12.7%) and for co-occurring alcohol and drug use (5.1%) at the final time point. The prevalence of SA treatment in this population declined from 23% at the beginning of the study to 15% at the second wave. A slight increase in SA treatment (16.5%) was detected at the third wave. The majority of those who received treatment reported using both formal and self-help programs at the first two time points. Conversely, approximately 65% of SA treatment recipients reported use of formal programs only at the third wave. CONCLUSIONS: Alcohol and/or drug-related problems affect a significant portion of adult Medicaid enrollees with SMI. The mechanisms behind the decrease in use of self-help programs warrant further investigation. ACKNOWLEDGEMENTS: T32DA07292 and R01 MH49250

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- 201 NEURAL CORRELATES OF NICOTINE WITHDRAWAL- VERSUS CUE-BASED CRAVING**
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Hypotheses: Both nicotine cue exposure and nicotine withdrawal would increase the urge to smoke. Both types of nicotine craving would involve common and distinct brain regions involved in reward and the acute effects of nicotine. Subjects: 8 human nicotine-dependent male smokers. Procedures: Male volunteers with nicotine dependence, no other substance use disorders, who had breath CO > 10 ppm, and who reported consuming >10 cigarettes per day were invited to participate. Each subject received two MRI scans: nicotine-withdrawal and nicotine-satiated. Subjects rated emotions and craving on a 7-point scale from "very little or not at all" to "extremely." Each session consisted of 4 epochs- 2 containing nicotine cues and 2 containing matched control pictures. Order of epoch presentation was counterbalanced. Results: Nicotine craving, nervousness, and agitation were significantly higher in the withdrawal state than in the satiated state ($p < 0.001$). Happiness did not differ between sessions. Using a two-way ANOVA, withdrawal had a significant effect on craving ($p < 0.001$), but nicotine cue exposure did not ($p = 0.369$). Relative increases in BOLD f-MRI signal during nicotine withdrawal occurred in bilateral inferior, middle, and superior frontal gyri, in the right middle temporal gyrus, anterior and dorsal cingulate, right parahippocampal gyrus, and the left insula. Nicotine cue exposure during satiation was associated with increased BOLD signal in the right middle temporal gyrus, post-central gyrus, multiple areas of the right cingulate gyrus and the thalamus. Conclusions: Nicotine withdrawal had a significantly greater effect on subjective craving than did nicotine cue exposure. Nicotine withdrawal-based craving was associated with increased activity in limbic regions associated with emotion and reward processing, and widespread frontal activations associated with response inhibition. Nicotine cue exposure during nicotine satiation was associated with increases in limbic and subcortical regions involved in reward processing and those activated by nicotine.
- 202 MD-354 SELECTIVELY ATTENUATES THE ACTION OF NICOTINE IN THE MOUSE TAIL-FLICK ASSAY**
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meta-Chlorophenylguanidine (MD-354) is a novel, dual-mechanism type of analgesia-enhancing agent [EJP 2004, 495, 129-136]. A 5-HT3 partial agonist, MD-354 binds equally well at serotonin 5-HT3 receptors ($K_i = 35$ nM) and alpha2B-adrenoceptors (alpha2B-AR) ($K_i = 25$ nM), but displays somewhat lower affinity for alpha2A- and alpha2C-ARs. MD-354 lacks affinity for >30 other receptor types including nACh receptors. Literature evidence indicates that nicotine might act via the descending inhibitory pathways of serotonergic and adrenergic systems. Therefore, it was of interest to examine the spinal action of MD-354 on nicotine's antinociception in the mouse tail-flick assay. We examined (-)nicotine ($ED_{50} = 1.7$ mg/kg, s.c.) in the tail-flick test and obtained results consistent with that reported in the literature. Interestingly, when administered in combination with an active dose of (-)nicotine (i.e., 2.5 mg/kg; $MPE = 70\%$), MD-354 (6 mg/kg; $MPE = 0\%$) did not potentiate, but effectively attenuated the antinociceptive actions of (-)nicotine ($MPE = 1\%$). Lower doses of MD-354 also antagonized nicotine-induced antinociception ($AD_{50} = 3.4$ mg/kg). In the rat drug discrimination paradigm, MD-354, in combination with the training dose of (-)nicotine produced no less than 87% (-)nicotine-appropriate responding up to an MD-354 dose of 0.45 mg/kg. By itself, MD-354 produced <5% (-)nicotine-appropriate responding at doses of 0.3 and 1.0 mg/kg. Previously we showed that a dose of 6 mg/kg of MD-354 did not affect motor coordination in the mouse locomotor activity assay. Similarly, lower and higher doses (0.1-17 mg/kg) of MD-354 produced saline like effects when administered alone. In combination with 3 mg/kg (a locomotor activity suppressing dose) of (-)nicotine, all doses of MD-354 failed to antagonize the locomotor action of (-)nicotine. It would appear that MD-354 selectively attenuates the antinociceptive actions, but not the stimulus or motor effects of (-)nicotine. [Supported in part by J-778 from the Jeffress Memorial Trust and DA-05274.]
- 203 ATTENUATION OF THE MOTOR AND SEDATIVE-LIKE EFFECTS OF ALPRAZOLAM BY FLUMAZENIL AND BCCT IN RHESUS MONKEYS**
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Alprazolam, a benzodiazepine (BZ) with anti-anxiety effects, can cause motor impairment and sedation. Previous research has suggested that different GABA (A) receptor subtypes are involved in these behavioral effects. We investigated the role of alpha1GABA(A) receptors in the motor and sedative-like effects of alprazolam by examining the effects of alprazolam alone and in combination with the BZ antagonist flumazenil or the alpha1GABA(A)-preferring antagonist BCCT. Moderate sedation (atypical sleep posture, rousable) and deep sedation (atypical sleep posture, not rousable) were measured using quantitative behavioral observation techniques. Gross and fine motor coordination were assessed using an automated movement assessment panel adapted for rhesus monkeys (mMAP, Gash et al. 1999). Motor deficits were also measured with a new apparatus designed to quantify a monkey's ability to pull a spring-loaded handle. Alprazolam dose-dependently engendered sedative-like effects, impaired gross and fine motor coordination, and impaired the ability to pull the spring-loaded handle. Flumazenil attenuated alprazolam-induced increases in moderate and deep sedation, as well as gross and fine motor impairment and reduction of handle pulling. BCCT attenuated moderate and deep sedation and gross motor impairment, but did not block alprazolam-induced fine motor impairment or reduction in handle pulling. Taken together, these findings suggest alpha1GABA(A) receptors may be involved in alprazolam-induced gross motor impairment and sedative-like effects, but not impairment of fine motor coordination or handle pulling; the latter being a potential measure of myorelaxation. Supported by DA020304, DA011792 and RR000168.
- 204 HIV PREVALENCE AMONG INJECTION DRUG USERS IN VINNITSYA, UKRAINE**
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HIV/AIDS epidemic in Ukraine continues to grow rapidly, with total number of officially registered cases reaching 85,596 by the end of 2005. The true number of HIV cases is estimated to fall between 180 and 520,000. Injection drug use (IDU) remains to be a major risk factor, although the proportion of IDUs among newly registered cases steadily declined from 83.6% in 1997 to 46.3% in 2004. In the early stages the epidemic was concentrated in South and East of the country and in several big cities, leaving smaller cities understudied and underserved in terms of prevention activities. The aim of this study was to investigate the HIV spread and risk factor patterns in the IDU population in Vinnitsya, mid-size city in central Ukraine. In June-September 2005 315 IDUs were recruited using the snowball sampling technique (about 15% of total IDU population in the area). 'Seeds' were selected from IDUs attending addiction and infectious diseases treatment centers. HIV prevalence was measured using rapid tests, and reached 14.6%. Drug and sex risk factors were measured by the Risk Assessment Battery and Form 90; additional locally-specific questionnaire was added. 17.6% were females; median age was 28 years (sd 7.5); 24.6% of the sample were married (ns difference between HIV- and HIV+ groups). Mean duration of opiate use was 8.4 years (sd 4.7) for HIV+ and 8.5 years (sd 6.5) for HIV- (ns difference). Opiate use during last 30 days was significantly greater in HIV+ subgroup compared to HIV- (23.4 days vs 17.4, $p = 0.009$). Number of injecting partners was greater in HIV+, but did not reach statistically significant difference (13.6% of HIV+ had more than 4 partners during last year vs 4.2% among HIV-, $p = 0.07$). 52.6% of the sample had 2 or more sex partners during last year (ns difference between HIV+/HIV-), and only 41% reported constant use of condoms. This study documents for the first time the association between HIV and IDU in an understudied mid-size city in central Ukraine.

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- 205** POLYSUBSTANCE USE, MENTAL HEALTH, AND SCHOOL DROPOUTS IN ADOLESCENT MARIJUANA USERS
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Marijuana use during adolescence has been associated with various negative outcomes, including polysubstance use, poor mental health and school dropouts. As behavioral studies of adolescent marijuana users enter the literature, the extent to which different samples from this population reflect these prior data is unknown. The goal of this ongoing study is to characterize substance use patterns, concurrent psychiatric disorders, and other comorbid aspects among adolescent marijuana users. The present study analyzed telephone screens and in-person interviews of persons between the ages of 12 and 17 years. These participants responded to newspaper and radio advertisements targeting adolescent marijuana users and non-users for a study of impulsive behavior. Thus far, eighteen individuals (11 females and 7 males), have completed this screening process. Sixty-seven percent (n = 12) were users while the other 33% (n = 6) had never tried marijuana. The users averaged using six days per week with a standard deviation of two. In the marijuana user group, 42% (n=5) of participants have used cocaine and 17% (n=2) have used ecstasy. Furthermore, 57% (n=7) of users reported use of prescribed psychoactive medications within the last year, particularly Xanax (n = 6). Further screening with DSM-IV criteria revealed current mood disorders (n = 4) or alcohol dependence (n = 1) in 42% of users. Fifty-eight percent of the users (n = 7) had dropped out of school. In contrast, each of the adolescents who had never tried marijuana reported no use of any other drugs or prescription psychoactive medications, and all were still in school. In supporting prior research, these results reveal several potential confounds that may need to be controlled for in behavioral studies of adolescent marijuana users.
- 206** PILOT STUDY TO REDUCE CIGARETTE SMOKING AMONG METHADONE PATIENTS
K. E. Dunn, S. C. Sigmon and S. T. Higgins, University of Vermont, Burlington, VT
Prevalence of smoking among methadone maintenance (MM) patients is more than three-fold that of the general population and is associated with increased morbidity and mortality. This ongoing pilot study examines the efficacy of a contingency-management (CM) intervention in reducing smoking during a 2-week cessation effort. MM smokers are randomized into a Contingent or Noncontingent group and visit the clinic daily. Abstinence during Days 1-5 is defined as a Carbon Monoxide (CO) level of ≤ 6 ppm and during Days 6-14 as a urine cotinine level of ≤ 80 ng/ml. Contingent participants receive vouchers for each negative sample, which escalate in value and are redeemable for gift certificates to local stores. A maximum of \$362.50 can be earned for continuous abstinence during the study. Noncontingent participants provide CO and cotinine samples daily but receive vouchers independent of their smoking status. Thus far, we have enrolled 7 participants (4 Cont, 3 Noncont) into the study. Participants on average are 17% male, 25 yrs old, report smoking 16 cigs/day and are maintained on approximately 115 mg methadone. Three participants (2 Cont, 1 Noncont) have completed the study, 3 (1 Cont, 2 Noncont) are currently enrolled and have completed > 75% of study visits, and 1 Contingent participant terminated participation before completing the protocol. Results thus far are promising. Among Contingent participants, 1 subject was 100% abstinent from smoking for the entire 2-week study and 2 participants have tested negative on 86% of study visits, for a mean abstinence rate of 91%. Among Noncontingent participants, 2 subjects have achieved 0% abstinence during the study and 1 participant has tested negative on 38% of study visits, for a mean abstinence rate of 13%. Preliminary results of this pilot study indicate greater smoking abstinence among the Contingent compared to the Noncontingent group and suggest that this CM intervention may be effective in promoting early, continuous abstinence among MM smokers. We anticipate completing this study and presenting outcome data from the full sample of 20 MM smokers at the June meeting.
- 207** MAJOR DEPRESSION: CONTRIBUTIONS OF GENDER, MDMA AND CANNABIS USE
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Several studies have reported an association between MDMA (ecstasy) use and increased rates of depressive symptomatology. However, MDMA users tend also to use other illicit drugs, and some evidence suggests that depressive symptoms in MDMA-only users are not elevated relative to poly-drug users. Therefore, it is possible that MDMA use alone does not account for the increased levels of depression observed in heavy users of MDMA. Recent research has focused on comorbid cannabis use as a potential confound in studies of MDMA use and mood. To date, studies of MDMA use and depression have relied almost exclusively on rating scales of depressive symptomatology rather than clinical diagnoses. This study aimed to examine the associations among MDMA use, cannabis use and a DSM-IV diagnosis of lifetime Major Depressive Disorder (MDD) in young adult MDMA users. A total of 229 (80 female, 149 male; mean age = 23.1 ± 4.2 yrs) MDMA users (mean use episodes = 36.0 times, ± 46.3 , range = 2 to 400) underwent a semi-structured psychiatric interview (SCID) and completed a detailed drug history questionnaire. Results indicated that individuals who met DSM-IV criteria for MDD (current or past) did not differ in ecstasy use relative to those without such a diagnosis. In addition, whereas gender was not associated with a diagnosis of MDD, lifetime diagnosis of Cannabis Abuse or Dependence was significantly associated with an increased rate of lifetime MDD diagnoses. Finally, results of logistic regression indicated that neither gender nor mean number of MDMA episodes were significant predictors of a diagnosis of lifetime MDD, but meeting DSM-IV criteria for a cannabis use disorder was a significant predictor for also being diagnosed with MDD. These results indicate that comorbid cannabis abuse accounts for a greater proportion of the variance in the diagnosis of MDD compared to MDMA use, and underscore the importance of controlling for polydrug use, especially marijuana, in studies of the effects of MDMA use on mood function. Supported by Grant DA14874 and from Joe Young, Sr. funds from the State of Michigan.
- 208** DELETION OF THE NR1 SUBUNIT OF THE N-METHYL-D-ASPARTATE GLUTAMATE RECEPTOR ALTERS MORPHINE CONDITIONED PLACE PREFERENCE
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It is well-established that the NMDA glutamate system plays a role in both the antinociceptive and the conditioned effects of morphine. For example N-methyl-D-aspartate (NMDA) antagonists alter both the acquisition and expression of morphine's effects as measured by the conditioned place preference procedure. The aim of the present study was to examine the involvement of the NMDA receptor system in the conditioned effects of morphine using a genetic approach. Mice in which the NR1 subunit of the NMDA receptor had been reduced to approximately 5% (NR1 KD; n = 9) and their wildtype littermates (NR1 WT; n = 10) were preconditioned in a place preference apparatus consisting of a neutral center compartment and two distinctive conditioning compartments. Activity levels during 30-min preconditioning sessions were greater in the NR1 KD mice (5085 counts \pm 384.4 SEM) than the WT mice (3458 counts \pm 307.6 SEM). During conditioning, NR1 KD and WT mice received 3 pairings of morphine (6.6 mg/kg, sc) and saline in one of the conditioning compartments on alternating days. On test day, mice were given access to all compartments and time spent in the morphine-paired compartment following conditioning was compared to time spent in that compartment during preconditioning. The results indicate that the 6.6 mg/kg dose of morphine produced a CPP in the WT mice; whereas the CPP was attenuated in the NR1 KD mice. The present results suggest that NR1 deletion alters the development of morphine conditioned place preference in mice. Supported by R01-DA02749 (LAD) and T32-DA07244.

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209 PROBLEMS IN DEPENDENT AND NON-DEPENDENT DAILY CANNABIS USERS

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Cannabis is the most widely consumed illicit substance in America, with increasing rates of dependence and abuse. Theorists tend to link frequency of use with cannabis dependence. Nevertheless, fewer than half of daily cannabis users meet DSM-IV-TR criteria for cannabis dependence. Previous research has also demonstrated a relationship between heavy cannabis use and problems with mood and health. This study seeks to determine whether the negative aspects associated with cannabis use can be explained by cannabis dependence instead of by frequency of use. Over 2500 adult daily cannabis users completed an internet survey consisting of measures of cannabis and other drug use, in addition to measures of commonly reported negative problems resulting from cannabis use. We compared those who met DSM-IV-TR criteria for cannabis dependence (N=1111) to those who did not meet the criteria (N=1770). Participants ranged in age from 18 to 88 and reported diverse educational backgrounds. Cannabis dependent subjects consumed greater amounts of cannabis, alcohol, and a variety of other drugs. They also had lower levels of motivation, happiness, and satisfaction with life, with higher levels of depression and respiratory symptoms. Additionally, cannabis dependent users were younger and reported lower levels of educational attainment than non-dependent users. These data suggest that dependence need not arise from daily use, but consuming larger amounts of cannabis and other drugs undoubtedly increases problems.

210 EQUAL UNDER THE LAW: TREATMENT RETENTION AND OUTCOME AMONG COCAINE-DEPENDENT PATIENTS WITH AND WITHOUT ACTIVE CRIMINAL JUSTICE INVOLVEMENT

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This study examined differences between cocaine and alcohol dependent patients with and without active criminal justice involvement. Data were combined from two randomized controlled trials, in which 243 participants were randomly assigned to manual-guided behavioral therapies and medication (either disulfiram or placebo). Fifty-five participants (23%) of the combined sample had active criminal justice involvement, defined as being referred to treatment by a court official, probation or parole officer. Regarding treatment outcome, there were no significant differences between participants with and without criminal justice involvement with regard to frequency of cocaine or other substance use during the three months of study treatment or the one year follow up. Although the criminal justice referred group had significantly more new arrests during the one-year follow-up, when antisocial personality disorder was utilized as a covariate, there were no significant differences between criminal justice groups in number of arrests at the one-year follow-up. These data suggest that participants with active criminal justice involvement do not necessarily have poorer retention or substance use outcomes compared with individuals who are self referred or referred by other sources when treated in well-defined protocols (Support was provided by the National Institute of Drug Abuse grants K05 DA00457, P50 DA09241 and K12 DA00167).

211 FACILITATING BUPRENORPHINE IMPLEMENTATION: THE PHYSICIAN CLINICAL SUPPORT SYSTEM

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The Physician Clinical Support System (PCSS) is a SAMHSA-funded nationwide network of physicians (mentors) who provide assistance to recently trained individuals (participants) to assist in buprenorphine implementation. We describe the characteristics of the PCSS mentors and participants as well as the clinical issues on which they have been asked to provide guidance/education. To date, 51 mentors have been selected and identify their specialty as Psychiatry (33%), Internal Medicine (31%), Family Medicine (18%), and Addiction Medicine/Psychiatry (18%). 84% are certified in addiction. Their primary practice settings include a treatment program (60%) private practice (12%) or academic institution (28%). The 175 PCSS participants enrolled to date identify their specialty as Psychiatry (42%), Internal Medicine (18%), Family Medicine (27%), Addiction Medicine (6%), and other (7%). 74% identify private practice as their primary practice setting. Of the participant who completed a baseline survey, the mean age is 50, 34% are female, 35% indicate that they have <1 year of experience treating opioid dependence, and 26% report that more than a quarter of their patients are abusing prescription opioids. To date, mentors have completed a web-based log for 94 of their contacts with participants. 43% of the contacts were via email, 39% via telephone and 17% via in-person visits. 72% of the contacts were clinica support and 28% were logistical support. The top 5 clinical areas in which support was requested were logistical assistance (37%), medication dose management (34%), induction procedure (dosing) (32%), induction procedure (timing) (32%), and medical comorbidity (12%). The top 5 logistical areas in which support was requested were scheduling (18%), provider availability (17%), medication supply (11%), paperwork (10%), and reimbursement (7%). The primary materials provided or referenced were clinical tools and CSAI guidelines. We conclude that the PCSS provides an important resource to extend physician education beyond the training mandated by DATA 2000.

212 DESCRIPTION OF IDUS IN AN HIV PRE-EPIDEMIC SETTING

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Israel faces a critical juncture in HIV prevention through the immigration of individuals from areas identified as experiencing steep increases in HIV infection such as the former Soviet Union and Africa. There has also been a corresponding increase in the HIV rates of non-immigrants. WHO estimates that approximately 5000 individuals living in Israel are infected with HIV/AIDS, with a steady increase noted since the mid-1990s. The aim of this study is to present descriptive demographic characteristics of individuals entering drug treatment who are at high risk for contracting or transmitting HIV for the purposes of informing policy planners and clinicians to help stem the HIV transmission rate and abate the threat of an epidemic. Data was collected from the Haifa Drug Abuse Treatment Center (HDATC) during the period between August 2004 and August 2005. 270 individuals presented for admission, with 198 eventually admitted. Subjects had a mean age of 41; 73% unmarried, 67% were of Jewish descent, 13% Muslims of Arab and non-Arab descent, and 8.5% Christians of Arab and non-Arab descent. A full 40% were immigrants with 34% coming from Eastern Europe and 6.5% coming from Africa. Between 1996 and 2005, co-morbid psychiatric conditions were observed in over 20% of IDUs. A 3.9 fold increase was observed in HCV carriers (from 15.6% to 60.1%), and during this same period, a 13 fold increase in the number of individuals with HIV was observed (from 0.4% to 5.2%). This rate of 5.2% exceeds the WHO standard of 5% sero-prevalence which is considered an immediate public health danger with the potential for an expansion of risk in the highest risk populations of injection drug users and sex workers. Efforts need to be dedicated to the cross-cultural translation of effective risk-reduction and intervention strategies for these highest risk IDUs. The potential for translation of Low Threshold-Low Intensity drug treatment interventions that have proven effective in the United States holds great promise for addressing the epidemic in Israel.

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213 MORPHINE EXACERBATES HIV-1 TAT-INDUCED NEUROINFLAMMATION AND GLIAL ACTIVATION IN THE STRIATUM THROUGH CCL2/MCP-1 CHEMOKINE-RECEPTOR INTERACTIONS

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Opiate drug abuse reportedly exacerbates the pathogenesis of human immunodeficiency virus-1 (HIV-1) encephalitis (HIVE) through preferential actions at mu opioid receptors (MOR). Evidence suggests that astroglia, which can express MOR, play a central role in the opiate-mediated acceleration of HIVE. The CC chemokine ligand 2 (CCL2), also known as monocyte chemoattractant protein-1 (MCP-1), in particular, mediates inflammatory signaling by opiate and HIV-1 protein-exposed astrocytes. CCL2 levels correlate highly with neurobehavioral deficits accompanying HIV-1 or simian immunodeficiency virus infections. Prompted by the importance of CCL2 in neuroAIDS, and findings that opiates potentiate the production of CCL2 by HIV-1 Tat-exposed astrocytes, we assessed the role of the CCL2 receptor, CCR2, in opiate and HIV-1 interactions in morphine and Tat exposed wild type CCR2(+/+) and CCR2 null C57Bl/6 mice. The effects of intrastriatal HIV-1 Tat(1-72) protein and/or systemic morphine (25 mg time-release implant; 5 days before termination of the experiment) on macrophage/microglial and astroglial activation were examined 7 days after Tat injection. Tat or morphine markedly increased the proportion of CCL2 immunoreactive astroglia; while in combination there were additive increases in CCL2-expressing astroglia, which were prevented by co-administering naltrexone. The number of F4/80 immunoreactive macrophages/microglia and glial fibrillary acidic protein-immunoreactive astroglia were significantly reduced in CCR2(-/-) compared to wild-type mice after exposure to Tat or morphine and Tat. This indicates that CCR2 mediates local increases in macrophage/microglial and astroglial activation caused by Tat and that concurrent opiate exposure enhances the glial activation. Overall, our results suggest that enhanced astrocytic release of CCL2 and subsequent events triggered by CCR2 activation are critical elements that drive the opiate-induced exacerbation of HIVE. Supported by NIDA P01 DA19398.

215 BUPROPION FOR THE TREATMENT OF METHAMPHETAMINE DEPENDENCE

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Bupropion, an approved antidepressant with monoamines uptake inhibition properties and mild stimulant effects was tested in a double blind placebo controlled study for the treatment of methamphetamine dependence. 151 patients with a DSM-IV diagnosis of methamphetamine dependence were screened after signing the required consent forms. 72 patients were randomized to placebo and 79 to Bupropion SR 150mg BID. Patients were asked to come three times/week to the clinic for assessments, urine collection, and group psychotherapy (matrix). The primary outcome was the mean weekly urine qualitative assessment of methamphetamine use, secondary outcomes include Addiction Severity Index, craving, withdrawal symptoms, and cognitive functions. Analysis of the primary outcome showed a trend for significance for the total sample ($p=0.09$) favoring bupropion. When the total sample was split based on their baseline use using time line follow back into high users ($n=77$) and low/moderate users ($n=71$) bupropion showed a statistically significant effect for the low/moderate group compared to placebo ($p=0.03$). There was no effect for the high users. Secondary outcome data are still being analyzed. This data suggest efficacy for bupropion in combination with behavioral therapy in the treatment of low/moderate methamphetamine dependent patients.

214 OPIOID WITHDRAWAL SCALES: SOWS, OOWS AND MORE SOWS

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Many scales are available for measuring opioid withdrawal. They are rooted strongly in physical symptoms and have been based on the original work of Himmelsbach (1938). A total of 16 opioid withdrawal scales were compiled for this review. Of these, 31% have been validated, 50% were semi-validated, and 19% have not been validated. 63% were developed using patients in detoxification programs and 50% were developed based on performing a naloxone challenge. Most (75%) scales are self-report. Only one of these scales was developed by evaluating withdrawal in Opioid Substitution Therapy (OST) patients; the Methadone Symptom Checklist (MSC). The MSC is an unvalidated measure consisting of 48 items to measure opioid withdrawal, direct agonist effects and effects that can be either agonist or withdrawal. A point of confusion in the literature, is the use of the same acronyms to denote different scales: SOWS is used to denote the Short Opioid Withdrawal Scale, the Subjective Opioid Withdrawal Scale, and in part the Strong Opioid Withdrawal Scale developed from the Addiction Research Center Inventory. The most commonly used scales for research in OST are the Short Opioid Withdrawal Scale (10 items) and the Subjective Opioid Withdrawal Scale (16 items). Both of these scales are strongly based on physical markers of withdrawal and were validated in patients during opioid detoxification following a naloxone challenge. Withdrawal in this setting may be qualitatively different from that experienced during a dosing interval, as well as different in the relative strength of physical and subjective symptoms. Individual patient factors may influence the experience of opioid withdrawal and may play a relatively larger role in the context of OST. Hence, it is surprising that there are no tools currently available for measuring opioid withdrawal from the perspective of OST. An OST-specific scale may be of utility in monitoring patients, particularly since as many as 1/3 of patients in methadone treatment report experiencing significant withdrawal towards the end of their dosing interval.

216 REINSTATEMENT OF COCAINE SEEKING FOLLOWING ABSTINENCE OR COCAINE PRIMING IS ATTENUATED BY BLOCKADE OF D1, BUT NOT NMDA, RECEPTORS IN THE DORSAL STRIATUM

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Recent studies have implicated the dorsal striatum as an important neural substrate for drug-seeking following chronic cocaine exposure, including evidence from our laboratory showing that inhibition of the dorsolateral striatum (dlCPu) significantly attenuates cocaine-seeking following prolonged cocaine self-administration and abstinence in rats. However, the specific striatal receptors that mediate cocaine seeking remain to be determined. Therefore, the present investigation sought to determine the role of dlCPu dopamine D1 and NMDA receptors in reinstatement to cocaine seeking. Animals were implanted with jugular catheters as well as bilateral cannulae directed at the dlCPu and trained to self-administer cocaine (0.2 mg/infusion) on a fixed ratio 1 schedule for 10 days (2 h/day). Following 14 days of abstinence, animals received intradlCPu infusions of vehicle or the selective D1 antagonist SCH23390 (0.2-2.0 μ g/side) and were returned to the test chamber for a two hour reinstatement test in the absence of cocaine reinforcement. Animals pretreated with vehicle displayed a significant increase in responding compared to responding during self-administration, and pretreatment with SCH23390 significantly attenuated responding on the previously cocaine-paired lever without affecting inactive lever responses. Importantly, the effect of SCH23390 does not appear to be due to non-specific locomotor impairment as the highest SCH23390 dose tested did not affect spontaneous locomotor behavior or produce catalepsy. Additional preliminary experiments suggest that SCH23390 also attenuates cocaine-primed reinstatement in extinguished animals and that NMDA receptor blockade with AP-5 (3.0 μ g/side) does not affect reinstatement behavior following abstinence. Collectively, these data demonstrate that dopamine signaling through D1 receptors in the dlCPu is an important mechanism underlying cocaine seeking, perhaps by activating expression of previously learned habit responding. (Supported by NIH Grant DA10462 to RES)

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217 MULTIMODAL ASSESSMENT OF REWARD FUNCTION IN ALCOHOL AND HEROIN DEPENDENCE

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It is unknown whether heightened motivation for drugs in dependent individuals can be extended to non-drug rewards. To address this question, we administered non-drug psychosocial and biochemical probes of reward function to four groups of male participants with alcohol (N=20; age±SD: 33.7±4.64) and heroin (N=18; 28.1±4.69) dependence along with occasional alcohol/heroin users (N=22; 27.6±3.28) and healthy controls (N=24; 27.1±5.23). Four paradigms employed in this project included: a) sucrose solutions administered in the context of the sweet preference test, social reward tasks in the form of visual processing of b) attractive faces, c) positive images, and d) monetary incentive stimuli incorporated into a gambling task. In comparison to controls detoxified alcohol and heroin dependent subjects alike displayed greater ($p<0.01$; corrected for multiple comparisons) "wanting" responses operationalized via subjects' ratings (sweet solution) and via amount of work (computer key presses) in order to change the relative duration of images' viewing; "liking" ratings generally paralleled "wanting" responses. "Wanting" assessments in the occasional alcohol/heroin users were normal, suggesting that motivational/incentive sensitization could be an acquired, state-related condition. Conversely, similarly decreased self reports of expectation and satisfaction with monetary gains in the three alcohol- and/or heroin-exposed groups suggest that diminished capacity to experience pleasure may prove to be a trait feature or could be an early marker of exposure to heroin and/or alcohol. The novel aspects of this study include 'spillover' of excessive drug motivation to non drug rewards and generalizability of this phenomenon to dependence on distinct classes of addictive substances. Neuroimaging research is needed to determine neural correlates of this reward function alteration and whether non-drug addictions have related pathophysiologies.

219 A PILOT PLACEBO-CONTROLLED TRIAL OF MEMANTINE FOR ALCOHOL DEPENDENCE

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This 16 week double-blind outpatient clinical trial examined the efficacy of the NMDA antagonist, memantine, compared to placebo for alcohol dependence. After a 2-week single-blind placebo lead-in phase, treatment-seeking alcohol-dependent volunteers were stratified into one of two treatment conditions: memantine (maximum dose of 40 mg/day) or placebo. This 12-week double-blind treatment phase was followed by a 2-week single-blind lead-out phase when patients were tapered off medication, but continued with other assessments and therapy. In addition to alcohol consumption, a number of other measures were assessed throughout the study: the Alcohol Craving Scale, the Obsessive Compulsive Drinking Scale, Clinical Global ratings done by a psychiatrist, breath alcohol levels, urine drug toxicology, and various biochemical markers of alcohol use. Weekly, patients had individual relapse prevention therapy. To enhance retention, patients received vouchers of increasing value for coming to the clinic, providing a urine and breathalyzer sample at each visit, and attending the weekly relapse prevention therapy. If an individual attended all visits, he/she could earn vouchers worth a total of \$570 over the 4-month study. A total of 44 patients were enrolled and 34 were randomized (19 to the memantine group and 15 to the placebo group). Of the 34 randomized patients, the mean age was 42.5 years and at baseline, the mean weekly alcohol consumption was 48.5 standard drinks. Of those randomized, 85% (29) completed the entire 16-week trial. This level of retention is on the high end for alcohol treatment trials, suggesting that the modified voucher-incentive plan was successful. Abstinence rates were similar in the memantine group (31%) and the placebo group (27%). Longitudinal analysis of drinks per week and heavy drinking days per week indicated that both groups showed a significant decrease in drinking behavior, but there were no significant differences between the two groups. Supported by NIAAA RO1 AA12599.

218 CHARACTERISTICS OF OVERWEIGHT LONG-TERM NARCOTIC USERS

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Weight control has often been cited as an important factor for continued use of tobacco and methamphetamines, but it has never been considered an issue among narcotics users. Nevertheless, our 33-year follow-up study of a subset of 108 male narcotics users revealed that 55% of them met the Body Mass Index criteria for being overweight. A set of medical tests were conducted to assess their health conditions. In the present study, we examined the characteristics of these overweight narcotics users to explore the relationship between weight, recovery, and relapse. The subjects were admitted to the California Civil Addict Program in 1962-1964 and were re-interviewed in 1996-1997. Study subjects were 58% Hispanic, 34% White, and 7% African American. Preliminary analysis revealed that compared to not overweight people, overweight people in the sample were younger (57 vs. 59), Hispanic (62% vs. 53%), employed (44% vs. 32%), and earning a higher salary (49% vs. 23%). They also had higher rates of high cholesterol (17% vs. 10%) and diabetes (19% vs. 10%), more were taking prescribed psychiatric medications (28% vs. 23%), had experienced more weight gain in past 5 years and since age 25, and had more episodes of treatment for psychiatric (28% vs. 18%) and drug problems (51% vs. 47%). Fewer overweight subjects reported having been arrested (51% vs. 61%) at follow-up. Overweight subjects also reported lower drug use rates, particularly for heroin (49% vs. 65%). Multivariate analysis will be conducted to examine the relationships among weight, relapse, and other health conditions.

220 AN EVALUATION OF THE IMPACT OF LIFETIME OR CURRENT SMOKING PATTERNS ON THE ACUTE SUBJECTIVE EFFECTS PRODUCED BY METHAMPHETAMINE IN THE LABORATORY

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Methamphetamine (MA) is often co-abused with cigarettes, yet little is known about the behavioral effects of the two compounds in combination. Since nicotine is known to increase cardiovascular indices and positive subjective effects, we postulated that smoking consumption patterns may alter the acute subjective effects produced by MA in the laboratory. This study includes non-treatment seeking, MA-dependent volunteers (N=15). Average duration of MA use was 11.33 ± 2.2 years and the average recent use (of the past 30) was 17.20 ± 2.5 days. Participants had an average of 12.67 ± 0.5 years of education. In addition, 7% were Native American, 33% were Hispanic, and 60% were Caucasian. The sample consisted of 9 men and 6 women. Participants received intravenous doses of placebo or MA (30 mg) on two separate days. As expected, MA, but not placebo, increased subjective effects of "Desire" ($p<0.001$) and "High" ($p<0.001$) as measured using a visual analog scale. Considerable variability was noted among individuals prompting us to examine the potential contributions of smoking behavior to the responses produced by acute MA exposure. Regression analysis indicated no correlation between "Desire" ($r^2=0.003$) or "High" ($r^2=0.053$) versus number of cigarettes smoked per day. Similarly, there was no correlation between these subjective effects versus number of years of use of nicotine. Overall, the data reveal that years of use and current daily cigarette consumption were not associated with the acute subjective effects produced by MA in the laboratory. The current findings diverge from results obtained using experimental animal models, and merit further research to evaluate the extent to which acute and repeated exposure to nicotine influence the subjective effects of MA in MA-dependent patients. Supported by NIDA: DA-14593, DA-18185, DA-17754

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221 COMPARISON OF AVERSIVE EFFECTS OF NALTREXONE, 6-BETA-NALTREXOL, AND NALBUPHINE GIVEN 4 HOURS AFTER ACUTE PRETREATMENT WITH MORPHINE

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Aversive effects of naltrexone (NTX), 6-beta-naltrexol (6-beta-N), or nalbuphine (NALB) given 4 h after SC treatment with either saline or a dose of 5.6 or 10 mg/kg morphine (MS) were examined in a two-compartment place conditioning assay. During conditioning, rats were treated on alternate days with either MS or SAL. Four h later, they received a SC dose of antagonist immediately before being placed in the appropriate compartment of the CPA chamber. Doses of antagonists were chosen to be equi-potent to block acute effects of MS. Tests of aversion, defined as a post-conditioning decrease in total time spent in the MS-antagonist paired chamber, were conducted after 4 sets of pairing trials. The antagonists differed in their ability to condition a place aversion. NTX, when given after pretreatment with either 5.6 and 10 mg/kg MS, produced a dose-dependent aversion of the MS-NTX paired chamber. The lowest dose of NTX (0.032 mg/kg) produced no aversion, whereas the highest dose (0.32 mg/kg) produced marked place aversion, such that time spent in the MS-NTX paired chamber decreased by 200 s on average. Alteration of the pretreatment dose of MS produced few changes in the aversive effects of NTX. The highest dose of NTX (0.32 mg/kg), however, produced no aversive effect after SAL, suggesting that aversive effects of NTX required pretreatment with MS. In contrast, the highest conditioning dose of 6-beta-N (10 mg/kg) produced marked place aversion following only 5.6 mg/kg MS, and an intermediate dose of 6-beta-N (3.2 mg/kg) produced a preference for the drug-paired chamber following SAL. Finally, NALB (32 mg/kg) produced little place aversion following 5.6 mg/kg MS and no change in place selection following SAL. Thus, equi-potent doses of these opioid antagonists differed in ability to produce place aversion following acute MS, consistent with possible differences in inverse agonist actions. [Supported by USPHS DA003796]

222 SOCIAL SUPPORT AND SUBSTANCE ABUSE TREATMENT SERVICE USE IN A HOMELESS DRUG-ABUSING POPULATION

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Evidence in the scientific literature demonstrates the role support plays in substance users/abusers' success or failure in SAT and aftercare. Yet, besides "hitting rock bottom," little is known about factors facilitating substance users/abusers' initiation of treatment. Affiliation theory suggests support may play an important role in getting people to treatment. This inquiry's purpose was to explore the relationship between social support and initiation/use of SAT services in a homeless drug-abusing population. Four hundred homeless persons (300 men & 100 women) were recruited randomly from shelters and streets in St. Louis, Missouri. Participants were interviewed for residential history (Homeless Supplement to the Diagnostic Interview Schedule: DIS), social support (Arizona Social Support Interview Schedule), mental health and substance use history (DIS and Composite International Diagnostic Interview), and service use (Washington University Health and Social Service Use Instrument). Support was divided into five categories: 1) family and 2) friend instrumental (material aid), 3) family and 4) friend emotional, and 5) service provider support. SAT services included self-help, outpatient, residential, and inpatient. Regression diagnostics and tobit analyses were completed; demographics were used as control variables. Those with more family instrumental (log likelihood=-206.03, B=4.62, SE=1.67, X²=7.66) and more service provider support (log likelihood=-205.22, B=0.95, SE=0.41, X²=5.47) were more likely to use SAT services. Number of friend emotional supports was significant in the bivariate analyses, but not in the full tobit equation. These data bolster the idea that support plays a role in who seeks SAT. Although further study is needed, these results suggest that intervening in users/abusers' social networks (particularly family networks) may facilitate entry into SAT. It further emphasizes the role of providers as supports.

223 CLEARING THE MURKINESS OF DESIGNING, CREATING, AND CHECKING SCORING ALGORITHMS

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Diagnostic interviews like the Substance Abuse Module, (SAM), have provided reliable DSM-IV substance abuse and dependence diagnoses. Reasons for reliability include good question design, and a scoring algorithm that correctly evaluate each diagnostic criterion. We will present an example used to score a modified WHO Schedules for Clinical Assessment in Neuropsychiatry (SCAN), for club drugs, used in the NIDA funded Club Drug - St. Louis, Sydney, Australia, Miami, (CD-SLAM) study. The modification mimicked the SCAN question format and created a need to construct scoring algorithms adopting DSM-IV substance use disorder criteria for club drugs. First, a data entry program was created and the data from the paper and pen interview was transferred into an electronic database. Second, scoring algorithms were created by taking each question within the modified SCAN and matching it to individual DSM-IV criteria. The process was also reversed by beginning with the DSM-IV criteria and matching it to specific SCAN questions. The referenced list was passed to a peer-review panel which considered whether all diagnostic criteria had been assessed and urged revisions until a consensus was reached for each question. Because peer-review may fail to recognize problems with each other's inquiry, outside experts, were called upon to evaluate the appropriateness of the operationalization for each question, in this case Dr. Cottler (Robins and Cottler, 2004). Once a defined list of appropriate variables was created, scoring algorithms were designed. The algorithms programmatically evaluated the SCAN data and for each respondent, each diagnosis was scored as present, negative, or indeterminate if insufficient information was available for a diagnosis. These results were also peer-reviewed and any programming errors found within a specific algorithm were corrected. These steps will be presented with the hope to assist others who may not have a full understanding of the algorithm design process.

224 CHANGES IN DEPRESSIVE SYMPTOMATOLOGY AMONG YOUNG ADULTS WITH A HISTORY OF MDMA USE

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Research suggests that MDMA can cause serotonin depletion as well as serotonergic neurodegradation that may result in depression. This longitudinal study used the latest version of the Beck Depression Inventory (BDI-II) to assess depressive symptomatology every 6 months over a two year period among a community sample of young adult MDMA users (n=402) in Ohio. An individual growth model was used to analyze changes in BDI scores. Between baseline and 24 months, the mean BDI score declined from 9.8 to 7.7. Scores varied significantly across individuals at baseline and declined at a rate of 0.44 points every 6 months. Persons with higher baseline scores were more likely to have their scores decrease over time. Several factors were significantly associated with BDI score levels, independent of time: gender - men's scores were lower; ethnicity - whites' scores were lower than other groups; education - college students' scores were lower than non-students; benzodiazepines - current users' scores were higher; opioids - current users' scores were higher; and cumulative MDMA use - people who had used MDMA more than 50 times had scores that were higher than persons who had used the drug less often. The results reported here show low levels of depressive symptoms among a sample that, after 24 months, consisted of both active and former MDMA users. The low and declining mean BDI scores suggest that MDMA use does not necessarily contribute to long-term or clinically relevant depressive symptomatology, although heavier lifetime users were more likely to have higher scores.

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- 225 YEARS OF POTENTIAL LIFE LOST AND MORTALITY AMONG CALIFORNIA DRUG ABUSERS IN TREATMENT**
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This study analyzed death data of adult patients admitted to 43 drug treatment programs in 13 counties across California. Premature mortality in terms of years of potential life lost (YPLL) and cause-specific mortality were calculated for this cohort. From April 2000 to May 2001, a total of 7008 patients consecutively admitted to treatment programs were recruited into this study. Two years after admission, 174 subjects were dead as confirmed by death certificates. Among them, 41% were females and 59% males. More than half of study subjects were Whites (54.3%) and 21.4% Hispanics, 17.4% African Americans, and 6.9% others. On average, age of death in this cohort was 44 (SD=10.8). Potential life lost before 65 averaged 21 years (SD= 10.2). The leading causes of death by YPLL were: poisoning by substances (593), accidents (563), and suicide (411). In terms of mortality, leading causes of death were poisoning (n=26), accidents (n=21), and liver diseases (n=20). The YPLL was significantly higher among Hispanics than African Americans or Whites (p=0.01), which indicated that Hispanics died at a younger age than other two groups and had a higher premature mortality. Female and male addicts showed a similar trend of YPLL (21.3 vs. 21.1). This study reveals the leading causes of premature deaths among addicts were poisoning of substances (overdose), accidents and suicide, which should be considered in public health efforts.
- 226 ABUSE LIABILITY OF GAMMA-HYDROXYBUTYRIC ACID IN HUMANS: A COMPARISON WITH ETHANOL AND FLUNITRAZEPAM**
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GHB, an endogenous neurotransmitter, is marketed in different countries as an anesthetic, for the treatment of narcolepsy and in alcohol detoxification therapy. In addition, GHB is a recreational drug commonly consumed at nightclubs and "raves" in conjunction with drugs like 3,4-methylenedioxymethamphetamine (MDMA, ecstasy), or ketamine, also known as "Club drugs". GHB has become a major concern in emergency rooms of some countries due to an important increase in the number of cases of intoxication. GHB can induce strong sedation and reversible coma, and has been used as a rape-drug. Recreational users of GHB experience euphoria, relaxation, reduction of social inhibitions and decreased motor skills. This clinical trial was designed to evaluate the abuse liability of GHB. The study was randomized, double-blind, double-dummy and cross-over. Twelve healthy male recreational users of GHB participated in five experimental sessions. Drug conditions were: a single oral dose of GHB (40 mg/kg or 60 mg/kg), ethanol (0.7 g/kg), flunitrazepam 1.25 mg and placebo. Study variables included vital signs (blood pressure, heart rate, oral temperature, pupil diameter), psychomotor performance (DSST, balance, Maddox-Wing), and subjective effects (a set of 13-visual analog scales, ARCI-49 item and VESSPA questionnaires). GHB increased blood pressure and pupil diameter. Flunitrazepam decreased temperature. All active conditions impaired psychomotor performance and induced euphoria. Alcohol induced its prototypical effects and flunitrazepam produced strong sedation. GHB showed a mixed stimulant-sedative pattern with a biphasic time profile, with initial euphoria ("high", "liking") and stimulation followed by sedation. Results suggest a high abuse liability of GHB. Supported by grants: FIS (02/0824, G03/005 and C03/06) and CIRIT 2005SGR00032.
- 227 DRUG-RELATED DEATHS IN THE MONTH AND YEAR AFTER RELEASE FROM ENGLISH PRISONS BETWEEN 1999 AND 2001, A 48,771 COHORT STUDY**
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Previous reports indicate a period of increased risk in the immediate post release period (Singleton, Farrell, Marsden et al 2002) . A study of 48,771 prison releases over a three year period from 1999 to 2001, sampled from the English sentenced prisoner population were followed to determine the mortality relating to the release period and the year following release. . There were 261 drug-related deaths and 181 deaths from other causes recorded to study sample members. Rates of mortality for all causes were 9.4 per 1,000 per annum for men and 8.2 per 1,000 per annum for women. The mortality rates for drug-related causes were 5.2 per 1,000 per annum among men and 5.9 per 1,000 per annum among women. The corresponding rates for non-drug causes were 4.2 per 1,000 per annum for men and 2.3 per 1,000 per annum for women. In women, the mortality rate for all causes for released offenders during the first week after discharge was equivalent to 47 deaths per thousand per annum. The all causes mortality rate for males was 37 deaths per thousand per annum during the first week after discharge. Rates then declined to 26 deaths per thousand per annum in the second week after discharge and 13 deaths per 1,000 per annum in the third and fourth weeks after discharge. For the remainder of the first year after discharge the all cause mortality rate for males varied between 7 and 10 deaths per 1,000 per annum. The rates were 8 to 10 fold elevated in the first month compared to the matched annual mortality rates. There were no significant differences in overall or period specific mortality rates for men or women between 1998, 1999 and 2003. Release from prison for those who are opioid dependent and non tolerant due to low exposure to opiates is associated with a very significant increased risk of death in the first month. Strategies to reduce this risk need further development.
- 228 ESTROUS CYCLE AND HORMONAL INFLUENCES ON COCAINE-PRIMED REINSTATEMENT OF DRUG SEEKING IN FEMALE RATS**
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Clinical research suggests that gender differences exist in cocaine dependence. Similarly, preclinical studies have shown that female rats exhibit higher response rates during cocaine self-administration and enhanced cocaine-primed reinstatement of drug-seeking than male rats. This latter effect is estrous cycle dependent, as estrus females show greater cocaine-primed reinstatement than nonestrus females. However, the relationship between estrogen and progesterone levels with cocaine self-administration and reinstatement has not been explored. The current study examined whether responding during cocaine self-administration and cocaine-primed reinstatement would correlate with estrogen and progesterone plasma levels. Female, Sprague-Dawley rats (n = 27) were trained to lever press on a FR1 schedule for i.v. cocaine (0.5 mg/kg/infusion) during daily 2 h sessions. Following self-administration, responding was extinguished in the absence of cocaine reinforcement. Once responding was extinguished to criterion, rats received an injection of cocaine (5 or 10 mg/kg, IP) or saline 30 min prior to reinstatement testing. Vaginal smears and blood samples were collected prior to and during chronic cocaine self-administration and prior to each reinstatement test. Although no significant differences were found during self-administration, there was a significant increase in responding during cocaine-primed reinstatement for estrus versus nonestrus females. Moreover, these effects appear to be inversely related to hormone levels, as proestrus females (high plasma levels of estrogen and progesterone) exhibited less responding during reinstatement, while estrus females (lowest plasma levels of estrogen and progesterone) showed the greatest reinstatement. Taken together, these results suggest that while estrogen and progesterone levels do not appear to influence ongoing cocaine self-administration, lower hormone levels may contribute to increased susceptibility to relapse. (Supported by NIH Grant DA016511).

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229 NEUROPSYCHOLOGICAL FUNCTIONING AND RETENTION OF CONSENT INFORMATION IN A MISDEMEANOR DRUG COURT POPULATION

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It is generally assumed that informed consent to research ensures that participants' decisions are knowing, intelligent, and voluntary. However, evidence suggests that participants often fail to comprehend or remember much of the consent information. For example, research indicates that 33-75% of drug and alcohol abusers have cognitive impairment. Current procedures (e.g., brief consent quizzes, mental status exams) may be insufficient to identify these individuals or determine their specific deficits. Identifying specific cognitive deficits that predict poor consent comprehension and retention could permit us to more effectively determine competence and tailor consent procedures to participants' needs. Misdemeanor drug court clients (N = 77) completed a standard informed consent to participate in a research study. Participants completed the Addiction Severity Index at baseline and a 17-item consent quiz (Modified MacCAT-CR) and a brief neuropsychological battery 2 weeks later. Results indicated that this sample performed within the normal range on measures of intelligence, memory, attention, verbal fluency, reading level, and mental flexibility. Scores on the consent quiz indicated that participants failed to remember over 65% of the consent quiz information within 2 weeks of being consented. A series of linear regression analyses revealed that drug problem severity, verbal IQ, and reading level significantly predicted retention of consent information. Although these data suggest that misdemeanor drug court clients are not significantly impaired, the existing consent procedures appear inadequate to ensure the retention of important human subject protection information. Drug problem severity, verbal IQ and reading level may serve as useful screening tools to determine whether research participants require enhanced consent procedures. Supported by NIDA grants #R01-DA-16730 & #R01-DA-13096

230 MINIMAL VS. ENHANCED COUNSELING AND DIRECTLY OBSERVED THERAPY IN PRIMARY CARE BUPRENORPHINE TREATMENT

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Counseling and medication adherence can affect opioid agonist treatment outcomes. We investigated the effects of two of counseling intensities and two medication dispensing methods in patients receiving buprenorphine (BUP) in primary care. We conducted a 12-week trial of Physician Management (PM) with weekly BUP dispensing vs. PM and directly observed thrice-weekly BUP and cognitive behavioral therapy (PM+DOT/CBT) in opioid dependent patients. PM was a 15-minute counseling treatment provided bi-weekly by physicians. CBT was a 45-minute treatment provided weekly by psychologists. Subjects were assigned to PM (N=28) or PM+DOT/CBT (N=27), based on therapist availability. The groups were similar on mean age (37.8 vs. 40.3 years) and % male (68% vs. 78%). PM patients were more likely to be white (89% vs. 59%), had fewer years of opioid use (5.8 vs. 12.0), and were less likely to have a history of detoxification (30% vs. 74%;p.05). There were no differences in treatment completion between PM and PM+DOT/CBT (86% vs. 67%;p>.05). PM patients had a greater proportion of opioid negative urines (69% vs. 46%; p.05) weeks of continuous opioid abstinence. Proportion of cocaine negative urines did not differ between treatments (77% vs. 78%;p>.05). On adjustment for baseline differences, prior detoxification interacted with treatment assignment (p.05). We conclude that PM with weekly medication dispensing has improved efficacy compared to PM+DOT/CBT for patients receiving BUP in primary care. Response to PM+DOT/CBT appears to be moderated by patient treatment history. Supported by NIDA grants: DA019511-01, DA09803-04A2, DA00167, 2K12DA00167-1, 2 K24 DA000445.

231 ACUTE EFFECTS OF COCAINE IN TWO MODELS OF INHIBITORY CONTROL: IMPLICATIONS OF NON-LINEAR DOSE EFFECTS

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There is growing interest in the possibility that acute cognitive effects of drugs can play a role in their abuse potential (Fillmore 2003). Of the various cognitive functions affected by stimulant drugs, alterations in inhibitory control might be among the most likely to contribute to abuse potential. This study examined dose-response effects of oral cocaine on the inhibitory control of behavior in adult cocaine abusers using two different behavioral models of inhibitory control. Adults (N=12) with a history of cocaine use performed the stop-signal and cue-dependent go no-go task to measure inhibitory control of behavior in response to a range of oral cocaine HCl doses (0, 100, 200, and 300 mg). Although both tasks showed cocaine-induced facilitation of inhibitory control, dose-response functions differed depending on the measures. The stop-signal measure revealed a quadratic dose-response function and the cue go no-go measure showed a more orderly, linear improvement as a function of dose. The evidence suggests a two-phasic dose-response in which facilitating effects of stimulant drugs on inhibitory control might be limited to a range of intermediate doses, above which improvement is no longer evident and impairing effects could possibly emerge. This research was supported by Grant R01 DA14079 from the National Institute on Drug Abuse and by the General Clinical Research Centers Grant M01RR02602.

232 TWO-YEAR EXPERIENCE WITH BUPRENORPHINE-NALOXONE FOR MAINTENANCE TREATMENT OF OPIOID-DEPENDENCE WITHIN A PRIVATE PRACTICE SETTING

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Office-based opioid treatment with buprenorphine-naloxone (Suboxone) has significantly improved patient access to safe and effective therapy for opioid dependence. The practical experiences of physicians prescribing Suboxone are of great interest to healthcare providers since little real world data has been available to date. We describe here the experiences of an early adopter of Suboxone operating as a sole practitioner since 2003 in a private office in Durham, NC. After directly observed office dose induction, Suboxone prescriptions are given in progressively increasing lengths culminating in monthly prescriptions after evidence of continued stability. In-office urine drug screening (UDS) is done regularly. Patients are referred out for ancillary services. Retrospective chart reviews of 80 patients who received Suboxone treatment for up to two years will be discussed. Data from the first 25 patients revealed the following. Patients averaged 31 years old and slightly over a third were 17-22 years old. Almost half were white (44%), male (44%) and married (40%). Most were employed (70%) and insured (88%). Dependence histories were short, averaging 3.3 years. Most (2/3) were dependent on prescription opioids and a third were heroin users. The mean Suboxone maintenance dose was 10 mg (range 2-16). Ninety-five, 82 and 80 percent were still in treatment 3, 6 and 9 months following induction. Eighty-six percent of UDS were opioid-negative; rates of non-opioid drug use also decreased. Fifty-two percent of the patients attended at least 75% of their counseling sessions. There were no significant issues with patient safety, medication abuse or diversion. Overall, the office-based experience has been excellent and this practitioner would treat more than 30 patients if permitted by law. Suboxone maintenance was safe, associated with high rates of treatment retention and opioid abstinence, and is helping to reach a broader patient population including younger users. Supported by an educational grant from Reckitt Benckiser Pharmaceuticals, Inc.

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- 233 SCHOOL-BASED ECSTASY AND RELATED DRUGS EDUCATION IN AUSTRALIA: A QUALITATIVE STUDY**
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In Australia, contrary to the population use trends for other illicit drugs, ecstasy use has been increasing over the last decade amongst young people. This qualitative study aimed to explore issues related to the effective coverage of ecstasy and related drugs (ERDs) in school drug education. A total of 66 in-depth interviews were conducted in all jurisdictions across Australia among a range of stakeholders across the school community. A thematic analysis was conducted on the interview transcripts. The results provided a detailed description of the current approaches and activities of school drug education across all subjects in the curriculum. The results compare the way conversations occur in class rooms around alcohol, cannabis and ERDs. The study describes teachers views on effective techniques for drug education. This paper will present the range of views about appropriate harm reduction messages and the use of external speakers. A number of barriers to effective ERDs drug education were identified including inadequate leadership; curriculum; teacher's knowledge, attitudes and credibility; and concerns about disclosure of personal drug use. Currently, curriculum frameworks may not specify drug education outcomes, or only use them as an example for broader health outcomes. Study results indicate that there is support for the provision of ERDs school drug education. A number of recommendations for expanding and further enhancing schools-based ERDs education and the development of relevant resource materials will be discussed.
- 234 OPIOID- AND CANNABINOID- INDUCED ANTINOCICEPTION IN NR1 KNOCKDOWN MICE**
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The present study examined nociception, opioid-induced antinociception, and cannabinoid-induced antinociception in mice in which the NR1 subunit of the NMDA receptor had been reduced to approximately 5% (NR1 KD mice). Wild-type littermates (NR1 WT) served as controls. Nociceptive responses were measured with a hot plate analgesia meter. Mice were initially tested for differences in nociception across a range of hot plate temperatures (44°-56°). Latency to respond on the hot plate was reduced in a temperature dependent manner in both NR1 KD and NR1 WT mice and these groups did not differ from each other. Opioid-induced antinociception was assessed with morphine (0.32-18 mg/kg, s.c.), which produced dose-dependent increases in latency to respond on a hot plate maintained at 56° in both groups. Morphine was less potent in NR1 KD mice [ED50 = 11 (95% confidence limits = (8.5-14))] compared to NR1 WT mice [ED50 = 5.0 (4.2-6.0)]. The competitive NMDA antagonist LY235959 (0.1-1.0 mg/kg, i.p.) shifted the dose effect curve to the left in NR1 WT mice [ED50 = 1.7 (0.94-3.1)] but had no effect on NR1 KD mice [ED50 = 15 (11-20)]. The cannabinoid agonist CP55940 (0.032-1.0 mg/kg, i.p.) was also examined and produced dose-dependent increases in latency to respond on a hot plate maintained at 52°. Similar to morphine, CP55940 was less potent in NR1 KD mice [ED50 = 0.39 (0.23-0.66)] compared to NR1 WT mice [ED50 = 0.13 (0.08-0.20)]. These results suggest that the antinociceptive effects of both morphine and CP55940 are different in NR1 KD mice and NR1 WT controls. Supported by grants R01-DA02749 and T32-DA07244.
- 235 THE ROLE OF DOPAMINERGIC ALTERATIONS IN PREPULSE INHIBITION IN ADULT RATS FOLLOWING NEONATAL INTRACEREBRAL HIPPOCAMPAL GP120 INJECTIONS**
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The development of immunodeficiency virus (HIV)-associated dementia (HAD) is mediated by the HIV-1 proteins Tat and gp120 that interact with neurons in the central nervous system. Multiple studies suggest that HAD may result from damage to dopaminergic (DA) systems in the HIV infected brain. The present study was designed to determine the potential role of DA alterations in sensory gating and its interaction with the HIV-protein gp120 that was intracerebrally injected into the hippocampus on postnatal day 1. Sensory gating was measured by prepulse inhibition (PPI) of the auditory startle response (ISIs of 0, 8, 40, 80, 120, and 4000 msec, 6 trial blocks, Latin square design). Using a randomized-blocks design, one male and one female pup of 8 Sprague-Dawley litters were bilaterally injected with either vehicle (1µl saline) or one of the three gp120 doses: 1.29, 12.9, and 129 ng/kg. As a within-subject factor, saline and a dopamine D1/D2 agonist, apomorphine (APO) (0.1 mg/kg) were administered subcutaneously in adulthood 10 minutes prior to PPI testing. A main effect of drug indicated a significant reduction in the baseline magnitude, ASR by APO [F(1, 20) = 7.08, p = .02]. For gp120 in the saline condition, the magnitude of the peak response in the PPI trials (ISI 08-120) was significantly increased, as a function of gp120 dose treatment [F(1, 20) = 5.41 p = .03], indicating less inhibition compared to the baseline ASR. In addition, the inflection of the inhibition curve was significantly altered for the high dose gp120 treated animals [$\chi^2(1) = 4.12, p = .04$]. Interestingly, a gp120 dose x drug interaction [F(3, 20) = 3.62, p = .03] was evident on the magnitude of the inhibition response in the APO treatment condition, with an enhanced inhibition across ISIs [0-4000] as the neonatal gp120 dose increased. It is suggested that the DA D1/D2 agonist APO acts on long-lasting alterations in neuronal responses consequent to neonatal gp120 exposure. (Supported by DA13137, DA014401, HD043680).
- 236 CHARACTERIZING OPIOID ANALGESIC ABUSE: FINDINGS FROM ETHNOGRAPHIC FIELD RESEARCH**
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Introduction: Although numerous U.S. surveillance systems currently report on opioid analgesic abuse, there is a need for additional descriptive and interpretive data, not only to confirm and characterize the cases, but to guide targeted intervention efforts. The purpose of this analysis was to summarize 2005 findings from field research conducted by the Purdue Risk Information Synthesis & Minimization Action Program (PRISMATM). Methods: Field research inquiries were guided by standard ethnographic techniques and conducted in three-digit ZIP codes (3DZ) meeting a predetermined threshold level of opioid analgesic abuse or diversion. Data sources included RADARS® System studies and media reports. Semi-structured telephone interviews were conducted with a wide range of contacts, including law enforcement officers, physicians, pharmacists, and drug abuse treatment staff in the affected community. In total, 258 interviews were conducted in 40 states comprising 99 distinct 3DZs, with an average of 2.8 interviews conducted per field report. Qualitative Results: I. Major themes: 1) Hydrocodone, oxycodone (immediate-release) and OxyContin® reported to be the most frequently abused and diverted opioid analgesics; 2) Opioid analgesic abuse is most commonly reported in rural areas; 3) Opioid analgesic abuse appears to be rising among teenagers; and 4) Abusers perceive prescription drugs to be safer to use than illicit drugs. II. Other key findings: 1) Antidepressants abused to reduce the side effects of methamphetamine; 2) Abuse of prescription drugs rising in Mormon communities and on Native American reservations; and 3) Local government officials are being forced to redirect resources from diversion and abuse of prescription drugs to combat a rising methamphetamine problem. Conclusions: Interpretation of quantitative reports of opioid analgesic abuse and diversion are substantially enriched by the addition of detailed, descriptive field-based inquiries.

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237 PSYCHIATRIC DISTRESS AMONG ADULT RECENT-ONSET CANNABIS USERS

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AIM: In this work, we seek to estimate the degree to which recent-onset cannabis users might be experiencing clinical features of psychiatric distress, relative to the experience of past-onset cannabis users and never-users. Here, the focus is upon 4 interdependent clinical features associated with generalized anxiety disorders (GAD): (1) worrying about everyday problems more than other people, (2) excess worrying, feeling nervous, or anxious for most of the past year, (3) ruminative worrying ("couldn't put it out of your mind"), and (4) worry-associated clinical features such as feeling on edge and irritability, with a multivariate approach for estimation of cannabis-associated worrying. **METHODS:** The study estimates are based on data from the National Survey on Drug Use and Health (NSDUH) conducted in 2003, with a representative community sample (n= 55,230 respondents) and standardized assessment of cannabis use and psychiatric distress. **RESULTS:** A total of 563 respondents, 1.0% of the total sample, qualified as recent-onset cannabis users (i.e., starting use within 24 months of the assessment), and 18,428 were past-onset cannabis users. Based upon the generalized estimating equations and a generalized linear model to compare users with never-users, and borrowing information across all four clinical features associated with GAD, the recent-onset cannabis users were an estimated 1.8 times more likely to experience these clinical features ($p < 0.05$), even with statistical adjustments for sociodemographic variations such as male-female differences that also were statistically robust. As compared to never-users, the past-onset cannabis users were an estimated 2.4 times more likely to have experienced these clinical features ($p < 0.05$). **CONCLUSIONS:** Excess risk of cannabis-associated worrying is found for both recent-onset and past-onset cannabis users, relative to never-users. Two interesting possibilities merit special attention: (1) worrying signals vulnerability to use cannabis, and (2) cannabis use causes GAD-like worrying. **SUPPORT:** NIDA/NIH/FIC D43TW05819; T32DA07292; K05DA015799.

238 TREATMENT COST ANALYSIS TOOL (TCAT) FOR PROVIDER ESTIMATES OF ACCOUNTING AND ECONOMIC COSTS

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Because of the increased importance for and growing need to better understand treatment costs, a Microsoft® Excel-based workbook designed for use by research analysts on a national study was retooled for treatment program director and financial officer use. This cost allocation and analysis instrument can also be used as a planning and management tool to optimize resources and forecast the impact of future changes in staffing, client flow, program design, and other resources. The Treatment Cost Analysis Tool (TCAT) automatically generates a summary cost table and three charts, reporting average program costs, mean hourly personnel rates, and distributions of personnel costs compared with costs from a national sample of outpatient providers. To learn the purposes of TCAT, data entry, and interpretation of results, treatment agency staff participated in 4 hours of group training within a broader project workshop. TCAT is being used by these staff to capture and allocate both economic and accounting costs in a sample of 100 outpatient drug-free treatment programs. Preliminary analyses on about one-fourth of the sample indicate that 75% of the programs are affiliated with a parent organization; 54% offer regular outpatient services, 8% intensive, and 38% both regular and intensive; 71% are non-profit, 21% for profit, and 8% public. Preliminary costs are \$13 per enrollment day, \$80 per individual counseling hour, and \$9 per group counseling hour. Future directions include development of a web-based interview version, much like some of the commercially available tax preparation software tools, and extensions for use in other modalities of treatment. Cost data, coupled with other measures of organizational operations and functioning will allow for a more comprehensive understanding of dynamic and reciprocal relationships between organizations and service delivery. Supported by NIDA grant 5R01 DA014468

239 IMPACT OF A PEER-MENTORING PROGRAM FOR HIV-AFFECTED YOUTH ON FAMILY FUNCTIONING AND MENTAL HEALTH SERVICES PARTICIPATION

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Background: Stronger family functioning and supportive service participation are protective factors for vulnerable youth at risk for substance abuse (e.g., Biederman et al., 1999; Hawkins et al., 1992). **Objective:** To determine whether participation in peer mentoring (PM) predicts improved family functioning and mental health services participation for early adolescents with an HIV+ parent/guardian. **Methods:** Youth (N=157 in 94 families) were randomly assigned to: (a) Experimental - a PM program centered around 20 older trained Peer Mentors with adult supervision; or (b) Control - a recreational program. Because only 54% of the assigned experimentals participated in PM, the frequency of PM attendance rather than group assignment was used as the predictor variable to determine the effect of PM on outcomes. The outcome (dependent) variables measured at one year follow-up were five family functioning measures and an index of mental health services received (e.g., counseling, medication). Ordinary least squares (OLS) regression was used to control for baseline covariates and multilevel modeling (MLM) to control for the nested effect of youths (siblings) within the same families. In the OLS model the baseline equivalent of the outcome variable was force entered; other correlated variables were entered in a stepwise fashion. The baseline equivalent of the outcome variable was included as a fixed effect in MLM. **Results:** Subjects were 49% male, 62% African-American, 29% Hispanic; mean age was 11.4 yrs. Frequency of PM attendance was significantly associated ($p < .05$) with more services received ($r = .20$) and with two family functioning outcomes (family management, $r = .25$; and family discipline, $r = .22$). PM attendance predicted family management and receipt of mental health services in the OLS and multilevel models. **Conclusion:** Peer mentoring activities appear to increase two factors that can help protect vulnerable inner-city youth against future substance abuse: participation in mental health services and stronger family functioning. (Grant# R01 HD37350)

240 RACIAL DISPARITIES IN QUALITY OF LIFE OF SUBSTANCE ABUSERS IN TREATMENT

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Objective: The negative health consequences incurred by drug use appear to disproportionately affect racial and ethnic minorities. It is widely acknowledged that substance users need access to health, social, mental health and drug abuse treatment services, yet it is less well documented whether similar health disparities exist within drug treatment populations or whether substance abuse treatment redress some of these inequalities and improve the quality of life of substance users. This study will explore analytically whether there is racial variability in perceived quality of life. **Methods:** This paper draws upon a subset of baseline data from the "Partner-Oriented Drug Treatment and HIV Risk Reduction Project." The analytic sample was comprised of 321 participants recruited from 4-drug treatment clinics located in the Los Angeles, CA metropolitan region. Ordinary Least Squares multivariate analyses estimated the effect of race and ethnicity on quality of life after controlling for sociodemographic, health, and treatment-related factors. **Results:** African American and Hispanic drug users in treatment perceived their quality of life to be greater than Whites. Lower perceived quality of life was associated with being unemployed, having public insurance and perceiving barriers to care. **Discussion:** The findings of this study suggest that methadone treatment programs are important, not only to respond to the growing problem of drug abuse, but may also be a conduit for leveling racial and ethnic disparities in accessing health care and in turn quality of life.

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241 BOTH ERROR MONITORING AND DELAY DISCOUNTING ACTIVITY CO-LOCALIZE IN MEDIAL FRONTAL CORTEX

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Background: Error Monitoring is an essential cognitive capacity in the pursuit of goals in a changing environment (Rabbitt, 1966). Both electrophysiological and functional neuroimaging results have identified an error-associated signal located in medial frontal cortex. Using fMRI and a probabilistic Go/NoGo task, we have established that opiate-addicts entering methadone maintenance treatment exhibit decreased medial frontal cortex activation with occurrence of error events (Forman et al. 2004). The strength of this error signal is linked to discrimination performance (through speed-accuracy trade-off) and moment-to-moment cognitive control. In the clinical setting, the strength of this error signal predicted individual treatment adherence (e.g., time retained in treatment before drop-out). While the latter finding suggests a connection between the processing of error events and complex decisions involving choices between immediate and delayed goals, we did not have direct evidence supporting this connection. Methods: 23 subjects (8 opiate-addicts, 15 controls) performed both the probabilistic Go/NoGo task and a delay-discounting task while brain activity was monitored using event-related fMRI. Results: The medial frontal cortex region of interest (ROI) previously associated with error processing also displayed significant activation during delay discounting ($p < 0.04$). Moreover in this ROI, the individual strength of brain activation while processing errors positively correlated with that exhibited during processing decisions between immediate and delayed hypothetical rewards ($p < 0.03$). A common neurobiological substrate in medial frontal cortex appears to support both types of processing. Supported by NIH grant R29DA11721 and VA CPPF and MERIT awards.

242 ETHNIC DISPARITIES IN THE UTILIZATION OF TREATMENT SERVICES AMONG PROPOSITION 36 CLIENTS

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Objective: To examine ethnic disparities in treatment services received by individuals participating in drug treatment via California's Proposition 36. Methods: Using a non-experimental study design, intake data were examined among 1,057 Proposition 36 clients consecutively admitted to 30 drug abuse treatment programs across 5 diverse California counties. Results: Sample characteristics are as follows: 19.6% were Black, 25.9% Hispanic, and 54.5% white, average baseline age was 36.9 years, and almost 70% were male. Almost half had never been married, and 23.5% were employed at intake. Approximately 71% reported using any drugs in the past 30 days, with amphetamines (including methamphetamines) as their primary drug problem (52.2%). Overall, 51% of participants reported never receiving prior treatment for their alcohol or drug use. With respect to ethnic differences, more Blacks reported cocaine (44.0%) to be their primary drug problem, while more Hispanics (53.7%) and Whites (65.8%) reported amphetamine. The results of the logistic regression, after adjusting for age, gender, and addiction severity, indicated that Blacks were significantly less likely to receive outpatient services (OR: 0.56, $p < .05$) compared to Whites and Hispanics (OR: 1.00, 1.15, respectively). However, Blacks were almost twice as likely to receive residential care (OR: 1.55, $p < .05$) when compared to Whites and Hispanics (OR: 1.00, 0.70, respectively). In addition, Blacks were more likely to receive methadone maintenance (OR: 2.23; $p < .05$) than Whites and Hispanics (OR: 1.00; 2.05, respectively). Conclusion: Disparities in treatment services rendered to Proposition 36 clients of different ethnic groups were indicated. Although access to residential treatment has improved for Blacks, efforts to increase such treatment options may be needed for Hispanics to curtail their substance abuse. Attempts to address these ethnic disparities could maximize the benefits of Proposition 36.

243 LEARNING AND MEMORY DEFICITS IN ABSTINENT COCAINE AND ALCOHOL ABUSERS: RELATIONSHIP TO DRUG AND ALCOHOL CRAVING

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Prior research has shown that chronic cocaine and alcohol abuse affects brain systems associated with learning and memory abilities. The present study aims to examine these processes in abstinent cocaine and alcohol dependent individuals and also assesses the relationship of these learning and memory abilities to drug craving. Treatment-seeking cocaine (N= 30) and alcohol (N = 30) dependent individuals and 30 healthy community controls were administered the Rey Auditory Verbal Learning Test (RAVLT) to assess a range of learning and memory processes. These included immediate and delayed recall capability, recognition memory, perseveration and retroactive/proactive inhibition. Learning and memory scores were then correlated to levels of drug/alcohol craving at early abstinence. Linear Mixed Effects (LME) models and Analysis of Covariance (ANCOVA) were performed in order to establish group differences. Cocaine patients showed a significantly reduced learning curve compared to both alcohol patients and healthy control participants. They also produced significantly lower recognition scores and higher intrusion errors in the recognition component of the task. All recall and recognition scores were moderately but significantly correlated with drug and alcohol craving. Both recall and recognition deficits in cocaine patients may indicate encoding problems that are not solely associated with difficulty retaining new information. Moreover, the association of such memory decrements with craving is consistent with recent evidence suggesting that the neurobiological alterations associated with addiction overlaps with neuronal plasticity associated with learning and memory functions. Clinical implications of these findings for cognitive behavioral treatments and relapse vulnerability are discussed. (Supported by R01-AA13892, P50-DA16556, K02-DA17232 to Yale University)

244 NALOXONE, BUT NOT PROGLUMIDE OR MK-801, BLOCKS TOLERANCE TO MORPHINE'S AVERSIVE EFFECTS

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Both the cholecystokinin (CCK) antagonist proglumide and the non-competitive N-methyl-D-aspartate (NMDA) antagonist MK-801 block or reduce the development of morphine tolerance in several analgesic assays. The present experiments were performed to assess the ability of these compounds to affect tolerance to the affective properties of morphine as indexed by conditioned taste aversion (CTA) learning. Specifically, 230 male Sprague-Dawley rats were exposed over five sessions to either vehicle or morphine (5 mg/kg) in combination with either proglumide (5 mg/kg; Experiment 1), MK-801 (0.1 mg/kg; Experiment 2) or naloxone (1, 3.2 mg/kg; Experiment 3). Saccharin was then presented and was followed by an IP injection of either vehicle or morphine (10 mg/kg) to condition a taste aversion. For each experiment, a Group x Conditioning Day repeated measures ANOVA was used to examine the effect of these compounds on the ability of morphine preexposure to attenuate taste aversion conditioning. There was a significant Group x Conditioning Day interaction in each experiment ($F(20,308) = 18.533$, $p < 0.0001$; $F(16,236) = 28.084$, $p < 0.0001$; $F(20,308) = 14.293$, $p < 0.0001$). Animals preexposed to and conditioned with morphine acquired an attenuated morphine-induced aversion to saccharin. While neither proglumide nor MK-801 had an effect on this attenuation, naloxone blocked the effects of morphine preexposure, suggesting that neither CCK nor NMDA may be involved in the aversive effects of morphine (or their modulation by drug exposure). That the attenuating effects of morphine preexposure on morphine-induced CTA can be blocked suggests that the weakening of the aversive effects of morphine with chronic use can be prevented, an effect that may have implications for overall drug acceptability and the development of potentially therapeutic compounds to block the effects of drug preexposure.

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245 THE EFFECTS OF DISULFIRAM ON METHAMPHETAMINE-INDUCED CONDITIONED PLACE PREFERENCE

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Methamphetamine (MA) abuse is a serious public health problem, yet no useful pharmacotherapies exist. Disulfiram (DS) has recently emerged as a promising medication to reduce relapse in cocaine addicts, although its efficacy in MA addiction is unexplored. Given the importance of conditioned cues in relapse phenomenon, the present study tested the hypothesis that DS may reduce expression of an MA-induced conditioned place preference (CPP) in rats. We investigated the effects of DS on expression of an MA-induced CPP in which a single MA (1 mg/kg) injection was paired with one chamber and saline in the other, while control animals were paired with saline in both conditioning environments. Expression of this single-trial CPP was tested in drug-free animals allowed to roam the apparatus for 30 min either 24 or 48 hrs after the CPP training. Separate groups of rats were injected with DS (50 or 100 mg/kg) and either placed in the CPP apparatus 30 min or 24 hrs later. MA (1 mg/kg) supported the development of a CPP after the single pairing trial and DS (50 mg/kg) eliminated expression of CPP whether the expression test occurred on Day 3 or 4. DS (100 mg/kg) evoked conditioned place aversion. Future studies will explore a wider range of doses for DS, given the disruptive effects of DS at the chosen doses. These data suggest that DS may be useful in preventing relapse and promoting abstinence in MA-dependent individuals. Supported by DA 00260, DA020087, and DA 13595.

247 WITHDRAWN

246 DISCRIMINATIVE STIMULUS EFFECTS OF DOM IN RHESUS MONKEYS

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The discriminative stimulus effects of drugs that have hallucinogenic effects in humans have been studied extensively in rodents but much less in non-human primates. The purposes of this study were first to see whether monkeys could be trained to discriminate 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) from vehicle, and second, to characterize the DOM discriminative stimulus. Four rhesus monkeys reliably discriminated between 0.32 mg/kg (s.c.) of DOM and vehicle after an average of 116 (range=85-166) sessions while responding under a fixed ratio (FR) 5 schedule of stimulus shock termination. There was a dose-related generalization to DOM with doses of 0.32 and larger occasioning predominantly DOM-lever responding for up to 2 hrs. Two drugs with hallucinogen activity in humans, 2,5-dimethoxy-4-iodophenylisopropylamine (R-DOI) and 2,5-dimethoxy-4-(n)-propylthiophenethylamine (2C-T-7), substituted fully for DOM as did the serotonin (5-HT) receptor agonist quipazine. The selective 5-HT_{2A} receptor antagonist MDL100907, and not the dopamine receptor antagonist haloperidol, completely blocked the discriminative stimulus effects of DOM and the DOM-like effects of quipazine. Drugs that failed to substitute for the DOM discriminative stimulus include ketamine, phencyclidine, amphetamine, methamphetamine, cocaine, morphine, lisuride, and yohimbine. Collectively these data support and extend results obtained in rodents indicating a prominent role for 5-HT_{2A} receptors in the discriminative stimulus effects of drugs that have hallucinogenic activity in humans. It is not clear whether other 5-HT receptors contribute to these effects of DOM in rhesus monkeys. Supported by RCA DA17918 (CPF).

248 NEUROTENSIN AND METENKEPHALIN LEVELS ARE ALTERED IN SEVERAL BRAIN REGIONS IN METHAMPHETAMINE ADDICTS

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Animal data demonstrate that neuropeptide systems associated with dopamine (DA) pathways found in the basal ganglia or the limbic systems are influenced by drugs of abuse because of the propensity of these substances to dramatically alter the activity of associated DA projections. For example, potent psychostimulants such as methamphetamine (METH) vary the extracellular content, the tissue content and the messenger RNA of the neuropeptide neurotensin (NT) and metenkephalin (Met-Enk). Because of these findings, we examined the effect of METH in long-term abusers who overdosed on this stimulant, to determine how these drugs influence the DA-related neuropeptide systems of the brain. The present study is the first to report the effects of abusing METH for extended periods of time on basal ganglia and cortical tissue content of NT and Met-Enk in humans. Our findings demonstrate that NT levels and Met-Enk levels show some similarity in terms of the responses to METH. In general, METH decreased these neuropeptide levels in several regions: parallel decreases in both neuropeptide levels were observed in the caudate nucleus and some regions of cortex (Brodman's Cortex 22, Cortex 39). However, in other brain areas, NT levels in response to METH were down with no change in Met-Enk levels (Brodman's Cortex 18, medial pulvinar thalamus) while other regions exhibited the converse (putamen). Interestingly, Brodman's Cortex 9 was the only region displaying an increase in either peptide (Met-Enk levels were significantly increased). Taken together, we observed changes in peptide concentrations in several motor and limbic brain regions caused by heavy METH exposure that would not have been predicted from the animal work. The significance and mechanisms of these changes require elucidation. This work was supported by PHS grants from NIDA, DA09047 and DA00378.

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249 RANDOMIZED TRIAL OF BACLOFEN FOR SMOKING REDUCTION

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Indirectly dampening the mesolimbic dopamine system with a GABA B agonist may be a useful strategy to reduce craving and drug use. Because it is FDA-approved and well-tolerated, we chose the GABA B agonist baclofen, to test this hypothesis. We conducted a planned interim analysis of our ongoing Smoking Reduction Study at N=58 subjects (27 Females/31 Males) to examine preliminary clinical outcomes. Treatment-seeking smokers were randomized to either baclofen (20 mg q.i.d.) or placebo. Twenty-nine subjects completed the study with no significant differences between groups in attrition or side effects. Groups were also not different in age (40.5 yrs), education (14.5 yrs), cigarettes smoked per day (21 CPD), or depression as measured by the Beck Depression Index (5.1). All subjects received equivalent minimal smoking cessation counseling. Counseling was administered by a trained technician and guided by a manual ("You Can Quit" adapted from the U.S. Department of Health and Human Services Guide). Repeated measures analysis of CPD over the nine week study showed a strong trend toward greater decreases in smoking in the baclofen group compared to the placebo group [$F(1, 213)=5.97, P=0.06$]. Because smoking reduction is a first step in quitting smoking, this ongoing study suggests that ultimately, baclofen may be helpful for cessation. Upon study completion, we will examine results for possible male/female differences as the literature suggests that baclofen may be more helpful for females. A subset of these subjects were imaged (prior to and during treatment) with continuous arterial spin-labeled (CASL) perfusion fMRI during exposure to smoking and nonsmoking cues. These ongoing adjunctive studies will enable us to link medication response to brain substrates, with the prediction that baclofen will dampen limbic perfusion (amygdalae, insulae, ventral striatum) reported in smokers during exposure to cigarette cues (Franklin, SfN 2005). Supported by: NIDA KO1 DA-015426, P60 DA-05186, R01 DA10241; VA VISN 4 MIRECC; and Alexander Foundation.

251 ASSESSMENT OF EXTENDED-ACCESS COCAINE SELF-ADMINISTRATION ON DRUG INTAKE AND BREAKPOINTS MAINTAINED BY FOOD AND COCAINE IN THE LEW RAT STRAIN

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A growing body of research has demonstrated that the rate of cocaine intake by rats in the self-administration (SA) preparation escalates over numerous extended access sessions, demonstrating a behavioral plasticity that may in turn represent underlying neuronal adaptations resulting from and/or causing increased drug intake. Given that operant responding for cocaine varies as a function of animal strain, the present experiment assessed the effects of extended access in a rat strain reported to acquire cocaine SA relatively fast and at relatively low doses, i.e., the "addiction-prone" LEW rat. Interestingly, LEW rats fail to exhibit many of the neuronal adaptations accompanying repeated drug exposure seen in other strains. Accordingly, the current study assessed the effects of extended access to cocaine in male LEW rats ($n = 3$) on drug intake across sessions and on subsequent breakpoints maintained by food and cocaine under a progressive-ratio schedule. Breakpoints maintained by food and cocaine were examined in rats before and after 20 daily extended access sessions (6 h/session) of cocaine SA (0.75 mg/kg, intravenous) on an FR-1 schedule of reinforcement. A repeated-measures ANOVA revealed no escalation of drug intake across the 20 extended access sessions ($F(19) = 1.19; p = .355$). Furthermore, paired t-tests revealed no significant changes in breakpoints for food or cocaine between the pre-extended access and post-extended access progressive ratio tests [p 's = .334 (food) and .493 (cocaine)]. Extended access to cocaine in this preparation does not exhibit the same rate-increasing effects in male LEW rats seen in previously examined outbred strains. Furthermore, there are no evident changes in reinforcement value for food or cocaine resulting from extended access to cocaine as evidenced by the constancy of breakpoints for food and cocaine before and after extended access sessions of cocaine SA.

250 AN MR-COMPATIBLE DEVICE FOR DELIVERING SMOKED MARIHUANA OR TOBACCO TO PARTICIPANTS DURING FUNCTIONAL IMAGING

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Functional magnetic resonance imaging (fMRI) is increasingly important in the study of both acute and chronic brain response to drugs of abuse, including THC and nicotine. To date, the rapid brain function and mood changes accompanying inhalation of smoked products have eluded study with fMRI; only iv or oral administration have been available. We report on the development of a modular device, consisting of separate smoke delivery and exhaust components, that permits subjects to smoke marijuana or tobacco cigarettes during fMRI acquisition. The device is not intrusive; it does not touch the subject's face, fits easily inside the head coil and does not restrict movement. Plasma drug levels, heart rate, and behavioral timecourses of "high" and "craving" resulting from smoking a 3.51% THC marijuana cigarette with the device closely match those resulting from smoking outside the magnet in a natural setting (avg. peak plasma level (ng/ml) = 109.8+/-32.0 (device, N=3), vs. 173.33+/-53.6 (w/o, N=5), diff. N.S.). Expired smoke is quickly and completely removed from the magnet bore - in 35 fMRI studies (25 marijuana, 10 tobacco), there have been no detectable odors in the MR suite. Placebo cigarettes have been smoked and offer new insights into the role non-drug factors such as carbon monoxide play in smoked drug effects. Neither the device nor the act of smoking in the magnet impaired the quality of the fMRI data; subject motion is typically less than 2 mm translation and 2 degrees rotation over 30 minutes. This portable and easy to construct device will facilitate research into the neurobiological bases of drug abuse, providing a unique opportunity to study brain mechanisms associated with psychoactive drug use via the delivery method of choice for most marijuana and tobacco users. Supported by NIDA Grants K25DA14013 (BBF), K25DA017712 (LDN), DA03994 (SEL), DA019238 (SEL), and KO5DA00343 (SEL).

252 ADDICTION TREATMENT WORKFORCE CHARACTERISTICS FOR CALIFORNIA, ARIZONA, AND NEW MEXICO: IMPLICATIONS FOR WORKFORCE DEVELOPMENT

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The Pacific Southwest Addiction Technology Transfer Center conducted a survey of substance abuse treatment clinicians and program managers within California, Arizona, and New Mexico to better understand the changing demography and the educational/technical-assistance needs of the workforce. A total of 361 surveys were returned from program directors ($n=128$) and program staff/clinicians ($n=216$). Respondents were asked about workforce demographics, educational and professional background, agency characteristics, professional experience, compensation, and training preferences, needs, and barriers. Women were identified to be under-represented in management positions, and individuals of non-Caucasian ethnic/racial backgrounds under-represented in program staff and program director levels. Access to effective training programs (68%) and strategies for evaluating client performance (63%) were the most frequently identified technical assistance needs among program directors. Program staff identified strategies for improving client participation, problem solving skills, use of computerized client assessment tools, and providing co-occurring competent services as the most critical training needs. Seventy-two percent of program directors and 46% of program staff reported being employed in the addiction treatment field for 8 years or more; 31% of the directors and 57% of program staff reported being employed at their current agency for four years or less. While most respondents reported receiving some fringe benefits, 10% reported receiving no employer contributed health benefits and 31% reported receiving no employer sponsored retirement benefits. These findings provide support for the importance of focusing upon strategies for promoting career development and career stabilization strategies for the substance abuse treatment workforce and identify specific foci for staff development and staff retention based interventions.

253 SLOW ONSET, LONG DURATION METHYLPHENIDATE ANALOGS WITH SELECTIVITY FOR THE DOPAMINE TRANSPORTER

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Based on a molecular modeling/superposition model of methylphenidate with tropane-containing monoamine reuptake blockers, we hypothesized that methylphenidate analogs in which the ester is replaced by an alkyl group should be active. Since the ester group in methylphenidate is rapidly metabolized to an inactive acid, alkyl analogs should have longer durations of action. A large number of analogs were synthesized, and many of the RR/SS diastereomers proved to have low nanomolar potencies in binding and functional transporter assays. Compounds with a para-Cl group had good selectivity for the dopamine transporter, unlike methylphenidate which also has substantial activity at the norepinephrine transporter. Compounds with a 3-Cl or 3,4-diCl did not show this selectivity. In the 3,4-diCl series, the "inactive" RS/SR diastereomers began to show low nanomolar activity at all three monoamine transporters. On a locomotor assay in mice (4 doses, n=8), one 4-Cl compound (32,476) had a slow onset (>20 min), long duration (>8 hrs at 30 mg/kg) profile that should minimize abuse potential. The compound also had slow onset, long duration profiles in a rat microdialysis study (2 doses, n=6) and in a rat electrical brain stimulation study (3 doses, n=8). One 4-Cl compound (32,648) met the dopamine selectivity criteria of the Cocaine Treatment Discovery Program and is being advanced as a possible treatment for cocaine abuse. Supported by grant DA015795; NIDA Intramural Research Program; NIDA contracts Y1-DA1002-04, Y1 DA 0107-05 (to Aaron Janowsky); N01-2-8822 (to Michael J. Forster)

255 ENVIRONMENTAL INDICATORS OF AOD AND VIOLENCE EXPOSURE

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Despite the growing body of evidence linking environmental factors to alcohol and other drugs (AOD) and violence exposure, traditional prevention programs have not targeted environmental factors. This investigation seeks to classify both individual- and community-level distributions and determinants of AOD and violence exposure by identifying environmental factors associated with increased neighborhood violence and AOD exposure among youth. Independent objective neighborhood ratings were conducted on a random sample of city blocks within each of 246 residential Baltimore City neighborhoods to (a) gather information on the physical environment of the neighborhood; (b) clarify the environmental contexts in which youth live and experience violence and AOD exposure; and (c) provide insight on environmental targets for future intervention efforts aimed to reduce youthful exposure to AOD and violence. Environmental assessments were also conducted on block faces of 398 Baltimore City youth participating in the Baltimore Prevention Program (BPP). The BPP data are rich in longitudinal data on violence and AOD exposure as well as social and psychological well-being. In total, 844 unique city blocks were assessed in the first of 4 planned waves of data collection beginning summer, 2005. Environmental assessments were conducted using the Neighborhood Inventory for Environmental Typology (NifETy). The NifETy has six core domains including: physical layout, type of dwellings, activity, physical order and disorder, social order and disorder, and AOD indicators. Indicator-specific prevalence was as follows: alcohol - 21.9%, drugs - 18.8%, and violence 11.6%. These indicators were also found to co-occur in 13.5% of the sample. Indicator co-occurrence was most common on blocks with less than 50% residential land use. Neighborhood indicators of AOD and violence were predictive of youth self-reports of exposure. Geospatial analysis of AOD and violence indicators revealed distinct 'hot-spots' for alcohol and drugs and clustering of violence around these hot spots.

254 INTERACTIONS OF BASOLATERAL AMYGDALA WITH THE DORSAL PREFRONTAL CORTEX AND DORSAL HIPPOCAMPUS IN CONTEXT-INDUCED REINSTATEMENT OF EXTINGUISHED COCAINE-SEEKING BEHAVIOR

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Exposure to a drug-associated environment increases the probability of drug relapse in cocaine users and produces cocaine-seeking behavior in rats. We have previously shown that the functional integrity of the basolateral amygdala (BLA), dorsal prefrontal cortex (PFC), and dorsal hippocampus (DH) is necessary for context-induced reinstatement of extinguished cocaine seeking in rats. It is unclear, however, whether these brain regions directly interact with one another or contribute independently to this behavior. Using a GABA agonist-induced functional disconnection method, we tested the hypothesis that the BLA and PFC interact whereas the BLA and DH independently mediate context-induced cocaine seeking. Rats were trained to press a lever for cocaine infusions (0.25 mg/kg, IV) in a distinct environmental context then underwent extinction training in a different context. On the test day, rats first received infusions of baclofen plus muscimol (0.01/0.1 mM, 0.5 ul/hemisphere) or vehicle into the BLA unilaterally and into the contralateral or ipsilateral PFC or DH. Rats were then placed into the cocaine-paired context and cocaine seeking (responding on the previously cocaine-paired lever) was assessed in the absence of cocaine reinforcement. Vehicle- and GABA agonist-treated groups exhibited equally robust context-induced cocaine seeking. More importantly, regardless of the brain regions manipulated (BLA+DH or BLA+PFC), contralateral inactivation did not impair responding more than ipsilateral inactivation, which would have been indicative of functionally significant interaction between these brain regions. These findings are consistent with the interpretation that the BLA does not interact directly with the PFC or DH to control context-induced cocaine seeking. This implies the existence of multiple parallel pathways of information processing within the relapse circuitry which is consistent with the strong resistance of cocaine relapse to pharmacological interventions.

256 RESPONDER/NUMBERS-NEEDED-TO-TREAT ANALYSIS OF ACAMPROSATE IN ALCOHOL DEPENDENCE IN THE CONTEXT OF CURRENT CNS THERAPY

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Background: Despite availability of pharmacologic options for the treatment of alcohol dependence, the use of such agents for this disorder lags behind that for other CNS disorders. Acamprosate in combination with psychosocial support is indicated for the maintenance of abstinence from alcohol in the treatment of alcohol dependence. Multiple placebo-controlled clinical trials have demonstrated the efficacy and safety of acamprosate in maintaining complete abstinence and prolonging periods of abstinence in alcohol-dependent patients. The current analysis examines the efficacy data across the pivotal trials of acamprosate using various clinically relevant definitions of response in the context of the pharmacological treatments of other CNS disorders. Methods: Intent-to-treat (ITT) data from three double-blind, placebo-controlled pivotal European trials were retrospectively pooled to examine the proportion of patients who responded to treatment with acamprosate 1998 mg/day or placebo using different responder definitions. Numbers-Needed-to-Treat (NNT) analyses were carried out for each of the responder definitions. Results: 372 acamprosate and 375 placebo patients comprised the ITT population. The percentage of responders was significantly greater with acamprosate compared to placebo, using any one of the three criteria of response: patients abstinent at two thirds or more study visits (45% vs. 28%, respectively, p<0.0001); patients with percent days abstinent (PDA) ≥90% (41% vs. 22%, p<0.0001); and patients with PDA ≥90% and Clinical Global Impression of Improvement (CGI-I) scores of 1 (very much improved) or 2 (much improved) (36% vs. 15%, p<0.0001). Depending on the specific definition of clinical response used, NNTs for achieving good response were between 5 and 6. Conclusion: Acamprosate is an effective and safe medication for the treatment of alcohol dependence, with the magnitude of treatment effect comparable to that of therapies for other CNS disorders.

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257 COMPLEX TRAUMA EXPOSURE, PTSD AND DRUG USE

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Objective: Increasingly, evidence suggests that complex trauma exposure may play a role in determining both drug use behavior and PTSD. Several theories have been posited to explain the associations among trauma, PTSD and drug use, yet the nature of these relationships remain unclear. **Methods:** A community-based sample of non-drug users, former drug users, non-injection drug users and injection drug users aged ≥ 18 years were recruited. Trauma exposure, PTSD symptoms, and drug use were assessed through interviewer-administered questionnaires. We constructed a complex trauma score representing cumulative lifetime experience of qualifying criterion A traumatic events. **Results:** To date, of 405 recruited, 50.6% were Hispanic, 39.0% Black and 10.3% White/mixed/other race. The sample was mostly male (70.6%); median age was 37. Overall, 88.9% had experienced at least one traumatic event, 3.2% reported lifetime PTSD and 1.7% past-6 month PTSD. Violent assault was the most frequently reported trauma (67.7%), followed by a relative's death (52.6%), sexual assault (48.4%), injury/disease (42.7%), child abuse (39.0%), witnessing injury/death (35.1%), motor vehicle accident (21.5%), disaster (17.5%), and war/conflict (4.7%). Average trauma score was 3.4 (SD=2.4). In adjusted models, the trauma score was not associated with illicit drug use overall; however, in separate models, there was a significant 12-13% increase in risk for opiate, hallucinogen, and barbiturate use for every unit increase in trauma score after adjustment for key covariates including lifetime PTSD. **Conclusions:** These preliminary data suggest that while complex trauma exposure is not associated with overall increased risk of illicit drug use, it is associated with increase risk of specific drugs, all of which have depressant properties. Although this is partly consistent with a self-medication hypothesis, the persistent association between complex trauma and use of illicit depressants even after adjusting for PTSD suggests multiple mechanisms are operating.

258 AMPHETAMINE, BUT NOT COCAINE, ATTENUATES AKT ACTIVITY IN hDAT-EXPRESSING CELLS AND STRIATAL SYNAPTOSOMES

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The primary mechanism for clearance of extracellular dopamine (DA) is uptake by the dopamine transporter (DAT), which is governed by the number of functional DATs on the cell surface. Previous studies have shown that amphetamine (AMPH) causes a decrease in DAT cell surface expression, while insulin reverses this effect through activation of phosphoinositide-3 kinase (PI3K). Here we show, in both HEK-293 cells stably expressing human DAT (hDAT cells) as well as in murine striatal synaptosomes, that AMPH causes a time-dependent decrease in the activity of AKT, a protein kinase immediately downstream of PI3K, as assessed from immunoblots of both phosphorylated AKT on Thr-308 and Ser-473, as well as by phosphorylated GSK3 α , the immediate downstream effector of AKT. This effect is selective for the psychostimulant AMPH; the DAT inhibitor cocaine does not produce this effect, and pretreatment with cocaine also blocks the effect of AMPH, suggesting that AMPH must be actively transported by DAT to inhibit Akt. The ability of AMPH to decrease AKT activity is also dependent on intracellular calcium as well as CaMKII, since pretreatment with BAPTA-AM and KN-93, respectively, blocked the effect. In vivo studies are also currently underway to examine these paradigms; preliminary data suggest that AMPH administration (both single and repeated administration) to rats mirrors what we see in vitro and ex vivo. By examining kinases in the insulin signaling pathway, our data demonstrate that AMPH, but not cocaine, decreases AKT activity through a Ca²⁺/CaMKII-dependent pathway, thereby providing a novel mechanism for the insulin regulation of AMPH-mediated hDAT trafficking.

259 PREDICTORS OF TREATMENT OUTCOME AMONG COCAINE-DEPENDENT INDIVIDUALS

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We examined whether cocaine use during the first 4-weeks of a 14-week pharmacotherapy trial was predictive of treatment retention and cocaine use during the study. Demographic and baseline characteristics were also examined as predictors. During the first 4 weeks of the trial (2 weeks of lead in and the first 2 weeks post-randomization), all patients received a high value contingency reinforcement behavioral treatment to induce abstinence. Positive reinforcement, in the form of vouchers for clean urine samples (up to a maximum of \$510), was provided in response to a decrease or cessation of use. Of the 54 cocaine dependent patients analyzed for this study, 72% were male, 41% African American, 39% Caucasian and 20% Hispanic. Results indicate that cocaine use behavior during the voucher phase was predictive of cocaine use but was not predictive of treatment retention. There was a significant positive correlation between new cocaine use during the voucher period and the proportion of new cocaine use at the end of the trial ($r = .53$, $p < .0001$). Subjects that had more than 4 days of new use during the voucher period were less likely to achieve abstinence during the study (4% vs. 52%; $X^2 = 15.31$, $df = 1$, $p < .00001$). These findings suggest that reduction of cocaine use early in the trial, in response to the contingency reinforcement treatment, is a strong predictor of abstinence from cocaine during the study.

260 BASELINE PSYCHOLOGICAL STRESS PREDICTS DRUG COURT OUTCOMES ONE YEAR LATER

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Background: The detrimental role of psychological stress in illicit drug use is well established. It is hypothesized that greater stress at initial involvement in drug court will be associated with more negative outcomes one year later. **Method:** Subjects were 500 new drug court clients in two jurisdictions in Kentucky, one rural and one urban. Low, medium, and high self-reported baseline stress groups were compared using ANOVA predicting drug use, criminal involvement, employment, and health one year later. **Results:** The three stress groups differed significantly on all drug court outcomes, with the high stress group having the worst outcomes in all instances, namely, most days of illicit drug use, most types of criminal acts and days incarcerated, least days employed and lowest income, and most days with physical and emotional health problems in the intervening year and in the 30 days before one-year follow-up. These results also obtained after controlling for baseline levels of outcome variables. **Conclusions:** Future research should investigate the possible benefits of including effective stress reduction interventions in drug court programs.

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261 CROSS-SUBSTITUTION OF NICOTINE AND METHAMPHETAMINE

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Nicotine and methamphetamine are both abused in similar settings, sometimes together. Because there are known interactions between central nicotinic acetylcholine receptors and dopamine receptors, it is of interest to characterize the nature of the interaction of these two compounds. The purpose of this study was to characterize the ability of these two compounds to modulate each other's discriminative stimulus effects and to identify pharmacological mechanisms for their interactions. Male Sprague-Dawley rats were trained to discriminate methamphetamine or nicotine from saline. First, the ability of methamphetamine and nicotine to cross-substitute in rats trained to the other compound was tested. Subsequently, the ability of a dopamine antagonist (haloperidol) and a centrally-acting nicotinic antagonist (mecamylamine) to block the effects of methamphetamine and nicotine was also tested. Nicotine and methamphetamine each partially cross-substituted (50-60% DAR). Further testing of methamphetamine-trained subjects revealed that some subjects consistently cross-substituted when given nicotine (42%), whereas others sometimes selected drug and other times selected saline (50%). A minority of subjects (8%) consistently showed no signs of substitution. In nicotine-trained rats, mecamylamine fully antagonized the discriminative stimulus effects of nicotine, but haloperidol had no effect. In methamphetamine-trained rats, mecamylamine failed to antagonize the discriminative stimulus effects of methamphetamine, but haloperidol fully blocked the methamphetamine cue. These results suggest that nicotine and methamphetamine share subjective effects in some subjects. However, the behavioral data suggest that the two compounds do not act at the same site, but produce their interaction downstream from their respective receptors.

262 THE FRENCH CANNABIS POLICY

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The "2004-2008 French Government Plan for the Fight against illicit drugs, tobacco and alcohol", coordinated by the Interministerial Mission for the Fight Against Drugs and Drug Addiction (MILDT), develops a comprehensive policy. Increase in cannabis experimentation and in regular and daily use in the nineties led to set cannabis in the governmental policy. At 18, 59% of boys and 52% of girls have ever used cannabis in 2003. Furthermore, 18% of boys and 8% of girls aged 17-8 regularly used cannabis (at least 10 times a month). As cannabis use has been normalised among youth, the French cannabis policy aimed at reversing the trend in young cannabis use and decreasing cannabis use by changing the image of cannabis, raising awareness of cannabis risks, improving cannabis information and counselling services in order to enhance behaviour changes. The French Cannabis Programme has four components: 1) communication and information through mass media campaigns on the risks of cannabis abuse and large diffusion of information booklets, targeting young people, parents and teachers respectively 2) adolescents and parents with individual and anonymous information and counselling through a specific cannabis hotline and cannabis clinics 3) a comprehensive school education program 4) the development of research on cannabis dependence treatment. This policy was implemented in 2005: a TV and radio campaign was carried out in 2005. A general population survey shows satisfaction scores were about 85%. Information booklets targeting youth, parents and education staff have been widely distributed (around 4 000 000). From March to November 2005, 30 057 visits had been registered in 266 cannabis clinics recently created, including 21 449 for cannabis users (71%). The cannabis hotline has received 80 calls a day on average. In 2006, a second cannabis campaign will be launched on traffic accident related to combined alcohol-cannabis use; the first detailed data on functioning of cannabis clinics will be soon available and allow a full evaluation of this new service; the school education programme will be expanded according to the guidelines defined in 2005.

263 EFFECTS OF SEVERAL ABUSED SOLVENTS ON SEIZURES INDUCED BY PENTYLENETETRAZOL OR N-METHYL-D-ASPARTIC ACID IN MICE

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Volatile organic solvents are widely used in industrial processes and for recreational purposes. According to several studies, these substances potentiate GABAA receptors and act as NMDA antagonists in vitro. Evidence generated from behavioral studies indicates that abused solvents share several actions with CNS depressants. In particular, it has been described that toluene protects against PTZ- and NMDA-induced convulsions. The purpose of this study was to analyze if solvents like benzene, m-xylene, ethyl benzene, propyl benzene, cyclohexane and hexane were able to block the convulsant activity induced by PTZ (90 mg/kg) and/or NMDA (120 mg/kg) and to compare the results with the effects produced by toluene under the same circumstances. Male Swiss Webster mice (25-35 g) were i.p. injected with either PTZ or NMDA, placed in a static exposure chamber and observed for 30 min during air or solvent exposure (500-8000 ppm). The parameters registered were the percentage of animals that presented clonic and/or clonic-tonic (CT) seizures, as well as the latencies to these responses. In PTZ-treated animals, substituted aromatic compounds (propyl benzene, ethyl benzene, toluene and m-xylene), but not cyclohexane, benzene and n-hexane, protected against PTZ-induced convulsions in a concentration-dependent manner. The potency order was: propyl benzene > ethyl benzene > toluene > m-xylene. In contrast, only toluene was able to reduce the percentage of animals presenting NMDA-induced seizures and to increase the latency to the occurrence of convulsions, while other solvents had no effect. These results suggest that the anticonvulsant effect of substituted aromatic inhalants may be predominantly mediated by GABAA receptors. Supported by grant 43604-M (S.L.C.) from Conacyt.

264 AN ITEM RESPONSE THEORY ANALYSIS OF DSM-IV ALCOHOL ABUSE AND DEPENDENCE CRITERIA IN ADOLESCENTS

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RESEARCH QUESTIONS: (1) Do the abuse and dependence criteria in the DSM-IV reflect two categorical and non-overlapping levels of severity in adolescents? (2) Are there significant differences in item severity between clinical, adjudicated and community samples? METHODS: Adolescents from three samples, an adjudicated population, a clinical sample from successive admissions to a substance abuse treatment center, and a community sample, were administered the CIDI-SAM. In total, 795 adolescents (ages 11-19) who had endorsed at least one DSM-IV alcohol criterion were included in an Item Response Theory (IRT) Differential Item Functioning (DIF) analysis of the 11 alcohol abuse and dependence criteria. RESULTS: (1) The DSM-IV abuse and dependence criteria reflect a wide range of alcohol pathology and do not reflect two categorically distinct levels of severity. (2) Significant differences in item parameters between the three groups existed for two items: "Abuse 1-failure to fulfill major obligations" and "Abuse 3-legal problems". These items were indicative of more severe levels of alcohol pathology in the adjudicated sample. CONCLUSIONS: The commonly accepted distinction that alcohol abuse and dependence reflect distinct levels of severity is not supported in our samples of adolescents. In general, the abuse and dependence criteria function similarly across the three samples of adolescents; this is especially supported for the dependence criteria. There are a variety of possible explanations for the DIF results and these will be discussed. The alcohol dependence criterion "withdrawal" and the abuse item "legal problems" had the highest parameter estimates. This may suggest that these items are highly indicative of severe alcohol problems in adolescents. Support: DA11015, DA12845, DA05131, DA015522, MH01865, DA016314

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- 265** SMOKING INITIATION AMONG ALCOHOL-DEPENDENT MEN REFERRED TO SUBSTANCE ABUSE TREATMENT AFTER A DOMESTIC VIOLENCE ARREST
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This study examined differences between alcohol dependent offenders of intimate partner violence (IPV) with early initiation of cigarette smoking versus alcohol dependent offenders of IPV with later initiation of cigarette smoking. Data were obtained from a randomized controlled trial, in which 85 participants were randomly assigned to manual-guided behavioral therapies (Cognitive Behavioral Therapy or Twelve Step Facilitation). Sixty-two clients reported smoking cigarettes (85%) while 52 reported smoking cigarettes (71%) on a daily basis. Early initiation of smoking was defined as smoking cigarettes before the age of 16 years of age, while later initiation of smoking was defined as smoking cigarettes from 16.5 years and older. Regarding baseline characteristics, participants assigned to the early initiation of smoking condition had significantly more domestic violence arrests and significantly higher anger expression scores at baseline compared to the late smoking initiation group. There were also trends for individuals in the early smoking initiation group to have more severe legal problems, more years of alcohol related problems, more times treated for alcohol related problems, a higher number of lifetime arrests for violent behavior and higher trait anger scores compared to the late smoking initiation group. Regarding alcohol and violence treatment outcomes, there were no significant differences between smoking initiation groups at the end of treatment. Despite more severity of substance abuse, legal and violence characteristics at the baseline assessment in the early initiation group, both smoking initiation groups responded equally as well across 12 weeks of manualized behavioral treatments. The implications of these findings are discussed. This work was supported by the following grants: The Donaghue Foundation (DF# 0026) and by NIDA grants P50-DA0924 and K12 DA00167-11 (to CJE), and K02-DA-16611 (to TPG).

- 266** SELECTIVE ATTENUATION OF THE DISCRIMINATIVE STIMULUS EFFECTS OF BENZODIAZEPINES, AND NOT OTHER POSITIVE GABA_A MODULATORS, BY PENTYLENETETRAZOLE IN RHESUS MONKEYS
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Despite similarities in behavioral effects of positive GABA_A modulators, there are differences among these drugs, such as their ability to activate GABA_A receptors directly, that influence their clinical use. Under conditions where drugs produce qualitatively similar effects, differences can sometimes be detected by studying drugs in combination with antagonists. In the current study, differences among positive GABA_A modulators were further characterized by studying them in combination with a GABA_A receptor antagonist that does not act at modulatory sites. This antagonist might be expected to attenuate the effects of all positive GABA_A modulators similarly. Four rhesus monkeys discriminated 0.178-0.32 mg/kg of midazolam. When administered alone, midazolam and pregnanolone produced >80% responding on the midazolam lever. Monkeys responded predominantly on the saline lever after receiving 10-32 mg/kg of pentylenetetrazole (PTZ) alone; the larger dose of PTZ shifted the midazolam dose-effect curve 3-fold to the right. In contrast, the same dose of PTZ failed to alter the pregnanolone dose-effect curve for midazolam-like discriminative stimulus effects. Thus, PTZ attenuated the discriminative stimulus effects of midazolam and not those of pregnanolone. Although positive GABA_A modulators produce qualitatively similar discriminative stimulus effects, those effects are not attenuated similarly by the GABA_A receptor antagonist PTZ. These differences might be attributed to the ability of these different positive modulators to directly activate GABA_A receptors and could have an impact on the clinical use of positive GABA_A modulators, especially neuroactive steroids. Supported by USPHS grants DA09157 and DA017240 and a Senior Scientist Award to CPF (DA17918).

- 267** SUICIDAL BEHAVIORS, INTERNALIZING DISORDERS AND ALCOHOL INVOLVEMENT IN YOUTH

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Recent evidence suggests that suicidal behaviors, often associated with internalizing disorders such as depression, may have an independent association with alcohol and drug use disorders. Few reports assess profiles of suicidal and internalizing behavior symptoms as they relate to alcohol involvement and the emergence of alcohol dependence. The analysis is based on public-use data files for the 1994b-1996 National Household Survey on Drug Abuse, where 13,831 respondents aged 12-17 years old self-rated their psychological functioning over the preceding six-month period as assessed by an adapted version of the Youth Self-Report. Standardized questions assessed recent use of alcohol, how often drinking five or more drinks a day, and the DSM-IV diagnostic criteria for dependence. As an alternative to the use of scale thresholds or standard diagnostic criteria, latent class analysis was used to elucidate six distinct subgroups of adolescents based upon symptom profiles of the 18 items that correspond to clinical features of DSM-IV anxiety and depressive disorders (including items on suicidal ideation and attempts). Suicidal ideation and attempts were most prevalent in two of three classes reflecting a high probability of comorbid symptoms of anxiety and depression; combined these two classes captured 11% of the youth. Class profiles representing higher levels of internalizing behavior were associated with a greater odds of reporting a higher prevalence of drinking and alcohol related problems. Youth categorized into classes with severe symptoms of suicidal behaviors tended to have twice the odds of alcohol involvement and were almost 2.5 times more likely to be alcohol dependent than youth with comparable profiles of the anxiety and depression features. These findings add to the evidence that, for some adolescents, the link between suicidal behavior and alcohol involvement may have a different underlying mechanism (e.g., impulsivity) than that which links suicidal ideation and attempts with depression (e.g., hopelessness). Acknowledgment: DA016323

- 268** NONDISCLOSURE OF CANNABIS USE: PREDICTORS AND RELATIONSHIP TO TREATMENT OUTCOME IN METHADONE-MAINTAINED PATIENTS

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Prior studies have shown that underreporting of drug use is common and is influenced by multiple factors. Cannabis (THC) use nondisclosure (at least 1 positive urine with no self-reported use) and its relationship to use of heroin and cocaine were investigated in 690 patients enrolled in methadone maintenance therapy and any of three 25-29 week clinical trials evaluating contingency management to decrease opiate or cocaine use. Urine specimens (analyzed for cocaine, opiates and THC) and self-reports of drug use (checklist-driver interview) were collected 3 times per week. Self-reported drug use had no formal consequences. Potential predictors of THC use nondisclosure were analyzed by multiple logistic regression; relationships between THC use nondisclosure and cocaine and opiate use (% cocaine- and opiate-positive urine specimens) were analyzed by multiple regression. Patients with THC-positive urines (n=373) were more likely than non-THC users (n=317) to be male and have more years of THC use but did not differ on other characteristics. Nondisclosure to user ratios were: THC 191/373 (51.2%); opiates 17/494 (3.4%); cocaine 20/488 (4.1%). The predictors of THC use nondisclosure were low rate of THC-positive urines, fewer days of THC use in the last 30, African American race, and absence of antisocial personality disorder. Nondisclosure of THC use was associated with significantly greater opiate (F_{2,238}=3.06, p<0.05) and cocaine (F_{2,238}=6.64, p<0.01) use. Cocaine use in THC disclosers and nondisclosers was similar when contingency management was added to standard methadone maintenance therapy (F_{3,150}=0.32, p=0.812). Although recent studies have found that THC use per se is not associated with treatment outcome in methadone maintenance outpatients, nondisclosure of THC use is a significant predictor of greater cocaine and heroin use. This association can be eliminated by addition of contingency management therapy to standard methadone maintenance. Supported by the NIDA Intramural Research Program.

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269 DISCRIMINATIVE STIMULUS EFFECTS OF Δ^9 -THC IN C57BL/6J MICE

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Drug discrimination has utility for characterizing the *in vivo* pharmacology of cannabinoids, and the goal of this study was to establish Δ^9 -THC as a discriminative stimulus in C57BL/6J mice using a two-choice (drug-no drug) procedure. Mice (n=6) could insert their snouts into one of two holes (one paired with vehicle and the other with Δ^9 -THC) located on a wall of a rectangular enclosure and interrupt a photobeam 30 times (FR30) to gain access to condensed milk for 10 s. Initially, the training dose of Δ^9 -THC was 3.2 mg/kg, and then was increased to 10 mg/kg. Mice satisfied the criteria for testing in 18-98 (median = 54) sessions. In addition to Δ^9 -THC, the cannabinoid agonist CP 55940 dose-dependently increased Δ^9 -THC-appropriate responding; CP 55940 was 57-fold more potent than Δ^9 -THC (ED₅₀ values = 0.058 and 3.3 mg/kg, respectively). In contrast, up to doses that significantly decreased response rate, the NMDA antagonist ketamine and the monoamine uptake blocker cocaine occasioned predominantly vehicle-appropriate responding. The CB1 antagonist SR 141716A (0.1-3.2 mg/kg) dose-dependently attenuated Δ^9 -THC-appropriate responding occasioned by the training dose (10 mg/kg) of Δ^9 -THC, such that vehicle-appropriate responding predominated at larger doses of SR 141716A. This study demonstrates that drug discrimination can be used to establish an assay that has pharmacologic selectivity for cannabinoid activity in mice. These results are consistent with previous studies in rats and monkeys and suggest that CB1 receptors mediate the discriminative stimulus effects of Δ^9 -THC. Supported by DA15468 and 19222.

270 REVIEW OF ANTIDEPRESSANT TREATMENT OF METHAMPHETAMINE DEPENDENCE: HYPOTHESIZED MECHANISMS AND FUTURE DIRECTIONS

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Recent reviews have indicated a paucity of controlled trials of pharmacotherapeutic agents for methamphetamine (MA) abuse and dependence. However, extant studies have focused largely on antidepressant medications. To date, preliminary evidence suggests that dual acting antidepressant agents such as bupropion may be effective in attenuating subjective effects of MA administration as well as cue-induced craving. Nevertheless, the mechanism of action of antidepressant medications in altering responses to MA use and potentially reducing or preventing continued use is not well understood. This literature review summarizes the current state of research into pharmacological treatment of MA dependence and integrates recent neurobiological, epidemiological, and neuroimaging research to propose mechanisms of action of antidepressants in reducing MA use. Studies have shown that chronic MA use causes neurotoxicity in monoaminergic systems, resulting in alterations in dopamine, serotonin, and norepinephrine levels. Because of the complex interactions between these neurochemical changes and the effects of various antidepressant agents, identifying medications that reduce MA use has proven to be challenging. Given the direct effects of antidepressants on neurochemicals that impact mood and drug craving, future studies are needed to differentiate the impact of these agents in treating affective and reward-related aspects of MA dependence.

271 ALPHA-ETHYLTRYPTAMINE (AET) AS A DISCRIMINATIVE STIMULUS IN RATS

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Alpha-Ethyltryptamine (variously known as Love Pearls, Love Pills, AET, or simply ET) is a controlled substance gaining growing notoriety as a club drug. AET is known to possess hallucinogenic properties, and reports suggest that it also produces MDMA or N-methyl-1-(3,4-methylenedioxyphenyl)-2-aminopropane-like effects in humans. We have previously demonstrated that substitution occurs when AET is administered to rats trained to discriminate either the hallucinogen 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) or the empathogen MDMA from vehicle. Furthermore, the DOM stimulus generalized to (+)AET but not (-)AET, whereas the reverse was true in animals trained to discriminate (+)amphetamine from vehicle; an MDMA stimulus generalized to both optical isomers of AET (Pharmacol. Biochem. Behav. 2001, 70, 311-316). The present studies were conducted to determine the nature of the AET stimulus. Employing standard 2-lever operant equipment, male SD rats (n=6) were trained to discriminate AET from vehicle using a VI-15s schedule of reinforcement. Both isomers of AET substituted for the AET stimulus and were nearly equipotent: (+)AET and (-)AET ED₅₀ = 1.3 and 1.6 mg/kg, respectively. DOM (ED₅₀ = 0.4 mg/kg), MDMA ED₅₀ = 0.7 mg/kg), N-methyl-1-(4-methoxyphenyl)-2-aminopropane (PMMA) (ED₅₀ = 0.7 mg/kg), but neither (+)amphetamine nor cocaine, fully substituted for the AET stimulus. The results with the AET-trained animals are consistent with claims that AET is a hallucinogenic agent with empathogenic character. [Supported in part by DA 01642.]

272 LOW RESTING PERFUSION IN THE VENTROMEDIAL PREFRONTAL CORTEX AND AMYGDALA OF COCAINE-DEPENDENT PATIENTS PREDICTS POOR RESPONSE INHIBITION IN A NOVEL AFFECT-CONGRUENT GO NOGO TASK

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Compared to controls, chronic cocaine users have frontal hypodensity and hypoactivity and smaller amygdalar volumes. Fronto-limbic circuits are critical for inhibiting the impulse to seek rewards when the consequences of this behavior are negative. Thus, fronto-limbic deficits may mediate cocaine users' continued pursuit of drug, despite recurrent negative consequences. To model this brain-behavioral dysfunction, we correlated performance on an Affect-Congruent Go-NoGo task with resting regional cerebral blood flow (rCBF). Good performance on the task requires that pre-potent responding to affect-positive Go stimuli (flowers) be inhibited when a rare affect-negative NoGo signal (scorpion) is presented. We hypothesized that cocaine patients with lower resting perfusion in fronto-limbic regions would exhibit poorer response inhibition (more errors of commission). Arterial spin labeled perfusion fMRI was used to measure resting rCBF in detoxified cocaine patients (n=10; male). Using SPM2, we examined the relationship of errors of commission with resting rCBF in a single regression analysis. We found a significant inverse correlation between errors of commission (mean 5.0 + 2.9) and resting rCBF in the right ventromedial prefrontal cortex (t=3.8, p<.003) and bilateral amygdalae (right t=5.5, p<.0001; left t=4.9, p<.001). Thus, subjects with lowest resting perfusion in these regions had the greatest difficulty with response inhibition, perhaps reflecting their real-life struggle to inhibit the pre-potent response to drug reward despite negative consequences. These findings add to the evidence of fronto-limbic deficits in cocaine patients, and demonstrate the sensitivity of the Affect-Congruent Go-NoGo task for probing these dysfunctions. NIDA T32, NIDA RO1 DA-10241, NIDA RO1 DA-15149, NIDA P60-DA-05186, NIDA P-50 12756, Research Div. VAMC, VA VISN 4 MIRECC.

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273 DRUG FLUENCY: A POTENTIAL MARKER FOR SUBSTANCE ABUSE

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Semantic fluency is a neuropsychological task measuring verbal ability and executive function and requires respondents to name as many words as possible from a particular subject category (e.g., animals). Specifically, this task involves the activation of a search strategy for conceptual knowledge based on previously formed semantic associations and involves frontal and medial temporal brain regions. The goal of the current study was to examine semantic fluency specifically for the category drugs in drug addicted and control subjects. Thirty-nine cocaine-addicted and 142 healthy control subjects were instructed to call to mind and name different drug-related words for a period of one minute. Responses were audio-recorded and later counted and organized into separate semantic categories. Although there was no difference in the total number of drug-related words produced by control vs. cocaine subjects (15.9 ± 0.89 vs. 15.2 ± 0.47 , $p > .05$), several qualitative differences were observed (one-tailed t-tests, Mean \pm SEM, cocaine vs. controls, $p < .05$). Control subjects reported significantly more words classified as Over-The-Counter drugs (e.g., Tylenol; 0.23 ± 0.09 vs. 0.60 ± 0.10), whereas cocaine subjects retrieved more words associated with the experience of using drugs, particularly as related to drug acquisition (e.g., cash, borrow; 0.67 ± 0.20 vs. 0.34 ± 0.06), preparation (e.g., cook-up; 0.46 ± 0.15 vs. 0.15 ± 0.04), and paraphernalia (e.g., pipe; 4.05 ± 0.53 vs. 2.77 ± 0.16). This effect was accentuated in the cocaine abusers who tested positive as compared to those who tested negative for cocaine on the day of testing (total number of drug-related words: 16.8 ± 1.09 vs. 15.5 ± 1.9). These preliminary findings on this newly adapted version of a classical neuropsychological test suggest that cocaine abuse triggers the retrieval of drug-specific semantic networks; findings further reflect greater salience and sensitivity to drug-related cues during testing, particularly for subjects with recent use of cocaine.

275 A GENDER PERSPECTIVE ON VIOLENT BEHAVIORS IN COCAINE ADDICTS

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The purpose of this study is to establish a practical and theoretical basis for the prevention of violent behaviour among males and females with a diagnosis of cocaine addiction. Qualitative methodology was used. With the objective of determining which dimensions would be evaluated in the first stage of the study, 6 in-depth interviews with drug abuse professionals were conducted. In the second stage, and drawing from the results of these interviews, a semistructured interview was developed which included three areas: cocaine and violence; drug abuse treatment; and violence and treatment. The interview was administered to a representative sample (N=30), of professionals working in public outpatient treatment centres (Unidades de Conductas Adictivas (UCA's)). A Grounded Theory based data analysis was conducted. Which revealed a relation between cocaine abuse and violent behaviours and differed between males and females. Men tended to be violent with their partners, and women tended to be violent with their children. The type of violence differs by gender; men tended to be more violent in frequency and intensity. Male tend to have more support networks than women when they request treatment. Men go into treatment because they have pressure from external factors. Women usually start treatment because of internal reasons. Women who request treatment are usually victims of domestic violence. Professionals need specific training to deal better with addicts' violent behaviours in the treatment process. This study indicates that cocaine users' violent behaviours may vary by gender. It is important to investigate in depth those differences in order to improve the quality and outcomes of treatment programs. Supported by Conselleria d'Empresa, Universitat I Ciència.GV05/279 Direcció General d'Investigació i Transferència Tecnològica.CSISP, Direcció General de Salut Pública, Conselleria de Sanitat,G.V.

274 COMPARISON OF THE ENDOCRINE EFFECTS OF THE MIXED MU/KAPPA OPIOID NALBUPHINE IN COMBINATION WITH COCAINE AND COCAINE ALONE IN MEN

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Nalbuphine, a mixed mu-kappa opioid, is a potential new medication for the treatment of cocaine abuse (Mello et al., 2005). Kappa opioid agonists functionally antagonize some abuse-related and locomotor effects of cocaine, and both kappa-selective and mixed mu/kappa opioids reduce cocaine self-administration by rhesus monkeys. We compared the neuroendocrine effects of a single acute dose of cocaine alone (0.2 mg/kg, i.v.), with nalbuphine (5 mg/70 kg, i.v.) + cocaine in combination, in seven adult men (ages 18-35) who met DSM-IV criteria for current cocaine abuse. Cocaine alone, and cocaine in combination with nalbuphine were administered on separate test days in an irregular order under placebo-controlled, double-blind conditions. Blood samples for HPA axis hormones, plasma cocaine, and serum nalbuphine were collected prior to and for 2 hours following cocaine or nalbuphine and cocaine administration. Nalbuphine levels exceeded 50 ng/ml within 10 min after injection, and cocaine levels exceeded 130 ng/ml within 4 min. Cocaine's pharmacokinetic profile did not change after nalbuphine administration. The endocrine effects of cocaine alone were diametrically opposite to those of nalbuphine + cocaine in combination. Cocaine stimulated ACTH, cortisol, and LH whereas cocaine + nalbuphine in combination did not alter ACTH and decreased cortisol and LH. Thus it appears that nalbuphine attenuated cocaine's effects on ACTH, cortisol, and LH. These data are consistent with our earlier report that the subjective and cardiovascular effects of cocaine + nalbuphine in combination were not addictive, and nalbuphine modestly attenuated cocaine's positive subjective effects (Mello et al., 2005). This research was supported by grants P01-DA14528, T32-DA07252, K05-DA00064 and K05-DA00101 from the National Institute on Drug Abuse, NIH.

276 A COMPARISON OF THE ACUTE BEHAVIORAL EFFECTS OF GAMMA-HYDROXYBUTYRATE, GAMMA-BUTYROLACTONE, AND 1,4-BUTANEDIOL IN BABOONS

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The abuse of GHB and its precursors GBL and 1,4-BD is a growing public health concern. GBL and 1,4-BD are found in commercially available products and, when ingested, are metabolized into GHB. Additionally, instructions for converting GBL and 1,4-BD into GHB before ingestion are readily available on the internet. The current study used three behavioral measures to characterize and compare the acute behavioral effects of GHB (32-420 mg/kg), GBL (32-240 mg/kg), and 1,4-BD (32-240 mg/kg). Following drug or vehicle (distilled water) administration as a single bolus infusion via a chronic indwelling intragastric catheter, a fine-motor task was presented at multiple time intervals, food pellets were available on an FR 10 schedule of reinforcement for 20-hrs, and behavioral observations were conducted by trained observers. Acute doses of GHB, GBL, and 1,4-BD produced dose-dependent decreases in the number of food pellets earned, impaired performance on the fine motor task, and increased the frequency of overt signs of sedation, muscle relaxation, and gastro-intestinal symptoms. Tremors and jerks were also observed at high doses of each compound. A higher dose of GHB was required to produce consistent changes in behavior when compared to the doses required by GBL or 1,4-BD. The on-set of action of GHB was more delayed when compared to GBL and 1,4-BD, as measured by the fine-motor task at multiple intervals after drug administration and the duration of behavioral changes following drug administration. Studies to describe blood levels of GHB following acute administration of these compounds are on-going. These data indicate GHB, GBL, and 1,4-BD are behaviorally active in baboons and produce similar behavioral effects. Comparing equimolar doses of the three compounds, GBL and 1,4-BD appear to be more potent and have different on-sets and durations of action when compared to GHB.

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277 ANXIETY AND THE RISK OF TOBACCO USE AND TOBACCO DEPENDENCE AMONG ADULTS IN THE UNITED STATES

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BACKGROUND. Anxiety disorders and nicotine dependence are associated among adults. Beyond these associations, little is known about the specific nature of these relationships. The objectives of this study were therefore to determine the association between anxiety and tobacco use, nicotine dependence, and the transition from tobacco use to nicotine dependence among adults. **METHODS.** Data were drawn from the NESARC, a nationally representative sample of 43,093 adults in the United States aged 18 and over. Logistic regressions were used to examine the relationships between symptoms or diagnoses of anxiety disorders (generalized anxiety disorder (GAD), social phobia (SoP), specific phobia (SiP), panic disorder (PD)) and the risk of tobacco use, nicotine dependence, and the risk of dependence among tobacco users. Analyses were adjusted for demographic characteristics, major depression and other substance use disorders. **RESULTS.** SiP (OR=1.2, 95% CI 1.1, 1.4), PD (OR=1.6, 95% CI 1.4, 1.9), and GAD (OR=1.1, 95% CI 1.0, 1.3) were associated with tobacco use. Among tobacco users, the risk of tobacco dependence associated with anxiety disorders (SiP (2.0, 95% CI 1.7, 2.2), PD (1.6, 95% CI 1.4, 1.9), SoP (1.6, 95% CI 1.4, 2.0), and GAD (1.6 (95% CI 1.3, 1.9)) was even stronger. Having at least one symptom of any of the anxiety disorders was also associated with increased risk of tobacco dependence among users (GAD (1.5, 95% CI 1.3, 1.7), SoP (1.5, 95% CI 1.3, 1.7), SiP (1.4, 95% CI 1.3, 1.5), and PD (1.6, 95% CI 1.3, 1.7). Anxiety symptoms and disorders were associated with significantly earlier onset of tobacco use and dependence. **CONCLUSIONS.** Among adults, symptoms and diagnoses of anxiety disorders are associated with increased odds of tobacco use and dependence, controlling for the effects of major depression and substance use disorders. Results suggest that anxiety may play a meaningful role in tobacco use and dependence in the general population. Tobacco use prevention and intervention programs may benefit from the assessment and treatment of anxiety.

279 IMPLEMENTATION OF BEST PRACTICES FOR CLIENTS WITH CO-OCCURRING SUBSTANCE USE DISORDERS AND MENTAL ILLNESS

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Background: SAMHSA's 2004 Treatment Improvement Protocol for co-occurring substance use disorders and mental illness (COD) lists best practices or "Essential Programming for COD" such as screening, assessment, referral, medication and medication monitoring, psychoeducational and self-help groups for COD. The present study sought to identify the extent to which COD best practices are provided in Missouri and to examine factors related to their implementation. **Method:** As part of a SAMHSA-funded Co-occurring Disorders State Incentive Grant (COSIG), program managers from all state-contracted substance abuse and mental health treatment sites were surveyed in Fall 2005 (259 sites; response rate 75%) regarding screening and assessment, treatment services, staffing, and constructs related to implementation (Rogers, 2003). **Results:** Implementation of COD best practices in Missouri varies widely (e.g., 37% of sites do not screen for substance abuse; 59% do not screen for mental illness). A summary variable of 12 best practices appears normally distributed ($X = 5.8$; $SD = 2.7$). Moreover, implementation of best practices is related to program manager factors (personal readiness to change, perceived advantage of providing COD services, beliefs about the utility of research findings for treatment, use of information sources to learn about substance abuse and mental health) and agency factors (agency readiness to change, COD training, site size). **Conclusion:** Although based on cross-sectional data, results suggest factors that may facilitate implementation of best practices by individual practitioners (readiness to change, contact with the literature), agencies (improved access to training about COD best practices), and the state (mandates for screening/assessment and referral).

278 ELECTROCARDIOGRAPHIC CHANGES DURING COCAINE WITHDRAWAL

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Cocaine acutely alters electrocardiographic (ECG) parameters such as PR and QTc intervals and QRS duration, but little is known about changes in ECG parameters during early cocaine withdrawal. We studied this issue in 62 physically healthy, male cocaine addicts (86% African-American, 8% white, 6% other, mean [SD] age 34.2 [6.9] years, 42.4 [40.6] months of regular cocaine use, 16.1 [10.7] days of use in the prior month, spending \$1069 [\$1195] and averaging 2.5 [2.5] g/day) undergoing inpatient treatment as part of a clinical trial with bromocriptine (started 2 weeks after admission). Subjects had a standard 12-lead ECG 4.0 [3.5] days after admission (9.9 [8.4] days after their last cocaine use); 47 had a second ECG 3-4 weeks later. The initial ECG showed heart rate of 70.7 [12.1] beats/min, PR interval of 150 [18] ms (normal 120-200 ms), QRS duration of 90 [12] ms (normal < 120 ms), and QTc interval of 409 [21] ms (normal < 450 ms). Age was significantly correlated with PR interval ($r = -0.30$, $p = 0.02$) and QTc interval ($r = +0.46$, $p < 0.0001$). The only significant correlation between ECG parameters and cocaine use variables was between days of use in past month and PR interval ($r = -0.29$, $p = 0.02$). Between the first and second ECG, PR interval lengthened significantly (6.4 [1.1] ms, $t = 3.9$, $p = 0.0003$) and heart rate decreased (2.4 [8.9] beats/min, $t = 1.85$, $p = 0.07$). All ECG parameters were highly correlated between the two ECGs: r 's 0.53-0.87, all p 's < 0.0001. There were no significant correlations between the interval between ECGs and changes in ECG parameters. As expected, bromocriptine treatment (1.25-7.5 mg/day) had no significant effect on ECG parameters. These findings suggest that normalization of some of the ECG effects of cocaine use is still occurring several weeks after the last cocaine use. Supported by Sandoz Pharmaceutical Co. and the Intramural Research Program of the National Institutes of Health, National Institute on Drug Abuse.

280 DIVERSION OF CONTROLLED SUBSTANCES AT THE PHARMACY LEVEL: 2005 FINDINGS FROM RXPATROL®

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Introduction: Pharmacy theft, including robberies, burglaries, and employee and customer pilferage, represents an important source for diversion of prescription medications. To combat this problem, pharmacies and law enforcement need information on when and how such crimes are likely to occur as well as specific security precautions that may reduce the likelihood of victimization. **Methods:** RxPATROL is a national information clearinghouse on pharmacy-related theft of controlled substances. In addition to collecting, analyzing, and disseminating pharmacy-related crime data, RxPATROL assesses physical security features of pharmacies and provides a profile of those at greatest risk for theft. We conducted an analysis of RxPATROL data from 06/01/03-12/31/05. **Results:** 1,728 incidents have been reported to the RxPATROL database from a geographically diverse cross-section of the continental U.S. Of these, 37.6% involved fraud, 25% robbery, 16.6% forgery, 13.4% burglary, and 7.4% "other" (including employee theft, counterfeiting, and shoplifting). To date, pharmacy robbery reports have been submitted by 40 states with most such reports received from MA (21%), IN (11%), OH (10%), and FL (7%). The majority of robberies (52%) occurred between 4 P.M.-12 A.M.; 37% between 8 A.M.-4 P.M., and 11% between 12 A.M.-8 A.M. 82.7% of robberies occurred on a weekday. The front door was the most common mode of entry and exit for robberies (88% and 71% respectively). Suspects were predominantly male (95%), Caucasian (88%), working alone (86%), and in the between 20-29 years of age (53%). The handgun was the preferred weapon type (70%). 63% of pharmacies reporting a robbery did not have a video camera, 86% did not have deadbolts, and 40% had no alarm system. **Conclusions:** In 2005, pharmacy robberies involving controlled substances were most likely to occur on weekdays during the late afternoon-evening. Suspects were likely to be young, male Caucasians working alone and armed with a handgun. Lack of video camera, deadbolt and alarm systems place a pharmacy at higher risk for such crimes.

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281 USING AN OFFSPRING-OF-TWINS DESIGN TO EXAMINE THE IMPACT OF PARENTAL DIVORCE ON OFFSPRING EARLY NICOTINE AND CANNABIS USE AND PROBLEMS

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Previous research has shown that nicotine dependence (ND) and cannabis abuse/dependence (CAD) are both heritable and associated with high-risk environments. Offspring-of-twins (OOT) designs can separate the two processes in a way that traditional twin designs cannot. We analyze combined data from two high-risk OOT studies to examine whether parental divorce (DIV) is related to offspring nicotine (NIC) and cannabis (CAN) use and dependence after controlling for alcohol dependence (AD) and other drug dependence (DD) in the twin fathers. OOT (n=1919, mean age=21.4 yrs at interview in 2000-2004) were classified based on the lifetime AD/DD status of their father and father's cotwin: GP1=1003 OOT with an AD or DD father, GP2=245 OOT with a non-AD/non-DD dad and an AD or DD uncle who was their dad's MZ cotwin, GP3=229 OOT with a non-AD/non-DD dad and an AD or DD uncle who was their dad's DZ cotwin, and GP4=440 OOT whose father and father's cotwin were unaffected. Logistic regression analyses indicated that GP1>GP4 for offspring NIC and CAN use, ND, and CAD (*=pGP4 for CAN use (OR=1.56*), ND (OR=1.62*), and CAD (OR=1.78*). DIV was associated with NIC (OR=1.56, p<.06) and CAN use (OR=1.99*), and ND (OR=2.12*). Cox regression analyses that controlled for family history of AD/DD indicated that offspring from DIV families were at increased risk of early-onset NIC (HR=2.23* for NIC before age 12; HR=1.42* for NIC age 12-14) and of having ever used CAN (HR=1.69*). In addition, OOT with a family history of DD were more likely than OOT with a family history of AD only to have CAD (OR=2.38*) and to have first used CAN prior to age 15 (HR=1.31*). These analyses suggest that parental DIV remains a risk for CAN and NIC use even after controlling for other genetic and environmental risks associated with paternal AD/DD. Support: DA14363, AA11667, AA07728, AA11998.

282 DOSE-RELATED ATTENUATION OF COCAINE AND FOOD REINFORCEMENT FOLLOWING PRETREATMENT WITH TACRINE

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Acetylcholine (ACh) is involved in brain reward and learning functions, and disruption of this neurotransmitter may contribute to substance abuse disorders. Tacrine is a centrally acting, reversible cholinesterase inhibitor that also inhibits monoamine oxidase (MAO) and blocks reuptake of dopamine and serotonin. Male Wistar rats were trained to self-administer cocaine under a fixed-ratio-5 schedule during two-hour multiple-component sessions in which 0.1, 0.2, and 0.4 mg/kg per injection of cocaine were each available for 40 minutes. Saline or tacrine were administered as single intravenous doses prior to cocaine or food self-administration sessions. Before initiating self-administration sessions, behavior was scored over a 20-minute period by a blinded observer for signs of cholinergic stimulation. Self-administration behavior was allowed to return to baseline levels over at least two subsequent sessions prior to administration of additional doses of saline or tacrine. Pretreatment with tacrine produced dose-related increases in signs of cholinergic stimulation, with parallel attenuations of cocaine and food reinforcement. The 50% effective dose (ED50) values for attenuating cocaine reinforcement were 0.68, 1.63, and 3.46 mg/kg for self-administration of low, intermediate, and high doses of cocaine, respectively. Tacrine attenuated food self-administration with an ED50 of 6.19 mg/kg, more than three-fold greater than the corresponding value for attenuation of an intermediate dose-level of cocaine. ED50 values for production of signs of cholinergic stimulation in cocaine- and food-reinforced animals were 0.63 and 3.59 mg/kg, respectively. In summary, pretreatment with tacrine produced a dose-related attenuation of cocaine self-administration, with moderate selectivity for effects on cocaine relative to food reinforcement. Tacrine produced signs of cholinergic stimulation with greater potency in cocaine-dependent animals.

283 PREVALENCE AND RELATIONSHIP OF OVERWEIGHT AND OBESITY AMONG MEN AND WOMEN IN A LONG-TERM RESIDENTIAL SUBSTANCE ABUSE TREATMENT PROGRAM

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The purpose of this retrospective chart review was to examine the correlation between length of time abstinent from alcohol and drugs and weight changes among patients in long-term residential treatment for substance abuse. A random sample was generated to have equal numbers of men and women (males=65; females=65) who entered the facility between January 1, 2002 and December 31, 2002. Of the 130 cases, 99 (76.2%) dropped out (did not complete one year of treatment) and 31 (23.8%) persisted (completed one year of treatment). The mean initial BMI for the total sample was 27.03 (26.83 for men, 27.23 for women). The mean initial BMI for dropouts was not statistically different than for persisters (26.93 versus 27.33). There was a significant increase in body mass index among patients who completed one year of treatment (paired t=3.2; p<.001); 57.7% of persisters were at least overweight at the end of one year, with 27% being obese or morbidly obese. The mean BMI for persisters was 29.24, with an average increase of 1.91 BMI points. Although the mean BMI change for women was greater than for men (2.05 compared to 1.8 BMI points), it was not statistically significant. An increase in BMI was not correlated with drug of choice. Given the results of this study, and the problems associated with both obesity and substance abuse, further study of the relationship between abstinence from alcohol and drugs and weight gain is warranted.

284 APPLICATION OF STATISTICAL PROCESS CONTROL METHODS TO MONITOR EMERGENCY DEPARTMENT VISITS INVOLVING INTENTIONAL ABUSE OF OXYCONTIN® OR HYDROCODONE

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Introduction: Statistical process control (SPC) encompasses a broad set of statistical techniques that can be used to distinguish unusual from unusual patterns of measurements given some natural process variability. We applied SPC to compare patterns of abuse-related emergency department (ED) admissions associated with the abuse of two widely prescribed opioid analgesics. Methods: We accessed unweighted, real time ED cases reported to the Drug Abuse Warning Network (DAWN) via its on-line, real time query system (DAWN Live!). DAWN collects information on drug-related ED visits from a nationally representative sample of short-term, non-Federal hospitals. The monthly number of OxyContin® (branded oxycodone extended release product) and hydrocodone (both generic and branded) ED cases designated as case type "Other" (i.e., those involving intentional drug abuse) were used as the numerator; the total number of monthly ED visits whose charts were reviewed for DAWN were used as the denominator. Study time frame was between 12/04-7/05. Using the SPC U chart technique, the data were analyzed to determine whether unusual measurements were present on a month-to-month basis. Results: Control charts indicating the rate of non-conformities per month ("U" chart) were generated for the 20 month study time period for each of the two monitored drugs. The OxyContin® control chart showed a process that was in control: reported cases fell within the control limits and no systematic pattern of unusual measurements was present. In contrast, the control chart for hydrocodone indicated out of control patterns with hydrocodone-related abuse cases showing a marked escalation beginning in March 2005 and continuing through July 2005. Conclusion: Between 12/04-7/05, the rate of ED cases involving OxyContin® abuse appeared essentially stable nationally while that for hydrocodone showed a marked increase. Systematic application of SPC techniques represents a promising method for monitoring opioid analgesic abuse in real time.

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285 EFFECT OF ENVIRONMENTAL ENRICHMENT ON TRANSCRIPTION FACTORS IN THE NUCLEUS ACCUMBENS UNDER BASAL CONDITIONS AND AFTER ACUTE OR REPEATED COCAINE ADMINISTRATION

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Prior work has shown that environmental enrichment in rats produces a robust behavioral phenotype where enriched rats exhibit low rates of intravenous cocaine self-administration, particularly at low unit doses, compared to rats reared in isolation. Given that the individual elements of the enrichment paradigm (novelty, social contact, exercise) all evoke dopamine release in the nucleus accumbens, gene transcription resulting from these stimuli is a likely mediator of this phenotype. The current experiments examine basal and cocaine-induced expression of transcription factor mRNA (CREB, CREM, ICER, ATF2, ATF3, ATF4, FosB, deltaFosB) in enriched and isolated rats using quantitative PCR. First, rats in the enriched condition (EC) had higher basal mRNA levels for FosB, deltaFosB, CREB and CREM. Acute cocaine (20 mg/kg) increased mRNA levels of ICER, FosB and deltaFosB in EC and IC rats; however, acute cocaine increased ATF2 mRNA only in EC rats. The ATF2 induction showed tolerance with repeated cocaine. In addition, chronic cocaine also produced tolerance to ICER mRNA induction, and this tolerance was more pronounced in IC rats. FosB and deltaFosB showed similar induction compared to the respective saline controls, but the higher basal FosB and deltaFosB levels meant that EC rats had a greater absolute increase in FosB and deltaFosB mRNA. These studies provide evidence that environmental enrichment affects basal and cocaine-induced transcription factor mRNA levels. Ongoing studies are investigating protein levels of these transcription factors in EC and IC rats. Taken as a whole, transcription factors are likely to be responsible for the robust low self-administering phenotype resulting from environmental enrichment.

286 COMT VAL(158)-MET POLYMORPHISM MAY INFLUENCE MEASURES OF IMPULSIVE BEHAVIOR AND DRUG USE IN HEROIN-DEPENDENT INDIVIDUALS: A PRELIMINARY ANALYSIS

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Catechol-O-methyl-transferase (COMT) is a key enzyme modulating dopamine (DA) concentration in ventral striatum and prefrontal cortex, brain regions that are centrally involved in drug abuse and impulsive behavior. A relatively common methionine (Met) substitution for valine (Val) at codon 158 is known as the Val(158)-Met polymorphism. Individuals with Val/Val have the highest activity of COMT (resulting in low synaptic DA), those with Met/Met have the lowest activity of COMT (high synaptic DA), and those with Val/Met have intermediate COMT activity. This ongoing study is determining whether heroin abusers varying in COMT Val(158)-Met genotype exhibit differences in impulsive behavior and drug use. During screening for laboratory studies, heroin-dependent individuals provide blood for genotyping and answer questionnaires related to drug use, impulsivity, and heroin delay discounting under imagined conditions of opioid withdrawal and satiation. In preliminary analyses (total n=42), Met/Met participants (n=5) are significantly ($p < .05$, more likely to be current IV (vs. intranasal) heroin users, have used cocaine in the prior 30 days, have higher total scores on the Impulsive Relapse Questionnaire and discount heroin markedly at the shortest delay (3 hr) during imagined withdrawal, relative to Val/Met (n=21) and Val/Val (n=16) groups. The frequency distribution of this polymorphism was independent of gender and other genotypes being assessed (e.g. 5HT transporter and MAO-A). Caucasians were somewhat ($p < .06$) more likely to be Met/Met (similar to previous literature), but race was not associated with these behaviors. These data suggest that the Met/Met polymorphism may be associated with a pattern of more impulsive behavior and riskier drug use, perhaps more so during periods of opioid withdrawal. More samples are needed to determine whether these initial results will be confirmed. (Supported by a supplement to NIH/NIDA DA15462 and Joe Young, Sr. funds from the State of Michigan.)

287 PREDICTORS OF RETURN-TO-PRISON FOLLOWING COMMUNITY TREATMENT FOR SUBSTANCE-ABUSING FEMALE OFFENDERS

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Hypothesis: Female offenders with substance abuse problems are at high risk for relapse and recidivism after leaving prison. We hypothesized that participation in an aftercare program, the Female Offender Treatment and Employment Project (FOTEP), would reduce the risk of return-to-prison. The program provides community-based substance abuse treatment to women parolees for 6 to 15 months following their release from prison in California, using a therapeutic community approach. Procedures: Return-to-prison (RTP) was examined over periods of 12 months (N = 2,654), 24 months (N = 1,915) 36 months (N = 1,078), and 48 months (N = 406) following exit from FOTEP. All data on participants was based on administrative and program records. Statistical analyses: Survival analyses were conducted to determine the predictors of RTP. Results: Overall, RTP rates were: 33% at 12 months; 46% at 24 months, 50% at 36 months, and 54% at 48 months. Individuals who completed the FOTEP program were less likely to RTP, with hazard ratios (HR) ranging from 0.29 at 12 months to 0.34 at 48 months (all HR, $p < .0001$). Individuals who were classified as having a co-occurring mental disorder were more likely to RTP, with HRs ranging from 2.3 at 12 months to 3.8 at 48 months (all HR, $p < .0001$). Individuals convicted of a felony were more likely to RTP compared to civil addicts who were mandated to treatment; HR at 12 months = 1.4 ($p < .01$); HR at 48 months = 2.1 ($p < .05$). In addition, each year increase in age reduced the risk of RTP by 2%. Ethnicity was also associated with RTP, with African Americans having approximately 37% greater risk of RTP at 12 months and 68% at 48 months. Conclusion: Although risk of returning to prison following community-based substance abuse treatment for female offenders remains high, the risk is considerably reduced among those who complete treatment; however, those with co-occurring mental disorders remain at particularly high risk. Supported by California Department of Corrections and Rehabilitation (Contract C03.052)

288 RATES OF HIV, HEPATITIS A, AND HEPATITIS C AMONG AFRICAN-AMERICAN AND WHITE DRUG USERS

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The present study sought to examine rates of HIV, hepatitis A, and hepatitis C among African American and White drug users. This study is based on data from the International Neurobehavioral HIV Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of HIV, and Hepatitis A, B, and C in the U.S., South Africa, and Russia. The U.S. sample of the present study consists of 610 injection and non-injection drug users between 15 and 50 years of age in the Baltimore metropolitan region. The sample was comprised of 312 African American (51.1%) and 298 White (48.9%) subjects and was 56.4% male. Multinomial logistic regression indicated that African American drug users (OR = 3.78; 95% CI = 1.58; 9.03) were significantly more likely than White drug users to test positive for HIV while controlling for age, gender, and education. Specifically, 12.8% of African American drug users tested positive HIV compared to 2.6% of Whites. Conversely, White drug users (OR = 2.15; 95% CI = 1.40; 3.32) were significantly more likely than African American drug users to test positive for hepatitis A. Specifically, 42.3% of White drug users tested positive hepatitis A compared to 29.4% of African Americans. In addition, White drug users (OR = 4.10; 95% CI = 2.66; 6.31) were significantly more likely than African American drug users to test positive for hepatitis C with 58.8% of White drug users testing positive hepatitis C compared to 35.5% of African Americans. The ethnic differences in the present study sample in rates of HIV versus hepatitis are particularly interesting in light of the entire sample exhibiting low socioeconomic status independent of race. That is, differences in disease prevalence are not likely to be explained by differences in economic status that are typically associated with ethnic status. Further research is needed to understand mechanisms that may place African Americans at heightened HIV risk and Whites at heightened hepatitis risk.

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289 THE RELATIONSHIP BETWEEN PARENTAL SUBSTANCE ABUSE AND LONG-TERM COPING IN ADULT DOMESTIC VIOLENCE SURVIVORS

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Previous URI research (Jospitre et al., 2005) indicates that adult domestic violence survivors with substance abusing parents report significantly higher levels of childhood neglect than those with non-substance abusing parents. The present study expands upon this research by exploring the interrelationships between their history of parental substance abuse, childhood emotional neglect and long-term coping in an ethnically diverse sample of adult female domestic violence survivors (N=276). Participants completed a structured interview that assessed parental substance abuse, as well as the Childhood Trauma Questionnaire and the Coping Strategies Inventory. As hypothesized, adult participants with substance abusing mothers (n=56) reported significantly greater reliance on disengaged or avoidant coping strategies (specifically, social withdrawal, self-criticism and wishful thinking), than adult participants with non-substance abusing mothers (n=220), $p < .01$. Contrary to our predictions, paternal substance abuse was not predictive of greater use of disengaged coping. A mediational model was tested which revealed that, as hypothesized, emotional neglect mediated the relationship between maternal substance abuse and avoidant coping ($p < .01$). These findings indicate the importance of close collaboration between substance abuse and domestic violence/child welfare agencies. In addition, adult domestic violence survivors with substance abusing parents may benefit from coping skills training.

290 ALTERED AFFECTIVE RESPONSIVITY IN CHRONIC MARIJUANA SMOKERS: AN fMRI STUDY

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More than 40% of Americans report having smoked marijuana, and it remains the most widely used illicit drug in the United States. Investigations of the cognitive effects of marijuana have found alterations in frontal brain function, most notably during tasks that require executive control, inhibition and decision making. Nevertheless, little is known about smokers' responses to affective stimuli. Given the range of behaviors often demonstrated by marijuana users we hypothesized altered frontal responsivity in chronic smokers relative to control subjects during the viewing of masked angry faces. Thirteen chronic heavy marijuana smokers (mean age 25.1 years), who reported smoking at least three thousand joints in their lifetime and smoked a minimum of five of the last seven days, and 10 control subjects (mean age 26.2 years), who reported smoking not more than five times in their lives, completed the study. Imaging data was acquired on a 3.0 Tesla Siemens MRI scanner, motion corrected and analyzed in SPM99 (height threshold $p < .005$, extent $k = 20$ voxels). The fMRI protocol included a backward masked affect paradigm, consisting of a 40 msec presentation of angry faces masked by neutral faces. In comparison to healthy controls, marijuana smokers demonstrated reduced activity of the anterior cingulate cortex (MNI coordinates -2, 14, 24) and increased activity of the medial temporal lobe (MNI coordinates -40, -20, -10). As hypothesized, chronic marijuana smokers demonstrated reduced activation of the anterior cingulate, an area noted to be important for the regulation of impulsive behavior. This finding is consistent with the high CB-1 receptor density found in this region, as well as previous studies of CB-1 knockout mice reporting alterations of emotional behaviors in these animals. These results suggest differences in affective processing in chronic marijuana smokers even when the stimuli are presented below the level of conscious processing.

291 NOVEL DOPAMINE D3 RECEPTOR LIGANDS WITH FUNCTIONALIZED LINKING CHAINS AS POTENTIAL COCAINE ABUSE THERAPEUTIC AGENTS

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Dopamine D3 receptor antagonists and partial agonists have been shown to modulate the reinforcing and drug-seeking effects induced by cocaine and other abused substances. We have recently discovered that by introducing functionality into the butylamide linking chain of the 4-phenylpiperazine class of ligands, improved D3 receptor affinity and selectivity, as well as water solubility, was achieved (Grundt et al. 2005). To further this line of investigation, we designed and synthesized a series of linking-chain derivatives wherein functionality such as OH, OAc, and cis or trans-cyclopropyl groups have been introduced into the linking chain. In general, these modifications were well tolerated at D3 receptors ($K_i = 100$ -fold selectivity over D2 and D4 receptors, using competition binding assays in HEK 293 cells transfected with either hD2L, hD3 or hD4 dopamine receptors. Furthermore, addition of these groups affected efficacy of the compounds as measured by quinpirole stimulation of mitogenesis at human dopamine D3 receptors transfected into Chinese hamster ovary (CHO) cells. Further analysis of structure-activity relationships regarding in vitro function and behavioral evaluation in animal models of drug abuse of these novel D3 ligands is underway. These compounds will provide additional tools with which to elucidate the role of D3 receptors in drug reinforcement in vivo. - Supported by the NIDA-IRP.

292 SILDENAFIL USE BY VETERANS IN SUBSTANCE ABUSE TREATMENT

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Objectives: Sexual dysfunction, including erectile dysfunction (ED), is a common complaint among men in substance abuse treatment. Information about the effectiveness of sildenafil for treating ED in substance abusers is lacking. Methods: Pharmacy records for all veterans in substance abuse treatment at VA PSHCS from 7/2004 to 7/2005 (n=1899) were reviewed for presence of a current or past prescription for sildenafil. These men (n=247, 13%) were invited to complete a self report questionnaire regarding their experience with sildenafil. Questionnaires were returned by 40 (16.2%). Sample demographics: age (m=54 years, sd=5.6), race (white, 60%; African American, 37.5%, Asian 2.5%), substances abused (alcohol, 55%; cannabis, 17.5%; cocaine, 35%; methamphetamine, 2.5%; opioids, 35%). Results: This report focuses on the prior 90 days during which 26 (65%) were sexually active with a single partner and 6 (15%) with multiple partners. Sildenafil use in the prior 90 days was reported by 29 (72.5%) of the sexually active and by 3 (7.5%) of those without partners. For sildenafil users the mean number of times used was 7.4 (sd=5.4). Use of sildenafil under the influence of substances of abuse was reported by 53.1%. Effectiveness of sildenafil was rated on a 1 (almost never) to 5 (almost always) scale. A rating of 5 or 4 (most of the time) was given: 62.5 % for "obtaining an erection," 65.7% for "erection sufficient for penetration," 56.3% for maintaining an erection," 40.6% being able to ejaculate during intercourse," 50.1% being able to ejaculate during masturbation." Episodes of multiple orgasms during a single sexual session were reported by 56.2%. Conclusion: The majority of men in substance abuse treatment prescribed Sildenafil who responded to a questionnaire reported it was an effective treatment for ED.

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293 DISCRIMINATIVE STIMULUS PROPERTIES OF COCAINE IN RATS WITH INDIVIDUAL DIFFERENCES IN COCAINE-INDUCED LOCOMOTOR ACTIVITY

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Humans exhibit a wide-range of responses to psychotropic drugs and certain individual differences might be useful predictors of subsequent abuse or addiction. Using animal models to explore correlates of addiction, we and others have reported that rats can be classified as either low or high cocaine responders (LCRs or HCRs, respectively) based on their open-field behavioral response to an i.p. injection of cocaine. Our goal here was to determine how LCRs and HCRs respond to the discriminative stimulus properties of cocaine. Male, Long-Evans rats ($n = 18$) were characterized as LCRs or HCRs and then trained to lever press for food pellets on an FR10 schedule. When behavior stabilized, they were trained to discriminate cocaine (10 mg/kg, i.p.) from saline (1 ml/kg, i.p.) by repeated pairings of injections with one of two response levers. Upon meeting a training criterion, rats began generalization testing where they were given doses of cocaine that differed from the training dose (1.25-15 mg/kg, i.p.) and were reinforced for responses on either lever. We found no significant group differences in sessions to criterion, with LCRs and HCRs learning the discrimination in 22.2 ± 3.2 and 25.7 ± 2.7 sessions, respectively. Furthermore, the dose-response curves obtained in generalization tests were similar in LCRs and HCRs. When generalization tests were performed with co-administration of the serotonin (5-HT) transporter blocker fluoxetine (5 mg/kg), we noted a leftward shift in the dose-response curve in both groups, with a relatively greater effect in HCRs. Lastly, we re-tested each rat's locomotor response to 10 mg/kg cocaine in the open-field. We found evidence of context-independent behavioral sensitization in both groups, with LCRs exhibiting a relatively greater effect. These results suggest that individual differences in cocaine-induced locomotion do not reliably predict performance in cocaine discrimination tests, but that manipulations of 5-HT systems might differentially modulate cocaine's discriminative stimulus properties in LCRs and HCRs.

294 EVALUATION OF A BUPRENORPHINE TRAINING PROGRAM

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Even after completing eight hours of buprenorphine training, many physicians are reluctant to prescribe buprenorphine for opioid dependence. This limits treatment diffusion and suggests a need to evaluate new training methods. As little data exist on buprenorphine training methods, this study surveyed physicians after a CSAT-sponsored training to evaluate their perception of the curriculum, the training methods, and perceived barriers to prescribing. The training content was standardized to national American Psychiatric Association curriculum requirements and incorporated 4 hours each of online and in-person instruction. The in-person component was primarily case-based, and included a session in which participants interviewed buprenorphine maintenance patients. Of 70 physicians, 76% completed the 33-item survey, including 57% psychiatrists, 40% generalists, and 9% addiction or pain management specialists. Most (73%) were practicing physicians, 27% in-training, and 40% lacked experience treating opioid dependence. On a scale of 1 (very poor) to 7 (superlative), the overall training rated a mean 5.8. The mean online course rating (5.0) was significantly lower than all in-person training components ($p < .001$) except for the office logistics session (5.4). Among in-person training components, meeting with patients rated highest (mean 6.3, $p < .001$). Most physicians (67%) stated that they intended to begin prescribing buprenorphine after the training. Intention to prescribe did not vary by physician background characteristics. They were more likely than hesitant physicians (33%) to agree that the course provided enough information ($p < .05$) and to agree that telephone access to experienced providers would improve their confidence ($p < .05$). Among those hesitant to prescribe, the primary barriers were a lack of experience (41%), concern about induction difficulty (24%), and lack of reimbursement (24%). Overall, physicians preferred in-person instruction. They might benefit from greater emphasis on induction, as well experiential training and support. (Supported by CSAT and NIDA DA-020000)

295 DEVELOPMENT OF STRATEGIES FOR PREVENTION AND CONTROL OF SUBSTANCE USE PROBLEMS IN INDIA: NEED TO FOCUS ON COUNTRY SPECIFIC FACTORS

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Success of programs for prevention and control of alcohol, tobacco and other drugs (ATOD) in a country depends on strategies that guide these programs. A wide range of country specific factors needs to be considered in order to develop appropriate strategies for prevention and control of ATOD in any country. This presentation will highlight how country specific factors can be helpful in development of such strategies in India. The following categories of factors will be included in the presentation: (i) Availability of substances (ii) ATOD use patterns (iii) Profile of ATOD users (iv) Health care system (v) Familial and sociocultural systems (vi) Socio-demographic factors (vii) Medical training (viii) Multiplicity of problems and scarcity of resources (ix) governance and law enforcement (x) Ongoing transitions- economic, societal and others. The possible influence of these factors on the effectiveness of prevention and treatment programs in India will be discussed. Following strategies based on these factors will be presented: (i) Low cost interventions involving non-specialist care providers (ii) Abstinence oriented prevention and treatment approaches for majority of the population, even for licit substances (iii) A combination of generic and specific approaches suitable to various population subgroups (iv) Decentralization of planning and implementation of interventions (v) Integration of ATOD services with primary health care system (vi) Community and family oriented interventions (vii) Community participation in ATOD prevention and control activities (viii) Approaches that combine science and spirituality Feasibility and implications of these strategies will be discussed.

296 COLOMBIA 2003: DRUG INVOLVEMENT OF SCHOOL-ATTENDING YOUTHS IN IBAGUÉ, COLOMBIA

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BACKGROUND & AIMS: In most parts of Latin America, there has been limited research on adolescent drug involvement. In this project, we seek to estimate occurrence and school-level clustering of drug involvement among school-attending adolescent youths in the City of Ibagué, Colombia, adapting methods from the NIDA-sponsored original PACARDO research project, a multinational collaborative epidemiological study. **METHODS:** Within an epidemiological sampling frame at the city level, 24 schools and classrooms were designated probabilistically, using Royall's balanced stratified sampling approach, with an intent to secure and to use standardized questionnaire methods from the original PACARDO project to assess a sample with mean age of roughly 16 yrs. An analysis protocol appropriate for this type of multi-level school survey was used to produce the survey estimates. **RESULTS:** Virtually all sampled students completed the survey: 378 males, and 383 females, with 575 from public schools and 186 from private schools, as in the survey city. The most commonly used drug was alcohol (66%), then tobacco (30%), marijuana (13.8%), cocaine (7.8%), coca paste or "bazuco" (6.3%) and heroina (6.0 %). Cumulative occurrence of alcohol use reflected a male excess: males, 72%; females, 46%. Overall, males were more likely to have used all drugs under study. **DISCUSSION:** As in the original NIDA-sponsored seven country PACARDO research project, we found alcohol to be the most commonly used drug. The excess occurrence values observed for males is intriguing, and merits attention in future. The occurrence of heroin use is remarkably large, and requires more study in relation to possible methods artifacts. Strengthening of school-based surveys and other prevention efforts in Colombia may help the country slow the spread of youthful drug involvement, reduce school-level clustering of drug use, and avoid a recent history of periodic outbreaks of illegal drug use.

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- 297** HIGH SCHOOL AND COMMUNITY HEALTH PREVENTION PROGRAM IN GUADALAJARA, JALISCO
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- Most drug prevention programs in México are aimed at young people. Nevertheless most school and university programs have many deficiencies and limitations such as scarce human and economic resources, too large student populations, wide geographical distribution of schools and high mobility of personnel among others. To overcome those limitations this project aims to offer a program of prevention of drug addictions and sexually transmitted diseases on the one side and Health promotion on the other, that reaches young people right on their school-settings. Program description The program includes periodic visits to different public high schools and local parish communities mainly in the Guadalajara metropolitan area in a mobile clinic with a medical, nursing, chem-path and nutrition team. During a one-week visit on their premises medical checkups with histories and selective blood samples for RBC, blood chemistries, and urine tests for everyone and pap smears and breast examination in females are performed. There is also drug and sexual preventive counselling as well as healthy lifestyles promotion. On average 207 young people are attended every week. Data Summary.- During 2005 there were 9131 (73 % female, 27 % male) youngsters attended in 11 major public high schools and 25 communities; of those attended 16 % admitted using tobacco and 12 % admitted use of alcohol. Few students admitted using illegal drugs. Non-previously diagnosed hyperglycemia was detected in 2.12 % and high blood pressure in 3.7 % of the students. Commentary.- This kind of program can be very helpful as a complement to other core drug and health prevention programs in large Universities or school systems with the advantages of high flexibility, ease of mobility and low cost.
- 298** ADOPTION OF RESEARCH-BASED PRACTICES IN TWO RANDOMIZED CLINICAL TRIALS
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- This qualitative study was designed to investigate the process and extent to which research based substance abuse treatment interventions are adopted by clinics participating in multi-site randomized clinical trials (RCTs). Two RCTs were examined: 1) the Center for Substance Abuse Treatment's (CSAT) Methamphetamine Treatment Project (MTP) that tested a manual-driven intervention for methamphetamine users (Matrix Model) at eight clinics, and 2) an Motivational Enhancement Therapy (MET)/Motivational Interviewing (MI) intervention used to enhance client motivation for change at five clinics. Seventy-one interviews were completed at multiple levels of assessment within the RCT's organizational structure, ranging from protocol developers to program clinicians. Respondents were asked about their experiences in project implementation and adoption of the intervention. Analytic methods used were simultaneous collection and analysis of data, coding of data according to emerging themes, and use of analytic memos and theoretical frameworks. Regarding the extent of adoption in the two RCTs, we found: 1) in the MTP trial, full adoption at one clinic through adaptation of the intervention, partial adoption at another clinic, no adoption at four clinics, and no opportunity for adoption at two clinics; 2) in the NIDA MI/MET trial, full adoption at one clinic, partial adoption at two clinics, intention to adopt at one, and no adoption at one clinic. The most common report of adoption across the two RCTs was partial adoption of the intervention in the form of the "counselor toolbox". Factors likely influencing adoption include state policies regarding the use of evidence base practices, organizational culture of the clinic especially its culture of innovation, and the existence of local supervision and intervention expertise at the clinic. Understanding adoption and influencing factors in these two case studies may assist planners in the diffusion of promising research-based treatment practices into community settings.
- 299** INDIVIDUAL AND SOCIAL FACTORS ASSOCIATED WITH DRUG TREATMENT PARTICIPATION
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- Background: Little is known about the interaction of individual and social factors in the role of drug treatment participation. Objectives: To assess whether different levels of addiction severity, problem use, plans to stop, and plans to control drug use combined with different levels of friends' encouraging treatment participation, drug buddies' discussing reducing drug use, getting free drugs from others and being encouraged to use drugs are associated with treatment participation among injecting and non-injecting drug users in Baltimore City. Method: Data from the SHIELD Study (1996-2004; N=581) was analyzed using logistic regression models controlled for injecting drug use, gender and age. Multivariate adjusted odds ratios and 95% confidence intervals (aOR [95%CI]) are reported. Results: Participants who do not report problem use and do not talk very often with friends about reducing drug use (aOR=0.56 [0.35, 0.90]), and those who do not plan to stop using and do not get encouraged by friends to enter treatment (aOR=0.38 [0.22, 0.66]) are less likely to be in treatment. Those who have high addiction severity and whose friends talk very often about reducing drug use (aOR=2.4 [1.2, 4.7]) are more likely to be in treatment, and so are females (aOR=1.9 [1.3, 2.6]). Conclusion: Those with problem use or who plan to stop are equally likely to be in treatment regardless whether or not they get encouraged by friends to go to treatment. However, those with no problem use or who do not plan to stop, respectively, are just as likely as those with problem use or those who plan to stop (regardless of encouragement to enter treatment) to be in treatment if they are encouraged by friends to enter treatment. For those with high addiction severity, friends' talking about reducing drug use may be crucial to enter treatment. Depending on individual susceptibility, social influence is just as important as lack of thereof.
- 300** PAIN AS A REASON FOR SEEKING ADMISSION TO METHADONE TREATMENT
J. D. Haddox(1), M. Y. Smith(1), S. Colucci(1), A. Rosenblum(2), C. Fong(2), C. Maxwell(2) and M. Parrino(3), (1) Risk Management & Health Policy, Purdue Pharma LP, Stamford, CT, (2) National Development and Research Institutes, and (3) AATOD, New York, NY
- Introduction: Pain is a common comorbidity among patients in substance abuse treatment. The purpose of this study was to assess the extent to which pain was endorsed as a reason for seeking admission to methadone maintenance. Methods: Cross-sectional survey of 5,803 individuals admitted to 69 US methadone maintenance treatment programs (MMTPs) between 1/05 -09/05. Respondents completed a structured, self-administered, 1 page questionnaire at intake. Pain (Non-withdrawal intensity) was measured on a 5-point scale (None - Very Severe). "Chronic pain" was defined as non-withdrawal pain of >moderate intensity and pain duration of >6 months. Generalized estimating equations (GEE) were used to examine associations between pain as a reason for enrollment and socio-demographic and drug-related variables; predictors with a p value of < 0.01 were reported. Results: 32.9% of study respondents endorsed pain as a reason for seeking enrollment in methadone maintenance. Of these, most were male (62.3%), Caucasian (65.7%) with a mean age of 37.2 years (SD ± 10.6). The primary drug of abuse within the past month was heroin (58.1%), or an opioid analgesic (41.9%). 69.3% reported experiencing severe or very severe withdrawal pain within the past week; and 63.8% reported severe or very severe bodily pain during that same period. Factors that were significant predictors of pain as a reason for enrollment in multivariate analyses included: having chronic pain (p<0.0001), being non-white (p<0.0001), being unemployed (p=0.006), methadone abuse within the past month (p=0.002), and to have obtained their primary drug of abuse from a doctor's prescription (p=0.01). Conclusions: Methadone maintenance patients who cite pain as a reason for seeking substance abuse treatment are significantly likely to report having persistent bodily pain of moderate to severe intensity. They are also likely to have recently been abusing methadone, to be nonwhite and unemployed, and to obtain their primary drug of abuse through a prescription.

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- 301 EFFECT OF NALTREXONE ON AMPHETAMINE-INDUCED CONDITIONED PLACE PREFERENCE**
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Naltrexone reduces amphetamine-induced locomotor activity, but its effect on other amphetamine-induced behaviours has been less investigated. To study the effect of naltrexone on amphetamine-induced conditioned place preference (CPP) in male Wistar rats, a two chamber apparatus was used. One compartment had black walls with a striped plastic floor and the other had white walls with a smooth floor. A pre-test showed baseline preference for the black side of the compartment. Rats received amphetamine (2 mg/kg i.p.) and were placed in the non-preferred compartment for a period of 30 minutes. On alternative days, the animals were injected with saline and placed on either side. This procedure was repeated for 6 consecutive days. On day 7, the door separating the two compartments was removed and the animals were given free access to both sides for 15 minutes. Animals conditioned to amphetamine showed a significant place preference to the drug-paired side compared to the control animals that had received saline on both sides. The extinction and reinstatement of amphetamine-induced CPP was also studied using this model. The animals were first conditioned as described above and the behaviour subsequently extinguished by injecting the animal with saline in the drug and saline paired compartment, respectively, on alternate days. When the animals displayed extinction behaviour for the drug paired side, they received a priming dose of amphetamine (0.5mg/kg i.p.) and were given access to both compartments. This priming dose reinstated the previously amphetamine induced place preference. Preliminary data suggest that pre-treatment with the opioid antagonist, naltrexone dose-dependently attenuates the acquisition but not the expression of amphetamine induced place preference.
- 302 CREB DIFFERS IN NEURAL AREAS SUBSERVING COCAINE PLACE CONDITIONING IN LEWIS AND FISCHER RATS**
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Our previous research demonstrated that Lewis and Fischer 344 (F344) rats differ in neural and behavioral characteristics related to cocaine abuse. Lewis rats more readily acquire cocaine self-administration and show greater cocaine place conditioning (PC) compared to F344 rats. Studies indicate these behavioral effects are linked to activation of the cAMP pathway and induction of cAMP response element binding protein (CREB). Compared to F344 rats, Lewis rats have lower D2 receptor and Gi-alpha levels in the nucleus accumbens (NAc) and increased activation of the cAMP-PKA pathway. Thus, we assessed low-dose cocaine-induced PC and CREB immunoreactivity in both strains. Rats (n=6/strain and dose) were trained in an unbiased place conditioning procedure with 0, 2.5, 5, or 7.5 mg/kg cocaine (IP) in a 3-day; 2 trials/day (vehicle and cocaine) procedure. Lewis rats showed only place preference whereas F344 rats showed both place preference and aversion. A significantly greater proportion of F344 rats showed place conditioning compared to Lewis rats ($P < 0.01$). CREB was examined in NAc (shell and core), hippocampus (HIP), medial prefrontal cortex (mPFC), and caudate-putamen (CP) in separate groups of rats (n=4/strain). Baseline CREB was greater in the NAc shell but lower in the HIP in Lewis rats. No strain differences were seen in mPFC, NAc core or CP. These data suggest that (1) genetic differences contribute toward differential responses in these strains to the rewarding and aversive effects of cocaine and (2) dissimilar baseline CREB levels in brain areas that subserve cocaine-induced PC may also play a role. Support: NIDA P50-DA18197.
- 303 ATTACHMENT AND SOCIAL SUPPORT AMONG WOMEN DRUG OFFENDERS IN COMMUNITY TREATMENT**
E. A. Hall and M. L. Prendergast, University of California, Los Angeles, CA
Recent evidence suggests that attachment and social support play important roles in mediating substance abuse (Caspers, et al., 2005; Suchman, et al., 2005; Miljkovitch, et al., 2005). Attachment theory (Ainsworth, Blehar, Waters, & Wall, 1978; Bowlby, 1988; Main, 1995) describes types of parent-child connections and their effects on the security of a child's attachment to a parent. There is also evidence that the strategies that adults rely on in their romantic attachments result primarily from their childhood attachment experiences (Fraley & Shaver, 2000; Shaver & Hazan, 1993) and that those who experienced disruptions in attachment during childhood have difficulties providing an environment for secure attachment for their children (Main & Hesse, 1990). Our current study involves women drug offenders in community treatment randomly assigned to treatment-as-usual and women-focused treatment. Instruments include: Experiences in Close Relationships Inventory, Adult Adolescent Parenting Inventory, ISAP social support scale, and the Brief Symptom Inventory. We hypothesize that women with secure adult attachments will have healthier parenting attitudes. In addition, we plan to examine the relationships among adult attachment, social support, and psychological functioning. Preliminary analysis of data on 42 subjects shows that subjects had a mean score of 1.60 (scale 0 to 4) on attachment avoidance and a mean score of 2.25 (scale 0 to 4) on attachment anxiety, greater than normative samples.
- 304 DOES PERSONALITY INFLUENCE OUTCOMES FOR RX OPIOID ABUSERS WITH PAIN?**
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We explored the relationship between personality, baseline characteristics and treatment outcomes for patients in a combined behavioral/pharmacological treatment for pain and Rx opioid abuse. The NEO-FFI assesses the "Big 5" personality factors: neuroticism (N), agreeableness (A), openness (O), extroversion (E), and conscientiousness (C). We hypothesized that patients would score high on N and low on C. We further hypothesized that more extreme scores in this pattern would be associated with greater pain, more dysfunction and psychopathology, worse coping, and poorer outcomes. In general, patients scored high on N (M= 60, SD= 10.12) and low on C (M= 42, SD= 10.16), although all scores except N were normal range. When NEO T-scores were subjected to K-means cluster analysis, 2 groups emerged with significantly different scores on N, E, A & C ($p < .01$). Cluster 1 (n=16; 30%) was characterized by high N (M=65, SD= 9.43) and low C (M=37, SD= 11.9), E (M=32, SD= 6.17), and A T-scores (M= 39, SD= 10.33), whereas Cluster 2 (n = 23; 70%) had T-scores within the normal range (M's=46-57). Independent samples t-tests compared the clusters on the Millon Behavioral Medicine Diagnostic (MBMD) and the Multidimensional Pain Inventory (MPI). While pain, medication abuse, and compliance were comparable across groups, Cluster 1 reported greater physical dysfunction and psychological distress, used less effective coping strategies, and had lower self-efficacy; in addition, Cluster 1 had a higher incidence of dysthymia (44% vs. 13%; $p < .05$). No differences were found between the clusters regarding treatment outcomes: 50% of Cluster 1 and 73% of Cluster 2 patients completed treatment ($p = .14$) and 88% of Cluster 1 and 69% of Cluster 2 were "successes" who were maintained on opioids ($p = .32$). In summary, we found 2 personality subtypes with co-morbid pain and Rx opioid abuse; Cluster 1 was "dysfunctional" and had a pervasive depressive style of relating to the world. However, both groups tolerated and benefit from participation in a novel treatment for this comorbidity.

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305 CHANGES IN ACOUSTIC STARTLE AND FEAR-POTENTIATED STARTLE DURING WITHDRAWAL FROM CHRONIC OPIATE EXPOSURE IN RATS

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Disruption in diurnal rhythms and anxiety are two pronounced effects of opiate withdrawal. The acoustic startle reflex shows circadian regulation and is potentiated by fear-eliciting stimuli (fear-potentiated startle). Thus, one can investigate both signs of withdrawal using the same behavioral measure. The present study sought to characterize changes in startle during spontaneous withdrawal after chronic exposure to the long-acting opiate l-alpha-acetylmethadol (LAAM). Following cessation of 7 days of LAAM or water treatment, startle was assessed twice daily (6am/6pm; lights on: 8am) for 6 days (n=6/group). The circadian rhythm seen in non-withdrawing rats (i.e., peak before lights-on and nadir before lights-off) was disrupted at 6am on Day 2 of withdrawal (p.10). Corroborating the timing of withdrawal, severe weight loss occurred on the first 2 days of withdrawal (p<.005); weight gain normalized by Day 4. These results suggest the presence of concurrent anxiety- and depression-like states during spontaneous withdrawal following chronic LAAM exposure. The hypothalamic-pituitary-adrenal (HPA) axis, which is involved in circadian regulation and is disrupted during opiate withdrawal, may offer a potential mechanism driving the behavioral changes noted in this study. Supported by T32 DA07097 and NARSAD.

306 COCAINE VACCINE: SMOKED COCAINE ADMINISTRATION IN HUMANS

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The purpose of this 13-week study was to evaluate the safety, behavioral effects, and immunogenicity of repeated injections with the TA-CD cocaine vaccine (Xenova Research Limited) in combination with smoked cocaine in cocaine-dependent individuals. Vaccinations were given at weeks 1, 3, 5 and 9. Participants (n=10 males), who were not seeking treatment for their cocaine use, spent 2 nights per week for 13 weeks in the laboratory where the cardiovascular and subjective effects of smoked cocaine (0, 25, 50 mg) were determined prior to vaccination and at weekly intervals after vaccination. Each cocaine dose was administered twice per experimental session. Two doses of TA-CD were tested (82 microgram, n=4; 360 microgram, n=6). Preliminary data analysis demonstrate that cocaine-specific antibody levels peaked at week 13. When subjective-effects data collected prior to antibody development were compared to data collected during peak antibody levels, ratings of "I Feel a Good Drug Effect" and "I Like the Dose" decreased by 45-55% for the 25 mg cocaine dose, and 35-42% for the 50 mg cocaine dose. The vaccine was well tolerated throughout the study; there was no evidence that participants attempted to override the effects of the vaccine by using excessive amounts of cocaine outside the laboratory. These findings suggest that (1) the TA-CD vaccine substantially decreases smoked cocaine's intoxicating effects, (2) the vaccine is more effective at decreasing the effects of low versus high cocaine doses, and (3) even in a population with no motivation to stop using cocaine, the issue of a drug override may prove manageable. Supported by NIDA grant DA-10946-03S1

307 THE EFFECTS OF PROTRACTED COCAINE ABSTINENCE ON DEPRESSION, COGNITIVE PLANNING AND BRAIN METABOLISM

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Chronic cocaine use is associated with behavioral, cognitive, and neurofunctional abnormalities. The extent to which these abnormalities normalize following protracted abstinence is yet unknown. In this multimodal investigation, 40 cocaine abstainers (range:7-660d) and matched controls were screened for depression and executive function. Brain glucose metabolism was measured with FDG-PET. The cocaine abstainers were further clustered into short (ST: 10mo) groups. While all abstainer groups were more depressed than controls, after the first month, there was a significant correlation between decreased depression and length of abstinence (p<0.02). The ST abstainers were significantly impaired on multiple cognitive tests, but action planning time was the only cognitive parameter significantly correlated with length of abstinence. In the ST group, rates of cerebral metabolism were below control levels in all cortical and subcortical regions evaluated. This distributed cortical and subcortical hypoactivation persisted in the MT group and in many regions the metabolism was lower than in ST abstainers. In contrast to the ST and MT groups, the LT group had significantly increased rates of cerebral metabolism in many frontal, parietal, and temporal cortical areas (p<0.05) as compared to controls. The anterior cingulate cortex, hippocampus, amygdala, olfactory cortex, globus pallidus, substantia nigra, thalamus, and cerebellum, however, remained hypoactive in the LT group. These results suggest that specific behavioral, cognitive, and neurofunctional changes do occur following protracted cocaine abstinence. However, there are unique temporal relationships between depression, cognitive performance, and normalization of neural function following cocaine abstinence. Further investigation in to the synergy of these modalities may promote abstainer-tailored rehabilitation strategies. Supported by DA10230 and DA06634.

308 MARIJUANA USE AND DEPRESSION AMONG ADULTS: TESTING FOR CAUSAL ASSOCIATIONS

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BACKGROUND: The long-term mental health consequences of marijuana use are not well understood. AIM: This study tests whether a causal association exists between marijuana use and subsequent depression among adults, after accounting for other differences between marijuana users and non-users. METHODS: Data were analyzed from the National Longitudinal Survey of Youth 1979 cohort, and a total of 8759 adults had complete data on past-year marijuana use and current depression in 1994. Self-reported past-year marijuana use was tested as a causal predictor of adult depression measured using the Center for Epidemiologic Studies - Depression questionnaire. Individual's propensity to use marijuana was calculated using a nonparametric propensity score estimation method incorporating over 50 baseline covariates. RESULTS: Before adjusting for group differences, the odds of current depression among past-year marijuana users was 1.4 times higher (p<0.005) than the odds of depression among the non-using comparison group. After adjustment, the odds of current depression among past-year marijuana users was only 1.1 times higher than the comparison group (p=0.3). Similar propensity score adjustment eliminated significant associations between marijuana use and depression in four additional analyses: heavy marijuana use as the risk factor, stratifying by either gender or age, and using a four-year lag-time between marijuana use and depression. CONCLUSION: After adjusting for differences in baseline risk factors of marijuana use and depression, past-year marijuana use did not significantly predict later development of depression. Supported by NIDA grant T32DA07292.

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- 309** CHARACTERIZATION OF AN EXTINCTION BURST IN DRUG-SEEKING BEHAVIOR FOLLOWING NICOTINE SELF-ADMINISTRATION IN RATS WITH 23 HR/DAY ACCESS TO NICOTINE
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Animals trained to self-administer addictive drugs such as opiates exhibit a temporary increase in response rate when the drug is no longer available (i.e., an extinction burst). While some studies have indicated a parallel phenomenon in human smokers, the presence of an extinction burst in animal models of nicotine self-administration has not been well characterized. In the current study, two groups of rats were trained to self-administer one of two unit doses of nicotine (0.01 or 0.03 mg/kg/infusion) during daily 23 hr sessions until stable self-administration was obtained. Saline extinction was subsequently arranged for at least seven sessions, followed by reacquisition of nicotine self-administration. There was no significant increase in the daily overall response rate during extinction compared to baseline in either group. However, a within-session analysis revealed a 45% increase in the peak response rate during the first session of extinction in the group trained with the 0.03 mg/kg unit dose, indicative of a modest extinction burst. Such a burst was evident in the majority (6/9) of rats and ranged between 14 and 86%. In contrast, only 2/10 rats in the group trained with the 0.01 mg/kg unit dose exhibited an increase in peak within-session response rate during the first extinction session, suggesting that the induction of an extinction burst is dependent upon the unit dose maintaining nicotine self-administration prior to extinction. The current demonstration of an initial increase in drug-seeking during extinction of nicotine self-administration is consistent in some respects with studies demonstrating extinction bursts with other drugs of abuse, and also indicates some parallels between nicotine self-administration in rats and smoking behavior in humans. Supported by NIDA grants T32 DA 07097 and P50 DA013333.
- 310** PROSPECTS FOR AN OUTCOMES-BASED PERFORMANCE MEASUREMENT SYSTEM FOR SUBSTANCE ABUSE TREATMENT PROGRAMS
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The Substance Abuse and Mental Health Services Administration is developing the State Outcomes Measurement and Monitoring System (SOMMS), an outcomes-based performance measurement system designed to provide program benchmarks and other information useful for improving substance abuse treatment systems. In this analysis we assume that the substantial cost, implementation, and measurement challenges facing this plan can be overcome, and instead consider the analytic obstacles to using outcomes data for treatment system performance measurement. For this discussion, we draw on lessons learned from an outcomes-based treatment benchmarking study funded by NIDA that used data collected as part of the Adolescent Treatment Models Project sponsored by SAMHSA's Center for Substance Abuse Treatment. The project included data on 1,545 clients in 11 treatment programs followed over a 12-month period. This study identified several significant analytic challenges to using outcomes data for program performance measurement. (1) Program performance scores must be properly adjusted to account for the risk profiles of very heterogeneous treatment populations served by different programs. (2) Differential follow-up response rates across programs introduce potential biases in program performance estimates. (3) High rates of institutionalization in treatment populations renders many behavioral outcomes ambiguous, such as "abstinence" or "no illegal activity." (4) High outcome variance and small program-level sample sizes diminish the power with which program performance estimates can be made. (5) Outcomes conflate treatment effects with wider community effects resulting from community characteristics that can either support or discourage recovery. We conclude that there is a gap between the ideal and the practical reality of outcome-based performance measurement. Alternative strategies for measuring program performance are discussed. This research was supported by NIDA Grants R01 DA015697, R01 DA016722 and R01 DA017507.
- 311** THE EFFECTS OF STRESS IMAGERY ON THE SUBJECTIVE MEASURES OF CRAVING AND MOOD IN METHAMPHETAMINE-ADDICTED VOLUNTEERS
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The effectiveness of current therapies for methamphetamine (MA) dependence is limited by high rates of relapse. Factors contributing to relapse include drug availability, exposure to drug cues, and exposure to psychosocial stressors. The principal goal of this project was to determine the effects of a psychological stressor on physiological and subjective measures in MA-addicted volunteers (n=13). In random order, subjects described a stressful experience occurring in the recent past (not drug-related) and a neutral script (everyday activities). Immediately prior and 120 min afterward, patients completed visual analog scales (VAS) for mood and drug effects and the 45-item Craving-Questionnaire-Now (CQ-Now), and cardiovascular indices were monitored. Participants included 12 males and 1 female, of which 8 were Caucasian, 2 were African American, and 3 were Hispanic. Average age was 36.7 ± 2.3 and average years of education was 14.6 ± 2.4 . The data show that on ratings from 1 -10 (least stressful to most stressful), patients reported their stress script as stressful (8.7 ± 0.6), and their neutral script as non-stressful (1.9 ± 0.6). When asked about "imagery vividness", participants reported these at 9.4 ± 0.3 and 9.3 ± 0.4 , respectively. Despite these self-reports, recounting of the stress event, as compared to the neutral event, was not associated with increased VAS ratings for "Desire", "Stimulated", or "Would Use MA if Given Access". Similarly, recounting of the stress event was not associated with increased ratings on any aspect of the CQ-Now questionnaire. Moreover, recounting of the stress event, was not associated with increased heart rate or blood pressure. These data differ from those previously reported in cocaine-dependent populations. One explanation is that chronic MA use may lead to tolerance to the stressful effects of psychological stimuli such as those used in the current study. Supported by NIDA: DA-14593, DA-18185, DA-17754
- 312** INTRA-ACCUMBAL TAT (1 - 72) ATTENUATES IV COCAINE-INDUCED LOCOMOTOR ACTIVITY IN RATS: ROLE FOR D1 RECEPTORS IN COCAINE/TAT-INDUCED NEUROTOXICITY?
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Patients with HIV who also have a history of drug use are more likely to develop neuropsychiatric disorders and HIV dementia. Previous research indicates that the Tat protein may be integral to the HIV/drug synergism that produces neural dysfunction. First, Tat alone produces neurotoxicity via oxidative modification of proteins after microinjection into the striatum of adult rats and in hippocampal cell culture studies. Second, in vitro studies demonstrate that the combination of Tat and cocaine (COC) produces neurotoxicity and that COC enhances Tat-induced oxidative cell damage in part via a D1 mediated mechanism. Currently, little is known about the effects of Tat on COC mediated behaviors, or if D1 receptors play a role in Tat-induced toxicity of cultures of fetal midbrain neurons which include the striatum and nucleus accumbens. Therefore, the present experiments determined (1) if microinjection of Tat into the nucleus accumbens altered the subsequent acute and/or repeated effects of IV COC -induced locomotor activity in adult, ovariectomized rats; and (2) if SCH 23390, a D1 receptor antagonist, altered Tat-mediated toxicity of fetal midbrain neurons in cell culture studies. Intra-accumbal Tat (15 μ l/ml; bilaterally) attenuated the acute locomotor effects of IV COC (3.0 mg/kg/injection), but did not prevent the development of sensitization. Cell culture studies indicated that Tat alone produced toxicity to midbrain neurons, and that SCH 23390 attenuated the Tat-induced damage. These data suggest that Tat alters COC-mediated behavior by disrupting mesocorticolimbic dopamine system function, and that D1 receptors may play a role in Tat-induced toxicity in the midbrain. Pharmacotherapies aimed at preventing behavioral problems in individuals who are HIV+ and exhibit COC abuse should target the mesocorticolimbic dopamine system. This research is supported by the following grants: DA11337, DA09160, DA013137, DA014401, and HD043680.

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- 313 NEUROPHYSIOLOGICAL EFFECTS OF SMOKED MARIJUANA DURING COMPLEX COGNITIVE PERFORMANCE**
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Previously, we evaluated the ability of daily marijuana smokers to perform complex cognitive tasks following a single marijuana cigarette and reported that performance was only minimally affected. It is possible that the cognitive tests used in that study were insensitive to many marijuana-related cognitive effects. Therefore, in the current study electroencephalographic (EEG) signals were recorded as daily marijuana users performed additional tests of immediate working memory and delayed episodic memory, before and after smoking marijuana. Healthy research volunteers (N=24), smoking ~20 marijuana cigarettes per week, completed this 3-session outpatient study; sessions were separated by at least 72-hrs. During sessions, participants completed baseline computerized cognitive tasks, smoked a single marijuana cigarette (0%, 1.8%, or 3.9% THC), and completed additional cognitive tasks. Blood pressure, heart rate, and subjective effects were also assessed throughout sessions. Marijuana produced slower and less accurate responses to previously unseen words on the episodic memory task, due to a shift in response bias. This was accompanied by reduced slow wave evoked potential amplitude, suggesting reduced attentional allocation. Working memory task performance was not affected by marijuana, but EEG theta and beta band power decreased. Heart rate and "positive" subjective-effect ratings were significantly increased in a THC concentration-dependent manner. These data are consistent with previous studies on the neurophysiological effects of acute marijuana smoking and with the previous finding suggesting that a single dose of marijuana has more muted effects on daily smokers than it does on infrequent users, even when difficult memory tasks are employed. Supported by NIDA grants DA-03746 and DA-12840.
- 314 AN ITEM RESPONSE THEORY ANALYSIS OF DSM-IV MARIJUANA ABUSE AND DEPENDENCE CRITERIA IN AN ADOLESCENT SAMPLE**
C. Hartman(1), H. Gelhorn(1), J. Sakai(1), M. Stallings(2), S. Young(2), S. Rhee(2), R. Corley(2), J. Hewitt(2), T. Crowley(1) and C. Hopfer(1), (1) University of Colorado Health Sciences Center, Denver, CO and (2) University of Colorado at Boulder, Boulder, CO
RESEARCH QUESTIONS: In order to explore the utility of the DSM-IV abuse and dependence items for marijuana, we examined two questions: (1) Are there significant differences in item severity among clinical, adjudicated, and community samples? (2) Do the abuse and dependence criteria in the DSM-IV reflect two non-overlapping levels of severity in adolescents? METHOD: The sample included 619 adolescents (age 11-19) who had endorsed at least one DSM-IV marijuana item. Subjects came from three samples: an adjudicated population, a clinical sample from a substance abuse treatment center, and a community sample. All were administered the CIDI-SAM. An Item Response Theory (IRT) Differential Item Functioning (DIF) analysis was performed with the 11 abuse and dependence criteria. RESULTS: Results indicated no significant differences in item parameters among the three groups, excepting failure to fulfill major obligations, which indicated a less severe level of pathology in the treatment sample. Moreover, we found that both abuse and dependence items reflected varying levels of severity, rather than dependence items being distinctly more severe. CONCLUSIONS: These results suggest that, for marijuana, the DSM-IV abuse and dependence items function similarly across clinical and community samples of adolescents. In addition, the assertion that abuse and dependence reflect distinct levels of severity was not supported in these data. Support: DA15522, 05131, 12845, 11015, 16314, MH01865, AA07464
- 315 SEXUAL PRACTICES IN METHADONE MAINTENANCE AND OUTPATIENT PSYCHOSOCIAL DRUG TREATMENT SAMPLES**
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Objectives: Combining sex and drugs increases risk for HIV/STDs. Details about patterns of sexual behavior based on treatment type and drug use could inform allocation of HIV/STD intervention resources in drug treatment. Methods: Men in NIDA CTN protocol 0018, a gender specific HIV prevention intervention, were administered (via ACASI method) a structured self report questionnaire on involvement in sexual risk behaviors in the prior 90 days. The following results focus on the 236 methadone maintenance (MM) and 262 outpatient psychosocial (OPS) patients reporting only heterosexual encounters in the past 90 days Results: OPS patients reported significantly more frequent vaginal (t=2.7, p=.008) and receptive oral (t=2.0, p=.05) sex with their main partners, and other female partners (t=2.7, p=.007; t=2.6, p=.009, respectively), in the last 90 days. More OPS patients had "high risk" main partners ($\chi^2=6.6$, p=.01). OPS patients also used condoms less often than MM during anal sex with main partners ($\chi^2=5.2$, p=.02) and giving/receiving oral sex with other female partners ($\chi^2=13.0$, p=.0003; $\chi^2=5.9$, p=.02, respectively), though use in both groups was low. Men who were stimulant users had more partners (t=-3.05, p=.003), and their partners were riskier ($\chi^2=4.6$, p=.03), compared to mainly non-stimulant users. Despite differences in proportion of condom use in the past 90 days, in general OPS vs. MM and stimulant vs. non-stimulant users used condoms infrequently. Conclusion: Compared to MM patients, OPS patients described riskier sexual behavior. HIV prevention efforts often focus on IV drug users. Results from this study suggest that OPS patients in programs across the country are in as much need for interventions, perhaps more, based on their reported pattern of sexual activity.
- 316 ETHNIC DIFFERENCES IN TREATMENT FOR MOOD AND ANXIETY DISORDERS AMONG INDIVIDUALS WITH COMORBID SUBSTANCE DEPENDENCE**
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Previous literature indicates that having comorbid psychiatric diagnoses increases the likelihood of entering psychiatric treatment. It has also been shown that African Americans are less likely than Caucasians to receive treatment for mood/anxiety disorders. The treatment-seeking pattern of African Americans with comorbid psychiatric conditions, however, is not well studied. We examined differences in psychiatric treatment among African Americans and Caucasians with comorbid substance dependence and mood/anxiety disorders. Of the 32,752 Caucasian and African-American participants interviewed in the 2001-2002 NESARC, 2204 had lifetime comorbid substance dependence and mood/anxiety disorders as assessed by the AUDADIS-IV. Logistic regression conducted using SUDAAN to test for the effect of ethnicity on likelihood of treatment, controlling for sex, age, income, duration of psychiatric episode, age of first drug use, and insurance status. Results indicated that African Americans were significantly less likely to undergo treatment for a mood/anxiety disorder compared with Caucasians (54.8% vs. 38.3%, chi-square=9.42, p=0.003); there were no differences in proportion treated for substance dependence (30.2% of Caucasians, 30.6% of African-Americans). Comorbid Caucasians are significantly more likely to seek any mood/anxiety treatment (OR=2.14, 95% CI 1.51-3.04), talk to a professional (OR=2.10, 95% CI 1.49-2.96), or to take medications (OR=2.39, 95% CI 1.65-3.49) for mood/anxiety disorder, compared with African-Americans. There is no difference between the ethnic groups in the likelihood of seeking any treatment for substance dependence (OR=0.98, 95% CI 0.67-1.44), or specific types of substance treatment. African-Americans with comorbid mood/anxiety disorders and substance dependence are less likely to seek treatment for the mood/anxiety disorder compared with Caucasians, but are equally likely to seek treatment for the substance dependence. Further research is needed to understand how prevention and intervention strategies can be used to address this disparity.

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317 MORTALITY AMONG OPIOID-DEPENDENT CLIENTS IN A LONGITUDINAL STUDY

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Zanis and Woody (1998) reported high death rates (8.2%) among clients who are discharged prematurely or drop out of methadone treatment. Mortality among clients enrolled in a 2-year longitudinal study was assessed. The parent project examined the effectiveness of opioid replacement therapy in a therapeutic community (TC) setting. Participants were assessed at 6-month intervals for 24 months total. Of 231 total clients recruited, 96% (n = 221) were assessed at 6-month follow-up and 93% (n = 215) were assessed at 12-month follow-up; 18-month and 24-month follows are still ongoing. Comprehensive follow-up tracking methods proved especially useful for examining mortality. To date, 9 clients are deceased; 4 men and 5 women. Approximately 55% (n = 5) of deceased clients were on methadone maintenance at the time of study enrollment. Most participants (89%) died after the 12-month follow-up and none were in TC treatment at the time of death. Preliminary data shows that 2 clients were in methadone treatment at the time of death. Medical Examiner necropsy reports indicate that 2 clients died from acute polysubstance toxicity, 1 from chronic alcoholism, 3 from chronic polysubstance abuse, 2 from cardiovascular disease, and 1 from esophageal cancer. One client was documented HIV-positive and all 9 deceased participants were Hepatitis C positive according to medical records. The average age of clients at the time of death was 45.8 (Range = 26 to 56). Findings support previous research and suggest high rates of mortality among opioid-dependent clients. Participant tracking methods for longitudinal research will be discussed as a key factor in determining study mortality rates. Supported by R01DA14922.

318 RISK FOR INVOLVEMENT IN VIOLENCE IN PERSONS WITH SINGLE DISORDERS (SUBSTANCE USE OR MAJOR MENTAL DISORDERS) AND WITH CO-OCCURRING SUBSTANCE USE AND MENTAL DISORDERS

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Concerns about treatment and public safety have motivated studies investigating substance use and major mental disorders as predictors of violence. Our study examined whether type of disorder, gender, race, age and homelessness predicted perpetration and victimization in a sample (N=419) recruited at treatment entry from acute crisis substance abuse and mental health treatment programs. Subjects (Ss), by administration of the DIS-IV, were classified as having substance use disorders only (30%), major mental disorders only (17%), or both disorders (54%). Using the MacArthur Community Violence Interview, Ss described their experience of violence in the 30 days before treatment entry. For each incident, Ss stated whether they were the perpetrator or the victim. Ss were classified as perpetrators if they reported no victim incidents, as victims if they reported no perpetration incidents, and as perpetrators and victims if they reported both. A total of 171 Ss (41% of sample) reported at least one incident of violence, 6% reported being involved only as a perpetrator, 20% reported being involved only as a victim, and 14% reported being both perpetrator and victim. In the incidents they reported. Using logistic regression with simultaneous entry, Whites were less likely to be involved in any violence than Blacks or other race/ethnic groups (OR=0.56, p<.04) and being perpetrators only (OR=0.29, p<.02). Homelessness emerged as a significant predictor of being involved in any violence (OR=1.94, p<.01), and being a victim only (OR=2.19, p<.01). Homelessness did not predict perpetration. Type of disorder, age, and gender were not found to be significant predictors being involved in violence, being a perpetrator only, or a victim only. Our findings indicate that it was more typical of this sample to be victimized than to perpetrate violence and that homelessness was the preeminent risk factor for involvement in violence. Both of these findings have significant treatment and public policy implications.

319 PREVALENCE AND CORRELATES OF SUBSTANCE USE DURING PREGNANCY: RESULTS FROM A NATIONAL SAMPLE

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Background and Objective: Research demonstrates that substance use can have deleterious effects on pregnancy outcomes. The purpose of this study was to examine substance use during pregnancy in a nationally representative sample of women. Methods: Data from the 2002 and 2003 National Survey on Drug Use and Health (NSDUH) were utilized to determine the prevalence and correlates of substance use among pregnant women (N=1800) aged 15-44 years. Variables included demographics, substance use in the prior 30 days, severe mental illness (SMI) and severe stress in the prior 12 months. Since only pregnant women were included, unweighted contingency table and multiple logistic regression analyses were utilized. Results: Most respondents were between 18 and 34 years and married. The overall prevalence of past month illicit drug, cigarette and alcohol use was 4.7%, 18.9% and 10%, respectively. However, the prevalence of use decreased significantly (p<0.001) in the second and third trimesters versus the first trimester. Compared with women not reporting use during pregnancy, substance users were significantly more likely to meet the criteria for SMI (Adjusted Odds Ratio [AOR]: 1.89, 95% Confidence Interval [CI]: 1.35, 2.66) and have experienced recent stress (AOR: 1.47, 95% CI: 1.09 – 1.97). In addition, those women who were employed and married were less likely to have used any substance during pregnancy, adjusting for age, race and income. Conclusions: Although there were significant reductions in drug use during pregnancy, women with severe mental illness, stress and less social support appear vulnerable to continued use during pregnancy. Prevention and intervention programs aimed at these populations are warranted in order to reduce negative pregnancy outcomes associated with substance use.

320 MONTHLY PATTERNS OF SMOKING TOPOGRAPHY AND SMOKING RATE AMONG COLLEGE WOMEN SMOKERS:

A PILOT STUDY

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Smoking topography measures of nicotine self-administration (e.g., inter-puff latency, puff volume, peak flow of puffs, puff duration) have been shown to vary with smoker characteristics such as mood state and nicotine dependency level. Animal and human studies have shown that drug self-administration patterns are associated with menstrual cycle phase in female animals and humans. The goal of the present ongoing study is to track smoking topography and nicotine self-administration patterns over time in women smokers. We hypothesize that these topographical patterns and daily smoking rate will fluctuate in a predictable monthly pattern, possibly in concert with menstrual cycle phase and hormonal fluctuation in women smokers. Participants are college undergraduate women who smoke > 10 cigarettes per day and are not taking oral contraceptives. To date, we have screened 132 women, and 17 of them have met the smoking and oral contraceptive inclusion/exclusion criteria. Eighty-eight percent of the participants are Caucasian and 12% are African-American. Participant age: m = 20.5, daily smoking rate: m = 16.2, number of years smoking: m = 4.4, nicotine dependence level, as measured by the Fagerström Test for Nicotine Dependence (FTND): m = 3.8, and carbon monoxide level: m = 20.3 ppm. Participants were assessed with the smoking topography device at baseline and for a subsequent period of > 2 months, at twice weekly intervals. Participants also self-monitored their daily smoking rate. Eight participants have completed the study (topography and self-monitored smoking was obtained for > 2 months). Time to first puff, puff count, and average puff interval were significantly correlated with smoking rate on 4 days of each month. Visual inspection of individual graphs displaying smoking rate and topography data over 2+ months reveals a 7-14 day period of increased smoking.

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321 ADHERENCE AND RESPONSE TO HEPATITIS C TREATMENT AMONG INJECTION DRUG USERS

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Injection drug users (IDU) are at high risk for hepatitis C virus (HCV) infection and chronic liver diseases such as cirrhosis and hepatic cancer. Effective treatments for HCV are available; although IDU face many treatment barriers. Until recently, a history of IDU was viewed as a contraindication for medical treatment of HCV. Guidelines have now expanded treatment access to IDU and other vulnerable populations; however, many IDU continue to be excluded for treatment by providers because of treatment response concerns. Therefore, the purpose of this paper was to review studies examining HCV treatment adherence and efficacy among IDU. We examined all available English-language studies ($n \geq 50$) that evaluated the sustained viral response (SVR) of adult IDU either alone or in comparison to non-IDU receiving HCV therapies to determine if provider concerns about treating IDU are justified. Using these criteria, a total of 11 studies were found via Medline/PubMed and were reviewed in this paper. Among these studies, SVR was similar between IDU and controls. Most studies did not find significant differences in treatment response, adherence to treatment, relapse rates, or rate of discontinuation due to side effects among IDU and non-IDU controls. These data confirm that HCV treatment should not be uniformly withheld from IDU. Although the reviewed studies indicated similar treatment responses between IDU and non-IDU samples, further research into the response rates for hepatitis treatment are needed. In particular, more studies are needed to investigate the SVR among IDU receiving pegylated interferon in combination with ribavirin, which has become standard of care treatment for HCV. Finally, more research is needed to understand the barriers to HCV treatment initiation and maintenance among IDU.

322 NOT GETTING RESEARCH TREATMENT: EARLY-SCREENING-PHASE DROPOUTS IN A MODAFINIL TRIAL OF COCAINE DEPENDENCE

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Substance abusers often have severe instability in multiple life domains making any task completion daunting. The potential subject seeking a research treatment program must complete phone screening, endure a long consent process and complete a screening period prior to treatment initiation. While researchers see completion of screening as a measure of motivation, subjects see it as a barrier to treatment attainment. Dropout during screening in substance abuse trials is rampant due to both the nature of the dependence and the barriers to treatment inherent in substance abuse clinical trials. As part of a project to assess barriers to treatment in screening for the Modafinil clinical trial of cocaine dependence, dropout subjects were compared to treatment initiation subjects with respect to baseline characteristics. Subject baseline data was compared for the screen drop ($n=47$) and treatment initiation ($n=37$) subjects. Dropout subjects were similar to treatment initiation subjects with respect to gender, race, number of alcohol and cocaine days in the past 30 and Epworth Sleepiness Scale. Dropout subjects ($\text{mean}(\text{sd})=35.98(6.76)$) statistically differed from treatment initiation subjects ($\text{mean}(\text{sd})=39.73(7.28)$) with respect to age, $z=2.56$, $p=.01$. Also, dropout subjects ($\text{mean}(\text{sd})=36(17.54)$) statistically differed from treatment initiation subjects ($\text{mean}(\text{sd})=23.78(12.97)$) with respect to Cocaine Selective Severity Assessment total score, $z=-3.04$, $p=.002$. Finally, the probability of dropping out during screening increased as self-rated perception of cocaine dependence severity increased ($z=2.32$, $p=.02$). Using this information, a "Barriers to Screening" interview is under development. This interview will be conducted on subjects identified as having the most severe symptoms of cocaine dependence as measured by the CGIS in an effort to remove or cognitively reframe barriers to screening for those subjects most susceptible to dropout.

323 EARLY ABSTINENCE'S EFFECT ON LATER ABSTINENCE IN CIGARETTE SMOKERS

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Each year millions of smokers try to quit, but the majority relapses within days. Sustaining complete abstinence through the initial 2 weeks of a quit attempt is associated with a precipitous decline in relapse risk. There is much correlational evidence supporting this relationship. Our group has conducted a series of lab studies designed to experimentally examine the relationship between early and later abstinence in non-treatment-seeking smokers. Collectively, results of these studies support a direct, causal relationship between early and later abstinence. In the present ongoing study, which moves the model into a treatment-seeking population, we are using a CM procedure to experimentally manipulate the percentage of smokers achieving complete abstinence during the initial 2 weeks of a quit attempt. Participants are randomized to earn monetary payments (\$260 max) contingent on biochemically-verified abstinence or non-contingently in a yoked control condition. Point-prevalence abstinence is assessed 1 and 3 months later. We hypothesize that by increasing the percentage of participants who achieve complete abstinence in the contingent condition, long-term abstinence will also increase relative to the non-contingent condition. Preliminary results indicate that twice as many participants in the contingent condition sustain 2 weeks of complete abstinence compared to the non-contingent condition, 9/18 (50%) vs. 4/17 (24%). Point-prevalence abstinence at the two follow-up assessments was examined in the subset of 6 contingent participants who both (1) were continuously abstinent and (2) have completed both assessments and compared to their yoked controls. While we do not yet have enough data for statistical comparison, verified abstinence rates at 1 and 3 months were 3/6 (50%) vs. 2/6 (33%) and 3/6 (50%) vs. 1/6 (17%). There are no differences in characteristics between conditions that would account for this trend. Our preliminary results suggest a trend towards greater long-term abstinence as a direct result of sustained abstinence early in a quit attempt.

324 BECK DEPRESSION INVENTORY SCORES AND DRUG USE IN METHADONE-MAINTAINED OUTPATIENTS

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Polydrug-abusing participants ($N=199$) were administered the Beck Depression Inventory (BDI) and Addiction Severity Index during screening for a 35-week outpatient clinical treatment trial (daily methadone, weekly counseling, and protocol-specific behavioral interventions, with observed urine collection 3x/week). Participants also provided urine samples and completed the BDI at screening, treatment completion and at 3-month, 6-month and one-year follow-ups, resulting in data for up to five time points per participant. As the BDI assesses symptoms during a one-week period, percentage of positive urines in the 7 days preceding BDI administration was used as the dependent variable. Mean \pm SEM BDI score was 11.6 ± 1.1 on occasions when participants had tested 0% positive for cocaine throughout the week, but 17.5 ± 0.7 on occasions when they had tested 100% positive. The corresponding BDI scores for heroin were 7.7 ± 0.8 and 19.1 ± 0.7 ; the corresponding BDI scores for cannabis were 15.6 ± 0.6 and 16.5 ± 1.7 . These differences were analyzed in three separate repeated-measures regressions (SAS Proc Mixed)-one for cocaine, one for heroin, and one for cannabis. BDI score was used as a time-varying predictor of past-week drug use; each analysis controlled for sex, race, age, years of education, and years of use (cocaine, heroin, or cannabis, as appropriate). Results showed that BDI score was significantly associated with past-week positives for cocaine (unstandardized beta = 0.42, $t[216] = 2.03$, $p < .05$) and opiates (unstandardized beta = 0.53, $t[216] = 3.01$, $p < .003$), though no cannabis (unstandardized beta = 0.22, $t[216] = 1.27$, $p = .21$). Results suggest that depression, as evaluated by the BDI, is robustly related to drug use. These characteristics should be taken into consideration when identifying patients who may require more intensive psychological treatment for their depression while receiving drug treatment.

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325 DENICOTINIZED CIGARETTES ATTENUATE NICOTINE WITHDRAWAL SYMPTOMS, BUT NOT WORKING MEMORY DEFICITS, FOR 8 DAYS

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Denicotinized cigarettes have been shown to attenuate nicotine withdrawal symptoms for several hours; however, few studies have investigated this effect for longer periods. In this study, we examined the effects of denicotinized cigarettes on nicotine withdrawal signs and symptoms for 8 days. Smokers (mean cigarettes per day = 25; mean FTND = 5.7) were randomly assigned to one of three groups: tobacco deprivation (n = 6 to date), denicotinized cigarettes (n = 7 to date), or nicotine cigarettes (n = 8 to date). Participants adhered to these conditions for 8 days, after which they resumed (or continued) smoking nicotine cigarettes. Compliance was monitored via expired air CO and urine nicotine levels. A time-based control group of nonsmokers (n = 14) was also tested. A battery of subjective and cognitive measures was assessed at baseline, repeatedly during the 8-day experimental phase, and after resumption of smoking. Measures included the Minnesota Nicotine Withdrawal Scale (MNWS), Tobacco Craving Questionnaire (TCQ), and N-Back task, a measure of working memory. Deprived smokers reported increased withdrawal symptoms and tobacco craving throughout the 8 days, whereas scores on the MNWS and TCQ were unchanged from baseline for the denicotinized and nicotine cigarette groups. In contrast, the denicotinized and abstinent smokers showed significant impairment (decreased accuracy and increased response time) on the N-Back task compared to continuing smokers and nonsmokers. These preliminary results suggest that components of tobacco smoke other than nicotine attenuate the expected withdrawal symptoms, but not the memory deficits, observed during 8 days of tobacco deprivation.

326 CANNABIS USE IN THE COMMUNITY – ADVERSE OUTCOMES AND UNMET NEEDS

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Objectives: To estimate in a community sample of baseline adolescent and young adults the 10 year prospective risk of a) incident b) continued and c) problematic use of cannabis as well as subsequent use of other illicit drugs. Methods: The community-based EDSP-study employed a prospective-longitudinal design to study substance use and other mental disorders in a sample of adolescents and young adults (N=2934 at baseline) in Munich, Germany. The DSM-IV version of the M-CIDI was used to assess cannabis use as well as substance related problems and concomitant use of other illicit drugs Results: The cumulative lifetime incidence of cannabis use among a sample aged 24-34 years was 50.5%. Almost one third were incident users of cannabis within the follow-up period (16.6%). The population of continuous users was high and the proportion of cannabis users with subsequent use of other drugs was about 24%. The rate of cannabis users who developed psychosocial problems (about 20%), dependence (2.5%) or abuse (7.0%) was substantial. Conclusions: In the first three decades of life, one out of two adolescents or young people will use cannabis most of which go on to be regular users or problematic users. Results indicate a further increase in young cannabis users and reveal a growing need of interventions among cannabis users.

327 RISK MANAGEMENT AND DRUG ABUSE RESEARCH: CHALLENGES AND OPPORTUNITIES

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Risk management programs (RMPs), including Risk Minimization Action Plans (RiskMAPs), are increasingly used by FDA to supplement the scheduling provisions of Controlled Substance Act to reduce the risk of diversion, abuse, and misuse of psychoactive drugs. Drug scheduling has consequences for restrictions on marketing and prescription writing, as well as labeling, handling and pharmacy procedures for storage. However, RMPs can add many additional restrictions on marketing (e.g., restricted product launch time table), restricted distribution, as well as many additional requirements of the sponsor such as intensive methods of surveillance, and educational commitments. Thus, the level and nature of the RMP is becoming an important issue to sponsors and regulators as drug scheduling due to its potential impact on misuse, abuse, diversion, and commercial marketing potential of the drug RMPs are an emerging area of science and regulation. Guidance documents for the development of RMPs, issued in March 2005, recommend premarket risk assessment and a variety of potential "tools" for consideration in developing RMPs and RiskMAPs. Premarket risk assessment includes abuse liability assessment of the active drug, but goes further by recommending assessment of the drug formulation as a potential determinant of ease and attractiveness of a given drug product to be diverted for illicit sale and abuse. Other factors in development of RMPs and RiskMAPs may include the indication, population, and experience with other drugs in the category. The advent of risk management as a major regulatory tool for reducing misuse, abuse and diversion of psychoactive substances presents a challenge to substance abuse researchers to develop the science foundation. This presentation will provide an overview of the current state of the art of the science base for risk management development as well as specific research questions that need to be addressed.

328 A LONGITUDINAL STUDY OF PRE-SEXUAL RISK BEHAVIORS AND SUBSTANCE USE AMONG ADOLESCENTS WHOSE MOTHERS ARE HIV POSITIVE

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The initiation of substance use and risky sexual behaviors during adolescence is often a precursor to long-term addiction to substances and HIV infection during adulthood. It is particularly important to examine these risk behaviors among adolescents of HIV+ mothers, as their mothers face the challenge of coping with their illness as well as mediating the impact of their illness upon their family. This longitudinal study examined the association of pre-sexual and sexual behaviors (intimate touching, oral sex, and sexual intercourse) with substance use, family life variables, religiosity, and attitudes towards women among adolescents of HIV-positive mothers. Participants were 118 predominantly Latino and African-American adolescents (mean age=14.0; SD=1.8 at 12-month follow-up) in Los Angeles County. Adolescents and their mothers were interviewed in person separately at baseline, 6-month and 12-month follow-up. Pre-sexual behaviors were examined over time in relation to predictor variables while adjusting for age and gender differences. Pre-sexual and sexual behaviors increased over time from 19% at baseline to 25% at 12-month follow-up. There were significant positive associations between adolescent pre-sexual behaviors and the following variables: adolescent tobacco, alcohol, and marijuana use; disengaged family style; and traditional attitudes towards women (e.g., belief in a more submissive role for women). Adolescents with higher scores on family routines and parental monitoring scales were less likely to engage in pre-sexual behaviors across the three assessment periods. Adolescent religiosity, mothers' health status, and mothers' use of drugs or alcohol were not associated with adolescent pre-sexual behaviors. These findings suggest that HIV+ mothers with strong parenting skills may effectively protect their adolescents from the early initiation of pre-sexual and sexual behaviors. Implications are discussed. Funded by NIMH (R01MH057207) and NIDA (P30DA016383).

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- 329 PROVIDING INTEGRATED OFFICE-BASED METHADONE TREATMENT IN PUBLIC HEALTH MEDICAL SETTINGS: EXPERIENCES AND FINDINGS FROM THE SAN FRANCISCO OFFICE-BASED OPIATE PILOT PROGRAM**
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- For over a decade, San Francisco has grappled with a huge heroin problem. Untreated heroin dependence has resulted in tremendous morbidity, significant mortality, and a myriad of psychosocial problems. It has also placed a large burden on the public health system. Though a wealth of data support the efficacy of methadone treatment, literally thousands of heroin users are unable to access care under the present delivery system. The San Francisco OBOT Pilot is one of several novel initiatives implemented by the San Francisco Department of Public Health (SF-DPH) to bridge the access gap. At the pilot's core is the development of a model that expands methadone (and buprenorphine) availability by providing high quality, integrated addiction and medical services. It brings the OBOT paradigm to inner-city primary care sites and, unique to this program, allows for the enrollment of patients following a relatively brief (2-6 months) period of evaluation and stabilization. The pilot set out to enroll a total of 100 patients, 60 to receive integrated care utilizing methadone or buprenorphine at two primary care sites. In July 2003, following several years of discussions and negotiations with Federal, State, and local agencies, the first OBOT methadone patient was enrolled. To support providers, the SF-DPH conducted a series of trainings, developed treatment guidelines, created a methadone stabilization track for pre-enrollment evaluation and ongoing patient support, and provides ongoing consultation. To date, a total of 103 patients had been enrolled in the pilot, 33 having received methadone services at one of the two primary care sites. Preliminary data review reveals impressive treatment retention rates, low levels of heroin use, and high patient satisfaction. The presentation will focus on program description, implementation, and outcome measures, including patient retention, and program impact on drug use and medical utilization.
- 330 RESEARCH PARTICIPANT RECRUITMENT PROGRAM FOR DRUG ABUSE STUDIES AT NIDA-IRP**
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- The national Institute on Drug Abuse, Intramural Research Program (NIDA IRP) has a centralized IRB approved screening protocol for all of its adult therapeutic and non-therapeutic clinical studies. This presentation describes the process and outcomes of recruitment efforts for the 2004 and 2005 calendar years, including screening and primary protocol admission. After an initial phone screen with verbal consent, potential participants are scheduled for an in-person appointment. Before any additional screening is initiated, a written informed consent is obtained through a standardized procedure. The collection of demographic, health and other specific study suitability measures begins thereafter. The applicant is considered for multiple protocols simultaneously, but is initially offered participation in a primary protocol based on an institution determined priority sequence. Subjects may enter more than one study sequentially and participate in non-conflicting studies simultaneously. In 2004, there were 21 active primary studies; 4 of which were therapeutic protocols. Approximately 13,000 phone screens (13% for treatment studies), yielded 706 unique volunteers (19% for treatment) who consented to at least one study during that year. In 2005, 22 active primary protocols (2 were treatment studies) admitted 576 research participants (22% for treatment research) screened from 13,580 phone screens (23% treatment seeking). Implications of these findings for enhancing recruitment efforts for clinical research on drug abusing populations will be discussed.
- 331 SUBSTANCE ABUSE AND OLDER ADULTS: A REVIEW OF THE LITERATURE**
L. Hess(1), K. Munly(1), I. James(3), S. Nemes(3), L. Pelletier(1) and E. Moolchan(2), (1) Public Health Research, Danya International, Inc., Silver Spring, (2) HHS/NIH/NIDA/IRP, Baltimore, and (3) Social Solutions International, Inc., Olney, MD
- Alcohol-related problems among older adults remain largely undetected, and clinical symptomatology remains largely underdiagnosed. This is an important oversight given that the current cohort of adults ages 55 and older is the fastest growing age group. With Phase I funding from the National Institute on Alcohol Abuse and Alcoholism, Danya developed and piloted an educational intervention, Alcohol & Aging, in both English and Spanish, designed to increase awareness and knowledge about alcohol-related problems among older adults and their professional caregivers. The intervention employs both self-efficacy theory and the Stages of Change model. Additionally, with funding from the National Institute on Aging, Danya developed and pilot tested an online course, Alcohol Abuse Among Older Adults: A Guide for Home Healthcare Nurses. The goal of this project was to develop and evaluate educational tools to enhance the skills of home healthcare nurses in recognizing and addressing alcohol-related problems among older adults and making appropriate referrals. With a Phase I supplement, the online course was translated into Spanish. As a fundamental part of these projects, Danya researched and developed three comprehensive literature reviews on the topic of substance abuse and older adults. The literature review provides an overview of pertinent research in the field; treating older adult substance abusers, including age-specific issues and barriers to treatment; and antecedents and correlates of older adult substance abuse. Resulting conclusions will be discussed, underlining that before practitioners can adequately address the growing problem of elderly substance abuse, the science of the antecedents, consequences, and best methods of treating substance abuse in this age group must catch up. The research and information we have at our disposal with regard to the elderly of the past will no longer suffice in serving the baby boomer elderly of the future.
- 332 WORKING MEMORY AND DRUG USE IN METHADONE CLINIC PATIENTS**
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- Performance on working memory tests is correlated with performance on executive functions tasks, abstract reasoning tasks, and IQ (Engle et al., 1999). This is relevant to addiction. For instance, the use of stimulants and opiates, including methadone, is associated with deficits in working memory (Mintzer & Stitzer, 2002; Ornstein et al., 2000). On the basis of these findings, cognitive function in methadone patients was investigated. The hypothesis was that working memory performance would vary inversely as a function of duration and frequency of methadone and other drug use. The subjects included 76 methadone patients and 107 community volunteers. The experimental procedure included a series of short-term and working memory tests, IQ tests, and detailed questionnaires regarding drug use history. The community and clinic subjects showed age-correlated declines in working memory. However, the decline was more rapid in methadone patients. The largest difference was on the verbal working memory task. The correlations were $r = -0.18$ and -0.33 , for the community and clinic subjects respectively (partialing out IQ). Although there were modest correlations between cumulative measures of drug use and cognitive decline (e.g., $r = -0.28$), none of the relationships proved significant when age was entered into the analysis as a covariate. Urine screens showed that differences in performance were not due to recent drug use. The results suggest that the decline in working memory for the methadone clinic patients was related to a correlate of drug use or perhaps some more complex measure of drug use. For example, a proportionate measure, the percentage of the drug career that included heavy and regular drug use ((years of regular use + years of heavy use)/years of all use) was significantly related to the decline in cognition in methadone clinic subjects. The pattern of findings suggests a two-way relationship between basic cognition and drug use: lower working memory scores increase the likelihood of long-term, heavy illicit drug use, and, in turn, heavy illicit drug use and/or its correlates undermine working memory.

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333 TREATMENT FOR PTSD AND SUD: SITE DIFFERENCES AND IMPLICATIONS FOR OUTCOMES

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Background and Methods: Post traumatic stress disorder (PTSD) is prevalent in substance-dependent samples and associated with poor outcome. Here, we report baseline characteristics of the patient sample of a randomized, controlled, community-based, multisite trial in NIDA's Clinical Trials Network of Seeking Safety (SS), a 12-session group intervention for PTSD and substance abuse vs an attentional control, Women's Health Education (WHE). Patients meeting current DSM-IV criteria for drug or alcohol dependence and PTSD were eligible. All patients continued to receive treatment as usual at their respective programs. **Results:** 541 women with a history of trauma were screened, of whom 379 (70%) met eligibility criteria, and 353 (65%) were randomized (SS=176, WHE=177). The primary reason for exclusion was a lack of PTSD diagnosis. Randomized participants (N=353) had substantial substance use in the last month (45% use alcohol, 38% cocaine, and 25% marijuana) and reported an average of 10 lifetime drug treatment episodes. CAPS scores (M=56.4) indicate a highly symptomatic sample with 80% meeting full DSM-IV criteria for PTSD. About half experience a chronic medical issue (45%), with multiple hospitalizations in the last month (M=3.0), and multiple legal convictions (M=5.2). Sites differed in types of substance used by patients ($p<.001$ for alcohol, heroin, and cocaine), opiate dependence ($p=.009$), PTSD severity (CAPS) ($p<.001$), and measures of service utilization including mental health visits ($p<.001$), 12-step meeting attendance ($p<.001$), and lifetime treatment episodes ($p<.001$). Sites with more severe participant substance use and PTSD utilized fewer outside services. **Implications:** Most individuals in treatment for substance use disorders who experience trauma meet current PTSD criteria with substantial distress, continue to use substances, and carry multiple dependence diagnoses. Study findings highlight the need for population specific treatment. Implications for interpretation of study outcomes given site differences are discussed.

335 CITY-WIDE EVALUATION OF INTERIM METHADONE MAINTENANCE

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Interim methadone maintenance was developed to address the problem of long waiting lists for entry into comprehensive methadone treatment programs (MTP). Interim maintenance has been shown to be efficacious in a randomized clinical trial (Schwartz et al 2006). In order to determine its "real world" effectiveness the current study is evaluating its implementation in six MTPs in Baltimore MD. Interim Maintenance consists of daily administration of methadone with only emergency counseling for up to 120 days for individuals unable to gain admission to a comprehensive MTP. To date, these six programs have enrolled 984 heroin-addicted individuals into interim maintenance. A total of 620 participants have completed treatment. Of the 620, 433 (69.8%) transferred to comprehensive treatment after a mean of 84.7 (SD 34.4) days in treatment and 187 (30.1%) have been discharged from interim after a mean of 60.1 (SD 44.0) days of treatment. The remaining 364 individuals are still receiving interim treatment. The average length of time prior to transfer varies widely among the clinics from 49.8 days to 117.2 days. This variation may be accounted for by clinics' use of interim treatment. Clinics with shorter time to transfer are using interim maintenance to allow for a rapid transition to comprehensive maintenance, while clinics with longer time to transfer appear to be taking other individuals off waiting lists until the clinics must transfer interim patients at the 120th day. In summary, thus far, interim maintenance has been easily integrated into the city's system, however, it appears to be implemented in a heterogeneous manner.

334 EARLY SMOKING STATUS PREDICTS SMOKING-CESSATION OUTCOMES IN PREGNANT WOMEN

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Smoking during the initial two weeks of quitting predicts poor short- and longer-term outcomes in the general population of smokers. The present study examined whether that rule applies to pregnant women trying to quit smoking. Data were obtained from 129 women participating in clinical trials examining the efficacy of abstinence-contingent vs. non-contingent voucher-based reinforcement therapy. Smoking status was assessed in weeks 1 and 2 of the cessation effort and again at an end-of-pregnancy assessment at 32 week gestation using self-report and biochemical verification. In both conditions, any smoking in weeks 1 or 2 predicted a high likelihood of classification as a smoker at the end-of pregnancy assessment; that is, there was a 79% and 92% chance that those who smoked in weeks 1 or 2 would be classified as smokers at the end-of-pregnancy assessment in the contingent and non-contingent conditions, respectively. Among those who abstained in weeks 1 and 2, the chances of smoking at end-of-pregnancy were only 11% and 50% in the contingent and non-contingent voucher conditions, respectively. There was no evidence that the relationships between early and later smoking or abstinence differed significantly between the contingent and non-contingent treatment conditions, although the estimates regarding abstinence in the non-contingent condition were relatively variable related to the small number of subjects who successfully abstained in that condition. Overall, these results offer robust evidence affirming that the general rule regarding the negative predictive significance of early smoking to treatment outcome applies to pregnant women. The results also suggest that clinicians involved in helping pregnant smokers quit may want to monitor smoking status in the initial weeks of the cessation effort and consider enhancing/changing the intervention when smoking is detected.

336 RELATIONSHIP OF PROLACTIN RESPONSE TO METACHLOROPHENYLPYPERAZINE WITH SEVERITY OF DRUG USE IN COCAINE DEPENDENCE

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Rationale: Serotonergic (5-HT) mechanisms appear to mediate central effects of cocaine. Therefore, 5-HT disturbances could be associated with drug severity. **Objectives:** We investigated whether prolactin (PRL) response to meta-chlorophenylpiperazine (m-CPP), a mixed 5-HT agonist/antagonist were associated with severity of cocaine use. **Methods:** 36 cocaine-dependent subjects and 33 controls underwent a challenge with 0.5 mg/kg of oral m-CPP. Severity of drug use was assessed using the Addiction Severity Index (ASI). **Results:** The PRL response to m-CPP was significantly blunted in cocaine patients compared to controls ($F = 21.86, p < .001$). Δ PRL (peak PRL -baseline PRL) was negatively correlated with ASI-drug ($r = -.45, p < .01$), ASI-alcohol ($r = -.32, p < .05$), and ASI-psychological ($r = -.41, p < .01$) composite scores, and with the quantity, frequency and duration of drug use (r ranged from $-.41$ to $-.32, p$ ranged from $< .01$ to $.05$). Hierarchical regressions showed that ASI-drug composite scores significantly predicted the variance in Δ PRL after controlling for behavioral and demographic variables ($F = 4.27, p < .05$). **Conclusions:** The results indicate that disturbances in 5-HT function as reflected by a blunted response to m-CPP seem to be primarily associated with severity of drug use and to a lesser, although significant extent with behavioral traits in cocaine dependent patients.

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337 THE MANUFACTURE AND SALE OF METHAMPHETAMINE

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Dissimilar to most other drugs of abuse, methamphetamine (MA) can be easily made by the user with recipes downloaded from the internet, and ingredients purchased at the local drugstore. The quick, easy, and inexpensive production of MA increases the accessibility of the drug, a contributing factor to the nationwide explosion in MA use. Currently, it is unknown how many MA using individuals produce their own drug supply for sales or personal use. Estimates of MA manufacturing and sales are currently available only from law enforcement agencies such as DEA reports of drug lab busts. The current study fills a gap in empirically-based information about the MA phenomena by assessing specifics of MA production and sales in a sample of 584 MA-dependent adults participating in the longitudinal follow-up of the Methamphetamine Treatment Project (MTP). Findings indicate that approximately 67.6% of the sample have sold MA, with the majority (59%) selling the drug within a year of first use. Although the mean number of months that participants sold MA was 61 (SD = 44.3), many of those who ever sold MA did so for a year or less (31.9%). Over 13% report ever making MA. Importantly, 35.5% report that obtaining the ingredients for MA was not difficult. This paper presents other MA sales and manufacturing data, and provides a first glimpse into the nexus between the production and use of MA.

338 DRD2 TAQ 1A ALLELE IS ASSOCIATED WITH PAIN RESPONSE IN CHINESE MALE HEROIN-DEPENDENT SUBJECTS

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This study explored the association between candidate-gene variants and pain response in male Chinese heroin-dependent subjects (fulfilled DSM-IV criteria), divided into those who had abstained from heroin for one year or more after treatment (no-relapse group) and those who were on methadone or heroin for more than one year and had a history of relapse (relapse group). Healthy male subjects with no history of substance use were recruited as controls. The cold-pressor test was administered to all participants to ascertain pain threshold and tolerance. Subjects were genotyped for dopamine D2 (DRD2) Taq 1A, μ -opioid receptor A118G, and catechol-O-methyltransferase (COMT) val158met polymorphisms. The relapse group had the lowest pain tolerance, when compared with the no-relapse and control groups. There was no significant difference between A118G or COMT genotypes with pain response. However, across case-groups, individuals with at least one A1 allele (A1+) had a lower pain threshold and lower pain tolerance than those with no A1 allele (A1-). Heroin-dependent subjects (relapse group: 64%; no-relapse group: 58%) showed a significantly ($p=0.003$) higher A2 allele frequency than controls (51%). Relapse-group A1- individuals had a significantly ($p<0.05$) lower pain tolerance than no-relapse and control subjects. Relapse-group A1+ individuals had a significantly higher pain threshold than no-relapse and control A1+ subjects. Backward linear regression analysis of the three polymorphisms studied showed that only DRD2 A1 allele was a significant ($p=0.014$) predictor of pain threshold in the no-relapse group. It can be concluded that there is a difference in pain tolerance in heroin-dependent subjects related to relapse history. The DRD2 A1 allele may modulate the pain response in heroin dependence in a manner associated with relapse.

339 HOW EFFECTIVE IS SMOKING CESSATION IN ROUTINE PRIMARY CARE IN GERMANY? A CONTROLLED TRIAL IN 467 SMOKERS IN 167 PRIMARY CARE SETTINGS

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Context. Evidence has accumulated for the efficacy of smoking cessation treatments including Bupropion, nicotine replacement therapy (NRT), and psychological interventions. To date it remains unclear to what degree these results can be achieved by non-specialist physicians in "real life" clinical settings. Aim. To examine the effectiveness of Bupropion, NRT, CBT and a minimal intervention in German primary health care settings. Study Design. Within the national research program SNICAS a four-armed randomized controlled trial was conducted among 467 smokers in 167 primary care practices between 2002 and 2004. The minimal intervention (MI;n=81) included a structured advice to quit smoking, three non-smoking diaries, plus two follow-up sessions. In the cognitive-behavioral therapy condition (CBT; n=175), 4-5 individual counseling sessions plus a CBT self-help manual were added. In two pharmacotherapy conditions, Bupropion (BUP;n=108) and nicotine replacement (NRT;n=103) were added to CBT. Interventions were specified and structured by manuals. Logistic regression was used to compare complete abstinence as short- and long-term outcomes. Results. Overall, 39% of participants (ITT) were completely abstinent at the end of treatment (MI:39%, CBT:36%; Bupropion:47%; NRT:35%). Among completers, 69% of participants were abstinent (MI:71%; CBT:66%; Bupropion: 79%; NRT:69%) (LOCF). In a 12-month follow-up, 26% of subjects were continuously abstinent (Bupropion:28%; CBT:23%; NRT:29%; MI:28%). No significant between-groups differences emerged with respect to initial or prolonged abstinence from smoking. Overall, the retention rate was 54.0%, with no significant between-group differences. Besides common side effects no serious adverse events occurred during or after the medication phase. Conclusion. Smoking cessation treatments are feasible, effective and safe when applied by non-specialist physicians. The data support the value of any highly structured and continuous smoking cessation intervention in primary care.

340 SIMULATING THE OPERATION OF A LOCAL HEROIN MARKET: NEW USES FOR ETHNOGRAPHIC RESEARCH

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To acquire the illegal substances they use drug users must engage the illicit drug economy through sales or exchange. Many drug users also sell drugs to support or defray the costs of their addictions. However, there is a scarcity of research on illicit drug distribution, as well as how local drug markets operate to shape user's behaviors. Studies on these topics rely heavily on ethnographic research which produces highly detailed and descriptive accounts, but is limited by the geographic, social and historic contexts in which data are collected. Funded by NIDA, this presentation describes an experimental research project that is developing agent-based models to facilitate the reanalysis of an ethnographic data set on heroin dealing. The aims of this project are to: 1) develop a unique agent-based analytic approach to investigate the dynamic nature of illicit drug distribution, 2) test research questions generated from the original ethnographic study, and 3) provide researchers with methods, protocols, and program templates for agent-based simulation studies of illicit drug markets and organizations. This project is based on a three-year case study of a heroin dealing network that characterized the market, as well as how customer and dealer relationships were established, maintained, and broke down. To transfer this data into agent-based simulation models, decision-making processes, interactions, and environmental considerations are extracted from the data set. These findings are then used to program agents' activities and interactions within the simulations. Once programmed, agents act and interact with the simulated environment autonomously. The presentation will discuss the protocol for abstracting and programming agent behaviors using ethnographic data, assumptions of the models, strengths and limitations of agent-based simulation, and how prospective research can be designed to incorporate these new technologies. This presentation will also include simulation demonstrations and present preliminary results.

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- 341 EFFECTIVENESS OF COCAINE ESTERASE AGAINST COCAINE-INDUCED CONVULSIONS AND LETHALITY IN MICE**
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Cocaine esterase (cocE) has superior catalytic efficiency and selectivity for cocaine compared to other cocaine-metabolizing enzymes (Larsen et al., 2002; Nat. Struct. Biol., 9:17-21). We investigated the in vivo potency of cocE in blocking cocaine-induced toxicity in the mouse. Cocaine toxicity was quantified by measuring the occurrence of convulsions and lethality (n=6/condition). Intravenous administration of cocE (0.1-1 mg) 1 min prior to cocaine administration dose-dependently produced rightward shifts in the dose-response curve for cocaine toxicity; e.g., 1 mg of cocE showed a 10-fold increase in the lethal dose of cocaine. In addition, intravenous administration of cocE (0.1-1 mg) 1 min after the occurrence of convulsions dose-dependently shortened the recovery time from convulsions. Immunologic responses of cocE were determined using ELISA specific for cocE antibodies. Effects of repeated dosing of cocE were evaluated by measuring the titer number and the full protective effect of 0.32 mg cocE against toxicity elicited by 320 mg/kg of cocaine. CocE retained its effectiveness against cocaine toxicity in mice with single prior exposure of cocE (0.1-1 mg), and these mice displayed a weak antibody response. CocE also retained similar effectiveness in mice with triple exposures of cocE (0.1-1 mg/week x 3), and these mice displayed a 10-fold higher antibody titer. In contrast, cocE lost some effectiveness in mice with four prior exposures of cocE (0.1-1 mg/2 weeks x 4), and these mice displayed 100-fold higher titers of cocE antibodies. Thus, cocE produced robust prevention and reversal of extreme cocaine toxicity and only extensive repeated administrations of cocE increased the risk of immunologic effect (Supported by USPHS Grants DA00254 and DA21416).
- 342 BRAIN STRUCTURE IN SUBSTANCE-DEPENDENT PATIENTS WITH AND WITHOUT ANTISOCIAL PERSONALITY DISORDER**
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Anti-Social Personality Disorder (ASP) and substance use disorders (SUD's) usually co-occur and may be co-morbid. Both are associated with structural and functional brain abnormalities. The brain correlates of co-occurring ASP and SUD are not well known. Recent developments in automated non-linear methods of structural MRI analysis allow rapid analysis of large cohorts. We studied 25 opiate-dependent and 28 cocaine-dependent patients, 11 of whom had ASP, with a battery of neuropsychological tests (MINI Neuropsychiatric Interview 5.0.0, the WASI, modified Go-No-Go Task, Brown Attention Deficit Disorder Scale, Beck Depression Inventory, SCL-90-R Symptom Checklist-90-R, Zimbaro Time Perspective Inventory, Zuckerman-Kuhlman Personality Questionnaire) and high-resolution structural MRI at 3Tesla (TR/TE = 1620/3.87ms, slice thickness 1mm, 0 skip, FOV 250mm, 1x1x1 mm voxels). Structural brain volumes from 45 regions of interest were extracted from the MRI data using Hierarchical Attribute Matching Mechanism for Elastic Registration (HAMMER); whole-brain volume was maintained during the transformation into standard space. Images were also segmented to allow group comparisons of whole-brain grey and white matter volume. Preliminary results show a trend for a larger right amygdalar volume in the ASP with SUD group than SUD only group. Results also suggest an effect of gender on prefrontal white matter volume. Ongoing analysis will determine the presence of interactions between group (ASP+SUD vs. SUD alone), brain structures, and neuropsychological task performance. The impact of psychiatric diagnoses often co-morbid with ASP in substance abusers (e.g. ADHD) will also be examined, as this may be helpful in determining the specificity of variations in brain structure to ASP. Supported by: NIDA K23, RO1 DA-10241, P60-DA-05186, Research Division of VAMC, VA VISN 4 MIRECC, and the Alexander Foundation.
- 343 PREDICTORS OF MARIJUANA USE AMONG MARRIED COUPLES: THE INFLUENCE OF ONE'S SPOUSE**
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Background: With the transition into marriage, marijuana and other substance use tends to decline. However, changes in marijuana use may not be the same for all individuals during this transition. The objective was to identify trajectories of marijuana use during the early years of marriage and to identify baseline factors that predict these trajectories. Methods: Couples (N = 634 marijuana use, other substance use, and psychological variables were assessed at the time they applied for their marriage license and then again at the first and second anniversaries. Discrete mixture models estimated trajectories of marijuana use. Multinomial logistic regression models identified baseline predictors of these trajectories. Results: A 2, 3, and 4 group trajectory models were evaluated. The 3 group model had the best fit for both men and women (stable high use group (High), stable low use group (Low), and a stable no use group (No)). Compared to men in the No group, men in the Low group drank more often and had wives who also used marijuana. Compared to men in the No group, men in the High group drank more frequently and at heavier levels and had wives who used marijuana and had greater levels of heavy drinking. Among wives, those in the Low group were more likely to be heavy drinkers compared to wives in the No group. Women in the High group were slightly more likely to report greater levels of anxiety (p=.08) and depression (p=.06) be smokers and have husbands who also used marijuana, compared to women in the stable No group. Although the impact of psychological variables was reduced in the multivariable models, strong bivariate relationship existed with marijuana use. Discussion: After controlling for one's own substance use and psychological factors, a spouse's use of marijuana was a strong predictor of marijuana use trajectories. (Supported by NIAAA grant R37-AA09922 awarded to KEL)
- 344 INCIDENCE AND PATTERNS OF POLYDRUG USE AND CRAVING FOR ECSTASY IN REGULAR ECSTASY USERS: AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY**
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Background: Previous studies employing retrospective assessments methods found that regular ecstasy users frequently use alcohol, marijuana and other drugs in combination with ecstasy. However, retrospective self-report data have several limitations, including the fallibility of reconstructive recall. In addition, prior studies have not compared rates at which other drugs are used on ecstasy-use nights differ from rates of their use on nights when ecstasy is not used. Methods: Twenty-two adult participants (13 males, 9 females) wore a wrist actigraph/data recorder to record real-time drug use and ecstasy craving for six weeks. Rates of alcohol and drug use before, during, and after ecstasy and on comparison nights were analyzed with generalized estimation equations, while craving was modeled with regression and linear mixed models. Results: Approximately 70% of ecstasy uses occurred on Friday or Saturday nights. Alcohol was more likely to be used before ecstasy intoxication than during (p = .001) or after intoxication (p < .0001), and during ecstasy intoxication than afterward (p < .001). With the exception of marijuana, use of other drugs was more likely before or during ecstasy intoxication than afterward (p < .001). No drugs were used at higher rates on ecstasy use nights than comparison Friday and Saturday nights. Craving for ecstasy was low overall, and evidence was found for waxing and waning of craving over 24 hours before and after use. Conclusions: Use of intoxicating drugs besides marijuana was more likely before or during ecstasy intoxication than afterward, but no drug was more likely to be used during ecstasy use nights than ecstasy non-use nights. These ecological momentary assessment data offer new insights into the temporal relationships of multiple drug use, with particular attention to the dynamics of ecstasy use and abuse. Supported by NIDA grants DA 03994 and DA00343.

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345 MENSTRUAL CYCLE PHASE EFFECTS ON NICOTINE WITHDRAWAL AND CIGARETTE CRAVING: A REVIEW

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There is conflicting research on gender differences on the experience of withdrawal and craving and some have suggested that menstrual cycle effects may moderate this relationship. Given hormonal changes during the menstrual cycle, it is possible that abstinence-related symptoms such as withdrawal and craving vary as a function of menstrual phase as well. This review summarizes the modest but expanding body of research in this area. Thirteen studies were identified that examined menstrual phase effects on withdrawal and/or craving either under ad lib smoking, abstinence, or both. Of 8 study arms across 7 studies that included a condition of ad libitum smoking, there were significant menstrual phase effects for withdrawal in three study arms and for craving in three arms. Of 12 study arms across 10 studies involving abstinence, there were significant menstrual phase effects for withdrawal in four study arms and for craving in five arms. One of the challenges inherent in interpreting this literature is that it is difficult to distinguish withdrawal symptomatology from premenstrual symptomatology. Methodological variation, including limited sample size and possible selection bias, may explain some of the inconsistent findings across studies. Nonetheless, of the 9 studies that found significant phase effects, 7 noted heightened experiences of withdrawal and/or craving within the latter days of the menstrual cycle; i.e., the luteal phase. While further research is necessary to address methodological concerns and replicate these findings, this may suggest the need for focused cessation treatment during the luteal phase and/or quit attempts that are well timed relative to specific menstrual phases. This review was supported by National Institute of Drug Abuse (NIDA) Training Grant T32DA007288 (MJC), Component #3 (HPU) of NIDA P50DA016511 (KTB), and M01 RR0107 from the MUSC General Clinical Research Center. *Correspondence: Matthew Carpenter, PhD: (843) 792-3974; carpente@musc.edu.

346 NEW DIRECTIONS IN THE ASSESSMENT OF EXECUTIVE FUNCTIONS—COMMENTARY

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Executive functions impairment has been implicated in the poor decision making behaviors characteristic of drug abusers. Recent research has identified lesions in the ventral-medial area of the frontal lobes of the human brain that appear to be associated with poor decision making. Similar research with drug abusers has demonstrated similar styles of poor decision making that mimic those of clearly brain injured patient with specific brain damage in the ventral-medial area of the frontal lobes. In addition, brain imaging studies of drug abusers have noted specific difficulties in the frontal lobes of drug abusers. Methods of the assessment of executive functions systems that are assumed to include the frontal lobes need to be further developed. This commentary will examine a new measure of executive functioning that may be of value in the assessment of drug abusing patients. The Test of Verbal Conceptualization and Fluency (TVCF) includes measures of verbal fluency, verbal concept formation and set-shifting that have a long history in neuropsychology as measures of executive functions. The measures require patients to name to categories and letters of the alphabet, to sort cards according to categories and to perform a version of the Trail Making Test. Specific advantages of this assessment measure include a recent normative sample and a wide age range.

347 LIMBIC-RELATED ALTERATIONS OF DOPAMINE AND OPIOID SYSTEMS IN MIDBRAIN OF HUMAN HEROIN ABUSERS

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Both the opioid and dopamine (DA) systems are known to be important for several neurobiological aspects of drug addiction such as euphoria and reward. DAergic neurons and opioid receptors in the brainstem are important for the rewarding effects of opiate drugs. Midbrain DAergic neurons are subdivided into a ventral tier (substantia nigra) which is motor-related and a dorsal tier (ventral tegmental area; VTA) which is limbic-related. The aim of the present study was to determine whether there are alterations in the opioid and DA systems in limbic vs motor related regions in the human midbrain in correlation to heroin abuse. Post-mortem brain samples were obtained from two groups of subjects: heroin abusers (N=22) and drug-free controls (N=10). Toxicological analyses were carried out to determine the levels of opiate metabolites and medications in the body at the time of death. In situ hybridization histochemistry was performed to determine mRNA expression levels of several DAergic markers such as the dopamine transporter (DAT), tyrosine hydroxylase (TH), orphan nuclear receptor NURR1, DA D2 receptor and synuclein-c (SNCA). [35S]GTP γ S agonist-stimulated autoradiography was used to examine the functions of μ (DAMGO) and κ (U69593) opioid receptors. The levels of mRNA expression of DAT and NURR1 were significantly lower in the PN in heroin abusers as compared to normal controls. The mRNA expression of TH was increased in SNd and SNl. There was also an increase in the mRNA expression of SNCA in the PN and SNv. DAMGO-stimulated [35S]GTP γ S binding was significantly increased in the PN and PAG. U69593-stimulated [35S]GTP γ S binding was also increased in the PAG with a trend in the PN. Overall, our study provides evidence of predominant mesocorticolimbic alterations in midbrain DA and opioid systems of human heroin abusers. Interestingly, these results are consistent with changes reported in human cocaine abusers. Supported by NIDA DA15446; MH was supported by the Swedish Institute and the Hungarian Scholarship Board.

348 TRAJECTORIES OF HEROIN ADDICTION: GROWTH MIXTURE MODELING RESULTS BASED ON A 33-YEAR FOLLOW-UP STUDY

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We investigated the trajectories of heroin use and associated consequences over a 33-year observation period. The study is based on 436 male heroin addicts who were admitted to the California Civil Addict Program at 1964-65 and were followed in three follow-up studies conducted every ten years over 33 years. Applying the growth mixture modeling approach to heroin use level (e.g., mean number of days per month using heroin) over the first half of the addiction careers (16 years) since first heroin use, we identified four groups with distinctive profiles (AIC = 47687, BIC = 48042, entropy = 98.2%): (1) the Stably High-level Heroin Users (n=277) who maintained fairly consistent high-levels of heroin use since initiation; (2) Accelerated Users (n=74) who started at a low level of use, increased their use gradually, and then maintained at a high level of use; (3) Decelerated Users (n=52) who started at a high level but decreased their use over time; and (4) Early Quitters (n=33) who quickly dropped to no use within 5 years of the initial use. Except for Group 2, all had started at a similarly high-level of use; ten years later, however, Group 1 converged with Group 2 at a high-level of heroin use, and Group 3 converged with Group 4 with almost no use. The mortality rate was 43.3% for Group 1, 40.5% for Group 2, 34.6% for Group 3, and 21.2% for Group 4. The patterns of heroin use trajectories for the surviving addicts remained largely unchanged over the second-half of the addiction careers (16 years) for all groups with the exception that the Accelerated User group demonstrated a decreased use over time. Characteristics of these four groups of individuals will be investigated. Furthermore, additional analyses will be conducted to identify correlates and turning points of the heroin use trajectories.

349 A CORRELATION BETWEEN MORPHINE-INDUCED ANTINOCICEPTION AND INCREASED CD-38 IN MOUSE BRAIN

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CD38 is an enzyme extensively studied in vascular smooth muscle and other peripheral tissue. It has also been found in both neurons and glia of the brain, however, CD-38's role in neuronal signal transduction is not fully characterized. We investigated whether there is a connection between morphine-induced analgesia and the level and activity of this enzyme in the periaqueductal gray (PAG) of male Swiss-Webster mice. PAG was removed 30-min following acute administration of 8 mg/kg morphine s.c. (a dose which produced 87.2 % analgesia). Gene expression of CD38 was increased 29.9% in both the PAG and cortex of morphine-treated mice compared to control mice. Western Immunoblotting demonstrated a 30.9% increase in the expression of the more active 110 kDa homodimer form of CD38. In addition, the ADP-ribosylcyclase conversion of beta-NGD+ to cGDPR was increased by 26.7%. All of these effects were blocked in mice co-treated with 1 mg/kg naloxone s.c. Other experiments supported the role of CD38 in morphine-induced analgesia. Nicotinamide, a negative feedback inhibitor of CD38 ADP-ribosylcyclase, injected i.p., dose-dependently antagonized the antinociceptive effects of 8 mg/kg morphine in the 56 degree C tail-withdrawal test. Furthermore, a 500 mg/kg nicotinamide dose decreased the potency of morphine by 9.7-fold. These results are supported by data from male CD38^{-/-} knockout mice, which exhibited a decreased analgesic response to morphine in comparison to male C57BL/6J wild-type mice. These results clearly implicate CD38 in the analgesic action of morphine. Funded by NIH grants: R01-DA-01647, T32-DA-07027, K05-DA-00480, HL-57244, HL-75316.

350 TISSUE COMPATABILITY, BIODEGRADABILITY, BLOOD LEVELS AND OPIOID OVERDOSE FOLLOWING TREATMENT OF HEROIN-DEPENDENT PERSONS WITH SUSTAINED-RELEASE NALTREXONE-POLY(DL-LACTIDE) IMPLANTS

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Four independent studies assessed in vivo human tissue compatibility, biodegradability, blood naltrexone levels associated with different implant doses, and overdose in heroin dependent persons treated with the Australian subcutaneous naltrexone-poly(DL-lactide) implant. The implant consists of multiple tablets containing compressed naltrexone-poly[trans-3,6-dimethyl-1,4-dioxane-2,5-dione] (DL-lactide) loaded microspheres. Assessment of tissue biopsy samples taken at 1 to 38 months post-implant from 54 (34 male) consenting human subjects showed an early phase (up to 12 months post-implant) of inflammation, foreign body reaction, and fibrosis. This subsided gradually over the next 12 months until tissue returned to normal by 25+ months. Ultrasound assessment of 139 clearly identifiable implant sites from 71 human subjects at various periods post-implant showed a significant decrease in mass and length of implant detectable from the time of implantation until total absence by ≥ 896 days. In humans blood naltrexone levels remained above 2ng/ml for 147 days compared to 164 days following 3.4g or 5.0g naltrexone implant insertion respectively, suggesting that no significant clinical efficacy is achieved by using the larger size implant mass. In a large cohort of heroin dependent persons (n=361; 218 males) no opioid overdose was observed in the six months post-treatment, with a reduced number observed seven to twelve months post-implant red to pre-treatment levels. The results of these studies indicated that the Australian naltrexone-poly(DL-lactide) implant is well tolerated, biodegradable, sustains blood naltrexone levels for extended periods of time and prevents opioid overdose suggesting it may have a role in the management of heroin dependence.

351 ESTROGEN'S EFFECTS ON INFLAMMATORY-INDUCED PAIN ARE IN PART MEDIATED THROUGH ACTIVATION OF CYCLOOXYGESE (COX) BIOSYNTHESIS OF PROSTAGLANDIN E2

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It is widely believed that pain affects men and women differentially; females demonstrate significantly higher behavioral responses to chronic and inflammatory pain than males. In female rats, we have recently shown that estrogen produces a persistent analgesic effect on injury (inflammation)-induced pain. Inflammatory-pain is caused by tissue injury that increases prostaglandin synthesis, elevates cyclooxygenase (COX) levels and pain hypersensitivity. COX, which has two isoforms COX 1 and COX 2, is the rate-limiting enzyme responsible for the synthesis of prostaglandins. In this study we aimed to determine if the activation of COX 1 and/or 2 are involved in estrogen effects in inflammatory induced pain responses. To this end, the effect of estrogen or the combination of estrogen plus NS398 [selective for COX 2; 20 mg/kg; i.p.], SC560 [selective for COX 1; 20 mg/kg; i.p.] or ibuprofen [non-selective COX 1 and 2; 40 or 100 mg/kg; i.p.] were tested using the formalin pain model. Using a computerized model, the number of paw flinches was measured during one hour of pre-treatment with the respective antagonist and one hour after formalin injections. Estrogen, ibuprofen, or NS398 alone reduced the number of flinches during Phase II. Estrogen potentiated ibuprofen's behavioral effects during Phase II, estrogen plus 40 or 100 mg/kg of ibuprofen significantly decreased the number of flinches after formalin administration when compared to estrogen or ibuprofen treated groups. Although estrogen plus NS398 decreased flinching responses, their effect was not further potentiated. SC560 alone did not alter the level of flinching responses in female rats. The behavioral responses were correlated with a decreased in prostaglandin E2 release; suggesting that estrogen antihyperalgesic effects during injury induced nociceptive responses are in part mediated through inflammatory control mechanisms such as activation of COX 2. This work was supported in part by SCORE 506-GM60654 and SNRP NF 39534

352 STRESS AND DRUG-CUE-INDUCED CRAVING IN OPIOID-DEPENDENT INDIVIDUALS ON NALTREXONE

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Background: Naltrexone is a non-addictive medication that blocks the euphoric effects of opioids. However, naltrexone has not proven efficacious possibly because it does not reduce stress and protracted withdrawal symptoms of opioid dependent individuals in early recovery. Prior clinical and preclinical research indicates that both stress and drug-cue related arousal response is associated with craving and vulnerability to relapse in a range of drug-using populations. Purpose: To examine the subjective and cardiovascular response to stress and drug-cues in naltrexone-treated opiate abusers. Participants & Method: Eleven men and three women seeking naltrexone treatment for opioid dependence were exposed to personalized stress, drug-cue, and neutral-relaxing imagery. Behavioral (craving, mood) and cardiovascular (heart rate, SBP and DBP) measures were assessed. Results: When naltrexone-treated opioid users were exposed to stress and drug-cue related imagery compared with neutral/relaxing imagery, they reported a significant increase in opiate craving, anxiety, and negative mood and a significant decrease in positive mood. They also showed a simultaneous increase in stress and drug-cue related cardiovascular response. Subjective and cardiovascular hyper-arousal was also greater in the stress compared with the drug-cue condition. Conclusions: Compared to a neutral imagery condition, naltrexone-treated opiate abusers demonstrated an increased craving and arousal response following stress and drug-cue related imagery. These findings support the need for pharmacological and behavioral interventions that address both drug-cue induced and stress-induced relapse vulnerability for opiate users in naltrexone treatment. This work was supported by NIH grant R01-DA18219.

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353 DOPAMINERGIC DRUGS REGULATE THE EXPRESSION OF "CLOCK" GENES IN STRIATAL NEURONS

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A regulatory role for transcription factor "clock" genes in psychostimulant-induced behaviors has been demonstrated. Clock genes not only regulate the outcome of psychostimulant-induced behaviors, they are also regulated by these drugs. Both cocaine- and methamphetamine-induced changes in striatal clock gene expression have been reported recently. To further study the involvement of dopamine receptors in these effects at the cellular level, we used primary cultures of striatal neurons as a model. Since these neurons express dopamine receptors as well as clock genes and they are harvested from the striatum, they are suitable for such mechanistic studies. Primary cultures of striatal neurons were prepared from embryonic mice and experiments were performed seven to nine days in vitro. The expression of the clock genes *Per1*, *Clock*, *NPAS2*, and *Bmal1* was measured after treatment with dopamine and the dopamine receptor agonists quinpirole (D2) and SKF 38393 (D1) at different time points and concentrations. We found significant changes in the gene expression levels in a time- and dose-dependent manner after treatment with the above-mentioned agonists, but not with dopamine itself. Namely, we found a generalized inhibitory effect on clock gene expression (except *Bmal1*) with the D2 agonist quinpirole. On the other hand, the D1 agonist SKF 38393 produced a generalized stimulatory effect on all genes studied. Collectively, these observations suggest that dopamine receptor-mediated intracellular signal pathways (i.e., cAMP, CREB) may play a role in altering the expression of clock genes. Since clock genes, such as *Clock*, have cAMP response element (CRE) binding sites in their promoters, it is possible that the cAMP/CREB signaling system may regulate clock gene expression through CREB binding. Using striatal neurons in culture as a model, further research is needed to understand the expression dynamics of clock genes in regard to dopamine signaling at the transcription level.

354 THE DIVERSION OF PRESCRIPTION OPIOIDS IN THE U.S.

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Hypothesis: Hydrocodone and oxycodone are the most widely diverted prescription opioids. Procedures: Prescription drug diversion involves the unlawful channeling of regulated pharmaceuticals from legal sources to the illicit marketplace. Diversion typically occurs through illegal sales of prescriptions by physicians and pharmacists, "doctor shopping" by individuals who visit numerous physicians to obtain multiple prescriptions, robberies and thefts from pharmacies and institutional drug supplies, supply-chain theft, and residential burglaries. Within this context, this presentation provides trend data on the diversion of prescription opioids for the period January 2002 through September 2005, drawn from quarterly reports submitted by a national sample of 300 police and regulatory agencies. Data extraction was conducted by university research staff. Because no identifying information on individuals is collected, the study received an exemption from the university IRB. Reporting agencies were paid a small monetary stipend for participation, and the research was supported by a grant from Purdue Pharma LP. Results: In the jurisdiction targeted by this survey, there were a total of 49,713 diversion cases during the 15-quarter survey period. Of these, 35.1% of the cases involved hydrocodone, followed by oxycodone (22.2%), methadone (3.2%), morphine (2.8%), hydromorphone (1.9%), and fentanyl (1.8%). The proportion of agencies reporting the diversion of hydrocodone ranged from a high of 89% during the 1st quarter of 2002 to a low of 66% in the 2nd quarter of 2003; for oxycodone, the range was 74% in the 1st quarter of 2002 to 55% in the 2nd quarter of 2003. The proportion of agencies reporting the diversion of all other opioids was significantly lower. Conclusions: Overall, the data demonstrate that: 1) the most widely diverted prescription opioid is hydrocodone, followed by oxycodone; 2) over time, there has been a slightly downward trend in diversion of hydrocodone and oxycodone, mentions, a steady increase in the diversion of methadone, and no changes in the diversion of other opioids.

355 A MOTIVATIONAL INTERVENTION REDUCES COCAINE USE AND IMPROVES HIV MEDICATION ADHERENCE

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Previously, we found that a 4-session Motivational Interviewing intervention for cocaine use and poor medication adherence improved the proportion of days using cocaine and rate of medication adherence. We modified the intervention to address stigma and relapse prevention. This paper presents preliminary outcomes of the 6-session Cocaine and Adherence Readiness Treatment (CART) intervention among 18 HIV+ nonadherent patients in medical care. Participants were 61% female, with 78% African-American and unemployed, and 61% heterosexual. At baseline, the average CD4 count was 332 and the mean viral load was 54,852, and medication adherence rate was 65%. At baseline, all were cocaine dependent and the mean proportion of days using cocaine was 29%. The most common comorbidities were Major Depression, anxiety disorders, and alcohol use disorders. Sixteen participants completed all 6 treatment sessions while the remaining 2 completed 5. At FU1, a post-treatment follow-up approximately 8 weeks after baseline, medication adherence had improved to 93% ($t=3.44$, $p<.004$) and proportion of days using cocaine declined to 12% ($t=2.8$, $p<.02$). At FU2, the 3 Month post-treatment follow-up approximately 5 months post-baseline, these improvements persisted with medication adherence rising to 98% and proportion of days using cocaine declining to 9%. Consistent with improvements in adherence, markers of immune health at FU2 improved, with the mean CD4 count increasing to 444.5 and mean viral load decreasing to 10,003. Participants rated their confidence in avoiding cocaine; it increased from 55.7 at baseline to 68.4 at FU1 and 83.1 at FU2. Temptation for cocaine declined from 58.7 at baseline to 41.1 at FU1 and 33.2 at FU2. We will examine patient characteristics that relate to outcomes. The CART intervention shows promise to reduce cocaine use and improve medication adherence among people with HIV.

356 WITHDRAWN

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357 FACTORS AFFECTING PLACE PREFERENCE AND ITS NEURAL MECHANISMS IN RATS

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The purpose of the present study was to investigate 1) factor affecting the acquisition of (NCT)-induced conditioned place preference(CPPs), and 2) neural mechanisms underlying the persistence of NCT-CPPs in rats. Exp.1) NCT at 0.4mg/kg, but not 0.8mg/kg s.c. induced CPP. A CPP was established when conditioning sessions were conducted in the evening or at night, but not in the morning. Locomotor activity, but not locomotor sensitization during conditioning sessions were positively correlated with degree of a CPP. There were an optimal dose window of NCT, chronological influence, and individual reactivity to NCT for establishing NCT-induced CPPs. Exp.2) 6-OHDA lesions of the amygdala (AMY) and the ventral tegmental area(VTA) DA system disrupted a CPP expressed by the environmental stimuli in 2 months and in 6 months after the establishment of conditioning, respectively. On the other hand 6-OHDA lesions of the nucleus accumbens (Acc) and the medial prefrontal cortex (mPFC) DA system did not affect the persistence of a CPP. These results indicate that the AMY and the VTA DA system are involved in the persistence of NCT-induced CPPs expressed by the environmental stimuli associated with NCT effects.

358 METHAMPHETAMINE-INDUCED NEUROTOXICITY: DEFICITS IN CONSOLIDATION OF PAVLOVIAN CONDITIONING ARE AMELIORATED BY N-ACETYLCYSTEINE BUT NOT D1 AND D2 DOPAMINE RECEPTOR AGONISTS

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Animal and human studies suggest that protracted use of methamphetamine (METH) inflicts damage to dopamine (DA) nerve terminals. Although clinical studies have implicated METH neurotoxicity in cognitive deficits, animal studies are essential for investigation of the underlying mechanisms of such deficits. The Pavlovian conditioning paradigm, such as conditioned place preference (CPP), is dependent on affective state and learning and memory. METH-induced selective dopaminergic neurotoxicity in mice is associated with impairment in the development of cocaine- and METH-induced CPP (Achat-Mendes et al., *Neuropsychopharmacol.* 30; 1128-1137, 2005). To determine if impairment in CPP following METH neurotoxicity is due to deficits in memory consolidation, saline, the D1 DA receptor agonist SKF38393 (5-20mg/kg), the D2 DA receptor agonist quinpirole (0.2-1.0mg/kg) and N-acetylcysteine (NAC; 50-100mg/kg) were administered daily immediately following each CPP training session. Results showed that a) neither the D1 nor the D2 DA receptor agonists improved CPP consolidation; however, NAC significantly increased the magnitude of CPP; b) only the immediate but not the delayed (2h) posttraining administration of NAC improved CPP magnitude in METH but not saline pretreated mice, suggesting that NAC had a specific effect on CPP consolidation in mice inflicted by dopaminergic neurotoxicity; c) brain content of the endogenous antioxidant, glutathione (GSH), in METH pretreated mice was significantly lower than controls; d) NAC administration restored brain GSH levels in METH pretreated mice but had no effect on controls. Results suggest that METH-induced dopaminergic neurotoxicity is associated with glutathione deficiency, and the behavioral deficit in consolidation of appetitive Pavlovian conditioning is ameliorated by treatment with NAC rather than D1 and D2 DA receptor agonists. Supported by DA12867 and DA DA19107 to YI.

359 CHRONIC ADMINISTRATION OF Δ^9 -THC INCREASES THE LOCOMOTOR-ACTIVATING EFFECTS OF COCAINE IN ADOLESCENT BUT NOT ADULT RATS

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Recent NSDUH (2005) data have shown that approximately 3.7 million youths aged 12-17 used marijuana in 2004. In addition, it has been shown that the earlier the first marijuana use, the more likely one is to use other illicit drugs. For example, if the first use is prior to age 15, there is about a four-fold greater likelihood of cocaine use than if first marijuana use is later. Thus, there may be unique responses to marijuana in preadolescents and young adolescents compared to adults. The purpose of this study was to determine whether cannabinoid administration during adolescence altered the subsequent effects of cocaine in a manner different than during adulthood. Male adolescent (PND 28-35) and adult (PND 60-66) rats were treated with daily injections of Δ^9 -THC (3 mg/kg) or vehicle and locomotor activity was measured daily for 8 days. Four days later the effect of cocaine on locomotor activity was measured using a cumulative dosing paradigm so that entire cocaine curves could be derived in one day. The effect of cocaine on locomotor activity was greater in the adolescent rats that had been treated with Δ^9 -THC compared to vehicle. In contrast, there was no change in the locomotor-stimulant actions of cocaine in the adult rats after Δ^9 -THC administration compared to their vehicle controls. These data show that chronic treatment with Δ^9 -THC alters the subsequent behavioral effects of cocaine in adolescent male rats and further suggest that the adolescent rat may be particularly vulnerable to the effects of cannabinoids. A greater understanding of the differential effects of drugs during adolescence and of how this use impacts subsequent psychostimulant action may lead to different treatments for different age groups, as well as a better understanding of how cannabinoid use in adolescence may lead to stimulant abuse in adulthood.

360 AN EVALUATION OF THE EFFECTS OF RIVASTIGMINE ON NEUROCOGNITION IN METHAMPHETAMINE-DEPENDENT VOLUNTEERS

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Methamphetamine (MA) abusing patients demonstrate significant neuropsychiatric dysfunction, including impairments in psychomotor speed, attention, memory, and executive function. Medications that ameliorate neurocognitive deficits associated with MA abuse may enhance treatment outcomes, particularly with interventions making use of cognitive behavioral therapy. Cortical acetylcholine is critical to cognitive processes, and cholinergic drugs have been shown to reduce memory impairments. To evaluate this, we tested the effects of the acetylcholinesterase inhibitor rivastigmine (Exelon) in recently abstinent MA-dependent volunteers. To date, 10 participants have been enrolled in this inpatient study. All volunteers were male with an average age in years of 35.8 ± 8.5 , average years of education of 14.8 ± 2.3 , and average years of MA use of 5.9 ± 4.7 . Subjects were admitted to the General Clinical Research Center at UCLA for 16 days and randomized to placebo or rivastigmine (1.5 or 3 mg) administered daily. The blind has not yet been broken so these treatments have been arbitrarily designated as groups A, B, and C. Prior to randomization, subjects were given a battery of neurocognitive tasks to assess attention/psychomotor speed, working memory, and verbal memory. These tests include simple and complex reaction time, N-back, and Hopkins Verbal Learning Task. Five days after randomization to rivastigmine or placebo, subjects were reassessed with the same battery of neurocognitive tests. To date, data from two of the cognitive tasks have been analyzed. A within-groups analysis revealed that participants in Condition B significantly improved performance (faster reaction time) on a choice task (897.5 ± 45.7 ms during washout vs. 817.7 ± 44.2 ms following treatment)($p < 0.05$). Following the completion of 4 additional subjects, the blind will be broken and a complete analysis will be performed. Supported by NIDA: DA-14593, DA-18185, DA-17754

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- 361 IS THIS URINE REALLY CLEAN? ADULTERATION IN URINE DRUG SCREENING AND TESTING**
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Is this Urine Really Clean? Adulterants in Urine Drug Screening and Testing
The increase in laboratory drug screening in recent years has led to a proliferation in the number of products and methods available to falsify drug test results. Adulterants and urine substitutes designed to defeat drug tests are readily available and can be easily researched or purchased over the Internet. These products fall into three basic categories, in vivo adulterants (ingested), in vitro adulterants (added to a sample), and urine substitution devices. Additionally, a number of common household products such as soap, bleach, aspirin, and simple dilution through ingestion of water may also be used to obtain a "clinical false negative" (i.e., a negative drug test in the context of drug use). Utilizing PsychInfo, Medline and Google, we searched the psychiatric and medical literature, as well as the internet to identify a comprehensive list of methods of urine adulteration and substitution. These products, compounds and methods are described, and literature on their effectiveness as well as means of detection is reviewed. Most of these products and methods are at least moderately effective at producing a clinical false negative result for certain substances under certain conditions. Virtually all of these products and methods, however, are readily detectible using either direct observation, laboratory integrity checks, and/or on-site dipstick devices. It is recommended that clinicians and researchers involved in urine drug screening and testing consider these threats to validity in designing treatment programs and research protocols and employ methods to detect adulteration when appropriate.
- 362 DOES A SINGLE OR LOW DOSE OF ECSTASY AFFECT MEMORY BRAIN FUNCTION?**
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Background It is debated whether a single or low dose of ecstasy is neurotoxic to human brain function. In this study we prospectively investigated the non-acute effects of a single or low dose of ecstasy on associative memory function in ecstasy-naive volunteers, using fMRI. Methods 50 Subjects, 26 novice ecstasy users and 24 persistent ecstasy-naive matched controls were assessed twice: first at baseline (all subjects still ecstasy-naive) and second after a period of first ecstasy use (mean 2.7±3.8 tablets) or a comparable follow-up period in the persistent ecstasy-naive group. Time since last ecstasy use in the novice users was ≥ 2 weeks. Associative memory function (performance and brain activity) was examined by fMRI. Results Both novice users and persistent ecstasy-naive controls performed normally during baseline and follow-up. Based on a brain activity map of the whole group, 9 regions of interest were defined in the prefrontal cortex, the parahippocampal area, the occipital gyrus and the anterior cingulate cortex. GLM analysis revealed no significant differences in activity between groups across baseline and follow-up scanning. Within the group of novice ecstasy users no correlations were found between the number of ecstasy tablets and memory performance or brain activity. Conclusion No sustained effects were found of low dose ecstasy use on associative memory function. In a previous study with heavy ecstasy users, we demonstrated clear non-acute impairments in associative learning and abnormal brain activity, using the same fMRI-paradigm (in preparation). Therefore, the current lack of findings cannot be explained by insensitivity of the method used. Apparently, low dose ecstasy use in otherwise healthy volunteers has no sustained effect on associative memory brain function. It should be noted, however, that small but significant effects on verbal memory were observed using a cognitive task in the same study population (Schilt et al, submitted). As of yet it is not clear how this apparent discrepancy should be interpreted.
- 363 PATIENT COMMITMENT LANGUAGE IN RESPONSE TO A PROJECTIVE NARRATIVE PREDICTS LENGTH OF STAY IN A RESIDENTIAL TREATMENT PROGRAM**
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Verbal predictors of addiction treatment outcomes are understudied in adolescents. While recent studies indicate patient speech is related to behavioral outcomes (Amrhein, Miller, Yahne, Palmer, & Fulcher, 2003; Amrhein, Aharonovich, Brooks & Nunes, 2005; Collins, Carey & Smyth, 2005), they have focused on adult substance abusers. Amrhein et al.(2003, 2005) found that specific types of patient speech--verbal commitments--are robust indicators of future drug use and treatment retention. Of interest was determining whether patient commitment expressed in a projective narrative task is related to treatment retention in substance abusing adolescents remanded to a therapeutic community. Eighteen residents (17 males, 1 female, mean age=18.3 years, range=17-20 years, SD=.77 years) were read two short narratives as a means of eliciting speech. The first narrative was a description of a young man emphasizing the positive aspects of smoking marijuana; the second was a description of a young man struggling to engage in a therapeutic community. Patients were instructed to speak freely for two minutes about their reactions to the passage. Audiotaped responses were coded according to Amrhein et al. (2003). Results indicated greater frequency of commitment language in the smoking than therapeutic narrative. In responding to the smoking narrative, patients expressed commitment to maintain drug use; however, drug use ambivalence--revealed through some patients' references to weakened commitment to smoke--predicted longer treatment program stays ($r=-.61$, $p<.02$). Usage of first person singular syntactic constructions was particularly associated with longer stays in treatment. Results extend findings (Wilson, Levin, Donovan & Nunes, In Press) demonstrating the prognostic utility of the projective narrative task in revealing linguistic evidence of patient commitment to treatment participation.
- 364 METHADONE CONCENTRATIONS IN BREAST MILK AND BLOOD AND ASSOCIATED NEONATAL NEUROBEHAVIOR**
L. M. Jansson(1), R. Choo(2), M. Velez(1), C. Harrow(3), J. Schroeder(4) and M. Huestis(2), (1) The Johns Hopkins University School of Medicine, (2) NIH/NIDA/IRP, (3) Johns Hopkins Bayview Medical Center and (4) Office of the Clinical Director, NIH/NIDA/Intramural Research Program, Baltimore, MD
Methadone maintenance offers major benefits to the population of opiate dependent pregnant and postpartum women, yet controversy exists regarding the practice of lactation in this group. This study evaluates 1) concentrations of methadone in breast milk and blood among a sample of mothers receiving methadone and 2) neurobehavior in their infants compared to a matched group of formula-fed infants. Nine methadone maintained (dose range 40-110 mg), lactating women yielded blood and breast milk specimens on days 1,2,3,4,14 and 30 after delivery at trough (just before single oral dose) and peak (3 hours after dose) maternal methadone concentrations. Three additional women yielded samples on days 1,2,3 and 4 after delivery. Paired specimens of foremilk (prefeed) and hindmilk (postfeed) were obtained at each sampling time. Infant blood was obtained on day 14. Urine toxicology screening thrice weekly for 30 days after delivery indicated that women were not using illicit substances. Breast milk specimens were analyzed utilizing LC-APCI-MS/MS for methadone and its primary metabolites EDDP and EDMP. Amounts of methadone in breastmilk were small (range 20.6-462.0 ng/mL). There was a significant increase in methadone concentration in breastmilk over time for all four sampling times: trough prefeed ($t(41) = 2.56$, $p = 0.014$), trough postfeed ($t(37) = 3.28$, $p = 0.0023$), peak prefeed ($t(39) = 4.03$, $p = 0.0003$), and peak postfeed ($t(35) = 3.02$, $p = 0.0047$). Eight subjects who delivered specimens at all collection points were matched for age, race, parity and methadone dose to eight formula feeding women. Infants in both groups had NICU Neonatal Neurobehavioral Scale assessments on day 3, 14 and 30. There were no significant effects of group or group by time interactions. Results contribute to the recommendation of breastfeeding for methadone maintained women.

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- 365 ABUSE LIABILITY OF INTRAVENOUS L-LYSINE-D-AMPHETAMINE (NRP104)**
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NRP104 (N) is an pro-drug that is itself inactive. Rate limited enzymatic hydrolysis of N in the gut to d-amphetamine (A) and lysine explains the slower onset and extended action of N. N IV should show little activity. N 50 mg, A 20 mg and placebo (P) were given IV over 2 minutes at 48 hour intervals to 9 stimulant abusers in a double blind crossover design to assess abuse liability. Drugs were given according to 3 X 3 balanced latin squares. N 50 mg and A 20 mg contain equal A base on a mole weight basis. Each dosing day, vital sign measures and subjective and behavioral effects were assessed with questionnaires before dosing and at 0.5, 1, 1.5, 2, 3, 4, 5, 6, 9, 12, 16 and 24 hours after dosing. At these times and at 5 minutes, a blood sample (5 ml) was taken for A levels. For A, mean peak plasma level of 77.7 ng/ml of A occurred at 5 minutes and then rapidly subsided. A produced expected A-like effects with mean peak responses at 15 minutes. The mean maximum response to A on the primary variable of Subject Liking VAS was significantly greater than placebo ($p = .01$). For N, mean peak plasma level of 33.8 ng/ml of A occurred at 3 hours and remained at this level through the 4 hour observation. N produced A-like subjective, behavioral and vital sign effects with mean peak responses at 1 to 3 hours. For the primary variable of Subject Liking VAS the response was not greater than placebo ($p = .29$). Changes in blood pressure following N were significant. At the end of the study, subjects were asked which treatment they would take again. Six subjects chose A 20 mg, two subjects chose none of the treatments, and one subject chose N 50 mg. In summary, N 50 mg did not produce euphoria or amphetamine like subjective effects although there were late occurring blood pressure increases. The findings support the hypothesis that NRP104 itself is inactive. After 1 to 2 hours, NRP104 is converted to A. Taken IV, NRP104 has significantly less abuse potential than immediate release A containing an equal amount of d-amphetamine base. Study sponsored by New River Pharmaceuticals, Inc.
- 366 MENSTRUAL SYMPTOMATOLOGY AND CIGARETTE SMOKING IN ADOLESCENT GIRLS: PRELIMINARY FINDINGS**
M. Jaszyna-Gasior, F. H. Franken, M. K. Leff, K. S. Bagot, E. J. Luther, M. B. Royo, C. C. Collins, E. D. Thorner and E. T. Moolchan, Teen Tobacco Addiction Research Clinic and, DHHS, NIH/NIDA/Intramural Research Program, Baltimore, MD
Equivocal findings have emerged on the relationship between tobacco smoking and menstrual symptomatology. Our aim was to investigate a potential relationship of smoking behavior and menstrual symptomatology among adolescent girls. Data were collected from 12 smokers (mean years smoking 2.1 SD 1.4, mean Fagerström Test for Nicotine Dependence 6.5 SD 1.4, mean cigarettes per day 12.8 SD 4.2; mean age at menarche 12 SD 1) and 5 non-smokers (less than 5 cigarettes lifetime) prior to participating in a randomized placebo-controlled treatment trial. Smokers and non-smokers were similar in age, Tanner staging, menarche and weight. Menstrual symptomatology questions were obtained using the menstruation module from the (Diagnostic Interview for Children and Adolescents) based upon DSM IV. Two-tailed Fisher's Exact analyses revealed a significant association between smoking and severe menstrual pain ($p=0.05$); differences between groups in reported heavy periods, irregular periods, missing school because of bad cramps, severe menstruation pain, or seeking medical attention did not reach statistical significance. Further analyses from a larger group of girls are needed to fully explore the impact of smoking on menstrual symptomatology and quality of life. Supported by NIDA Intramural Funds

367 WITHDRAWN

- 368 CANNABIS INFO SERVICE: PART OF THE FRENCH CANNABIS PROGRAMME**
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Cannabis Info Service is one of the four components of the French Cannabis Programme launched at the beginning of 2005 to tackle about the expanding cannabis use. It is part of the "2004-2008 French Government Plan for the Fight against illicit drugs, tobacco and alcohol", coordinated by the Interministerial Mission for the Fight Against Drugs and Drug Addiction (MILDT). A special phone line dedicated to cannabis has been set up in February 2005. It is a step up in prevention focusing on young people. In addition, it is an information and a support resources to make parents aware of problematic use and help them to act. Before setting up a specific cannabis phone line, DATIS2 recorded 30 000 phone calls a year about cannabis. Phone talks are confidential and anonymous. They provide information on legislation, risks linked to use, advice on screening or treatments. A data analysis of the hot line has been carried out. Callers are: 57% family or friends relatives, 38% cannabis users and 5% others including health professionals. The sex ratio is 81% for women among relatives, aged more than 40 and mothers in 52% cases; they call for male users (80%), aged from 15 to 24 years (75%). The phone call lasts 20 minutes on average. Users who call are male (68%), aged under 20 (23%), 20-30 (36%) and over 30 (41%). The phone call lasts 12 minutes on average. The topics of calls can be classified according to five types: "do I dare?" under 15 years; "could you tell my parents?" in 15-20; "could I be positive in a screening test?" in 15-25; "what do I risk?" users aged 20 and over; "I would like to stop" regular users aged 20 and over. Callers have been referred (44%), especially to specific cannabis clinics (64%). Cannabis Info Service could be considered as a brief intervention therapy. Concrete aims and up-to-date formation are needed to the answering team.

369 WITHDRAWN

370 RISK BEHAVIOR STUDY AMONG HEROIN ABUSERS IN WUHAN, CHINA

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Background: Drug abuse is a re-emerging problem in China. It contributes significantly to the death and infectious diseases such as HIV and hepatitis C virus (HCV) infection. Previous studies have showed a high prevalence of HCV infection arranged from 60-80%, even 97% among injection drug users (IDUs) in the West of China. The primary reason for the high prevalence of the viral infection among IDUs is their risk behaviors. The information about risk behaviors among the heroin users in Wuhan, the largest city in the center of China, is not available. Therefore, we investigate the patterns of risk behaviors and their relation to HCV infection among the heroin users in Wuhan, China. Methods: Fifty-five heroin users, who seek or were referred to detoxification treatment in Wuhan Psychiatric Hospital, signed informed consent and were interviewed by trained and experienced interviewers. The blood was sampled for HCV antibody detection by ELISA. Risk behavior measures include Inconsistent condom use, initial age of needle heroin use, one-time syringe use, needle and instrumental sharing, regular cigarette smoking, alcohol use and ASI composite scores. Results: The mean ASI composite scores are from 0.07 for alcohol to 0.64 for employment. 97.4% of the heroin abusers was inconsistent condom users, 45.4% shared needle and 32.7% shared drug instruments, only 38.2% used one-time syringe, 90.9% smoked cigarette regularly, 21.8% are drinking alcohol and 76% of the heroin abusers are infected with HCV. The subjects with needle and instrumental sharing were over 2 times more likely to be infected with HCV after the adjustment covariate of gender. No significant relation was found between HCV infection and ASI composite scores. Conclusions: The patterns of risk behaviors are similar to published data in other counties. There is a positive association between needle and instrument sharing and HCV infection. Further studies are needed to investigate the impact of risk behavior reduction on HIV/HCV transmission among heroin abusers.

371 WITHDRAWN

372 PROGRAM EMPHASIS ON SPIRITUALITY AND ADOPTION OF EVIDENCE-BASED PRACTICES

J. A. Johnson, L. J. Ducharme, H. K. Knudsen and P. M. Roman, University of Georgia, Athens, GA

Previous research on addiction counselors' attitudes toward specific evidence-based practices (EBPs) found a significant negative relationship between an individual counselor's belief in or adherence to the 12-step model and their attitudes toward the use of EBPs, particularly pharmaco-therapies. The present study extends this research to the organizational level by examining the relationship between 12-step orientation and other measures of spirituality on treatment programs' adoption of EBPs. Data are derived from a sample of 240 community treatment programs (CTPs) participating in the National Institute on Drug Abuse Clinical Trials Network. Descriptive statistics show significant variability in emphasis on spirituality among the CTPs. Certain spirituality components, such as requiring or encouraging 12-step meeting attendance, are present at more than 80% of CTPs. Other, more overt examples of spirituality are less common in CTPs. For example, less than half offered religious reading material while only 15% offer on-site religious worship. Separate logistic regressions found only one association between 12-step meeting attendance requirements and the use of EBPs, specifically methadone. However, logistic regressions that included some of the more overt measures of spirituality found significant relationships between these measures of spirituality and the use of certain EBPs. In some cases, however, the relationship was opposite to the expected direction. For example, the use of naltrexone was significantly more likely in programs offering psycho-educational groups on spirituality and in those programs offering instruction in meditation. There was no relationship between the use of psycho-social EBPs such as motivational enhancement therapy or voucher-based motivational incentives and the various measures of spirituality. The mixed results found in this study suggest the need for more in-depth analyses on the relationship between emphasis on spirituality in treatment and other indicators of program philosophy on the adoption of EBPs.

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373 GAMMA-HYDROXYBUTYRIC ACID AND ETHANOL: COMPARISON OF BEHAVIORAL, SUBJECT-RATED, AND OBSERVER-RATED EFFECTS IN SUBJECTS WITH HISTORIES OF SEDATIVE ABUSE

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GHB is an approved medication for the treatment of narcolepsy, and it has also been abused. However, little is known scientifically about the relative abuse liability of GHB in humans. This laboratory study is comparing the behavioral, subject-rated, and observer-rated effects of GHB and ethanol in participants with histories of sedative abuse. Comparison of GHB and ethanol is of interest because ethanol is a drug of well-characterized abuse potential, and both compounds are sedatives consumed in similar fashions (e.g., in liquid form, in social settings). Participants lived on a residential unit for about 1 month. Sessions were conducted Monday through Friday, and measures were taken before, and repeatedly up to 24 hours after drug administration. On session days, participants were administered GHB (1, 2, 4, 6, 8, and 10 g/70kg), ethanol (12, 24, 48, 72, 96, and 120 g/70kg), or placebo under double-blind conditions. For safety reasons, GHB and ethanol were administered in an ascending sequence, although the two drugs and placebo were intermixed across sessions. The ascending dose sequence for each drug was stopped if significant behavioral impairment occurred (i.e., sleeping or gastrointestinal distress). Currently, 5 participants have completed the study, and we continue to run additional participants. Preliminary analyses indicate that the highest doses of GHB and ethanol both have onset within 30 minutes, with peak effects at 60 minutes. However, GHB effects dissipated between 4 and 6 hours, while ethanol effects dissipated between 6 and 8 hours. Analyses revealed dose related effects for a variety of measures, with the highest doses of both drugs showing significantly greater subject-rated and observer-rated drug strength, subject-rated liking, and performance impairment (e.g., DSST) compared to placebo. Dose effect functions for GHB were generally steeper than for ethanol. Although trends suggest some differences, preliminary data also indicate many similarities between these two drugs. (NIH #DA-03889)

374 BUPRENORPHINE AWARENESS AND AVOIDANCE AMONG STREET HEROIN USERS IN NYC

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Problem: Physicians certified to prescribe buprenorphine report difficulty in attracting and maintaining heroin-using patients for ongoing therapy. Most current buprenorphine patients are employed prescription opioid users. **Background:** Buprenorphine was systematically developed in part to attract street-level heroin users, and provide detoxification or maintenance, as an optional medication for methadone. But few street active heroin users approach and/or are retained in buprenorphine therapy in public clinics in NYC. **Hypotheses:** Multiple barriers discourage street heroin users from learning about and entering buprenorphine therapy. The social advantages of buprenorphine (blocks high) are perceived as a drawback by many heroin users. **Methods:** Screener interviews were conducted with over 350 heroin and methadone users recruited at different street locations in New York City in 2005. Taped interviews with nine subjects with buprenorphine therapy experience provide rich qualitative data. **Findings:** For two years (4Q03-3Q05) very few street heroin users had heard of buprenorphine. Almost none had heard of the brand names (Subutex and Suboxone™); a mild increase in awareness occurred in 4Q05. Among 9 persons with some personal buprenorphine experience, 3 had been dropped out of research studies before 2004. Four reported bad experiences with buprenorphine; they appreciated that buprenorphine alleviated their withdrawal syndrome, but expected the drug to get them high-they lost interest when it did not. The two subjects who had legal employment had gone to private doctors and were retained and doing well on buprenorphine therapy. **Conclusions:** In NYC, several buprenorphine certified physicians exist in private practice and public clinics to provide buprenorphine therapy to several hundred, and probably thousand, heroin users. Outreach to, awareness of, and building a positive street reputation toward buprenorphine therapy within the street heroin subculture remains to be accomplished.

375 DISENTANGLING THE COMORBIDITY OF PTSD AND SUBSTANCE USE DISORDERS

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This study examines the association of traumatic exposure, PTSD and substance use to disentangle the relationship that various substance use disorders have with traumatic event exposure and subsequent PTSD expecting that the most serious events will have greater association with illicit substance abuse/dependence. Data for these analyses are based on 858 women from two epidemiologic studies aimed at reducing high-risk sexual and drug use behaviors among female injection drug and crack cocaine users and in heavy alcohol drinkers. Both studies involved non-probability methods as women were simultaneously recruited through a street outreach method. The DIS elicited data on PTSD based on DSM-IV criteria. The CIDI-SAM elicited DSM-IV substance abuse and dependence criteria. Logistic regression analyses were utilized to conduct between group comparisons for categorical data. Over 90% of the women experienced at least one DSM-IV qualifying traumatic event with 33% of those developing subsequent PTSD. While some events such as being mugged and being held captive were associated with alcohol, cannabis, cocaine and opiate abuse and dependence, being shot or stab was only associated with cocaine abuse/dependence when compared to those without the disorder. Neither the likelihood of an event nor PTSD development was distinct across substance use disorder when women with alcohol abuse/dependence were compared to those with illicit drug abuse/dependence. However women with both disorders (alcohol and illicit) were more likely to have an event (OR=2.96) and develop PTSD (OR=1.38) than women with one disorder or the other. These women were also more likely to be mugged (OR=1.74), raped by a non relative (OR=1.56) or held captive (OR=2.06). The association of traumatic event exposure and subsequent PTSD is not distinct among alcohol abuse/dependence and illicit substance abuse/dependence but is enhanced in the presence of both disorders.

376 DAT GENE KNOCKOUT DOES NOT AFFECT THE AVERSIVE AFFECTIVE EXPERIENCE OF COCAINE AS ASSESSED IN THE CONDITIONED TASTE AVERSION PREPARATION

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Despite being highly rewarding, cocaine administration is also thought to be accompanied by a significant negative affective experience. Since these aversive drug properties are believed to play a significant role in abuse potential, their manipulation may prove to be a powerful tool against cocaine addiction. Cocaine blockade of dopamine uptake through its high affinity for the dopamine transporter (DAT) has been the focus of numerous investigations into the physiological basis of its reinforcing effects. Although cocaine is a "dirty" drug, affecting multiple systems, recent studies suggest that its effects on central DA uptake may be involved in its aversive properties as well. Conditioned taste aversion learning is a preparation often used to assess the aversive effects of drugs and has been widely used in the examination of the aversive effects of cocaine. To that end, in the present experiment cocaine-induced taste aversions were assessed in mice with a dopamine (DAT) transporter deletion. Specifically, DAT KO mice and wildtype controls (n = 61) were given access to a novel saccharin solution to drink and immediately injected subcutaneously with saline or cocaine (18, 32 or 50 mg/kg). This procedure was repeated every fourth day for a total of four conditioning trials. On intervening recovery days, all mice had access to water. A 2 X 4 ANOVA revealed that cocaine induced dose-dependent taste aversions in all mice, both wildtype and DAT KO [F (2, 55) = 8.62, p < .01], with no differences in the degree of aversions between the wildtype and DAT KO subjects, suggesting that under these specific conditions, dopamine reuptake inhibition does not have a significant role in the aversive effects of cocaine.

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- 377 THE SAFETY AND TOLERABILITY OF 7.5, 15 AND 30 MG OF SUBLINGUAL LOBELINE**
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Lobeline, a medicinal alkaloid that is active at nicotinic receptors and also inhibits the vesicular monoamine transporter, is a potential new pharmacotherapy for methamphetamine dependence. In animal models Lobeline decreases methamphetamine self-administration. In this 9-subjects, double-blind, ascending dose, crossover study we assessed the pharmacokinetics, cardiovascular (CV) safety and tolerability of 7.5, 15 and 30 mg of sublingual lobeline. Plasma and urine lobeline and its epimer were measured with LC/MS/MS. Lobeline was rapidly absorbed with mean Tmax of 1.4 hrs. Epimer concentrations were 8-10 fold greater than parent drug levels. Elimination was rapid with mean T_{1/2} of 2.4 hrs for Lobeline and 1.7 hrs for the epimer with only 0.5% of the dose excreted in urine. Lobeline non-dose dependently increased mean VAS ratings (0-100 scale) of bad drug (17.4), nausea (10.8), bad taste (29.6), lethargy (18.5), numbness (8.4) and restlessness (10.8). Lobeline 7.5 mg briefly increased diastolic blood pressure by 3.1 mmHg; no other CV effects were seen. We conclude that Lobeline is rapidly absorbed and hepatically cleared with the majority of the dose rapidly converted to an epimer. Lobeline is well tolerated with minimal adverse and CV effects. In this ascending dose paradigm unpleasant effects were more evident at lower doses, suggesting tolerance may develop to many CV and unpleasant effects. Supported by NIDA contract N01DA-4-8306 and NIH RR-00079 (GCRC, UCSF).
- 378 WORKSITE WELLNESS HEALTH PROMOTION: A TOOLKIT FOR EMPLOYERS AND EMPLOYEES**
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Employees at risk for a high body mass index (BMI) are more likely to have other health risks, illness, absence, and short-term disability, resulting in both direct and indirect expenses to employers (Burton, Chen, Schultz, and Edington, 1998). In December 2000, the Surgeon General presented a national plan targeting the public health epidemic of overweight and obesity; worksites were highlighted as one of five thematic areas for implementing strategies for change (Jackson, et al., 2002). Furthermore, an obesity research task force was created last year at NIH to develop a strategic plan for NIH obesity research; NIH emphasizes the diverse efforts necessary to effectively target the numerous factors contributing to this health problem (<http://www.obesityresearch.nih.gov/about/about.htm>). As a result, the workplace presents a significant opportunity to develop and implement a worksite health promotion program. According to the National Cancer Institute (NCI), a considerable amount of research has examined obesity prevention and treatment through environmental and behavioral approaches to lifestyle modification; this research has served to help identify evidence-based approaches. This study funded by an SBIR with NCI, has developed a Worksite Health Promotion Toolkit to promote widespread adoption of research-based energy balance promotion (i.e., obesity reduction) approaches in worksites. Following Phase I, social marketing materials and sections of a Facilitator's Guide, (focusing on employee-driven self-help groups) and a Resource Guide, (providing guidelines for employers) as well as a Vignette Video script, (illustrating support group implementation) have been developed. During Phase II, the project team will finalize the social marketing materials, Facilitator's Guide, and Resource Guide, produce the Vignette Video, and conduct an outcome evaluation of the toolkit. Results of the focus groups and a feasibility pilot study with employers and employees will be presented.
- 379 STREET KNOWLEDGE: USING ETHNOGRAPHY TO INFORM AND ENHANCE STREET-BASED RECRUITMENT AND RETENTION OF HEROIN INJECTORS AND CRACK SMOKERS IN HIV PREVENTION RESEARCH TRIALS**
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Recruitment and retention of those at high risk for HIV acquisition is essential for behavioral and clinical HIV prevention research. It is also important to learn about neighborhoods and its members when research activities are neighborhood-based and the neighborhood is central to engagement in high risk activities. Ethnographic research was used to meet the challenge of recruiting and retaining heroin injectors in a HIV prevention behavioral study and female crack smokers in a HIV prevention vaccine trial. Before and during recruitment and data-collection, ethnographers embedded themselves in 29 neighborhoods and used observations, interviews, and geographical mapping to assess perceptions of drug use, HIV, and research; and identify potential sites for recruitment activities. Ethnographers also built relationships with drug users and helped them connect to a mobile unit for pre-screening interviews and office visits. Between 12/02 and 10/05, the HIV prevention trials pre-screened 3,064 heroin injectors and/or crack smokers in Philadelphia, PA and Camden, NJ. Using this ethnographic model, researchers believe they are closer to understanding heroin and crack cocaine use as it relates to research participation, and its function in the lives of street-based drug users. Themes include: drug users' negotiation between research participation, sex work, and boosting as financial means to drugs, housing and food-with the availability of the mobile unit, a need for drugs, and police presence influencing hustle selection; attempts to access drug treatment, with purposeful drug relapsing and using incarceration to initiate drug rehabilitation; and the significance of familial histories of substance abuse. This paper will highlight lessons learned, describe potential measures to examine the efficacy of this model, and discuss its implications in HIV prevention behavioral and clinical trial research with active, street-based drug users.
- 380 THE IMPACT OF PARENTAL SUBSTANCE ABUSE ON THE LIVES OF DOMESTIC VIOLENCE SURVIVORS**
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Previous URI research studies (Griffing et. al 2002 and Jospitre et. al 2005) found parental substance abuse to be a contributing factor to childhood abuse and neglect among adult victims of domestic violence. Current research shows that parental substance abuse is increasingly being recognized as a factor in most foster care placements and that lifetime substance abuse is widespread among youths in foster care (NSDUH Report 2005). In light of these findings, we interviewed adult female residents (N=277) of two New York City domestic violence shelters regarding their experiences with parental substance abuse, parental involvement with the criminal justice system, and their own involvement with foster care. Consistent with our hypotheses, chi-square analyses revealed an association between parental substance abuse and parental criminal justice involvement (p<. 01) and an association between parental substance abuse and survivor placement in foster care (p<. 01). Independent sample t-tests revealed that survivors with substance-abusing mothers stayed in foster care significantly longer than survivors without a maternal substance abuse history (M= 43.17 mos. vs. M= 18.84 mos.) (t= -2.02, p= .037). Paternal substance abuse was unrelated to survivors' length of stay in foster care. Clinical implications for the prevention and treatment of substance abuse among domestic violence survivors are discussed.

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381 SHORT-TERM IMPACT OF SAME INTENSITY BUT DIFFERENT DURATION INTERVENTION FOR CANNABIS USERS

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This study evaluates efficacy of a brief intervention for cannabis users. A rct compared 3 conditions: 4 weekly individual sessions in 1 month-1MRP, same 4 sessions in 3 months-3MRP, and Delayed treatment control-DTC. From 277 interviewed, 183 were included. 160 were analysed. Subjects were mainly male, white, single and highly educated. They have mean age of 32.45 and started using cannabis at 16.44 and had 16 years of use. They smoked in 92.19% of last 90 days prior to baseline interview and smoked 1.99 joints per day in that period. Total adherence rate was 64%, with DTC having less drop out. In treatment groups, there was a significant reduction in percentage of days smoked from baseline to 1st follow-up: 1MIPR decreased from 94.19% to 63.74% and 3MIPR from 88.17% to 51.86% in the last 90 days, in mean number of joints smoked: 1MIPR decreased from 2.06 to 0.78 joints per day and 3MIPR from 2.08 to 0.58 and mean number of quarters per day: 1MIPR decreased from 2.05 to 1.17 and 3MIPR from 2.05 to 0.94 quarters per day. Improvement was similar for all primary outcomes while for secondary ones, 3MIPR had better improvement in terms of cannabis-related problems, 1MIPR decreased from 9.80 to 8.44 and 3MIPR from 10.21 to 6.70, and for dependence symptoms, 1MIPR decreased from 5.69 to 4.38 and 3MIPR from 5.78 to 2.75. Abstinence rate at 1st follow-up was small and there were no differences among 3 groups (total of 3.7%). There was an increase of drug use in the 1st follow-up mainly cocaine. This is a sample with highly educated people and with a long and heavy history of cannabis use. In general terms, treatment is better than no treatment. Comparing the 2 treatment groups, there is some evidence that the longer the treatment the better: 3MIPR was better on secondary outcomes. Curiously, waiting list has effect on cannabis use, which contributes to the idea of a very brief intervention being effective. Although the drop-out rate was high compared to other studies, it did not affect results (effects of missing data). Sample needs to be followed for longer, to check whether changes last over time.

382 RAPID BEHAVIORAL SENSITIZATION TO AMPHETAMINE- AND NICOTINE-STIMULATED LOCOMOTOR ACTIVITY IN FEMALE RATS

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Repeated exposure to stimulants produces a persistent and progressive enhancement in their psychomotor and positive-reinforcing effects. This phenomenon is termed behavioral sensitization and has been proposed to underlie various aspects of drug abuse, such as drug seeking behavior, and drug-induced psychosis. This adaptive process is dependent on the sensitizing dose use and periods of prolonged withdrawal between treatments. Recent studies have demonstrated a rapid-onset type of sensitization that develops within hours after a single priming injection of amphetamine. This study further explores this rapid behavioral sensitization and evaluates the effects of other stimulants, such as nicotine, on rapid behavioral sensitization to amphetamine and nicotine challenge. In the present studies, locomotor activity was evaluated in the home cage environment in female Holtzman rats (225-300g) implanted with radiotelemetry devices (Mini Mitter / Respironics). Rats were injected i.p. with saline or various doses of nicotine or d-amphetamine followed 1-4 h later by an amphetamine or nicotine challenge. Challenge injections were administered after pretreatment-induced locomotor activity dissipated. Nicotine (0.032-0.32 mg/kg) administered as a 1 h pretreatment significantly enhanced amphetamine-stimulated locomotor activity. Similarly, amphetamine (0.1-1.0 mg/kg) injected 4 h prior to nicotine dose-dependently potentiated nicotine-stimulated locomotor activity. These data demonstrate that rapid sensitization can be induced by pretreatments with amphetamine and nicotine. Furthermore, these findings suggest that frequent use of these drugs of abuse may further potentiate their reinforcing and psychomotor responses, potentially leading to exaggerated use. Research supported by University of Michigan Tobacco Research Network.

383 VAGAL TONE DURING SUSTAINED ATTENTION TASKS AMONG 8-YEAR-OLDS PRENATALLY EXPOSED TO COCAINE

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Arousal regulation problems have been the most consistent finding across studies on children with a history of prenatal cocaine exposure and these may be related to problems in behavior and attention observed in clinical samples. Most of these findings, however, are limited to the infants and toddlers. We studied the impact of prenatal cocaine exposure on the arousal responses of 8-year-olds with a history of prenatal cocaine exposure using physiological responses (heart rate (HR), respiratory sinus arrhythmia (RSA), skin conductance level (SCL), and skin conductance response (SCR)) during a baseline period and two sustained attention tasks. Contrast groups included a group who were recruited from the same birth hospital (CON) and a group recruited from the community with identified behavioral disturbance (BD). To examine the relationship between attention and arousal, physiological responses during the Visual and Auditory Discrimination Learning Tests from the Computerized Attention Battery were used. Four 30 second epochs were used to monitor HR, RSA, SCL, and SCR during a baseline and each of the two sustained attention tasks. A multivariate repeated measures analysis of variance yielded group differences ($F(2,152) = 5.7, p < .004$) on heart rate. Post-hoc comparisons indicated that the BD group had significantly higher levels of HR than both other groups across all conditions and epochs. An epoch by group interaction was found on RSA ($F(6, 516) = 2.6, p < .02$). Post-hoc comparisons indicated the EBD and cocaine groups had poorer vagal tone by epoch 4 for then did the controls, possibly representing a fatigue effect over time. Results suggest that 8-year-olds with a history of prenatal cocaine exposure have persistent effects on their ability to regulate arousal while sustaining attention.

384 ASSESSMENT OF THE PHARMACOKINETIC AND PHARMACODYNAMIC INTERACTION OF ORAL NALTREXONE WHEN CO-ADMINISTERED WITH ORAL HYDROCODONE/APAP

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Purpose: To characterize the potential for PK interactions and to quantify the reduction in the opioid-agonist effects of 15-mg oral hydrocodone/acetaminophen (HCD/APAP) in healthy subjects upon co-administration of various oral doses of naltrexone (NTX). Methods: A randomized, single-blind, controlled, 10-way crossover, 3-day washout period after each dose, PK-PD pilot study in 21 healthy, nonopioid-dependent, fasted, adult female subjects (aged ≥ 18 y, mean 26.5 y). Sixteen subjects completed. Treatments: 15-mg HCD/1500-mg APAP; NTX (0.4 mg to 12.8 mg NTX); control (750-mg Trilisate®). Plasma concentrations of HCD and NTX (metrics AUC, C_{max}, t_{max}, t_{1/2}), and mean residence time were quantified. PD assessments: pupil diameter and Modified Specified Drug Effect Questionnaire (MSDEQ) scores. Safety assessments: incidence of side-effects, clinical laboratory and vital sign results, physical examinations, and electrocardiograms. Results: increasing concomitant NTX doses: did not alter the extent or rate of HCD absorption, or HCD t_{1/2}; resulted in dose-proportional increases in NTX AUC and C_{max} values without changes in NTX T_{max} and t_{1/2} values; reversed HCD-induced pupillary constriction in an ordered dose-dependent fashion; decreased selected HCD-induced changes in MSDEQ, as well as the incidence of HCD side-effects. Common opioid-related side-effects were nausea, vomiting, dizziness, and pruritus. There were no unexpected safety concerns. Conclusions: These results demonstrate that there is no PK interaction between HCD and NTX at the doses administered, and further characterizes the NTX: HCD dose and blood concentration ratio at which NTX begins to block the opioid-agonist effects of HCD. These results may prompt investigations to determine the NTX dose that maintains opioid analgesia in pain patients while reducing abuse liability in HCD abusers.

385 EFFECTS OF BUPROPION SR ON NEUROCOGNITION IN VOLUNTEERS WITH METHAMPHETAMINE DEPENDENCE

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Methamphetamine (MA) dependence is associated substantial risk for neurocognitive impairment, including deficits in speed of information processing, attention, memory, and executive function. Medications that reverse the neurocognitive deficits associated with MA use may enhance treatment outcomes, particularly when cognitive behavioral treatments are utilized. Preclinical studies have shown that MA exposure is associated with long-term disruption of monoaminergic systems, including effects on dopamine (DA) and norepinephrine (NE). Bupropion inhibits reuptake of NE, and to a much lesser extent, DA, and is an attractive candidate medication for the treatment of neurocognitive impairment in MA-dependent individuals. To date, 13 volunteers (7 male, 6 female) have been enrolled in this inpatient study. Average age in years was 32.1 ± 6.6 and average years of MA use was 6.8 ± 3.7 . Subjects were admitted to the General Clinical Research Center at UCLA for 16 days and randomized to placebo or Bupropion SR (300 mg, p.o.). After a five-day washout period (days 1-5, during which no treatment was administered), subjects were given a battery of neurocognitive tasks to assess attention/speed of information processing, declarative memory, and executive systems functioning. These tests include simple and choice reaction time tests, as well as a series of N-back measures. Participants were then randomized to receive placebo or bupropion. After 26 days of treatment, subjects were reassessed with the same battery of neurocognitive tests. Performance of both groups improved over time; however, patients treated with bupropion tended to show greater improvement on measures of accuracy of decision-making than patients treated with placebo. Similar results were obtained on measures of episodic memory. Because of the modest sample size, the statistical significance approached, but did not reach, the .05 level. Implications for treatment of MA dependence are discussed. Supported by NIDA: DA-14593, DA-18185, DA-17754

386 A PILOT TRIAL OF QUETIAPINE FOR THE TREATMENT OF ALCOHOL DEPENDENCE

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Background: Atypical antipsychotics may prove to be useful for the treatment of alcohol dependence. Published studies indicate clozapine reduces alcohol consumption among schizophrenic patients, and olanzapine reduces alcohol craving in alcoholics. Quetiapine is an atypical antipsychotic, structurally related to clozapine, but with a favorable side effect profile; therefore it may be a promising treatment for alcohol dependence. This is the first controlled study that evaluated quetiapine for treating alcohol dependence in patients without another major mental disorder. Methods: Sixty-one male and female alcoholics were included in a 12-week placebo-controlled trial. After detoxification, patients were randomized to receive quetiapine (n=29), escalated over 9 days up to 400 mg/day at bedtime, or placebo (n=32), with weekly counseling. The primary outcome measure was alcohol consumption (any drinking and heavy drinking) measured in standard drinks per day by the Timeline Follow-back. Results: Forty-seven subjects (77%) completed the trial, with no significant between-group difference in treatment retention (quetiapine: 23/29 [79%]; placebo: 24/32 [75%]; Chi square =0.160, ns). Quetiapine-treated patients significantly reduced their alcohol use (group by time interaction: $Z=2.2$, $P=0.03$) and amount of heavy drinking, defined as 4 or more drinks a day for women and 5 or more for men ($Z=2.6$, $P=0.01$), compared to placebo-treated patients. Nine quetiapine-treated patients (31%) compared to 2 placebo-treated patients (6%) maintained complete abstinence throughout the trial (chi square =6.3, $P=0.012$). There was a significant interaction between quetiapine and alcohol subtype, with quetiapine-treated Type B alcoholics reporting less craving for alcohol and less heavy drinking than placebo-treated Type B alcoholics. Conclusions: Quetiapine may be an effective treatment for alcohol dependence. Supported by funding from AstraZeneca Pharmaceuticals LP.

387 OPIATE SENSITIZATION INDUCES Δ FOSB EXPRESSION IN CORTICAL AND LIMBIC BRAIN REGIONS IN C57BL/6 MICE

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Repeated and intermittent opiate administration produces behavioral sensitization that results in the neuroplasticity of motivational systems. These neuroadaptations underlie the enhanced and enduring behavioral effects of opiates. Acute and chronic administration of most drugs of abuse is known to produce a transient induction of many types of Fos proteins in the nucleus accumbens (NAc). Δ FosB is a long acting and stable Fos-related protein that gradually accumulates with repeated administration of drugs of abuse. Δ FosB accumulation represents a mechanism by which chronic exposure to drugs of abuse can alter gene expression and neural plasticity. This study examined the effects of opiate-induced motor sensitization on the induction of Δ FosB in the NAc, anterior cingulate (ACg), prefrontal cortex (PFC), and basolateral amygdaloid nucleus (BLA). Quantitative immunohistochemical studies were performed using an antibody specific for the Δ FosB protein. Mice received morphine (10 mg/kg s.c.) or vehicle treatment on days 1, 3, 5, 8, 10, and 12 and automated activity monitoring was performed for 180 min after drug administration. On day 16, all mice were challenged with morphine or vehicle prior to motor activity monitoring. Morphine pretreatment produced a two-fold increase in morphine induced motor activity on day 16 compared to single dose morphine administration on day 1 or day 16 (after repeated vehicle pretreatment). On day 16, morphine sensitized mice (vs. vehicle or single-dose morphine controls) demonstrated approximately a two-fold increase in Δ FosB immunoreactivity in the NAc-shell, ACg and BLA. These results suggest that the induction of Δ FosB in these neural systems may mediate opiate sensitization. Identification of transcription factors and their gene targets will lead to a better understanding of the mechanisms underlying opiate sensitization and addiction. Support Contributed By: Dept of Veterans Affairs and Boston Univ Sch Med

388 PRESCRIPTION OPIOID ABUSE: REVIEW OF CURRENT SURVEILLANCE SYSTEMS

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With prescription opioid abuse on the rise in the United States, appropriate public health surveillance is needed to monitor and detect emerging trends of abuse. Important criteria for effective public health surveillance systems have been identified, and include timeliness, relevance, and for opioid abuse, the ability to differentiate abuse rates of specific products. Databases were identified via Medline searches and recent reviews, including research from the Government Accounting Office (GAO),¹ the Office of National Drug Control Policy (ONDCP),² and the Center for Addiction and Substance Abuse of Columbia University.³ The resultant list of surveillance databases were then evaluated against criteria developed by an expert panel. Identified databases included: the National Survey on Drug Use and Health (NSDUH), Drug Abuse Warning Network (DAWN), Toxic Exposure Surveillance System (TESS), Drug Evaluation Network System (DENS), System to Retrieve Information from Drug Evidence (STRIDE), Treatment Episode Data Set (TEDS), National Forensic Laboratory Information System (NFLIS), Monitoring the Future (MTF), and key informant networks. Preliminary results suggest that current surveillance systems have significant limitations, including: not providing timely or product-specific data, lacking a focus on prescription opioids, no characterizing populations of opioid abusers, not readily linked to interventions, and lack of geographic specificity. No currently available system met minimum criteria. This systematic review suggests that new approaches are needed for the effective public health surveillance of prescription opioids. 1GAO (2003). Prescription drugs: OxyContin abuse and diversion and efforts to address the problem. 2ONDCP (2004). Synthetic Drugs Action Plan. 3Compton et al. (2005). Developments in the epidemiology of drug use and drug use disorders Am J Psychiatry, 162: 1494-1502.

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- 389** REPRODUCIBLE BRAIN ACTIVATION PATTERNS INDUCED BY THE MU OPIOID AGONIST FENTANYL IN AWAKE NON-HUMAN PRIMATES: AN fMRI STUDY
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We used fMRI in unanesthetized cynomolgus monkeys to assess brain activation patterns induced by intravenous infusion of the high-efficacy mu opioid receptor agonist fentanyl (0.0032 mg/kg). We studied 2 restraint-acclimated adult males to determine within- and between-subject reproducibility of fMRI activation foci. Scans were acquired on a Siemens Trio 3 Tesla scanner (Malvern, PA). Monkeys were restrained in the sphinx position in an MRI-compatible chair (Insight Neuroimaging Systems, Worcester, MA). Single shot gradient-echo echo planar scans were acquired. Data were analyzed with BrainVoyagerQX 1.6.3 and corrected for intersubject and interscan differences in brain size and positioning, respectively, using a Talairach-like transformation to spatially register the anterior commissure-posterior commissure plane. Data then were processed using a Generalized Linear Model accounting both for the hemodynamic response function and gradient heating effects. In both macaques, fentanyl bilaterally activated ventral striatum, anterior temporal lobe/amygdala, insula, and cerebellar hemispheres. Also activated were the posterior cingulate, cerebellar vermis, and medial brainstem. All regions reproducibly activated in duplicate fentanyl infusion sessions in each monkey (Bonferroni-corrected statistical significance of $P < 0.02$). When data from both monkeys were analyzed together, the same regions activated in duplicate fentanyl infusions (Bonferroni-corrected statistical significance of $P < 0.001$). Thus, we found both good within-subject and between-subject reproducibility of brain activation patterns following fentanyl infusion. These data suggest that our unanesthetized macaque fMRI model may be useful for characterizing brain effects of opioids and perhaps other psychoactive drugs. Supported by NIH grants DA17324, DA14013, DA09448, DA11460, DA015116, DA014178, and the John and Virginia Taplin Foundation.
- 390** HIV AND SUBSTANCE USE PREVENTION FOR MALE ADOLESCENT DETAINEES
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Incarcerated adolescents attending alternative schools have high rates of HIV risk behaviors, substance use and delinquency. Interventions addressing HIV and substance use are needed for this population of underserved, male minority youth. The purpose of this exploratory/developmental project is to test the feasibility of adapting an evidence-based HIV prevention program for use with eighty (80) Hispanic and African American males attending alternative high schools at 24-hour secure juvenile correctional facilities in Los Angeles County Probation Camps. The intervention (Street Smart) targets behaviors that are associated with HIV risk behaviors and substance use. The adaptation and implementation process is presented. Challenges and "lessons learned" from implementation of a research-based intervention into community settings are noted. Additionally, baseline and short-term results of HIV risk behaviors and substance use are presented. Future interventions with this population are discussed. This project is supported by The Universitywide Innovative, Developmental, Exploratory Awards (IDEA) Research Program in the State of California: ID04-FRII-073.
- 391** A COMPARISON OF LEWIS AND FISCHER RAT STRAINS ON AN ANIMAL MODEL OF DRUG ABUSE: AUTOSHAPING (SIGN-TRACKING)
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Lewis (LEW) and Fischer (F344) rat strains differ on a number of physiological characteristics, such as hypothalamic-pituitary-adrenal (HPA) axis activity, as well as on behavioral tasks, including those that measure impulsivity and drug reward. Since autoshaping, the phenomenon where animals approach and contact reward-paired conditioned stimuli, has been linked to HPA axis functioning, impulsivity and drug taking, the present study compared LEW ($n = 8$) and F344 ($n = 8$) rats on the rate of acquisition and performance of the autoshaping response. Rats were trained on an autoshaping procedure where insertions of one retractable lever (CS+) were paired response-independently with food, while insertions of another lever (CS-) were not paired with food. LEW rats acquired the autoshaping response significantly ($p < 0.05$) more rapidly and also performed the autoshaping response at a significantly ($p < 0.05$) higher rate than F344 rats. No differences between the strains were observed when rats were trained on a discrimination reversal where the CS+ and CS- levers were reversed or during a negative automaintenance phase where CS+ lever contacts cancelled food delivery. Potential physiological mechanisms that might mediate the present results, including strain differences in HPA axis and monoamine neurotransmitter activity, are discussed. The finding that LEW (as compared to F344 rats) more readily acquire autoshaping and perform more responses is consistent with research indicating that LEW rats behave more impulsively and more readily self-administer drugs of abuse.
- 392** PHARMACOKINETIC URINE MONITORING: A NEW TOOL FOR MINIMIZING TRAFFICKING IN PRESCRIBED OPIOIDS
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HYPOTHESIS: Diversion and trafficking in prescription opioids far exceeds current estimates presented in Federal and scientific publications [based upon patient interviews, arrest records, DAWN Reports, undercover investigations]. SUBJECTS: Adult patients being treated for non-malignant chronic pain syndromes in the US. METHODS: Urine samples were collected from 33,152 patients enrolled in 264 pain clinics and analyzed using standard GCMS methodology for commonly, prescribed opioids and their metabolites [codeine, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone and propoxyphene]. Urine data was pharmacokinetically-corrected so to minimize individual and population variance due to hydration state, lean body mass and urine pH. The normalized data was statistically analyzed so to establish functions relating corrected, urine concentration [parent + metabolite] to dose of parent opioid prescribed, including mean and acceptable variance. Results from this study were compared with previously published data of Kell RESULTS: Statistical analyses were completed for the opioids listed under Methods. Based upon such analyses, it was possible to construct linear functions expressing the relationship between pharmacokinetically-normalized urine GCMS concentrations and daily dose of opioid ingested for compliant patients. It was possible also to determine an acceptable variance about the mean for the population, allowing estimation of opioid misuse, diversion or supplementation. Based upon this data, gross diversion to persons outside the clinic averaged 0.246; ranging from a high of 0.475 for codeine to a low of 0.124 for methadone. Typically, only about half of the patients being prescribed opioids are compliant with their prescriptions based on quantitative urine testing. CONCLUSION: Approximately 1/4 of opioids prescribed within pain clinics are diverted to the street by traffickers. Another 1/4 is diverted between patients apparently being over-prescribed opioids to ones being under-prescribed. Pharmacokinetically-corrected urine monitoring is a viable tool for increasing compliance in pain clinics.

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393 DRUG-RELATED DEATH CASES IN BUDAPEST, HUNGARY BETWEEN 1999-2005

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Over the past decade fatal opioid overdose has emerged as a major public health issue both in Hungary and internationally. This study includes medicolegally examined drug-related death cases in Budapest, Hungary between 1999-2005. The number of deaths, age, sex, main intoxicant and other drugs present in the blood were recorded along with data from autopsy (organ weights, pathological changes) and results of serological testing for HIV, HCV, HBV and lues (the serological tests were performed from 2000). Heroin/morphine was the most frequently encountered single main intoxicant - 66-100% of the drug-related death cases each year were attributed to opiate overdose alone. Blood concentrations of morphine ranged from 0.02-19.56 µg/ml, and urine concentrations of morphine ranged from 0.214-7µg/ml. Codeine was detected in 70% of the subjects. The analytical screening revealed polydrug use appearing from 1999, decreasing in years 2000-2002 and reappearing in 2003. Frequently seen substances, in addition to the main intoxicant (which were still opiates) were tetrahydrocannabinol (THC), anticonvulsive drugs and volatile solvents. In years 1999-2002 there was no methadone-induced overdose mortality in Budapest. The first case appears in 2003. Pure heroin overdose cases declined dramatically in 2002, consistent with a marked reduction in availability of heroin in Hungary and a decrease in purity of street heroin. The first drug-related death case in the very young age group (<16 years) was noted in 2003. Females accounted for 0-22% of the overdoses throughout the years. According to the serological tests from the 75 cases available there was 1 HIV positive case, 19 HCV positive cases (25%), 18 acute or chronic HBV cases (24%), 9 cases with lues positivity (13%). In summary, these data show a disturbingly large increase in drug-related deaths during this time in Budapest. The main intoxicants are still opiates but there is a clear trend towards a politoxicoman pattern of use. This work was supported by NIH DA15446 and ETT 236/2003.

395 GENDER DIFFERENCES IN CLUB DRUG USE AMONG YOUNG ADULTS

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Gender shapes the practice of drug use in complex ways. Cultural bases of masculinity and femininity can profoundly influence the manner in which individuals manage their daily lives and engage in risk behaviors, such as the use of club drugs. Using data from a NIDA-funded study of club drug use among young adults, the authors explore gender differences in club drug use among young adults who patronize New York City dance clubs. The authors utilize both quantitative and qualitative data from the Club Drugs & Health project, a mixed-methods study with dual components. The surveillance of club drug use among club attendees (n = 1,914) occurred utilizing a time-space sampling methodology. Multivariate logistic regression analyses revealed that male gender was predictive of greater ketamine use, GHB use, and methamphetamine use (p < .05), as well as a trend towards active club drug use among young adults who patronize dance clubs. Female gender, however, was predictive of greater cocaine use (p < .05) within this population. Using qualitative data from a sample of 400 young adult club drug users, the authors conducted a thematic analysis of club drug use narratives. They explored the influence of masculinity and femininity in the respondents' experiences of club drug use. The use of club drugs plays a role in the construction of gender in club subcultures. Furthermore, the interface of the specific effects of each club drug, gender identity, and various social contexts coalesce in sexual narratives to frame not only the experience of sex but the associated risks as well.

394 INDIVIDUAL DIFFERENCES IN ALCOHOL EFFECTS AMONG HIGH- AND LOW-IMPULSIVE SENSATION SEEKERS

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Previous studies indicate that high sensation seekers are at increased vulnerability to drug abuse in part as a result of enhanced sensitivity to the reinforcing and other behavioral effects of drugs. This ongoing study examines the effects of alcohol in groups of high and low impulsive sensation-seeking adults matched on baseline alcohol and drug use. Eight of twenty healthy volunteers scoring in the top and bottom quartiles of gender-adjusted population norms on the impulsive-sensation seeking scale of the Zuckerman-Kuhlman Personality Questionnaire (6 high- and 2 low-impulsive sensation seekers) have completed 7 test days in which assessments are completed before (i.e., baseline) and after oral dose administration at times chosen to equate blood alcohol levels on the ascending and descending portions of the blood-alcohol curve. Placebo is administered on the first test day, during which data are collected but not analyzed. Each of three doses (0, 0.45 and 0.65 g/kg) is then tested under blind conditions on 2 days according to a randomized-block design. Preliminary analyses indicate that alcohol impairs performance on psychomotor, impulsive and attention tasks, increases heart rate, and engenders both stimulant- and sedative-like verbal reports of drug effect. Importantly, the magnitude of alcohol effects depends on whether blood alcohol levels are ascending or descending. The effects of sensation-seeking status on the behavioral effects of alcohol during ascending and descending blood alcohol levels, as determined using mixed-model repeated-measure ANOVA, will be presented. Supported by DA-05312 and RR-15592.

396 THE ROLE OF COMMUNITY SUPPORT IN TREATMENT ENTRY AND RETENTION

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Community support for recovery from heroin addiction is not well-studied. The Community Assessment Inventory (CAI) measures the perceptions of drug-addicted individuals' social support within their Household, Friends, Family (outside the home), and Community. In the context of a study on treatment entry and engagement, baseline CAI scales of 82 adults enrolling in six Opioid Treatment Programs and of 24 out-of-treatment, heroin-dependent adults were examined. The in-treatment group showed significantly higher scores on the CAI Household and Community scales than did the out-of-treatment group (both ps = .001), indicating that the in-treatment group perceives greater support and understanding from members of their household about addiction and its treatment and believes that there is less disorder in their community than does the out-of-treatment group. The correlations between baseline CAI scales and baseline ASI composite scores for all participants were not significant; nor were the correlations between the CAI scales and 3-month ASI composite scores for in-treatment participants. However, Household support at baseline was significantly correlated with self-reported heroin abstinence at 3-months (p = .005), indicating that greater support for abstinence in the household was related to short-term abstinence. Finally, there was a significant association between the change from baseline to 3-month assessment for the ASI Employment composite scale and the CAI Friends scale (p = .04) for the in-treatment group. These preliminary findings suggest that heroin-addicted individuals entering treatment perceive more social support than those addicts not entering treatment; and, that such support may be important to behavior change in drug use and employment.

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397 MORTALITY OUTCOMES AMONG HEALTHY YOUNG ADULTS WHO USE ILLICIT DRUGS (THE CARDIA STUDY)

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BACKGROUND: The long-term mortality risk of young adult drug use is little-studied. The longitudinal Coronary Artery Risk Development in Young Adults study (CARDIA) allowed us to test whether illicit drug use was associated with mortality over the next 17 years. **METHODS:** A young adult cohort (n=4547) was recruited in 4 cities, assessed for drug use in 1987/88, and mortality data obtained through 12/31/04. Participants reported current (last 30 days) and past use of illicit drugs, as reported in 1987/88 (cocaine, amphetamines, opiates, and marijuana), and were grouped as: Never Use (n=1173), Past Use only (n=2170), Current Marijuana only (n=802, 18%) and Current Hard Drugs (opiates, cocaine, amphetamines, n=404). Proportional hazards models adjusting for baseline characteristics (age, sex, race, alcohol, tobacco, economic status, education, marital status, self-reported general health, body mass index, physical activity, social support, chronic medical conditions, and mental illness). **RESULTS:** Mean age in 1987/88 was 27 (SD 3.5) years (range 20-32), 55% female, 49% black. Among Current Hard Drugs, 3.7% of Current Marijuana, 2.6% of Past Use and 2.0% of Never Use (p<0.01). This apparent association was explained by characteristics independently associated with mortality, such as chronic illness (HR 1.5, 95% CI 1.2-1.8), mental illness (HR 1.9, 1.1-3.1), and African-American race (HR 2.0, 1.3-2.9). Adjusted HR's, by drug use in 1987/88, relative to Never Use, were: Current Hard Drugs (HR 1.2, 0.8-2.0), Current Marijuana (HR 1.2, 0.7-2.2), Past Use (HR 1.0, 0.5-2.0). **CONCLUSIONS:** Drug use was not independently associated with 17-year mortality among young adults. (NIDA-K23-DA-15487; NHLBI N01-HC-95095)

398 GENDER DIFFERENCES IN THE EFFECT OF BIRTH COHORT ON RISK FOR ALCOHOL AND DRUG DEPENDENCE

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Due to dramatic changes in drug and alcohol use patterns in the U.S. during the 1960s and 1970s, rates of alcohol and drug dependence in this country increased among individuals who came to the age of risk during or after this period. The impact of these changes on gender differences in the prevalence of alcohol and drug dependence is poorly understood, but has important implications for our understanding of these disorders. We hypothesized that birth cohort and gender would interact to show a differentially increased risk for substance dependence in women born after 1950. Data analysis was conducted using a large, nationally representative sample, using in-person interviews with 43,093 adults aged 18 and older living in households or group quarters in the U.S. Odds of alcohol and drug use and DSM-IV diagnosed dependence stratified by gender and birth cohort, defined as before or after 1950. Only individuals born after 1950 came of age during the period when use of alcohol was more socially acceptable and drugs were more widely available. Results indicated that in the full sample, men and subjects in the younger cohort (born after 1950) are significantly more likely to have substance dependence. However, the proportion of women with a substance use disorder is rising among the younger cohort. There was a significant interaction of birth cohort and gender in the prediction of alcohol use (beta = -0.35 [SE=0.07], p<0.0001), drug use (beta = -0.31 [SE=0.07], p=0.0001), lifetime alcohol dependence (beta = -0.62 [SE=0.09], p<0.0001), and lifetime drug dependence (beta = -0.56 [SE=0.25], p=0.03). Gender-specific odds ratios indicated increased odds of use and dependence for both genders in the younger cohorts, but ORs were greater among women than among men indicating a closing gender gap in the prevalence of alcohol and drug use and dependence. These results suggest that sex differences in the prevalence of drug and alcohol dependence are decreasing in younger age cohorts due to larger increases in prevalence among women than men; young women may be in need of targeted prevention and treatment plans.

399 DIFFERENTIAL EFFECTS OF MIXED NOP/MU RECEPTOR LIGANDS IN ANTINOCICEPTION AND REWARD IN MICE

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In the course of our program to develop NOP ligands we have synthesized compounds showing agonist and/or antagonist activity at the mu and NOP receptors. The behavioral effects of SR16435, a mixed high affinity NOP/mu receptor agonist, with low efficacy at both receptors, was compared to SR14150, a mixed NOP agonist/ mu antagonist with higher selectivity for the NOP receptor (30-fold relative to mu receptors). It was hypothesized that lower efficacy mixed NOP/mu opioid ligands would produce analgesia and yet unlike morphine would have diminished rewarding properties. Antinociception was assessed in mice using the tail-flick assay, whereas behavioral and rewarding effects were assessed using the place conditioning (PC) paradigm. To establish PC, drug injections were paired with one of two distinct compartments, whereas saline injections were paired with the other compartment. Behavioral effects were measured following acute and repeated drug administration during conditioning, and the test for PC was carried out 24 h following the last conditioning day. Both SR16435 and SR14150 produced an increase in tail flick latency with a similar ED50 of approximately 20 mg/kg. Maximal antinociceptive effects induced by both ligands were lower compared to morphine. SR16435 induced a conditioned place preference (CPP), reflecting the rewarding effects of the drug. Although the NOP agonist activity did not block CPP, NOP agonist activity was present, as the mu-mediated increase in global activity (as observed with morphine) was not present, and in fact SR16435 was initially sedative. However, following repeated administration, SR16435-induced sedative effects were not present. Unlike SR16435, SR14150 administration produced sedative effects following both acute and repeated administration and did not produce CPP. In conclusion, it seems that SR14150 a mixed NOP agonist/ mu antagonist displays a promising profile as a sedative analgesic since it has antinociceptive activity yet does not seem to have any rewarding properties.

400 TREATMENT-RELATED REDUCTION IN HIV SEXUAL RISK BEHAVIOR: A CTN SECONDARY ANALYSIS

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Several studies have shown that substance abuse treatment reduces HIV risk taking behavior, especially in methadone maintained populations. Less is known about HIV sex risk behavior in non-methadone treatment populations, or about differential risk behavior change associated with various treatment modalities. The present study included a large heterogeneous population of stimulant abusers in non-methadone psychosocial treatment programs, representative of the typical patient presenting at community treatment programs across the country. Treatment-seeking stimulant abusing outpatients were randomized to receive motivational incentives (MI) plus treatment as usual (TAU) or treatment as usual alone for 3 months. HIV risk behavior was assessed at baseline, 1,3, and 6 months using the HIV Risk Behavior Survey (HRBS). Data were examined using both parametric and non-parametric statistics for the N=343 who participated in both baseline and 12 week HRBS assessment. The entire study sample showed a decrease on the HRBS sex risk behavior score from 3.9 (4.0) at baseline to 3.4 (3.3) at 6-months (p=0.03). There were no statistically significant differences observed using the change in HRBS sex score between MI and TAU (p=0.85). A test of symmetry for the number of casual sexual partners (0, 1, 2+) reported at baseline compared to post test suggests a reduction in prevalence of multiple partners over time (p=0.03). Specifically, 36%, 50% and 15% had 0, 1 or 2+ partners at baseline. After treatment, this distribution was 36%, 55% and 9%, respectively. There were no changes in condom use profile over the course of the treatment. Therefore, the reduction in sexual risk behavior scores appears related primarily to the reduction in multiple partners.

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401 ADHERENCE TO A 30-DAY BUPRENORPHINE DETOXIFICATION IN A PUBLIC PROGRAM

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Within the context of a NIDA-funded study examining issues in improving treatment engagement, an urban community-based clinic established a 30-day, outpatient buprenorphine detoxification for heroin-addicted adults, thus providing an opportunity to examine the response to such treatment of public program patients. Of the 52 participants (100% African American, 48% male) who started the detoxification to date, 42 had the potential to complete it and are included in the analysis. Suboxone™, a tablet combining buprenorphine and naloxone, was administered sublingually. Medication was dispensed at the clinic on a daily basis for the first week, with peak dose achieved within the first 2- to 6-days depending on the dose required to control withdrawal symptoms based on the physician's judgment. Weekly take-home doses were dispensed during the maintenance phase (lasting 19- to 22-days) and the dose reduction phase (lasting 5- to 7-days). Patients were scheduled to meet with the physician or nurse once per week. They met with their treatment counselors for individual sessions once per week and attended group counseling sessions 5 times per week during detoxification. The average maximum dose of buprenorphine achieved was 14.8 mg (SD = 2.2; range: 12 mg to 16 mg). Of the patients who could have completed detoxification to date, 88% completed the first week, 81% completed the second and third weeks, and 60% completed the entire detoxification. Forty-nine percent of patients attended three or more of their scheduled individual counseling sessions. Patients also had high rates of adherence to medical and nursing visits. Moreover, 40% of the patients who completed the detoxification attended at least one session of drug-free treatment following detoxification. These preliminary findings suggest the willingness of heroin-addicted clients to engage in and complete an extended buprenorphine detoxification and thus support the feasibility of implementing a 30-day buprenorphine detoxification within a community-based clinic.

402 ENCOURAGING ADOPTION OF METHADONE MEDICAL MAINTENANCE: A TECHNOLOGY TRANSFER STUDY

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Methadone medical maintenance (MMM) is an effective intervention that minimizes the intrusiveness of opioid agonist treatment without compromising good treatment response. Despite the benefits of MMM to both patients and treatment programs, little information is available to help community-based programs implement MMM and select patients who might benefit from this intervention. The present study evaluates the impact of an 8-session training seminar on the opinions of community-based treatment staff (n = 107) in five programs in Baltimore, Maryland regarding both the adoption of an MMM protocol and the use of an adaptive stepped care model to deliver it. The training sessions were developed based on results from a recently completed randomized clinical trial (King et al., 2002) together with other studies of MMM to help program staff: 1) understand the risks and benefits of MMM, 2) develop criteria to choose who may benefit from MMM, and 3) implement an adaptive stepped care delivery system that includes MMM as the least restrictive level of care. A survey of clinic staff opinion about MMM and stepped care delivery was administered at baseline, 6-months, and 12-month post study initiation. Overall, the training sessions were rated highly favorable for content and presentation (3.3 on a 4-point scale). At the 12-month follow-up, staff were more likely to believe that MMM facilitates patient participation in positive community activities (p=.003) and were more likely to support treatment that matches patients who are stable with minimal intensities of care (p=.035). One clinic modified their routine care to an adaptive stepped care model in response to the sessions. The results suggest that training sessions may be a beneficial mechanism for helping staff at community-based programs appreciate and adopt effective interventions developed and tested using rigorous research designs.

403 EXAMINATION OF DUALY DIAGNOSED PATIENTS' PARTICIPATION IN A CONTINGENCY MANAGEMENT PROGRAM

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Contingency management (CM) programs have demonstrated effectiveness in reducing substance use in primary substance users. However, relatively few studies have examined CM to reduce substance use in patients with severe mental illness (SMI). Studies of CM programs in SMI patients generally demonstrate their feasibility in reducing cigarette smoking, alcohol, marijuana, and cocaine use. However, most studies do not provide a description of the relationship of participants' characteristics to their level of engagement and participation in CM programs. An understanding of patient characteristics that are related to participation could inform how to design these programs for optimal effect. In the present study, we examined how the demographic and clinical characteristics of 59 patients with SMI and heroin or cocaine dependence were related to participation in the CM component of an integrated treatment. The CM procedures included patients receiving social reinforcement and incremental monetary rewards (\$1.50 to \$3.50) for providing negative urine samples at the beginning of each treatment session. Participation in the CM program was defined as engagement (session received first reward), level of reward achieved (average payment received), and overall participation (number of sessions paid over number of opportunities for reward). Mean differences in the participation measures were tested for each demographic variable using t-tests; separate bivariate regressions were tested for each clinical variable. Results show demographic characteristics generally not related to participation. Several clinical variables, including a diagnosis of schizophrenia, co-morbid alcohol dependence, severity of psychiatric symptoms, and severity of current substance use were related to lower engagement and participation. These results indicate that clinical characteristics of dually-diagnosed patients may predict their response to CM for reduction of illicit substance use.

404 ENHANCED COCAINE-INDUCED INCREASES IN DOPAMINE AND GLUTAMATE WITHIN THE NUCLEUS ACCUMBENS OF PRENATALLY STRESSED RATS

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Early environmental events have profound influences on a wide range of adult behaviors, including addiction liability. Previously, we found that rats subjected to prenatal stress have a modest enhancement in cocaine self-administration and a robust enhancement in cocaine-primed reinstatement of cocaine-seeking. In the current study, we assessed the influence of maternal stress during gestation on the neurochemical response to experimenter-administered cocaine in adult offspring. Pregnant female Sprague-Dawley rats were subjected to either no treatment or to restraint stress three times per day for the last 7 days of gestation. Control and prenatally-stressed male litter-mates were housed 2-3 per cage until they were 10 weeks of age, at which time they were implanted with cannula directed toward the nucleus accumbens. Following recovery from surgery, a microdialysis probe was inserted into the nucleus accumbens, then each male was injected with cocaine (15 mg/kg, i.p.). Samples were analyzed using HPLC for glutamate and dopamine levels. Control rats showed an increase in extracellular levels of dopamine but not glutamate in response to the cocaine injection, whereas prenatally-stressed rats displayed an enhanced capacity of cocaine to elevate accumbens dopamine and glutamate compared to controls. These findings indicate that early environmental insult can influence the neurochemical response to stimulant drugs in adulthood and may contribute to an individual's propensity to substance abuse. Supported by NIDA R03 DA021161 to TEK.

- 405 DIFFERENCES IN COCAINE USE AMONG METHADONE MAINTENANCE PATIENTS RECEIVING STANDARD VS. EXTENDED PERIODS OF ABSTINENCE-BASED REINFORCEMENT: AN INTERIM ANALYSIS**
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Basic behavioral research suggests that successful long-term behavior change does not focus on undoing old behaviors, but concentrates on developing new behaviors. This model predicts that in order to achieve long-term behavior change, patients must experience a sufficient duration of drug abstinence to develop new behaviors that are incompatible with drug use and that the new behaviors must have naturally-occurring sustaining contingencies. Despite the effectiveness of abstinence-based reinforcement interventions in initiating drug abstinence, the majority of these interventions are implemented for only 3 months. We are examining the effects of extending the duration of abstinence-based reinforcement. We randomly assigned cocaine-dependent methadone maintenance patients in community-based treatment to receive either a standard 3-mo. or an extended 9-mo. escalating schedule of voucher reinforcement for urinalysis-verified cocaine abstinence. In both groups, this was followed by a 3-mo. aftercare condition where a \$1 lottery ticket was delivered per cocaine-negative urinalysis test. Interim analyses of the first 6 months of treatment indicated a significant time x condition interaction ($F(4,25) = 4.34, p = .003$) with differences in cocaine abstinence emerging after 3 months. A precipitous drop-off in abstinence levels occurred for the standard group when the vouchers were discontinued. There was a trend toward longer maximum durations of cocaine abstinence in the extended group (mean = 5 wks) compared to the standard group (mean = 2 wks). These results suggest that in the context of community-based methadone maintenance treatment, 3 months of voucher treatment did not produce extended durations of cocaine abstinence and it is unlikely that new behaviors developed to compete with drug use.
- 406 INHIBITORY EFFECTS OF MECAMYLAMINE ON SERUM CORTICOSTERONE INCREASE PRECIPITATED BY NALOXONE IN MORPHINE-DEPENDENT MICE**
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The suppression of opioid analgesic withdrawal signs is quite important for the therapy of opioid abuse or withdrawal from clinically prescribed opioid analgesics. There are several lines of evidences that some drugs, e.g., L-type calcium channel blockers, alpha 2-adrenoceptor agonists, N-methyl-D-aspartate receptor antagonists among others, suppresses the occurrence of morphine-withdrawal signs in rodents. In this study, we examined the effects of mecamylamine, a nicotinic receptor antagonist, on naloxone-precipitated morphine withdrawal in ICR mice. We first examined the ability of mecamylamine and naloxone to antagonize the CS increases produced by a single injection of nicotine and morphine. Blood samples for the CS assay were collected 30 min after nicotine or morphine administration. The CS levels were elevated by the injection of nicotine (0.3 - 1 mg/kg) and morphine (3 - 10 mg/kg) in a dose-dependent manner. The nicotine-induced CS increase was antagonized by mecamylamine (1 mg/kg), but not by naloxone (1 mg/kg). On the other hand, the morphine-induced CS increase was antagonized by naloxone, but not by mecamylamine. We then examined the effects of mecamylamine on naloxone-precipitated CS increase in morphine dependent mice. Physical dependence was developed by the repeated administration of morphine (20 mg/kg, twice a day for 4 days). On day 5, morphine withdrawal was precipitated by naloxone (1 mg/kg). Blood samples were collected 30 min after naloxone and mecamylamine was administered 30 min before naloxone. Naloxone-precipitated CS increase was inhibited by pretreatment with mecamylamine (0.3 -1 mg/kg). These results suggest that nicotinic system may be involved in the CS increase precipitated by naloxone, but not in that induced by a single morphine dose.
- 407 WHAT ARE THE SPECIFIC COGNITIVE EFFECTS OF TRANSDERMAL NICOTINE AND SMOKING, AND DO THEY DEPEND ON SMOKER'S GENDER?**
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Cognitive performance is impaired by tobacco abstinence and reinstated by smoking or nicotine replacement therapy (e.g., transdermal nicotine; TN). The specific cognitive processes that underlie these effects, and whether they depend on smokers' gender, have not been determined. The purpose of this laboratory study was to use process-specific cognitive tasks to examine potential gender differences in response to TN and smoking in overnight-abstinent smokers. Participants (70 men, 54 women) completed four, 6.5-hour sessions in which TN was administered double-blind (0, 7, 14, or 21 mg, randomized across sessions) and a cigarette was smoked four hours later. Women participated during menstrual cycle days 2-16 to control for premenstrual symptomatology. Attention (alerting, orienting, and executive function) and spatial and verbal working memory performance were measured regularly, as were subjective effects, heart rate, and plasma nicotine. Three-factor ANOVA (dose, pre/post cigarette, gender) revealed that TN or smoking improved performance on different cognitive tasks. For example, active TN improved spatial working memory (e.g., mean correct response for 0 mg = 57%, 7 mg = 60%, 14 mg = 61%, 21 mg = 62%). Improvements in alerting and verbal working memory accuracy were only found after participants smoked, regardless of TN condition. TN and smoking reduced tobacco/nicotine abstinence effects and increased heart rate and plasma nicotine. Smoking-related changes in heart rate were smaller as TN dose increased (e.g., mean beats/minute of 13.9 for 0 mg, 6.3 for 7mg, 4.6 for 14mg, and 3.3 for 21 mg). No significant interactions involving the gender factor were observed on any cognitive or physiological outcome measure. In abstinent smokers, the cognitive effects of TN and smoking may differ, and do not depend on smokers' gender. Addressing impairments in alerting and verbal working memory may be important when supplementing TN-assisted smoking cessation.
- 408 VIOLENCE EXPOSURE, COPING PROCESSES, AND DRUG AND ALCOHOL USE IN EARLY ADOLESCENCE**
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Associations between witnessing and experiencing community violence, processes of coping with violence, and drug and alcohol use were investigated with 181 adolescents (51.4% female) from the first wave of a longitudinal study of risk and protective factors for drug use. Fifth and eighth graders ages 9-16 and their maternal caregivers participated. Most were African American and lived in high violence areas of a mid-sized city. Youth and their caregivers completed separate home interviews lasting 2-3 hours. The Problem Behavior Frequency Scale (PBFS) and the Personal Experiences Inventory (PEI) were used to assess substance use. The Survey of Exposure to Community Violence was used to assess witnessing and experiencing violence, and the Children's Coping Strategies Checklist (CCSC) and a measure of threat appraisals captured coping processes. In the past 30 days, 7.8% of the fifth graders and 31.3% of the eighth graders reported some alcohol or drug use. Results of logistic regression analyses indicated that after accounting for sex and age, both of which were significant, witnessing violence ($B = .08, SE = .03, Wald = 5.96, p < .02$) and victimization ($B = .39, SE = .14, Wald = 8.22, p < .004$) each were associated with past month drug use. Cognitive decision making coping ($B = -.37, SE = .11, Wald = 11.15, p < .001$) and threat of negative evaluation by others ($B = .22, SE = .10, Wald = 5.05, p < .03$) also contributed to early adolescent drug use. Hierarchical regression analyses with severity of problems with drug use as the outcome indicated that witnessing violence ($B = .11, SE = .04, b = .25, p < .003$) and cognitive decision making coping ($B = -.20, SE = .08, b = -.19, p < .02$) were the only two significant correlates. These findings suggest that coping processes contribute to our understanding of adolescent drug use beyond exposure to stressors. Interventions to reduce adolescent drug use should focus on both appraisals of and coping responses to stressors.

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- 409 ABUSER-REPORTED SOURCES OF ILLEGALLY OBTAINED OPIOID ANALGESIC MEDICATIONS**
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Illegally obtained opioid medications present an ongoing and challenging dilemma to society at large, while also impacting the legitimate prescribing of opioids for those individuals with moderate to severe chronic pain conditions. The principal purpose of this analysis was to ascertain how opioid analgesic abusers obtained their drug. Data were obtained from a cross-sectional, structured, self-report questionnaire administered at intake to individuals at 69 US methadone maintenance treatment programs (MMTPs) between January 2005 – September 2005. Of the 5,803 respondents, 59% reported an opioid analgesic as their primary drug of abuse within the past month. The most commonly reported sources for obtaining opioid analgesics included: dealers (81.6%), friends or relatives (50.4%), physician prescription (30.5%), emergency room visits (13.9%), theft (6.2%), forged prescription (2.9%), internet (2.4%), and other (not specified) (3.1%). Despite media reports suggesting that the internet is a primary source for illegally obtained prescription opioids, only a small percentage of opioid analgesic abusers reported this as a source of their drug supply.
- 410 A COMPARISON OF HOMELESS SUBSTANCE-ABUSING INDIVIDUALS ENTERING THE VA HOMELESS SERVICE AND STATE SHELTER SYSTEMS**
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Background: Despite considerable research on the demographic and psychosocial characteristics of homeless populations, few studies have identified characteristics unique to homeless veterans. Using data from two SAMHSA-funded studies of the homeless in New Jersey, this study compared the demographic and risk factor profiles of VA and non-VA homeless substance abusers to inform VA service planning. Methods: Data were collected on 119 homeless, substance abusing veterans enrolled in the MISSION Program, a SAMHSA-funded project aimed at helping veterans transition from NJ VA Domiciliary care into the community. Veterans were compared on demographic characteristics, substance use histories, and childhood experiences to a sample of 202 substance abusers residing in NJ homeless shelters. Homeless shelter data were obtained as part of a SAMHSA-funded study of addiction treatment need in NJ. Results: Compared to homeless shelter residents, homeless veterans were older, more likely to be male, better educated, and actively seeking employment. They were less likely to be learning disabled (5% vs. 15%) and became homeless substantially later in life (mean age 38.2 vs. 28.5). Veterans were also less likely to have used heroin (41% vs. 54%). Although veterans were more likely to have been raised by their natural mothers, they were more likely to report family alcohol abuse (67% vs. 53%), mental health problems in family members (20% vs. 7%) and a history of family violence (34% vs. 27%). Veterans also reported that their substance abuse problems began during, or were exacerbated by, their military service. Conclusions: Although homeless substance abusing veterans appeared to have more educational and cognitive resources than NJ substance abusing shelter residents, they reported greater family risk factors involving substance abuse, mental illness, and violence. This comparative study shows specific deficits and strengths unique to homeless veterans that can be used in planning appropriate and effective services for this population.
- 411 MEDICATION ADHERENCE AMONG HIV-POSITIVE METHADONE PATIENTS: ANALYSIS OF A NEW STATISTICAL TOOL**
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One of the key issues in assessing the efficacy of treatments designed to improve adherence to prescribed medications schedules is adherence measurement. Research has demonstrated that HIV-positive drug users have difficulty adhering to complex highly active antiretroviral therapy regimens, which is essential to successful treatment outcomes. Recently, Knafl, et al. (Statistics in Medicine, 2004, 27:783-801) proposed a method using adaptive Poisson regression models to capture adherence levels from electronic pill-bottle monitoring devices. We examine the use of this methodology in an extensive analysis of data from a 20-week randomized clinical trial designed to test the effects of vouchers on improving medication adherence among HIV-positive methadone maintenance patients. Adherence is modeled not only in the 66 randomized participants but also 17 subjects who were enrolled but demonstrated sufficient adherence during the baseline period. Fitted plots display changes over time and treatment effects consistent with the more standard analysis of “percent taken on time.” The predicted values from the Poisson models were clustered via an extensive search among clustering methods and those results were compared to a solution based on finite mixture modeling. The clustering identified the more extreme cases while the mixture modeling reflected levels of adherence. The mixture-modeling placed subjects into low, intermediate, and high adherence groups while the clustering-method tended to generate compatible but finer adherence groups. Results replicate the primary finding that the use of vouchers improved adherence rates. The use of an already adherent group helps to confirm the findings. Improvements in the methodology are shown and factors associated with medication adherence in HIV-positive methadone patients are discussed. Funded by P50-DA009253 and R01-AI057043.
- 412 PREDICTORS OF COCAINE ABSTINENCE IN INJECTION-DRUG-USING METHADONE PATIENTS EXPOSED TO EMPLOYMENT-BASED ABSTINENCE REINFORCEMENT**
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Employment-based abstinence reinforcement, like other abstinence reinforcement interventions, has been effective in some, but not all participants. Predictors of cocaine abstinence were examined in individuals exposed to such an intervention. Unemployed injection drug and cocaine using adults in methadone treatment were invited to attend the workplace 4 hours every weekday; earning hourly base and productivity pay vouchers. Participants who provided consistent cocaine-positive samples (collected 3 days per week) during a 4-week baseline were randomly assigned to a Work Only (WO; n=28) or Abstinence & Work group (AW; n=28) and invited to attend the workplace for a 26-week intervention period. AW participants were required to show recent cocaine abstinence to work and earn maximum base pay. The percent of cocaine negative samples was significantly higher in the AW group. AW participants appeared to achieve a dichotomous outcome, either achieving substantial cocaine abstinence (> 60% negative; “Responders”) or not (“Nonresponders”). Within AW participants, the percentage of baseline cocaine negative samples ($r = 0.41$, $p = .028$) and baseline opiate negative samples ($r = 0.56$, $p = .002$) were correlated with the percentage of cocaine negative samples during the intervention period; but neither the mean baseline benzoylcegonine values nor the percentage of minutes worked during baseline were correlated. Responders and Nonresponders were compared on the same four variables and differed in the percentage of baseline opiate negative samples (92% vs. 51% respectively; $p < .001$) and in the percentage of minutes worked during baseline (69% vs. 58% respectively; $p = .042$), but did not differ on the other variables. These results suggest that more aggressive treatment of opiate use and manipulation of factors that increase workplace attendance prior to implementing employment-based contingencies for cocaine abstinence may improve cocaine abstinence outcomes.

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- 413 THE CLINICAL TRIALS NETWORK AND TREATMENT INNOVATIONS: DIFFERENCES IN COUNSELOR ATTITUDES TOWARD BUPRENORPHINE**
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The National Institute on Drug Abuse's Clinical Trials Network (CTN) conducts multi-site clinical trials and aims to diffuse evidence-based treatment techniques into the treatment field. A critical research question is whether involvement in the CTN has implications for the attitudes of clinicians toward innovative practices. One such innovation is buprenorphine, which is FDA approved for the treatment of opiate dependence and has been the subject of multiple CTN clinical trials. This research compares CTN counselors and non-CTN counselors on their perceptions of the acceptability of buprenorphine. Hypothesis: Counselors affiliated with the CTN will perceive buprenorphine to be more acceptable than non-CTN counselors. Methods: Data were collected via mailback questionnaires from 681 counselors in CTN-affiliated centers and 2265 counselors in non-CTN facilities. Separate OLS regression analyses were conducted for privately funded and publicly funded centers, although the substantive results were similar across the two samples. Results: There was a significant positive bivariate association between CTN affiliation and perceived acceptability of buprenorphine. The addition of counselor characteristics, including educational attainment, certification in addiction counseling, personal recovery status, and 12-step orientation, did not mediate the association between CTN affiliation and perceived acceptability of buprenorphine. This difference was completely mediated by the addition of two variables to the model: specific training on buprenorphine and the routine use of buprenorphine at the center. Notably, CTN-affiliated counselors reported significantly greater amounts of training and greater implementation of buprenorphine. Conclusions: These data suggest that CTN counselors perceived buprenorphine to be more acceptable than non-CTN counselors, but this difference was explained by greater training and implementation in CTN-affiliated centers. Supported by NIDA R01 DA13110 and NIDA R01 DA14482.
- 414 THE MECHANISMS UNDERLYING THE BEHAVIORAL EFFECTS OF GAMMA-HYDROXYBUTYRATE AND BACLOFEN ARE NOT IDENTICAL: DIFFERENTIAL ANTAGONISM BY THE GABA_B RECEPTOR ANTAGONIST CGP35348**
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GHB is used to treat narcolepsy, but is also used as a "club drug". Although GHB has many actions in common with the GABA_B receptor agonist baclofen, there is evidence that their effects and underlying mechanisms are not identical. For example, their discriminative stimulus effects appear to be different, because rats can discriminate GHB from baclofen (Koek et al., JPET 314:170, 2005). Different underlying mechanisms are suggested by the finding that the GABA_B receptor antagonist CGP35348 less potently antagonized GHB than baclofen (Koek et al., JPET 308:904, 2004). The present studies were aimed at 1) quantifying the ability of CGP35348 to antagonize behavioral effects of GHB and baclofen, and 2) further examining the generality of the differential antagonism of GHB and baclofen by CGP35348. The antagonist effects of CGP35348 were quantified in pigeons trained to peck a response key. Schild analysis showed that CGP35348 was 4-6 times less potent to antagonize the response rate-decreasing effects of GHB and its precursor GBL (pA₂: 3.9 and 4.0, respectively) than those of the GABA_B receptor agonists baclofen and SKF97541 (pA₂: 4.6 and 4.7, respectively). In mice, GHB, GBL, baclofen, and SKF97541 all produced catalepsy. At a dose of 100 mg/kg, CGP35348 significantly shifted the dose-response curves of baclofen and SKF97541 to produce catalepsy to the right. However, 320 mg/kg CGP35348 was needed to significantly shift the dose-response curves of GHB and GBL. The finding that CGP35348 is a more potent antagonist of baclofen and SKF97541 than of GHB and GBL suggests the involvement of different GABA_B receptor subtypes, and/or non-GABA_B receptors, in their effects. Studying differences between GHB and baclofen may help to understand why GHB is effective for treating narcolepsy, and is abused, whereas baclofen is not. Supported by DA15692 (WK), DA19634 (AC), and DA17918 (CPF)
- 415 CHARACTERIZATION OF L-891,190, A NOVEL GABA_AERGIC COMPOUND**
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Anxiolytics that have less abuse liability than BZs are being sought using varying in vitro GABA_Aergic efficacy. Drug discrimination is a uniquely powerful model for comparing and contrasting interoceptive/subjective drug effects. Rats were trained under a 2-lever discrimination procedure with either zolpidem(ZOL)(n=5), lorazepam(LRZ)(n=6), TPA023(n=6), or L-891,190 (n=6) to determine whether differential efficacy at GABA_A receptor subtypes results in differences in behavioral profile. These drugs positively modulate GABA via the BZ binding site on GABA_A receptors. LRZ is nonselective; ZOL preferentially binds subtypes containing alpha1 subunits; TPA023 and L-891,190 bind all subtypes, but show efficacy at only alpha2 and 3-containing subtypes; L-891,190 is more efficacious at alpha3. ZOL, LRZ, and TPA023 groups were trained to discriminate drug from no-drug in 80% drug lever responding in the same dose range. Perhaps due to its long elimination half-life, L-891,190 tests dose-dependently increased the number of sessions to meet criterion in all three groups. The LRZ generalization gradient was shifted to the left after testing with L-891,190 and interaction tests shifted the LRZ curve to the right. These results are consistent with previous findings that the LRZ training condition is selective for compounds with full efficacy at alpha1 subtypes and demonstrates for the first time that the LRZ discriminative stimulus depends on alpha1 efficacy. The data also suggest that the ZOL training condition depends on alpha1 efficacy. That L-891,190 is behaviorally active at the tested doses is shown by its sharing discriminative effects with TPA023. Failure to train L-891,190 suggests that greater efficacy at alpha3 subtypes results in fewer interoceptive stimulus/subjective effects, but the pharmacokinetic profile of L-891,190 may play a significant role in this regard.
- 416 SUBJECTIVE EFFECTS OF METHYLPHENIDATE IN ADULTS WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER**
S. H. Kollins, J. English and H. Ravi, Duke University Medical Center, Durham, NC
MPH is widely used to treat ADHD, but also exhibits abuse liability comparable to other stimulants. However, the abuse liability of MPH in patients with ADHD has not been assessed. The goal of this pilot study was to assess the subjective effects of MPH in adults with and without ADHD. Adults with ADHD (N = 2) and with no psychiatric diagnoses (N = 2) received both 40 mg MPH (p.o) and matching placebo capsules on separate days under double blind conditions. Subjective effects were assessed every 30 minutes for 4 hours after dosing using: an 11-item Visual Analog Scale (VAS), a 32 item Adjective Rating Scale (ARS) comprised of two factors (Stimulant and Sedative), and a Stimulant Side Effects Rating Scale (SERS). Vital signs were also collected. Two-way, mixed ANOVA with group (ADHD versus Control) and dose (40 mg versus placebo) as the between and within subjects factors, respectively was used to analyze peak effects for each measure. On the VAS, 5 items showed at least trends for main effects of dose (40 mg > 0 mg): Feel Drug, Feel Good Effects, Feel Bad Effects, Like Drug, and Alert (p = 0.01 - 0.09). Three items showed significant Group x Dose interactions (Control > ADHD for 40 mg): Feel Drug, Like Drug, and Alert (p = 0.04 - 0.06). There was also a significant main effect of Group on Would Like to Take Drug Again (Control > ADHD; p = 0.01). On the ARS, there was a main effect of group for the Stimulant Scale (Control > ADHD; p = 0.04). There was a main effect of group for Loss of Appetite on the SERS (ADHD > Control; p = 0.02) and main effects of dose for systolic and diastolic blood pressure (40 mg > 0 mg; p = 0.05). These data suggest that individuals with ADHD may not experience the same subjective effects of MPH as their non-diagnosed peers. This may be related to differences in dopaminergic functioning between the two groups. These findings have important implications for testing abuse liability of drugs used to treat ADHD. This study is ongoing and we expect to have 8 subjects in each group for final analysis before the CPDD meeting.

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- 417** COMPARISONS OF THE IN VITRO BINDING OF [³H]WIN 354,428 WITH [³H] JHW 007, A DOPAMINE TRANSPORTER LIGAND THAT BLOCKS THE EFFECTS OF COCAINE
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The binding site through which cocaine produces its effects, the dopamine transporter (DAT), is shared by bupropion (BZT) and its analogues. However, BZT analogues which have high affinity for the DAT generally do not have behavioral effects substantially similar to those of cocaine. JHW 007 is a BZT analogue that displaces [³H]WIN 35,428 from the cocaine binding site with a 7-fold higher affinity than cocaine in the rat. As a pretreatment, JHW 007 reduces the behavioral effects of cocaine in mice. In vivo binding studies with mice indicate a high potency with a relatively slow apparent association and long duration of action at the DAT in striatum. In the present study the in vitro binding of [³H]JHW 007 was compared to that of [³H]WIN 35,428 in both rats and mice. WIN 35,428 binding was better fit to a one-site than two-site model, with KD values of 5.34 and 8.99 nM in rat and mouse, respectively. In contrast, the binding of [³H]JHW 007 was better fit to a two-site model with Hi-/Lo-affinity KD values of 12.5/9840 and 11.1/9680 nM in mouse and rat respectively. As with [³H]WIN 35,428, drugs with selectivity for the norepinephrine and serotonin transporters had relatively low affinity in displacement of [³H]JHW 007 binding. The association of [³H]WIN 35,428 was best fit by a one-phase model which yielded 1/2-life values of 2.82 and 2.94 min, in rat and mouse respectively. In contrast, the association of [³H]JHW 007 was best fit by a two-phase model, which overall combined was slower in either species than that for [³H]WIN 35,428, despite one phase of JHW 007 association being substantially faster than that for [³H]WIN 35,428. The dissociation of [³H]JHW 007 was about 3 to 4 times slower than that for [³H]WIN 35,428 in either species. Taken together the data suggest several differences in the binding parameters of JHW 007 and WIN 35,428, which may be related to the in vivo pharmacological actions of JHW 007.
- 418** REDUCED VISUAL AND AUDITORY BRAIN ACTIVATION IN COCAINE ABUSERS
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Many PET and SPECT studies of cocaine abusers (CA) during the past 20 years report reduced cerebral perfusion (rCBF) in several brain regions. We clarified the pathophysiology of rCBF reductions in the occipital and temporal cortex by concurrent SPECT and functional MRI (fMRI). First, we compared rCBF at rest in 41 CA to 20 controls using SPECT and found significant decreases of over 400 voxels each in the left middle occipital gyrus, left frontal supplementary motor and eye field cortices, and cerebellum (p < 0.0001). Eight of these male CA were compared to controls using fMRI during sad and cocaine cue videotapes. Although both groups reported equivalent sadness, the CA had significantly reduced brain activation in occipital and temporal (auditory) regions (P < 0.01) to sad tapes. Only the CA reported any subjective response to the cocaine tapes, but the CA still showed somewhat less occipital activation. Thus, primary visual and auditory cortices of CA are significantly inactive during emotionally charged experiences and may be relatively hypoactive even when craving cocaine. (NIDA P50-DA12762, K05-DA00454)
- 419** STRAIN DIFFERENCES IN REINFORCED AND NON-REINFORCED RESPONDING FOR COCAINE
T. A. Kosten, X. Y. Zhang and C. N. Haile, Yale University School of Medicine, West Haven, CT
We demonstrated that Lewis and Fischer 344 (F344) inbred rats differ in cocaine self-administration. Compared to F344 rats, Lewis rats acquire cocaine self-administration more readily but respond at lower levels under certain maintenance conditions (low fixed-ratio schedules; moderate doses). Now, we examine cocaine responding across several doses and under both fixed- and progressive-ratio schedules and include a Sprague-Dawley (SD) comparison group. Rats were trained to lever press for cocaine (0.5 mg/kg/infusion) under a fixed-ratio 3 (FR3) schedule of reinforcement in 3-hr sessions (10-sec infusion time; 5-sec time-out). Tests were conducted under the FR3 schedule across several cocaine doses (0.0626-1.0 mg/kg/infusion) and under a PR schedule (vehicle, 1.0 mg/kg/infusion). Numbers of self-administered infusions and non-reinforced presses (emitted during infusion and time-out periods) were tabulated. All strains showed dose-related responding under the FR3 schedule and respond more for cocaine than vehicle under the PR schedule. Under the FR schedule, F344 rats self-administered more cocaine than Lewis and SD rats and show greater non-reinforced responding. There were no strain differences under the PR schedule. Together with our previous work, results of the present study demonstrate that F344 rats are slower to acquire cocaine self-administration but once behavior is established they maintain responding at higher levels than either Lewis or SD rats. This effect is seen across a wide dose range suggestive of an upward rather than a rightward shift in the cocaine dose-response function. Further, greater non-reinforced responding seen in F344 rats compared to Lewis and SD rats may suggest that this strain shows greater cocaine "craving". Support: Yale IWHR program
- 420** GENDER DIFFERENCES IN TEMPORAL DISCOUNTING MAY EXPLAIN PATTERNS OF DRUG ABUSE
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The effort to find the neuronal mechanisms involved in temporal discounting may be guided by the identification of the evolutionary problem that discounting solves. Bjorklund and Kipp (1996) suggested that different survival goals for males and females may contribute to development of gender differences in cognitive mechanisms involved with inhibition. Different survival goals may also influence differences in temporal horizons between males and females; however, previously reported gender differences in discounting are limited and have not been clearly distinguished from mechanisms of inhibition. Hyperbolic discounting (k) values, reanalyzed from several studies, were used to determine the influence of gender on the discounting of temporally distant rewards independent of other demographic variables (e.g., age, education, monthly income). Females tended to discount temporally distant rewards less than males across reward classes (i.e., money vs. cigarettes) and direction in time (i.e., past gains or future gains). These results suggest that females exhibit extended temporal horizons compared to males. One possibility is that extended temporal horizons among females may influence mate preferences (e.g., preferences for mates that establish a long-term reputation for securing resources) and in concordance with memory mechanisms (e.g., a bias for remembering displays of success that occur despite great risk; Zahavi & Zahavi, 1996) contribute to the evolution of constricted temporal horizons among males.

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- 421** LOW-FREQUENCY HEROIN INJECTION AMONG OUT-OF-TREATMENT, STREET-RECRUITED IDUS
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Background: It is generally assumed that heroin use necessitates physiological dependence, multiple daily injections and a deepening of dependence over years. In the 1970's, Norman Zinberg pioneered the study of what he termed "controlled heroin use." A recent study by Warburton et al in England found that "controlled" heroin use was complex and suggested further study. This research has implications for helping heroin users control their use and ultimately cease all use. Objective: To assess the prevalence, factors associated with, and one-year trajectory of low frequency heroin injection (low-FHI) among out-of-treatment, street-recruited injection drug users (IDU). Methods: To assess prevalence and factors associated with low-FHI, we analyzed data from an epidemiological study of street-recruited IDUs in San Francisco in 2004. In this analysis, we selected all heroin IDU who were not currently in drug treatment (N=616). Low-FHI was defined using US Federal Government's criteria of non-hardcore heroin use, which is 1-10 heroin injections in past 30 days (including heroin alone or in combination with stimulants). To assess one-year trajectory of heroin frequency, we selected a sub-sample of low-FHI for whom we had data one year later (n=80). Results: Seventeen percent of street-recruited heroin IDU who were not in drug treatment reported low-FHI (n=107). Low-FHI were more likely ($p<0.05$) than higher frequency heroin users to be HIV positive and inject methamphetamine, and less likely to be homeless or use syringe exchange programs. Our longitudinal data showed that at one year, 33% of low-FHI users stayed low-FHI, 26% were no longer using heroin, and 41% reported higher frequency heroin use. Conclusion: Low-frequency heroin injection is prevalent among out-of-treatment, street-recruited IDUs in San Francisco. We explore the usefulness of the LFHI label and examine implications for prevention and treatment programming.
- 422** INCREASES IN DRUG-RELATED ACCUMBAL SIGNALING OCCUR OVER TIME WITH COCAINE BUT NOT SUCROSE SELF-ADMINISTRATION
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Multiple drugs of abuse induce adaptations in the nucleus accumbens, and these adaptations are believed to underlie the behavioral changes that define drug addiction. As the accumbens is involved in multiple drug and non-drug related behaviors, it is unclear how adaptations in the accumbens contribute to addiction. One explanation is that drug-induced adaptations are activity-dependent, and occur differentially amongst populations of neurons that are differentially activated in the presence of drug. With accumbal recordings in awake rats self-administering IV cocaine, our lab has previously reported evidence in support of this explanation: After 30 days of cocaine self-administration, neurons that were not activated by any events (lever-press or cues) in the cocaine sessions (cocaine-Task-Non-Activated) showed a significant decrease in average basal firing rates, relative to similar recordings made on day 2-3. In contrast, the firing rates of neurons that were activated by such events (cocaine-Task-Activated) did not change from day 2-3 to day 30. This relative increase in the firing rates of cocaine-Task-Activated neurons was associated with the emergence of addiction-like behaviors in these rats. The present study tested the hypothesis that these adaptations contribute to drug addiction, and do not represent obligatory effects of long-term exposure to all rewards. This hypothesis was tested with rats self-administering oral sucrose. After 30 days of sucrose self-administration, the average firing rates of both sucrose-Task-Activated and sucrose-Task-Non-Activated neurons had not changed from similar recordings made on days 4-6 of the experiment. This indicates that the adaptations reported in the previous study are not obligatory accumbal responses for all rewards, and may contribute to drug addiction.
- 423** PHARMACOKINETICS OF ORAL NRP104/SPD489 (LISDEXAMFETAMINE DIMESYLATE) VERSUS D-AMPHETAMINE IN HEALTHY ADULTS WITH A HISTORY OF STIMULANT
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NRP104/SPD489 (proposed generic name lisdexamfetamine dimesylate), is a d-amphetamine prodrug designed to have reduced abuse potential. Preclinical studies indicate that lisdexamfetamine is converted to amphetamine through rate-limited hydrolysis. The amphetamine-free base content of lisdexamfetamine 100 mg is equivalent to amphetamine sulfate 40 mg. This dose-escalation study obtained pharmacokinetic data as part of a study to evaluate the safety and tolerability of escalating doses of lisdexamfetamine (30 to 150 mg) in healthy adult stimulant abusers. Subjects were divided into 3 cohorts of 4 subjects each; all received single escalating doses of lisdexamfetamine at 48 hour intervals, with amphetamine 40 mg and placebo randomly interspersed. Amphetamine AUClast over the first 4 hours was substantially lower with 100 mg lisdexamfetamine (165.3-213.1 ng/mL) versus 40 mg amphetamine sulfate (245.5-316.8 ng/mL). Cmax and AUClast increased with doses of 30 to 130 mg lisdexamfetamine, attenuating between the 130 mg and 150 mg dose. The Tmax (h) of amphetamine range was longer for lisdexamfetamine (3.78-4.25) versus amphetamine sulfate (1.88-2.74). The half-life of lisdexamfetamine (range, 0.44-0.76 h) indicated rapid clearance of the prodrug. Adverse effects were mild in severity. Lisdexamfetamine had a slower release of amphetamine compared with amphetamine sulfate. At higher doses, there appears to be an attenuation of the maximum concentration, suggesting higher doses of lisdexamfetamine will not lead to further increases in Cmax and AUClast. These results are consistent with preclinical findings and indicate that in humans, there is a rate-limited hydrolysis of lisdexamfetamine that may lead to lesser abuse and greater safety.
- 424** DEVELOPMENT OF A HIGH SCHOOL SMOKING-CESSATION PROGRAM FOR ADOLESCENT SMOKERS USING CONTINGENCY MANAGEMENT PRINCIPLES
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Contingency management (CM) approaches have been successfully used to reduce tobacco use in adult smokers. However, there has been a paucity of research on CM as a treatment for adolescent smokers. We will present evidence from two recent studies focused on developing the use of CM approaches in a one month, high school-based smoking cessation program. The CM intervention in both studies involved monetary reinforcement for abstinence on an escalating schedule with a reset contingency. Abstinence was determined using breath CO and urine cotinine levels. Feasibility was increased by conducting all appointments in the high schools. The first study, examined the use of CM combined with weekly CBT. 28 adolescent smokers were randomly assigned to receive either CM in combination with CBT or CBT alone. At the end of one week and one month of treatment, complete abstinence verified using quantitative urine cotinine levels was higher in participants in the CM+CBT group (one week: 76.7%; one month: 53.0%) when compared to the CBT alone group (one week: 7.2%; one month: 0%). The second study examined two behavioral platforms for use with CM and further increased the feasibility of these procedures by incorporating a waiver of parental permission. 29 adolescent smokers received CM for abstinence and were randomly assigned to receive either weekly CBT sessions or a more frequent brief behavioral intervention (FBBI; Cooney, 2000) for a one-month treatment period. Overall end of treatment abstinence rates were at 55% with no differences in abstinence between the FBBI and CBT treatments. These preliminary results provide a strong initial signal supporting the utility of CM techniques for smoking cessation in adolescents and demonstrate that such interventions can be reliably implemented in a high school setting. (Supported by P50DA09421)

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425 HIV RISK BEHAVIOR AND PSYCHIATRIC SYMPTOMS AMONG HEROIN ADDICTS IN RUSSIA

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Relationships between HIV risk and other demographic features were examined in Russian heroin addicts. Methods: 332 addicts who completed detoxification and provided informed consent were enrolled in two separate naltrexone trials. All participants were assessed at baseline for HIV drug and sex risk, and psychiatric symptoms. Results: HIV drug risk was mainly related to employment status, HIV sex risk, use of hallucinogens, and severity of psychiatric symptoms. HIV sex risk was mainly related to HIV drug risk, use of stimulants, and severity of psychiatric symptoms. Females had a more significant factors relating to drug and sex risk than males (HIV drug risk: 10 vs. 3; HIV sex risk: 12 vs. 7). Stepwise linear regression analyses showed that increasing age, employment, having medical problems and being more ready for change were associated with reduced HIV risk. Conclusions: HIV drug and sex risk behaviors in Russian heroin addicts are closely related to each other, and also to use of stimulants and high levels of psychiatric symptoms particularly anger. Both males and females have multiple risk factors, but women have more than males. Increasing age, less employment, having more medical problems, and greater readiness for change were associated with reduced risk. These data suggest multiple interventions that could reduce the chances for HIV spread in Russia, and that women are at particularly high risk.

426 ESTRADIOL ALTERS COX-1 AND COX-2 ACTIVITIES IN THE LUMBOSACRAL REGION OF THE SPINAL CORD OF OVX FEMALE RATS

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Female rats display increased behavioral responses to inflammatory pain stimuli than male rats. Sex differences in inflammatory pain have been attributed to gonadal hormones effects; previous studies from our group have demonstrated that estrogen reduces formalin nociceptive response during Phase II of the formalin behavioral responses, an inflammatory nociceptive model. The mechanisms underlying this effect remain unclear. The aim of this study was to determine if estradiol alters inflammatory-mediated intracellular mechanisms. To this end, OVX female rats received 10 to 40% estradiol or empty SILASTIC capsules. Rats were sacrificed one week later. In the spinal cord, protein levels of COX 1 and COX 2 were determined using western blot analysis. Furthermore, levels of prostaglandin E2 and corticosterone, important mediators of inflammatory responses, were examined using enzyme immunoassays or radioimmunoassays kits, respectively. Preliminary results indicated that while no differences after estradiol replacement in COX-1 protein levels were observed, a 30% reduction of COX-2 protein levels were observed. Moreover, corticosterone levels were increased while PG-E2 levels were decreased. Thus, suggesting that estrogen's antihyperalgesic effects on inflammatory induced nociceptive responses are in part mediated by interactions of corticosterone-COX activation. This work was supported in part by SCORE 506-GM60654 and SNRP NF 39534.

427 CRIMINAL JUSTICE AS A PURCHASER OF COMMUNITY TREATMENT

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State departments of corrections are among the largest purchasers of non Single State Agency substance abuse treatment services. However, there has been little research on the impact of this funding on treatment. A recent study of 15 programs found that those with corrections (CJ) funding were less likely to use pharmacotherapies and follow-up techniques and more likely to use non-degree staff. This study expands this inquiry using a mixed methods case design with 36 treatment agencies - interviewing multiple staff members within the organizations. Community-based agencies were chosen because of their state corrections funding (n=11) and were matched with similar agencies within the same geographic region not receiving state corrections funding (nonCJ). All but one had multiple funding sources. Besides state correctional funding, four agencies received federal or municipal CJ funding (total of 16 CJ agencies). We found that pharmacotherapies were less likely (p=.03) and social services more likely (p=.01) in CJ programs than nonCJ programs. Length of stay in CJ funded treatment was longer (90-150 days) compared to Medicaid funded treatment (30-45 days). Unlike other funding sources, CJ funded providers were required to assess criminogenic factors and use manualized cognitive behavioral group therapy, regardless of individualized assessment. Monthly progress report and treatment plans are sent to supervising agents for CJ funded clients, as opposed to various pre-authorization and billing reviews for nonCJ funded clients. Although some CJ agency providers felt untrained in criminal justice issues and disliked feeling like "wardens", the overall consensus was "we would be out of business if it wasn't for corrections funding." Although CJ reimbursement rates were lower than other public funding, those with CJ funding were more likely to experience funding increases over the past 5 years. Providers appreciate the steady referral source and clear expectations of CJ funders, especially in contrast to the commercial insurance carriers. As the CJ population increases, the continued examination of the effects of CJ funding or agencies is warranted.

428 WHAT ELEMENTS OF MI BOOST CHANGE? SMOKING CESSATION MI INTERVENTIONS IN WOMEN POST PARTUM

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Aims: This study examines the association between patient's and therapist's verbal behavior during a MI based smoking intervention for women post partum. Additionally, the effect of positive and negative patient behavior i.e. change talk and resistance talk on behavior change is investigated. Methods: As part of a randomized controlled trial, n=297 women post partum, who were formerly smoking received a tailored MI based intervention. N=163 sessions of currently smoking (n=86) and non-smoking (n=77) women were audio taped. Behavior counts were obtained using the Motivational Interviewing Skill Code (MISC) and the Motivational Interviewing Treatment Integrity (MITI) Code that measure relevant MI dimensions, e.g. MI Spirit (collaboration, autonomy, evocation), change and resistance talk. Results: Change talk was positively related to open questions and MI Spirit. Therapist's MI-consistent utterances, i. e. giving support or compliments, strengthening patient's autonomy, were negatively correlated with resistance talk. Multivariate logistic regression found self-efficacy and resistance talk to be significant predictors for smoking status at 6 months follow-up in women who were not smoking at the time of intervention. In smokers, future smoking status was predicted by self-efficacy and the percentage of complex reflections made by the therapist. Conclusions: Several expected associations between patient's and therapist's behavior were found. In MI interventions, the positive aspects of quitting should be tackled preferably with open questions and complex reflections. Therapists should show increased MI adherence in order to reduce patient resistance and enhance change talk. This may boost resources such as self-efficacy and support behavior change.

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429 DOPAMINE MEDIATES CROSSTALK BETWEEN NERVE ENDINGS AND MICROGLIA AND SERVES AS THE MOLECULAR TRIGGER IN METHAMPHETAMINE NEUROTOXICITY

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Methamphetamine (METH) is a stimulant drug of abuse. Problems associated with METH abuse are compounded by its ability to cause persistent neuronal damage. The mechanisms underlying METH neurotoxicity are not fully understood but dopamine (DA) is thought to be an integral factor. Microglial activation is also emerging as an important participant in METH-induced neurotoxicity. We hypothesized that DA mediates METH-induced crosstalk between nerve endings and microglia, and serves as a molecular trigger of the cascade that culminates in neurotoxicity. Mice were treated with AMPT to deplete cytosolic DA, or with reserpine to deplete vesicle transmitter stores. At a time when striatal DA was reduced to 40% (AMPT) or 5% of control (reserpine), mice were treated with a neurotoxic regimen of METH. Neurotoxicity was assessed at 2d or 7d through measures of striatal DA and microglial activation. METH caused 65% reduction in DA that persisted for 2-7d. Mice previously treated with AMPT were completely protected from neurotoxicity whereas reserpine exacerbated METH-induced DA depletions. Mice treated with AMPT or reserpine showed near full recovery of DA at 2-7d after vehicle treatment. METH caused extensive microglial activation in striatum (252 vs 12 cell count for controls) 2d after treatment. AMPT prevented METH-induced microglial activation (32 cells) whereas reserpine increased this effect (289 cells). METH also caused a significant increase in striatal DA quinone content as revealed by the formation of 5-cysteinyld-DA. DA quinone also causes activation of cultured mouse microglial cells, and this effect was prevented by drugs known to prevent METH-induced neurotoxicity and microglial activation in vivo. Taken together, these results suggest that microglial activation is initiated by METH-induced formation of DA quinones, with cytosolic stores of transmitter serving as the primary target of METH.

431 EFFECT OF TREATMENT WITH A SELECTIVE SEROTONIN REUPTAKE INHIBITOR, PAROXETINE, ON NEUROGENESIS AND NEUROPROTECTION

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The mammalian brain contains neural stem cells that allow continued neurogenesis throughout the life of the animal. The purpose of present study was then to evaluate the effect of treatment with a selective serotonin (5-HT) reuptake inhibitor paroxetine, which shows "discontinuation syndrome" or "withdrawal syndrome", on neurogenesis and neuroprotection. MEB5 (IFO50472, Japanese Cancer Research Resources Bank), a multipotent stem cell line, can differentiate into neurons, astrocytes and oligodendrocytes obtained from the forebrain of mice. The expression of the 5-HT transporter and 5-HT1A receptors were found in nestin-positive neural stem cells, as detected by RT-PCR. Furthermore, treatment with paroxetine (10-8 M) on neural stem cells caused a significant increase in the extra cellular 5-HT levels as compared to that on control cultures (p-8-10-5 M) resulted in neurogenesis differentiated from neural stem cells obtained, as characterized by the increase in MAP2a/b-positive cells. As well as neural differentiation, the increase in cleaved caspase-3-like immunoreactivity induced by H2O2 (3 μM) was suppressed by the treatment with paroxetine in cortical neuron/glia cocultures. These effects were blocked by a selective 5-HT1A receptor antagonist WAY100635 (1 nM). These findings raise the possibility that paroxetine causes neurogenesis and neuroprotection mainly through the stimulation of 5-HT1A receptor of neural stem cells.

430 RACIAL/ETHNIC DISPARITIES AND DURATION OF DRUG USE DISORDERS

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Objective: Racial disparities in the natural history of drug use disorders have important implications on treatment and service needs. The study objective was to examine racial difference by duration of drug abuse and dependence and remission from these symptoms. Methods: Individuals meeting criteria for abuse and/or dependence to illegal and prescription drugs were identified (n=3,885) from the 2001-2 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Time from initial abuse/dependence symptoms to self-reported symptom remission was assessed. Persons who did not remit from symptoms were right-censored. Chi-square test and Kaplan-Meier curves were used to identify differences in remission and duration of abuse/dependence symptoms by race. The Cox proportional hazards model was used to identify independent correlates of symptom remission. Results: 3,165 (81.5%) reported remission by the time of interview. Whites were more likely to have gone into remission than African-Americans, American Indians and Asians (83.6% vs. 75.5%, p<0.001). Kaplan-Meier graphs indicated that Whites and Hispanics have shorter duration of drug use compared to other races (logrank test p<0.001). After adjusting for demographic variables, African-Americans and American Indians were significantly less likely to remit than Whites (African-American hazard ratio [HR]: 0.78; 95% CI: 0.68, 0.89; American Indian HR: 0.75; 95% CI: 0.58, 0.96). Women were more likely than men and individuals who met for dependence (versus abuse only) were less likely to experience remission from abuse/dependence. Conclusion: Whites and Hispanics tend to have shorter duration of abuse/dependence symptoms compared to African-Americans, American Indians and Asians. Understanding the natural history of abuse/dependence by race has implications for resource allocations for drug treatment. Future research should explore factors influencing disparities in duration of disorders.

432 CRACK-USING AFRICAN-AMERICAN MOMS: IS PARENTING A BARRIER TO SEEKING TREATMENT?

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African-American women who abuse crack cocaine face not only challenges to parenting but also accessing services. Many of these women report trauma histories, psychological distress, high-risk sex practices, and a lack of resources beyond day-to-day needs. This NIDA-funded study explores differences between African-American mothers (n=635) who use crack cocaine and are either living with or have been separated from their children. The women are compared on measures of treatment needs, perceived access to services, perceived barriers to care, and treatment seeking for substance abuse and other health care services. Of women who were mothers to dependent children, 257 (40%) had at least one child living with them (Caregivers), while 378 (60%) had none of their children living with them (Non-Caregivers). Caregiver mothers were more likely to have health insurance and public assistance benefits than Non-Caregivers. Significant differences were reported in instrumental support: If they were in a crisis, Caretakers perceived more assistance would be provided by relatives and neighbors than did Non-Caretakers. Non-Caregivers were significantly more likely to be homeless, to have ever been incarcerated, and to have initiated substance use and sexual activity earlier in life than Caregivers. Non-caregivers were twice as likely to initiate substance abuse treatment even though Caregivers were twice as likely to have some form of insurance. Overall, Non-caregivers were more likely than Caregivers to seek substance abuse treatment: alcohol detox 26% vs 13%; outpatient 33% vs. 30%; and residential 44% vs. 34%. However, both groups were equally likely to seek medical health care services, such as annual physical and gynecological exams. Findings such as these raise old questions about whether professional treatment is supportive of substance abusing women with children, whereas, relatives and community support still holds as an important support system.

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433 IN-TREATMENT PERFORMANCE PREDICTS POST-TREATMENT SUCCESS IN SMOKING CESSATION

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Post-treatment success is the goal of smoking cessation treatments. However, many more subjects are required to test the effectiveness of treatments at producing post-treatment change as opposed to in-treatment change. One might postulate then that it is best to demonstrate effectiveness at producing in-treatment increases in cessation before designing a study to test long-term effectiveness. This postulate, however, rests on the hypothesis that in-treatment performance predicts post-treatment outcome. In this study, we examine this hypothesis by looking at how in-treatment performance predicts not smoking at about three months after treatment ended. Participants received contingency management treatment for smoking cessation in which they received incentives each weekday for 70 visits and smoking status was determined six months following study entry, about three months after the intervention ended. An in-treatment abstinence criterion of a breath CO level 60 visits. For maximum number of sequential visits these numbers were 0% (0/67), 9% (2/22), 38% (16/42), and 50% (2/4). These results provide a strong indication that at least with contingency management treatment in-treatment success predicts post-treatment success.

434 EFFECTS OF FLUNITRAZEPAM (ROHYPNOL) ON HUMANS' RISKY DECISION-MAKING

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Risky decision making may lead to harmful consequences to both the decision maker and others. Many of these consequences (injury, substance abuse, violence, high-risk sexual behavior) have substantial impact on the public health and criminal justice systems. Misuse of the benzodiazepine flunitrazepam has been associated with impaired decision making and several of the above-noted harmful consequences. In our laboratory, we approach risk-taking as decision-making under conditions of uncertainty; operationally defined as behavior that occurs in a context with two response options: (i) option 1 (risky) has a probability of 0.50 of either a reinforcing or aversive consequence (monetary gain or loss), (ii) option 2 (non-risky) has a reinforcement probability = 1.0, but a substantially smaller reinforcer value than option 1. The present experiment employed a laboratory-based discrete trials decision making procedure that required a choice between the risky and non-risky option. Using a counterbalanced dose sequence and a within subject repeated-measures design, subjects were administered placebo and 0.5, 1.0, and 2.0 mg / 70 kg flunitrazepam. In two completed subjects, choices for the risky option were increased by 25-40% at the 1.0 and 2.0 mg / 70 kg doses, and were directly related to changes in subjective effects on the ARCI. The outcomes are similar to those we have previously observed with alprazolam and alcohol. Recruitment is ongoing, and it is expected that 6-8 subjects will be completed by the June 17, 2006 conference date. ACKNOWLEDGEMENTS: Supported by NIDA grant R 01 DA 15392

435 A PROSPECTIVE, MULTICENTER, OBSERVATIONAL STUDY ON COMPLIANCE TO HEPATITIS C TREATMENTS (CHEOBS): CHARACTERISTICS OF HCV-INFECTED PATIENTS WITH PSYCHIATRIC DISORDERS

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Background: CHEOBS is a French multicenter prospective observational study of patients with chronic hepatitis C virus (HCV). Objective: To analyze the baseline profile of HCV-infected patients with psychiatric disorders. Methods: From 2003 to 2004, 1945 HCV-infected patients were included. Results: Among the 1,945 HCV infected patients, 432 (22%) patients were identified with psychiatric disorders, but only 251/406 had been evaluated by a psychiatrist before starting antiviral treatment. 193 (10%) patients were excessive alcohol consumers or opiate users but were not considered to be suffering from psychiatric disorders. Patients with a past history of psychiatric disorders (764 39%) had depression (476), and/or attempted suicide (128) and/or psychiatric hospitalization (160). The distribution of present psychiatric disorders appears similar to that in the general population: patients suffered from depression (54.5%, 218/432), anxiety (54.5%, 218/432), chronic psychosis (5.6%, 23/406), or bipolar depression (2.4%, 9/406). Most patients (72%) with a current psychiatric disorder had never been treated for HCV. Among those with or without a psychiatric disorder who had previously been treated (551/1,945, 28%), the last course of treatment was stopped early in 173 (31%). Among those for whom treatment was stopped early, the percentage with or without psychiatric disorders was similar (43/121, 36% vs 130/430, 30%, respectively). However, premature withdrawal from treatment due to psychiatric reasons was significantly more frequent in the patients with psychiatric disorders than in those without such disorders [7/43 (16%) vs. 5/130 (4%), respectively; $p=0.01$]. Conclusions: In this study, patients who start HCV treatment frequently have psychiatric disorders. The involvement of a psychiatrist in these situations is insufficient. Given the negative impact that psychiatric disorders have on patient quality of life, involvement of a psychiatrist seems necessary as part of a comprehensive treatment strategy.

436 PHASE-I EVALUATION OF TRANSDERMAL BUPRENORPHINE

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We report a first-in-human evaluation of a transdermal buprenorphine formulation (patch) for treatment of opioid dependence. Physically-dependent opioid-users ($n=9$) completed a 10-day opioid detoxification study in a residential research unit. Each received a single patch application that remained in place for 3 days. The formulation has shown delivery of 1.9 mg/day of buprenorphine in preclinical evaluation. Blood samples were drawn prior to patch application, and then repeatedly through the following 10 days. Assessments 4 times daily included: self-report ratings of opioid withdrawal and agonist effects from a 37-item adjective checklist; visual analog scale ratings of the presence and severity of opioid withdrawal; observer ratings of opioid withdrawal using a modified Himmelsbach withdrawal severity scale; vital sign measures; and the amount of rescue medications ordered to treat withdrawal discomfort. Preliminary results show that volunteers' self-reports of the presence of any withdrawal symptoms, and the severity of these symptoms, was reduced by approximately 50% on the 3 days of patch application. Self-reported withdrawal symptoms increased marginally upon patch removal. Administration of opioid rescue medication dropped dramatically during patch application, and increased slightly upon patch removal. Buprenorphine blood level data will be examined in relation to the time course of withdrawal suppression. The apparent suppression of the opioid withdrawal syndrome during patch application and the syndrome's reappearance after patch removal are strongly suggestive of significant biodelivery and pharmacodynamic activity. Transdermal buprenorphine may be a useful opioid detoxification treatment by reducing compliance concerns, and administering buprenorphine in a formulation less likely to be diverted to illicit use. [Grants R44 DA15573 and T32 DA07209]

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- 437 NON-MEDICAL PRESCRIPTION DRUG USE AMONG YOUNG INJECTION DRUG USERS**
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Background: Non-medical prescription drug use is a rapidly emerging public health concern in the United States among adolescents and young adults. Hypothesis: Young injection drug users are at increased risk for exposure to non-medical prescription drug use. Procedures: 163 qualitative interviews were conducted between 2004 and 2005 with young injection drug users (IDUs) in New York, Los Angeles, and New Orleans. Eligibility requirements included aged 16 to 28 years old, and had injected ketamine within the past two years. Subjects were recruited using targeted and chain referral sampling. Analyses: Non-medical prescription drug is defined as noncompliance, recreational use, or abuse, and pertains to six categories of drugs: benzodiazepines, barbiturates, depressants (general), opioids, stimulants, and anti-depressants. Results: Sample demographics include the following: 23 years old (median); 71.3% male; 82.9% white; 78.7% heterosexual; 59% graduated high school or GED; 100% history of injection drug use; 98.8% history of homelessness; 51.8% history of drug treatment; 85.4% history of incarceration; 17.1% HCV positive (self-report); 0% HIV positive (self-report). Non-medical use of opioids was pervasive: 50% or more of respondents had ever used 9 out of 11 opioids surveyed with Vicodin (82.2%) and OxyContin (68.7%) being the most popular. Over 70% had ever used a benzodiazepine, such as Xanax, Valium, or Klonopin. Stimulants, such as Adderall or Ritalin, had been used non-medically by one-third and one-half of the sample, respectively. Histories of barbiturate or depressant were relatively lower such that no single substance had been used by more than one-quarter of the sample. Anti-depressants were used non-medically by one-fifth and one-quarter of the sample, respectively. Implications: In addition to pervasive use, non-medical prescription drug use was associated with a range of high-risk behaviors, including initiation into injection drug use, polydrug use, drug overdose, and drug dependence.
- 438 PRENATAL SUBSTANCE EXPOSURES AND DSM-IV DISORDERS IN ADOLESCENTS**
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We examined the relation of prenatal exposures to DSM-IV disorders in adolescents using data from 467 mother-child pairs. Alcohol, marijuana, and tobacco use were assessed prenatally. At 16 years, DSM-IV disorders were assessed in the offspring using the Diagnostic Interview Schedule (C-DIS-IV). Three diagnostic groups were created: Mood/Anxiety (Depression, Anxiety, PTSD), Disruptive Behavior (Conduct, Oppositional Defiant, Attention Deficit/Hyperactivity), and Substance Use (SUD: Alcohol Abuse/Dependence, Marijuana Abuse/Dependence, Tobacco Dependence). Covariates included race, sex, income, family history of alcohol problems, home environment, maternal psychopathology (grouped as above), maternal age, education, social support, and life events. Covariates were identified with logistic regressions. Prenatal substances and trimesters were evaluated separately. 52% of the adolescents were African-American; their average age was 16.9 years (16-19). Mean family income was \$2170/month (\$0-9990). Rates of adolescent Mood/Anxiety, Disruptive Behavior, and SUDs were 16% (n=74), 18.4% (n=85), and 20.6% (n=96), respectively. Third trimester alcohol exposure (≥ 0.5 drink/day; OR 2.8; 95% CI 1.2, 6.8) female sex, younger maternal age, and maternal Mood/Anxiety disorder predicted offspring Mood/Anxiety Disorders. First trimester alcohol exposure (≥ 1 drinks/day; OR 1.9; 95% CI 1.1, 3.3) and current life events predicted Disruptive Behavior Disorders. First trimester alcohol (≥ 1 drinks/day; OR 1.7; 95% CI 1.1, 3.0) and third trimester alcohol exposure (≥ 0.5 drinks/day; OR 3.4; 95% CI 1.4, 8.0), first trimester tobacco (≥ 0.5 packs/day; OR 2.1; 95% CI 1.3, 3.4) and third trimester tobacco exposure (≥ 0.5 packs/day; OR 1.9; 95% CI 1.2, 3.1), and Caucasian race predicted Substance Use Disorders. Prenatal marijuana exposure was not related to psychiatric disorders at age 16. Prenatal exposure to alcohol or tobacco significantly increased the risk of psychopathology at age 16. These results suggest that preventing drinking and smoking during pregnancy could reduce adverse psychological outcomes in adolescence.
- 439 N-ACETYLCYSTEINE'S IMPACT ON COCAINE-RELATED CUES**
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N-Acetylcysteine (NAC) reduces reinstatement in cocaine-dependent rats, and implicates NAC as a potential treatment for relapse to cocaine use. The present study investigated the impact of NAC on reactivity to cocaine cues in cocaine-dependent individuals. In a double blind placebo controlled safety and tolerability trial, 15 cocaine-dependent individuals were hospitalized for 3 days during 2 consecutive weeks. During the first stay, subjects received placebo or 600mg of NAC in 12-hour intervals (4 doses total). During the second stay subjects were crossed over so that those who received NAC during the first week received placebo in the second week and vice versa. After receiving their final dose of medication or placebo, subjects participated in a cue reactivity paradigm in which they viewed slides depicting cocaine as well as pictures of neutral objects. Slides were initially presented for 6 seconds over 15 minutes and measures of heart rate and skin conductance were measured. Upon completion of the initial slide presentation, slides were immediately presented a second time and each slide was viewed ad libitum (up to 20 seconds); as such, viewing time provided a behavioral measure of interest in the slides. After viewing each slide, subjects provided ratings of Craving, Desire to Use, and Interest in response to each individual slide. Cue reactivity procedures were identical across sessions, except slides were presented in a different order. Overall results indicated that subjects showed more skin conductance response to cocaine slides relative to neutral ($p < .01$); physiological measures were not affected by medication condition. In contrast, while NAC had no impact on ratings of Craving, slide viewing time and ratings of Desire to Use were lower when subjects were receiving NAC relative to placebo ($p < .05$ for both measures). The data suggest that when subjects were taking NAC, they were less motivated to view cocaine-related slides and experienced less subjective cue-induced desire to use cocaine.
- 440 RATES OF HIV DISEASE AMONG SOUTH AFRICAN DRUG USERS: AN EVALUATION OF GENDER AND DRUG USE TYPE AS HIV RISK FACTORS**
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Studies of HIV risk factors among South African drug users are in great need given the extent the pandemic has affected countries of the Sub-Saharan region. The present study sought to examine gender and lifetime use of opiates, cocaine, marijuana, and mandrax as risk factors of HIV status at baseline. This study is based on data from the International Neurobehavioral HIV Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of HIV, and Hepatitis A, B, and C in the U.S, South Africa, and Russia. The present study is based on the South Africa sample comprised of 144 drug users between 18 and 50 years of age in the Pretoria region. The Pretoria baseline sample was 91% Black and 65.3% male with 33.3% of the baseline sample testing positive for HIV. Multinomial logistic regression indicated that females (OR = 3.06; 95% CI = 1.42; 6.61) and opiate users (OR = 2.32; 95% CI = 1.00; 5.38) were significantly more likely to test positive for HIV while controlling for age and lifetime use of cocaine, marijuana, and mandrax. Specifically, 52% of females in the sample tested positive for HIV compared to 23.4% of males. In addition, 40.7% of opiate users tested positive for HIV compared to 20.8% of non-users of opiates. Lifetime use of cocaine, marijuana, and mandrax was not associated with HIV status. The study sample was not large enough to examine possible interaction effects between gender and opiate use statuses. However, the vast majority of female subjects reported no lifetime injection drug use suggesting unprotected sexual intercourse as the predominant HIV risk factor among South African women. The present study findings are among the first in a line of investigation designed to identify HIV risk factors among South African populations and develop prevention interventions that target identified risks.

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- 441** DIRECT AND INDIRECT EFFECTS OF NEIGHBORHOOD DISORDER ON DRUG USE AND HIGH-RISK SEXUAL PARTNERS
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Background: On a macrosocial level, neighborhood characteristics have been found to be associated with rates of HIV and other bloodborne and sexually transmitted infections. We used structural equation modeling to examine the relationship between neighborhood social and physical disorder and high HIV/STI risk sexual partners. Methods: A cohort (N=835) recruited for an HIV study of drug users (2002-2004) was interviewed about their neighborhood characteristics, drug use, depressive symptoms, and the HIV risk behaviors of multi partners, exchanging sex for money or drugs and partners who injected or smoked crack cocaine. Results: Model fit statistics from Mplus indicated that there were significant direct effects between neighborhood disorder and psychological distress and neighborhood disorder and sexual risk behaviors. There were also significant indirect effects of disorder on sexual risk behaviors. Conclusions: These results highlight the importance of viewing drug use, depression and hopelessness, and infectious diseases such as HIV and Hepatitis C as interlinked epidemics that are fostered by neighborhood social and physical disorder. Neighborhood, network, and community level interventions are needed to address these intertwined public health issues.
- 442** ADDICTION SEVERITY IN COCAINE-TREATMENT SEEKERS: AN APPLICATION OF FINITE MIXTURE MODELING
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Cocaine use remains one of the most pervasive and serious of the substance use disorders. Only half of those in need actually receive substance abuse treatment. In addition, rates of relapse and early attrition are extremely high. These challenges have prompted researchers to identify baseline variables that predict treatment outcome. The Addiction Severity Index (ASI) is a widely used measure of psychosocial functioning in substance abusing individuals. Efforts to identify predictive associations between baseline ASI composites and treatment outcomes have been inconclusive. Furthermore, previous studies using the ASI have examined composite scores independently, without taking into account the multidimensional qualities of the instrument by examining scores in multivariate fashion. Examining profiles allows for exploration of relative functioning across a number of domains and may inform treatment decisions by characterizing a potentially heterogeneous population. The present study examines baseline ASI composite profiles, and their relations to treatment outcome trajectories in a sample pooled from four randomized 12-13 week medication & psychotherapy clinical trials for DSM-IV diagnosed cocaine dependence. Finite mixture modeling was used to simultaneously model unexplained heterogeneity in multivariate baseline ASI profiles and treatment outcome trajectories. It was found that a two class model best informed the data (Vuong-Lo-Mendell-Rubin LRT Test $\chi^2(10) = 333.943, p < .0002$; Lo-Mendell-Rubin LRT Test $\chi^2(10) = 326.960, p < .0002$). Latent classes were then characterized in terms of their ASI profiles and treatment outcome trajectories. Results suggested possible associations between pretreatment addiction severity and treatment outcome. These findings advance efforts to define distinct subpopulations that may benefit from targeted interventions.
- 443** THREE-YEAR PATTERNS OF 12-STEP ATTENDANCE AND INVOLVEMENT AS PREDICTORS OF STABLE RECOVERY FROM POLYDRUG USE
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Twelve-step participation is useful in sustaining recovery. The bulk of evidence comes from treatment samples, often alcohol-, rather than drug-dependent persons, and timeframes are short for both follow-up periods and recovery outcomes (e.g., past 90 days use). Research is needed on longitudinal patterns of 12-step participation and their long-term outcomes among recovering polydrug users, in particular, on the role of involvement in 12-step recovery activities (e.g., having a sponsor, working the steps) independently of attendance. We describe patterns of 12-step attendance and involvement over 3 years and their role in predicting stable recovery (i.e., 2 years or longer of continuous abstinence at F2). Former poly-substance users in recovery from one month to 10+ years recruited from the community in NYC (preliminary N = 207), mostly inner-city residents with long and severe history of crack use interviewed 3 times at yearly intervals (BL, F1 and F2). Rates of both 12-step attendance and involvement decreased over time; 42% attended meetings continuously for 3 years, 40% were continuously involved in 12-step recovery activities. Greater lifetime addiction severity, younger age using drugs and being African-american predicted continuous attendance and involvement. Taken separately, continuous attendance and involvement predicted greater likelihood of stable F2 recovery, controlling for severity (OR = 7.5 and 6.8, respectively); in particular, having a sponsor continuously for 3 years increased the likelihood of stable F2 recovery by 23-folds. The strength of these findings was most pronounced among persons in recovery for under 18 months at BL. Findings on the role of 12-step participation over 3 years on 2+years of stable recovery among urban polydrug users extend in time and scope, data on the importance of 12-step participation. This bolsters the need for clinicians to foster stable 12-step participation as a useful post treatment recovery resource. Funded by NIDA R01DA14409 and by the Peter McManus Charitable Trust.
- 444** THE RELATIONSHIP BETWEEN THERAPIST ADHERENCE AND PATIENTS' RESPONSES TO MOTIVATIONAL INTERVIEWING, AND TREATMENT ADHERENCE IN CO-OCCURRING DISORDERS
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We evaluated the relationship between therapist adherence and patients' responses to motivational interviewing (MI), and aftercare attendance in inpatients with co-occurring disorders (N=57). The context was an RCT of Standard Treatment (ST) vs. ST+MI, where MI consisted of 1) motivation feedback, and 2) open-ended questions about aftercare (e.g., "What are the chances you will attend your first appointment?"), followed by prompts to the therapist to write verbatim, reflect on, query further, and summarize the patient's responses. Therapists completed session checklists, from which we calculated the number of MI components offered and questions administered, and coded patient responses to the questions. We used ANOVA's to evaluate therapist adherence differences among therapists and between patients who attended their 1st aftercare appointment versus those who did not, and Chi-square analyses to evaluate the degree of association between coded responses and rate of 1st aftercare appointment attendance. Results: Therapists did not significantly differ on their adherence and therapist adherence was not related to attendance ($p > .05$). However, patients who 1) gave personal reasons for why they would attend appointments (e.g., "I'll feel bad about myself if I don't go") were more likely to attend their 1st appointment than those who spoke about negative external consequences (e.g., "The doctor will be mad at me") or gave vague reasons (e.g., "It would be bad not to go...")(77%, 40%, 32%; $p < .05$). Also, those who offered positive and specific responses when asked about their aftercare plans (e.g., "Really need to go my clinic weekly" and named the clinic) were more likely to attend their 1st appointment than those who offered poor plans (e.g., "Will stay in my apartment"), plans unrelated to professional treatment or non-specific plans, or other plans unrelated to psychiatric problems (68%, 50%, 48%, 10%; $p < .05$). Supported by K23 DA15144 (MVP)

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- 445** PREVALENCE OF PSYCHIATRIC DISORDERS AND RELATIONSHIP WITH SEVERITY OF SUBSTANCE USE DISORDERS
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Objectives 1) to determine the prevalence of comorbid psychiatric disorders at entry in treatment; 2) to study the relationship between severity of substance use disorder (SSUD) and prevalence of psychiatric disorders. Methods. Consecutive patients seeking treatment between January 2001 and June 2005 were recruited and assessed with The Mini International Neuropsychiatric Interview (MINI) for current and lifetime Axis I disorders and antisocial personality disorder (APD), and the Addiction Severity Index (ASI). Participants were classified on the basis of SSUD. The Chi2 compared prevalence of psychiatric disorders in each group. SSUD was defined by two modalities: 1) ASI severity scores; 2) MINI polydependence. Results. 94 subjects were included (mean age 32,5 years (SD= 8.7), 81 % males). 48 % were dependent to cannabis, 42 % to opiates, 32 % to alcohol, 13 % to cocaine, 6 % to amphetamines and 4 % to benzodiazepines. Lifetime and current DSM Axis I disorders were highly prevalent (79 % and 64 %). Major depression was the most common current and lifetime Axis I disorder (37 and 62 %), followed by generalized anxiety disorder (34 and 36 %); 22 % were diagnosed with APD. Whichever modality used for SSUD, presence of at least one psychiatric disorder was associated with increased SSUD. SSUD was associated with increased prevalence of APD, anxiety disorders and comorbid anxiety and mood disorder, when modality of SSUD was based on ASI. Subjects dependent to more than one substance were more likely diagnosed with comorbid anxiety and mood disorder than those dependent to only one substance (63 % vs 39 % respectively, $p < 0.02$), when modality of SSUD was based on MINI. Conclusion. In this sample there was a high prevalence of psychiatric comorbidity and comorbidity was associated to SSUD. Although the design of this study does not permit to determine a direction to this relationship, these data strongly encourage for treatment services to be able to address both these aspects
- 446** RATES OF HIV, HEPATITIS A, AND HEPATITIS C AMONG DRUG USERS IN JAIL AND CORRECTIONAL FACILITIES
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The present study sought to examine associations between lifetime incarceration in jail and correctional facilities among a population of drug users and HIV, hepatitis A, and hepatitis C statuses. This study is based on data from the International Neurobehavioral HIV Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of HIV, and Hepatitis A, B, and C in the U.S, South Africa, and Russia. The U.S. sample of the present study consists of 610 injection and non-injection drug users between 15 and 50 years of age in the Baltimore metropolitan region. The sample was comprised of 312 African American (51.1%) and 298 White (48.9%) subjects and was 56.4% male. In the sample, 25.8% reported no lifetime history of incarceration, 46.6% reported lifetime incarceration in a local jail, and 27.6% reported incarceration in a correctional facility. Multinomial logistic regression indicated that drug users reporting a lifetime history of jail (OR = 1.78; 95% CI = 1.05; 3.01) and correctional facility (OR = 2.85; 95% CI = 1.55; 5.25) stays were each significantly more likely than drug users with no history of incarceration to test positive for hepatitis A while controlling for age, gender, ethnicity, and education. Specifically, 44.9% of drug users with a lifetime history of a correctional facility stay tested positive for hepatitis A, while 36.5% of drug users with a history of a jail stay, and 23.1% of drug users with no incarceration history tested positive. Drug users reporting a lifetime history of a correctional facility (OR = 4.27; 95% CI = 2.38; 7.64) stay were significantly more likely than drug users with no history of incarceration to test positive for hepatitis C. There were no differences in HIV status by type of incarceration. The vast majority of incarcerated drug users are returned to society. The present study suggests that working with incarcerated populations to treat undetected hepatitis conditions will likely provide substantial benefits to both inmates and society.
- 447** REFINING AN HIV RISK-REDUCTION INTERVENTION USING A STRUCTURAL EQUATIONS MODELING APPROACH
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Research on behavioral HIV risk reduction interventions for injection drug users (IDUs) has focused on primary outcomes (e.g., reduced injection drug use, increased condom use) but has rarely considered the respective roles played by intervention components on these primary outcomes. Thus, it remains unclear how to optimize the potency of risk reduction interventions targeting IDUs. In response, we used a structural equations modeling (SEM) approach to specify the causal pathways leading from theory-based intervention components to risk reduction outcomes before and after our intervention with 226 IDUs participating in a methadone maintenance program. Based on the Information-Motivation-Behavioral skills model of health behavior change (IMB; Fisher & Fisher, 1992), our SEM approach was used to establish the extent to which HIV risk reduction information, motivation, and behavioral skills were determinants of risk reduction behavior outcomes. Although we found similar significant causal pathways leading to both drug- and sexual-related risk reduction outcomes, the model indicates the need to tailor intervention content within each of the IMB constructs in order to optimize their impact. Findings indicate the importance of targeting participants' risk reduction motivation and behavioral skills as opposed to employing more passive informational strategies. Findings also suggest that increasing HIV knowledge may have a differential influence on sex- vs. drug-related HIV risk behaviors among IDUs participating in drug treatment and this may have important implications for intervention strategies aimed at each of these primary risk domains. By quantifying the specific linkage between intervention components and risk reduction outcomes, our SEM findings offered empirical guidance for future efforts to optimize this intervention. Further, our strategy may serve as an exemplar of a data-driven approach to intervention refinement that may inform similar efforts by others.
- 448** PREVENTION EFFORTS AMONG DRUG-USING AMERICAN ADOLESCENTS
D. Lee, Health Care Administration and Public Health, Cleveland State University, Cleveland, OH
Current (last month usage) drug users (n=2167) and nonusers (n=16037) were compared to examine their efforts of participating and involving in alcohol and drug prevention activities. The 2003 National Survey on Drug Use and Health (NSDUH) was used in the study and NSDUH measures the prevalence and correlates of drug use among members of United States households aged 12 and older. We analyzed a total of 18,204 adolescents (out of 55,230) and 51.6% were male. Descriptive analysis and logistic regression modeling were performed to analyze the data. The majority of the sample (67%) was white, followed by Hispanics (14.6%) and African Americans (14.1%). It was statistically significant that current users were less likely than nonusers to talk to their parents about dangers of tobacco/alcohol use (53.3% vs. 60%), to participate in a problem solving, communication skills or self-esteem group (22.1% vs. 26.1%), violence prevention program (14.3% vs. 17.8%), an alcohol, tobacco or drug prevention program outside of school (13.4% vs. 14.1%). It was also significant that users were less likely than nonusers to participate in school/community-based activities (mean score of 1.49 vs. 1.79 & 1.15 vs. 1.45) and faith-based activities last year (mean score of 0.98 vs. 1.35). Logistic regression was conducted and the results appear to be consistent with descriptive analysis results shown above. Overall, current drug using adolescents were less likely than nonusers to participate in alcohol and drug prevention activities. This result suggests policy implications at the local/state/federal level: (1) educating parents on how to effectively talk to their children about the dangers of tobacco, alcohol or drug use, (2) establishing more programs that specifically focus on alcohol/drug coping skills and techniques, (3) offering more counseling and treatment opportunities at school and in the community, and (4) utilizing effectively faith-based programs when intervening adolescent's alcohol and drug addiction. The study result indicates a successful intervention of alcohol and drug prevention efforts among adolescents in the U.S.

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449 SCREENING AND BRIEF INTERVENTION FOR MENTAL HEALTH DISORDERS WITHIN ALCOHOL AND OTHER DRUG SERVICES: THE PSYCHECK PROJECT

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Integrated treatment is now the recommended practice for patients with comorbid mental health and alcohol and drug disorders. Up to 80% of patients present to alcohol and drug services with mental health problems, primarily the higher prevalence disorders (anxiety and depression). Alcohol and drug workers do not always have extensive mental health experience and the focus of research and clinical programs is often on the more acute disorders, such as psychosis, meaning that few programs have been developed for this population. In order to provide truly integrated treatment, there is an urgent need to upskill alcohol and drug workers to both screen and intervene with both clinical and subclinical mental health disorders. The PsyCheck Project evaluated the implementation of mental health screening and intervention within a range of drug and alcohol settings, including regional and metropolitan services, counselling and pharmacotherapy services and services of varying sizes. Practitioners were offered training and clinical supervision for a 6 month period and changes in attitude, confidence and practice were evaluated. A stepped care model of intervention was used where intensity of intervention was matched to client presentation and increased as required. The results showed a doubling of recording of mental health conditions in a random file audit. Qualitative interviews with practitioners and managers involved in the study showed an increase in confidence, perceived competence and positive attitude to mental health screening and intervention. A best practice dissemination strategy incorporating a workforce development approach is currently underway. Future research will examine the impact on client outcomes as well as clinicians.

450 TREATMENT DROPOUT AMONG INNER-CITY RESIDENTIAL TREATMENT-SEEKING SUBSTANCE USERS AS A FUNCTION OF THE INTERACTION BETWEEN ANTISOCIAL PERSONALITY DISORDER AND COURT-MANDATED

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Conventional wisdom suggests that substance users with Antisocial Personality Disorder (APD) are increased risk for treatment dropout and a subsequent return to drug use and criminal behavior. However, recent studies have reported conflicting findings, suggesting that this relationship may be somewhat more complex than originally assumed. To address this issue, the current study examined the interaction of APD and court mandated treatment status, the latter of which has been more clearly shown to be related to treatment drop out with those court mandated to treatment evidencing a lower drop out rate. The study sample included 214 inner city male substance users receiving residential substance use treatment. The mean age of the sample was 40.6 years (SD = 10.0) and 92.7% of the sample was African American. Of the 214 participants 38.3% (n = 82) met criteria for APD and 79.4% (n = 170) were mandated to treatment by the drug court system. Consistent with the lack of previous evidence supporting a main effect of APD, no significant difference in dropout was evidenced comparing APD (12.9%) and nonAPD residents (14.6% drop out; $p > .10$). Also consistent with previous work, a main effect of court mandated status was evident, as a significantly lower number of court mandated residents dropped out of treatment (10%) compared to those with no legal obligation to treatment (27.2%; $\chi^2(1) = 9.0, p < .01$). Further, a robust interaction between APD and court mandated status was found ($p < .01$), with 45% of APD residents not mandated to treatment dropping out, compared with no higher than 12% for each of the other groups. These findings suggest that the relevance of APD status to treatment drop out should not be considered independent of court mandated treatment status, and that those with APD who are not mandated to treatment represent a group with extremely high risk for treatment drop out. Treatment implications and future directions also are discussed.

451 CLINICAL SUPERVISORS AS TRANSLATORS AND TRANSMITTERS OF EVIDENCE-BASED PRACTICES: A FIVE-STATE SURVEY OF CLINICAL SUPERVISORS WORKING IN SUBSTANCE ABUSE COMMUNITY TREATMENT

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Clinical supervision is considered a standard practice for most helping professions (e.g., substance abuse counselors, psychologists, and social workers). According to Fall & Sutton (2003) the majority of licensing and certification boards require clinical supervision. A recent literature review identified clinical supervisors' as playing an essential role in promoting the adoption of evidence-based practices. For example, Miller and colleagues (2004) and Sholomskas, et al., (2005) found counselors receiving clinical feedback from supervisors increased both their proficiency and rate of adoption of evidence-based practices (motivational interviewing and cognitive behavioral therapy). In addition, Carroll, et al., (In Press) highlighted the role clinical supervision played in helping counselors learn and implement treatment interventions. The importance of the clinical supervisor's role in training counselors, promoting the use of evidence-based practices and ensuring quality care is on the rise. However, there is a paucity of knowledge and studies on clinical supervision and the individuals that provide these services especially in the substance abuse treatment field. Of the studies that exist, most focus on the clinical supervision needs of substance abuse counselors or on supervisory relationships. This presentation will review data collected from a survey of clinical supervisors working in non-profit and for profit substance abuse treatment programs in Colorado, Montana, Nevada, Utah, and Wyoming. Specific survey results to be discussed will include clinical supervisors': age, education, gender, training, tenure in the field, recovery status, and years in current position. In addition, data regarding types and amounts of supervision performed, the number of counselors supervised, the frequency of supervision services, and the percentage of clinical supervisors that continue to provide direct treatment services will be discussed along with its implications.

452 EFFECTS OF HIGH-DOSE METHADONE MAINTENANCE ON COCAINE SEEKING, EXPRESSION OF MU RECEPTOR mRNA IN MESOCORTICOLIMBIC AREAS, AND OF OREXIN mRNA IN THE LATERAL HYPOTHALAMUS

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In this study, we employed a modified Pavlovian-to-Instrumental transfer procedure in rats to further investigate the effects of high-dose methadone maintenance on: 1) cocaine seeking behavior; and 2) cocaine-induced changes in mu-opioid receptor (MOR) mRNA expression in mesocorticolimbic areas and orexin (OX) mRNA expression in the lateral hypothalamus. During Pavlovian conditioning sessions (1 2h and 2 4h), rats received passive intravenous infusion of 1.0 mg/kg/inf cocaine, or vehicle, in conjunction with the presentation of a conditioned stimulus (10 sec). Two days following conditioning, methadone-filled mini pumps (sham or 30 mg/kg/day) were implanted and, 4 days later, lever pressing for the compound stimulus was assessed (5 3h sessions). On the last day of testing, all animals received a cocaine prime (20 mg/kg, ip) and lever pressing was monitored for 3h. Blood and brains were collected immediately after this test. Compared to animals that received vehicle during conditioning, rats conditioned with cocaine showed significant spontaneous and cocaine-precipitated cocaine seeking. Importantly, high-dose methadone maintenance: 1) completely blocked cocaine-seeking; 2) alone, did not produce significant alterations in MOR or OX mRNA expression in any of the regions analyzed; 3) prevented cocaine-induced elevations in MOR mRNA expression in the nucleus accumbens core and basolateral amygdala, but not in the pre-frontal cortex; and 4) and prevented the decrease in OX mRNA expression in the lateral hypothalamus induced by cocaine exposure. These experiments in rats suggest that high-dose methadone maintenance blocks cocaine seeking by reversing neural alterations induced by cocaine conditioning.

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453 EFFECTS OF PRENATAL EXPOSURE TO NICOTINE ON LOCOMOTOR ACTIVITY IN PRE-WEANLING RATS

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Previous studies examining the effects of prenatal nicotine exposure in pregnant rodents on locomotor activity in offspring have reported variable results. Some have reported increases in activity, others no effect, and others report a decrease in activity. The doses and routes of administration have varied widely across these studies, and none has used a protocol that models the frequency and daily patterns of nicotine exposure associated with smoking in humans. The purpose of the present experiment was to examine the locomotor activity of pre-weanling offspring of pregnant rats exposed to an i.v. nicotine dosing protocol that approximates the pattern of nicotine exposure in moderate to heavy smokers. Pregnant rats were administered an i.v. infusion of 0.03 mg/kg nicotine (N=13) or saline (N=10) every 14 min for 16 hr/day, resulting in a total daily dose of 2 mg/kg, from gestational day 3 to delivery. Four pups (two of each sex) from each litter were then tested for spontaneous locomotor activity on postnatal days (PD)19-21. Mean birth weight was significantly lower in pups from nicotine-exposed dams compared to controls, but body weights were equivalent between groups by the time of behavioral testing. Mean distance traveled, vertical counts, and stereotypy counts were lower on PD 19 in pups from pregnant dams exposed to nicotine compared to controls, but only the difference in mean stereotypy counts was statistically significant. Within session analysis revealed that all three activity measures were significantly decreased in nicotine-exposed pups compared to controls in the first five minutes of the session on PD 19. These findings demonstrate that prenatal nicotine exposure in a model that more closely approximates the pattern of nicotine exposure in humans results in offspring that exhibit hypoactivity in a novel environment. Supported by NIDA grant R01-DA15668

454 RURAL STIMULANT USE AND CRIMINALITY IN THREE STATES

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Background: Non-pharmaceutical methamphetamine use, meth cooking, and the illegal use of other stimulants are public health and public safety problems in many rural areas. Despite the increase in the use and production of stimulants in the US, little is known about rural stimulant use and criminality. Method: Data were collected from active (past 30 days) illicit stimulant users not in treatment from three rural areas in Ohio, Arkansas, and Kentucky (N=711). Participants were recruited using a referral method for sampling hidden community populations. ANOVAs were used to identify significant geographic differences on demographic characteristics, drug use, mental health, and criminality. Binary logistic regression was used to determine the independent correlates of an arrest for a drug-related crime within the past 6-months, arrest for a property crime in the past 6-months, and arrest for any other crime in the past 6-months. Results: Rural Kentuckians used significantly more (<.01) non-pharmaceutical methamphetamine in their lifetime (76%) and in the previous 6-months (more than 2 to 3 times a month) than others participants. Each of the three logistic models indicate that younger participants, those with more convictions, and those who use crack frequently are significantly more likely to have committed a drug-related crime, property crime, and another crime during the past six months. Geographic area was only significant in the logistic model predicting the odds of an arrest for a crime not related to drug use or property. Specifically, odds ratios indicate that rural participants from Kentucky and Arkansas, when compared to Ohio, were almost twice as likely to have committed a crime other than a drug or property crime. Conclusions: The U.S. drug abuse treatment system is not prepared for the increasing number of stimulant users in rural areas. Implications include increasing community and corrections-based treatment for stimulant users.

455 RELATIONSHIPS BETWEEN PILL TESTING, RISK PERCEPTION, AND DSM DIAGNOSIS AMONG MDMA USERS IN ST. LOUIS, MIAMI, AND SYDNEY

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This NIDA funded study examined the utilization of harm reduction methods among 636 MDMA users across three study sites: St. Louis (n=297), Miami (n=186), and Sydney (n=153). Participants were classified into MDMA dependence/abuse vs. neither using the Club Drug Substance Abuse Modul (CD-SAM). The Washington University Risk Behavior Assessment for Club Drug Users (WU-RBA-CD) obtained information on harm reduction methods (pill testing) and risk perceptions associated with taking 1 pill of Ecstasy once a week for a month (once weekly) and taking 2-3 Ecstasy pills during the weekend for a month (weekend use). Two 5-way frequency analyses were conducted to develop hierarchical loglinear models for the two MDMA use conditions. The final model for "once weekly" demonstrated a good fit between observed and expected frequencies [Likelihood Ratio $\chi^2(52) = 55.43, p = 0.35$]. The model showed that MDMA users in Sydney were more likely to test their pills (50%) compared to those in St. Louis (34%) and Miami (29%). Risk perceptions were significantly associated with sites. While most of St. Louis and Miami users considered using "once weekly" as dangerous/most dangerous (72% & 63% respectively), more than 59% of Sydney users did not think so. Male users who perceived "once weekly" as not very dangerous were less likely to test their MDMA pills. The model for "weekend use" [Likelihood Ratio $\chi^2(55) = 59.47, p = 0.32$] showed that Sydney also had a higher percentage of "low perceived risk" users (33%) compared to St. Louis (9%) and Miami (18%). These findings strongly suggest cultural differences in pill testing and perceived risks between US and Australian users. However, no significant 2-way association between risk perceptions, DSM diagnosis status, and pill testing was found in both conditions. Further investigation into the underlying mechanisms of MDMA use is needed.

456 ATOMOXETINE TREATMENT OF COCAINE-DEPENDENT ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: AN OPEN TRIAL

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The purpose of this 12-week open trial was to evaluate the safety and utility of atomoxetine in treating adult Attention Deficit Hyperactivity Disorder (ADHD) symptoms and current cocaine dependence (CD). The sample consisted of 12 participants who were predominately male (92%) and 75% Caucasian, 8% Hispanic, and 17% African American. All participants met DSM-IV criteria for ADHD and CD. The mean retention was 4 (± 4) weeks. Two patients (17%) completed the entire trial. Medication doses were raised to an average maximum of 0.75 mg/kg per day. For the 6 patients that made it to the maintenance phase, the mean maintenance dose was 81 mg/day. One patient required a dose decrease due to an increase in blood pressure. Three patients dropped following baseline ratings so only 9 patients were included in the data analysis. Using a combined outcome measure of 1) \square 30% reduction on the self report Adult ADHD Rating scale and 2) an end of study ADHD CGI Improvement rating of 2, 44% of the sample had clinically significant improvement in their ADHD symptoms. Although the Conners-observer ADHD rating scale did not show an improvement in baseline compared to end of study [70 (± 15) vs 62 (± 16); $t = 1.6, p = .16$], the self reported Conners scale did [83 (± 10) vs 69 (± 12); $t = 3.02, p = .02$]. Urine toxicology results found that only 22% of the sample achieved 2 weeks of cocaine abstinence during the trial and there was no significant reduction in the weekly proportion of cocaine positive urines between first and last week [.8 ($\pm .4$) vs .6 ($\pm .5$); $t = 1.49, p = .2$]. Atomoxetine was not as well-tolerated as earlier open trials with sustained-release methylphenidate or bupropion. Although ADHD symptoms improved, there was no substantial reduction in cocaine use. Supported by NIDA Grants: P50DA09236 and K02 00465 and Eli Lilly Co.

457 BEHAVIORAL EFFECTS OF THIENORPHINE IN RHESUS MONKEYS

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Efforts continue to discover new compounds with clinically-significant analgesic effects and low abuse potential. Thienorphine is an oripavine that reportedly has μ -receptor mediated antinociceptive effects in rodents without morphine-like dependence potential. This study evaluated the antinociceptive, rate-altering and discriminative stimulus effects of thienorphine in monkeys. In 3 monkeys, sensitivity to warm-water (40, 50 and 55 C) was assessed (tail-withdrawal) for 2 hr after s.c. injection of thienorphine (0.0032-0.32 mg/kg) and thereafter, daily or every third day, until no effect was observed. In 4 monkeys responding under a multiple food/stimulus-shock termination schedule, sensitivity to the rate-altering effects of thienorphine was assessed for 2 hr and thereafter daily until no effect was observed. Discriminative stimulus effects of thienorphine were studied in 4 morphine-treated (5.6 mg/kg/12 hr) monkeys that discriminated naltrexone. Thienorphine had antinociceptive effects that lasted up to 7 days, with the largest dose (0.32 mg/kg) producing a full (20 sec) effect at 50 C. Doses of thienorphine that were without effect when administered alone, enhanced the antinociceptive effects of morphine. Thienorphine had directly-observable effects (e.g., stupor) and also decreased responding in both components of the multiple schedule with effects being evident for as long as 7 days. Up to doses that increased tail withdrawal latency and decreased rates of schedule-controlled responding, thienorphine failed to substitute for a naltrexone discriminative stimulus and failed to reverse naltrexone-lever responding in monkeys acutely-deprived of morphine. These data show long-lasting antinociceptive effects of thienorphine but fail to support a role of μ receptors in the behavioral actions of thienorphine. Supported by DA05018 and RCA DA17918.

458 IMAGING RESPONSE INHIBITION IN COCAINE-DEPENDENT PATIENTS USING A STOP-SIGNAL TASK

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Background: Behavioral impulsivity has been associated with substance dependence. Methods: We employed a tracking stop-signal task (SST) to compare the behavioral performance and neural correlates associated with response inhibition between patients with cocaine dependence (PCD, n=13) and healthy controls (HC, n=13). In the SST, the frequent, "go" signal instructs the subjects to respond quickly and therefore sets up a prepotent response tendency, and the less frequent, "stop" signal instructs the subjects to withhold the response. The stop-signal reaction time (SSRT) is computed. BOLD signals were acquired for the whole brain with a 3T scanner. Results: PCD did not differ from HC in their general stop signal performance or in SSRT (240 ± 24 msec vs. 224 ± 37 msec). Successful compared with failed stop trials activated in PCD (at $p=0.001$, uncorrected, 10 voxels) visual cortices, perigenual cingulate cortices, left inferior/medial frontal cortex and the left middle frontal cortex (BA 8). Conversely, compared to successful stop trials, failed stop trials activated (at $p=0.001$, uncorrected, 10 voxels) left cuneus, left insula, right thalamus, left dorsal anterior cingulate, and left precentral cortex. These results largely replicated our findings in HC (Li et al., 2006). Comparing PCD with HC showed that no brain regions were significantly more or less activated during stop signal inhibition at the same statistical threshold. With a less stringent threshold ($p=0.01$, uncorrected, 5 voxels), HC showed greater activation in the inferior occipital gyrus (BA 17 and 18), right posterior cingulate gyrus (BA 31) and left superior frontal gyrus (BA 6). No brain regions showed greater activation in PCD as compared with HC. Conclusion: PCD and HC show marked similarity in regional brain activation during stop-signal inhibition. These preliminary results suggest that the SST in its regular context may fail to elicit deficits in response inhibition in PCD. Will PCD be impaired in stop signal inhibition when they experience cocaine craving?

459 ASSOCIATION ANALYSIS OF THE PROTEIN PHOSPHATASE REGULATORY SUBUNIT B1 GENE WITH NICOTINE DEPENDENCE IN EUROPEAN-AMERICANS AND AFRICAN-AMERICANS

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The protein phosphatase regulatory subunit B1 (PPP1R1B) gene (also known as dopamine- and camp-regulated phosphoprotein, 32-KD; DARPP32) is a target for the actions of dopamine. Because the mesolimbic dopaminergic system is implicated in the reinforcing effects of many drugs, including nicotine, the PPP1R1B gene is considered a plausible candidate for involvement in the development of vulnerability to nicotine dependence (ND). Further, this gene is located within a region on chromosome 17 that showed 'suggestive linkage' to ND in our previous genome-wide scan. In the present study, we analyzed six single nucleotide polymorphisms (SNPs) within PPP1R1B for association with the three ND measures, Smoking Quantity (SQ), the Heaviness of Smoking Index (HSI), and the Fagerström Test for ND (FTND) score, in 602 nuclear families of African-American (AA) or European-American (EA) origin. Association analysis revealed that SNP rs3764352 ($P = 0.04$) is significantly associated with HSI in AA samples, while rs879606 ($P = 0.03$), rs907094 ($P = 0.04$) and rs3817160 ($P = 0.02$) are significantly associated with SQ in EA samples. However, no significant associations remained for single SNPs after correction for multiple testing. Haplotype analysis indicated that in the EA sample, the high-risk C-T-G-C haplotype formed by rs2271309-rs907094-rs3764352-rs3817160 with a frequency of 32.0% was significantly associated with SQ ($Z = 2.50$; $P = 0.01$); this finding was still evident after Bonferroni correction. No significant haplotypes were found in the AA sample. In summary, our findings provide the first evidence for the involvement of PPP1R1B in the etiology of ND, and suggest the racial specificity of its impact. (Supported by NIH grant DA-12844).

460 GABAPENTIN HAS NO EFFECT ON COCAINE-PRIMED RELAPSE AND COCAINE-INDUCED INCREASES IN DOPAMINE IN THE NUCLEUS ACCUMBENS

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Gabapentin is a GABA analogue used for the treatment of seizure, anxiety, pain and alcohol withdrawal. It has a complex mechanism of action that may involve increases in the synthesis and nonvesicular release of GABA, as well as prevention of GABA catabolism (Tayler et al., *Epilepsy Res* 29:233-249, 1998). It has been reported that gabapentin dose-dependently inhibits the positive subjective effects of 50 mg/kg of smoked cocaine (Hart et al., *Drug Alcohol Depend*, 73:279-287, 2004). In the present study, we investigated whether systemic administration of gabapentin attenuates intravenous cocaine self-administration, cocaine-triggered reinstatement (relapse) of cocaine-seeking behavior and cocaine-induced increases in dopamine (DA) in the nucleus accumbens. The results indicated that gabapentin (30-60 mg/kg i.p., 30 min prior to testing) failed to alter cocaine (10 mg/kg, i.p.)-induced reinstatement (relapse) of cocaine-seeking behavior in rats previously experienced at intravenous cocaine self-administration. In vivo microdialysis demonstrated that acute cocaine administration significantly increased extracellular DA in the nucleus accumbens, which was not altered by pretreatment with gabapentin. The present findings are to be contrasted to our finding that the GABA-mimic compound gamma-vinyl GABA (GVG) successfully inhibits cocaine-triggered relapse to drug-seeking behavior in the laboratory rat reinstatement model.

461 TETRAHYDROALPAMATINE INDUCES A NEGATIVE BOLD SIGNAL IN THE NUCLEUS ACCUMBENS AND ORBITOFRONTAL CORTEX IN HEROIN-DEPENDENT RATS

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Objective: L-Tetrahydropalmatine (L-THP) treatment for heroin dependents showed a significant reduction in drug craving and increase in abstinence rate. To study its mechanisms, action sites and pharmacokinetics of L-THP on heroin-dependent rat brain were determined by the functional MRI method. **Materials and Methods:** Thirteen drug-naïve Sprague-Dawley rats (90–110 g, male) were treated with heroin over nine days using a progressive schedule. These rats became heroin dependent as evidenced by behavioral changes induced by naloxone. fMRI scanning was performed within 24 hours after the last daily injection of heroin. The rats were then divided into three groups. The first group received a 0.1 mg/kg heroin treatment 5 min into a 25-min scan. The second group received a sham treatment under the same conditions as the first. The third received a 40-mg/kg THP treatment 5 min into a 60-min scan. The heroin was licensed and obtained from NIDA. Under urethane anesthesia, all rats received tracheotomies and were artificially ventilated to maintain stable physiological levels during scanning. fMRI experiments were performed on a Bruker 3T scanner. **Results:** L-THP induced a significant BOLD signal reduction (about 15 ± 5%, n = 3) in the NAC core and shell regions, as well as the orbitofrontal cortex, in the heroin-dependent rats. The time course of L-THP in the NAC showed a long-lasting effect, taking an hour to reach the peak. In addition, it is intriguing that L-THP action showed a very high spatial specificity. The L-THP was sent to NovaScreen (<http://www.novascreen.com/>) and was confirmed that L-THP can significantly bind to dopamine D1, D2 and D3 receptors. **Conclusion:** L-THP significantly induced a negative BOLD signal in the region of the NAC and the OFC in heroin-dependent rats. It is suggested that the L-THP-induced, long-lasting negative BOLD signal in these regions may be related to the clinically observed therapeutic efficacy.

462 CONNECTIVITY ANALYSES REVEAL A LIMITATION OF FAST EVENT-RELATED fMRI DESIGNS WITH AROUSING STIMULI: "CARRY-OVER" EFFECTS

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"Fast" event-related fMRI has enjoyed increased popularity because of its potential to probe, with high temporal resolution, the brain response to very brief, categorically-distinct events. With highly arousing stimuli targeting the same (e.g., limbic) brain regions, we discovered that the functional connectivity triggered by explicitly arousing targets began to "carry-over" to non-emotional (neutral and null events) by the second half of an 8 minute session. We discovered this limitation of fast event-related designs in our recent BOLD fMRI on the brain response to cocaine-related, appetitive (sexual), aversive, and neutral cues in healthy young males (n=18) and in male cocaine patients (n=18). With TR=2 sec, 500 msec target stimuli were presented in a 'jittered' order to optimize sampling of the hemodynamic response function. 120 unique visual stimuli (24 in each of the 4 target categories, plus 24 null events) were presented without replacement, and then repeated. Data were realigned, smoothed, and normalized using SPM2 software. Functional connectivity analyses with amygdala as the reference region were performed separately for the first and second half of the 8 minute session, allowing us to check for habituation or recruitment of effect to the arousing targets. Connectivity analyses in controls revealed that amygdala connectivity increased (sometimes dramatically) between the first and second half of the session, not only for the arousing targets, but also for the intended control (neutral and null) conditions. This "carry-over" of arousal into the neutral and null conditions sometimes undermined random-effect contrasts in the second half of the design. "Sparse" event-related designs with several seconds between targets, may help avoid the confound of "carry-over" connectivity in fast event-related designs.

463 DEVELOPING A MENTAL HEALTH SCREENING INSTRUMENT FOR SUBSTANCE ABUSE TREATMENT

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Research points to high rates of co-occurring mental health disorders among individuals presenting for substance abuse treatment. The co-occurrence of mental health and substance use disorders presents particular challenges for screening and assessment. In March 2000, SAMHSA identified "improving the quality of services available to people with co-occurring substance abuse and mental health problems" as a priority. In its position paper on treating individuals with co-occurring disorders, SAMHSA suggested early identification of co-occurring problems is crucial for treatment success. With funding from the National Institute on Drug Abuse (NIDA), Danya International, Inc. (Danya) and its partners are addressing this need by finalizing the Behavioral Health Screening and Assessment Package. This package will provide the complete set of tools necessary to take clinician: through the entire screening process, including analysis of results and recommendations for treatment placement. This package includes an innovative, user-friendly computer-based screening system designed to rapidly identify potential mental health disorders that commonly coexist with substance-related disorders. In Phase I, Danya developed the pencil and paper versions of the Prescreening Battery and Screening Panel and conducted a pilot study on the feasibility of the instruments. In Phase II, Danya and its partners are converting the screening instruments to a computerized Co-occurring Disorders Screening Instrument, developing the Triage Instrument designed to help clinicians make decisions about patient safety and health status, and evaluating the psychometric properties of the screening and triage instruments in conjunction with a shortened version of the American Society of Addiction Medicine (ASAM) Patient Placement Criteria, Second Edition, Revised (PPC-2R). This presentation discusses the development of the instruments in Phase I and the ongoing psychometric evaluation underway in Phase II of the project.

464 GABA_A RECEPTOR SUBTYPES AND CLINICALLY RELEVANT EFFECTS OF BENZODIAZEPINES: OBSERVABLE BEHAVIOR AND DISCRIMINATIVE STIMULUS EFFECTS OF L-696 IN PRIMATES

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Benzodiazepines (BZs) exert their effects by binding to multiple subtypes of the gamma-aminobutyric acid type A (GABA_A) receptor, namely those subtypes containing alpha-1, alpha-2, alpha-3 and alpha-5 subunits. To understand the potentially different roles of these subtypes in the therapeutic and side effects of BZs, we evaluated GABA_A receptor subtype-preferring compounds in squirrel monkey models predictive of sedative/motor and subjective effects of BZ-type drugs. These compounds included zolpidem, which binds preferentially to GABA_A receptors containing alpha-1 subunits and L-696, which exhibits higher efficacy in potentiating GABA-induced chloride conductance at alpha-3 subunit-containing receptors (approximately 50% increase in a GABA EC₂₀ current) compared to alpha-1, alpha-2, and alpha-5 subunit-containing receptors (approximately 20%). In observation studies of BZ-induced sedative/motor effects, zolpidem engendered sedation, muscle relaxation and pronounced ataxia, while L-696 induced muscle relaxation and relatively mild ataxia only. In a drug discrimination model of the subjective effects of BZs, L-696 did not engender drug-appropriate responding for either the non-selective BZ triazolam or zolpidem. These results suggest that the alpha-3 subunit-containing GABA_A receptor plays a role in the muscle relaxant properties of BZ-type drugs, but not their sedative/motor and discriminative effects. Our results suggest that low-efficacy compounds with selectivity for alpha-3 subunit-containing receptors represent a promising approach for developing anxiolytics lacking BZ-like side effects. Supported by DA18473, DA11792, and RR00168.

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465 COMPARISON OF CANNABIS AND NICOTINE WITHDRAWAL AMONG ADULTS NOT SEEKING TREATMENT

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Recent clinical and neurobiological research indicates that cannabis has greater dependence potential than previously thought. Cannabis withdrawal syndrome has been characterized and validated in nonhuman and human laboratory studies. The clinical importance of this withdrawal syndrome, particularly in relation to frequently documented syndromes such as tobacco withdrawal, remains unclear. The aim of this ongoing study is to compare the severity of cannabis withdrawal syndrome to tobacco withdrawal syndrome. Smokers of either tobacco or cannabis but not both, who were not planning to quit, were recruited to participate in an outpatient study being conducted in either of two cities. Ten tobacco users and twelve cannabis users completed a 7-day baseline smoking-as-usual phase and a 14-day abstinence phase. Participants smoked a minimum of 25 days per month for the prior six months. Urine specimens were collected and analyzed to verify abstinence from the designated substance and other illegal substances. Thrice before and eight times during abstinence, participants completed a series of questionnaires assessing craving and withdrawal symptoms for either marijuana or tobacco. For preliminary analyses, averages of the three baseline measurements (1, 4, and 7 days before abstinence) were compared with averages from the first three days of abstinence. Greater initial abstinence effects were observed in the tobacco group on three measures: irritability ($p < 0.05$), restlessness ($p < 0.05$), and general discomfort ($p = 0.06$). No significant differences were observed on the other abstinence effects commonly observed with the two withdrawal syndromes. These data suggest that cannabis withdrawal has a less severe profile than nicotine withdrawal when assessed using this outpatient laboratory model. Future studies need to examine how these abstinence effects impact quit attempts in persons who are trying to quit on their own or with professional help.

467 SMOKING AND AT-RISK DRINKING AS INDICATORS FOR OTHER UNHEALTHY BEHAVIORS

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Heavy drinking, binge drinking and smoking are well documented risk factors that increase morbidity and mortality. However, the indirect relationship of these behaviors with other unhealthy behaviors has not been investigated in detail. The question of what other health risk behaviors smokers and at-risk drinkers may take was addressed by analyzing select variables from a 1% random sample ($N=2647$) of the Centers for Disease Control and Prevention, 2003 Behavioral Risk Factor Surveillance System database. Smokers were less likely than non-smokers to have leisure time exercise ($OR=.73$, $p<.001$), be trying to lose ($OR=.76$, $p<.001$) or maintain ($OR=.55$, $p<.001$) their current weight, ate less servings of fruits and vegetables ($OR=.73$, $p<.001$), and were more likely to have had sunburn in the past year ($OR=1.24$, $p<.01$). Binge drinkers reported that they ate more fruits and vegetables than non-binge drinkers ($OR=1.45$, $p<.001$), and took part in slightly more leisure time activity or exercise ($OR=1.68$, $p<.05$). Those with binge drinking risk were also more likely to report having had sunburn in the past year ($OR=2.22$, $p<.001$) and have taken less protective measures against high risk sex ($OR=.48$, $p<.001$). Smokers also felt that their ability to perform activities was impaired by their health more often than non-smokers ($OR=1.32$, $p<.01$), whereas, binge drinkers felt less impaired ($OR=.74$, $p<.001$) than those not at risk. In summary, significant differences for many health behaviors were found for those at risk for smoking and heavy/binge drinking. Additional research is needed to further understand the association between smoking and drinking, and other types of adverse health behaviors, and to examine the potential impact of interventions among smokers and drinkers that might target other aspects of healthy lifestyle.

466 ESTRADIOL ENHANCES THE DISCRIMINATIVE-STIMULUS AND SELF-REPORTED EFFECTS OF D-AMPHETAMINE IN HEALTHY PRE-MENOPAUSAL WOMEN

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Variation in the effects of psychostimulants in women and men might underlie differences in the addiction process. There is accumulating evidence that estradiol might be responsible for the enhanced response to psychostimulants sometimes observed in females. In the present study, 9 healthy pre-menopausal women who were using oral hormone-based birth control learned to discriminate 15 mg/70 kg oral d-amphetamine. In addition, subject-rated drug-effect questionnaires and a performance task were administered throughout each experimental session. Once a discrimination criterion was met (i.e., at least 80% correct responding at the final, 3-hr post-drug time point for 5 consecutive sessions), a range of doses of d-amphetamine (0, 3.25, 7.5 and 15 mg/70 kg) was tested alone and in combination with sublingual estradiol (0 and 0.25 mg). Test sessions were conducted during the placebo phase of oral birth-control cycles when endogenous levels of both estradiol and progesterone were at their lowest levels. Data were analyzed using three-factor, repeated-measures ANOVA. d-Amphetamine functioned as a discriminative stimulus and produced prototypical stimulant effects (e.g., increased ratings on abuse-related items from self-reported drug-effect questionnaires, elevated blood pressure). Estradiol enhanced the discriminative-stimulus effects of the 3.25 mg/70 kg dose of d-amphetamine and decreased the time of onset of the discriminative-stimulus effects of the 7.5 and 15 mg/70 kg doses of d-amphetamine. Similar effects of estradiol were found for subject ratings of Like Drug Effect on a Visual Analog Scale. In addition, estradiol increased composite score on the Stimulant subscale of the Adjective-Rating Scale at all active d-amphetamine doses. Finally, estradiol enhanced the effects of the lowest active dose of d-amphetamine on systolic blood pressure. These findings support the notion that estradiol increases sensitivity to the psychostimulant effects of drugs such as d-amphetamine. Supported by NCRR COBRE grant P20 RR15592.

468 BOLD fMRI OF TOBACCO SMOKING

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Tobacco is the most popularly abused drug worldwide. Despite the high prevalence of abuse, little is known about the effects of acutely smoked nicotine on brain. To address this question, experiments were performed in human smokers with functional magnetic resonance imaging (fMRI) during cigarette smoking. A nonmetallic smoking device was constructed and evaluated for its ability to deliver smoke and nicotine to subjects using a paced smoking paradigm. Dependent and nondependent smokers were scanned with concurrent cigarette smoking in both nicotine abstinent and nonabstinent states. Subjects smoked a 100mm Marlboro Red brand tobacco cigarette during fMRI scanning with concurrent assessment of heart rate and changes in subjective mood state. Changes in mood states were assessed by means of computerized visual analog scales presented every 2.5 minutes throughout the functional scan. This task was alternated with brief visual stimulation (a flashing radial checkerboard alternating with a fixation point) in order to assess the impact of peripheral cardiovascular effects of nicotine on measures of BOLD signal changes in the brain. Changes in ratings of both "high" and "craving" were maximal at the end of the 5-minute smoking period. Using General Linear Modeling techniques, changes in subjective reports of "craving" were highly correlated with reductions in regional BOLD signal in reward-related brain regions including anterior cingulate and caudate nucleus ($p<0.002$). This study is the first to assess and report changes in BOLD signal during active tobacco smoking. Supported by NIDA Grant R01 DA019238 (SEL), K25 DA14013 (BF), K25 DA17712 (LN) and KO5 00343 (SEL).

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469 THE ROLE OF ANCILLARY MEDS IN TREATMENT WITH BUPRENORPHINE

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The current study addresses the use of ancillary medications in a recently completed study of the NIDA Clinical Trials Network (CTN) that compared buprenorphine and clonidine in a detoxification protocol. The study design allowed clinicians the option of providing ancillary medications in a supplemental effort to reduce the discomfort of detoxification in cases in which the buprenorphine or clonidine received was not sufficient to suppress all symptoms of opioid withdrawal. Although all patients were provided with approximately the same doses of buprenorphine or clonidine, not all patients received ancillary medications. The current study examines the role of ancillary medications on treatment outcome. A total of five symptoms were treated, and percentages of patients receiving any ancillary meds ranged widely by site, from 2.27% to 100%. Other findings also ranged widely across sites. For example, from 0 to 92% of patients were given anxiety meds, 2.3 - 91.7% received meds for bone pain, 0 - 77% received meds for diarrhea, 0 - 79% received meds for nausea, and 0 - 92% received meds for insomnia. Medication was distributed an average of 6 out of 13 days and average amount decreased daily. Regression analysis indicated that the number of days medication was given for 2 of the 5 withdrawal symptoms successfully predicted treatment outcome ($p < .05$). The more frequently medication was provided to treat diarrhea, the less likely participants were to have a successful outcome (as indicated by providing a negative urine at treatment end). This paper addresses other findings addressing the provision of ancillary medications.

471 WITHDRAWN

470 DETECTION OF CATALEPTIC EFFECTS OF SELECTIVE CB2 RECEPTOR AGONISTS IN RATS

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Since high doses of selective CB2 agonists may be capable of activating CB1 receptors, the lack of a cataleptic effect with high doses of selective CB2 agonists is often used as *in vivo* evidence of cannabinoid receptor selectivity. A more sensitive model based on the findings of Marchese et al. (Br. J. Pharmacol, 2003;140:520-6) to detect threshold doses of selective CB2 agonists that produce catalepsy was established. The nonselective cannabinoid agonist WIN 55,212-2 and the selective CB2 agonists, AM 1241, GW 405833, and HU-308 were tested for the ability to potentiate the effect of haloperidol in the rat bar test. In these experiments, rats were treated with vehicle or cannabinoid fifteen minutes prior to administration of vehicle or a non-cataleptic dose of haloperidol (0.1 mg/kg s.c.) and the time spent with the forepaws on a raised bar (8 cm high) was measured. WIN 55,212-2 (1 mg/kg i.p.) was not cataleptic when administered alone (1.2 ± 0.2 sec). However, when it was administered with haloperidol, a pronounced cataleptic effect of 131 ± 18 sec was observed. AM 1241 and GW405833 which are 55- and 177-fold selective (based on pKi values in binding assays) for CB2 receptors compared to CB1 receptors significantly potentiated the effect of haloperidol at a dose of 10 mg/kg (i.p.). The results obtained with GW405833 in the presence of haloperidol demonstrated that significant catalepsy was observed at a dose that was ten times lower than the dose of GW405833 that produced catalepsy by itself (Valenzano et al., Neuropharmacology, 2005;48:658-72). HU-308, which is 194-fold selective for CB2 receptors, did not produce catalepsy on its own nor potentiate the effect of haloperidol at doses up to 60 mg/kg (i.p.). Our findings indicate that using the potentiation of the effect of haloperidol in the rat bar test to assess catalepsy may be a more sensitive and useful assay to detect cataleptic doses of selective CB2 agonists, than evaluating the cataleptic effects of the CB2 agonists by themselves.

472 ORAL AND DERMAL PRODUCTS ELABORATED WITH COCA LEAVES SOLD OVER THE COUNTER. LEGAL IMPLICATIONS

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Currently more than one hundred commercial coca leaf products are elaborated for human consumption by oral and dermal routes which are sold over the counter. Most are made in Bolivia, Colombia and Peru from whole coca leaves (containing natural cocaine). In the USA and almost all countries in the world, coca leaves products (cocaine free) are also sold over the counter. The most famous cocaine free, but not coca free product is a refreshing drink (Coca Cola). There are more cocainized products (>95%) than decocainized products sold over the counter, but they are limited to the Andean countries. Coca leaves, coca teas, coca mixtures, coca wines, candies, coca flour, cookies, energetic drinks, gums, tooth paste, soap, hair shampoos, coca tablets, coca tonics, anesthetic solutions, and several products for traditional medicine and cocaine (agonist) therapy are sold freely and at low prices in these countries. Many products containing cocaine are very popular among tourists that travel to these regions and are consumed during their stay: coca leaves chews, coca tea (mate de coca), coca candies and energetic drinks, mainly for physiological stimulant effects (to reduce high altitude effects). Urine toxicological tests done in native and tourist (volunteers) after they consume these products showed positive results to cocaine in all cases. Coca Cola and other cocaine free products showed negative results for cocaine in urine tests. Because cocaine positive urine tests could remain for 48-78 hours after the consumption of whole coca products many tourist could have legal problems if they return to their countries during this period.

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- 473** HOW NICOTINE INCREASES IMPULSIVE CHOICE: ANSWERS FROM IMPULSIVE AND RISKY CHOICE PROCEDURES IN RATS
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Impulsive choice, or preference for small immediate reinforcers over large delayed reinforcers, has been associated with cigarette smoking. Three experiments examined whether nicotine was at least partly responsible for this association, and whether an increase in temporal discounting - or the rate at which reinforcers lose value with increasing delay - could account for changes in impulsive choice. In Experiment 1, rats (n=5) chose between a smaller, sooner reinforcer and a larger, later reinforcer. Nicotine dose-dependently increased impulsive choice (all experiments used vehicle, 0.03, 0.1, 0.3, and 1.0 mg/kg). Experiment 2 tested whether temporal discounting could account for these findings. We used a risky choice procedure in which rats (n=9) made discrete choices between a variable delay (short and long delays; the risky option) and a fixed, moderate delay to a single pellet. The options differed only in the relative delays to the reinforcer, not in the amount of the reinforcer. Nicotine did not affect risky choice, however, suggesting that nicotine may have decreased amount sensitivity rather than increased temporal discounting in Experiment 1. By amount sensitivity, we mean the degree to which increases in reinforcer amount increase reinforcer value (which is not the result of a simple anorectic effect). A decrease in sensitivity would mean that large reinforcers would seem more like smaller reinforcers. In Experiment 3, therefore, we modified the risky choice procedure so that rats (n=9) chose between a variable delay to a smaller reinforcer and a fixed delay to a larger reinforcer. Nicotine increased risky choice when different amounts were involved, which parallels the finding of an increase in impulsive choice in Experiment 1. Overall, the results suggest that while nicotine does increase impulsive choice, this increase is better accounted for by a decrease in amount sensitivity rather than an increase in temporal discounting.
- 474** WITHDRAWAL SUPPRESSION EFFICACY OF TRAMADOL?
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Tramadol (T) is an unscheduled low affinity mu-opioid agonist that appears to have low abuse liability. Its pharmacological activity in opioid dependent persons is relatively unstudied. This study characterized T's ability to suppress spontaneous opioid withdrawal. Opioid dependent participants (n=10) on a residential unit were maintained on morphine (M) 60 mg/day (15 mg SQ QID), and had twice weekly study sessions. Prior to sessions, two M doses were omitted to produce mild spontaneous opioid withdrawal. Observer ratings of opioid withdrawal signs (possible range: 0-14) at the start of sessions showed scores of 5.3, confirming spontaneous withdrawal. Nine double-blind, double-dummy drug conditions were evaluated in random order: placebo, T (50, 100, 200, and 400 mg PO), naloxone (N) (0.1 and 0.2 mg IM), and M (7.5 and 15 mg IM). Outcome measures included physiological indices, subjective and observer-rated responses, and psychomotor/cognitive performance tasks. N and M produced prototypic opioid antagonist and agonist effects, respectively [e.g., mean peak visual analog scale (VAS) rating (range 0-100) for bad effects for N 0.2 was 61; and mean peak VAS rating of good effects for M 15 was 30]. T produced dose-related increases in several subjective measures. T 400 produced mean peak VAS rating scores of 35 for drug effects, 11 for good effects, 33 for bad effects, and 11 for liking. Observer mean peak opioid withdrawal scores increased from baseline for N and placebo, decreased for M, and increased for T 400 (similar in magnitude as placebo). As T dose increased, participants had higher rates of identifying T as not placebo, although T's profile was not clearly opioid agonist or antagonist like. These results suggest acute doses of T exert psychoactive effects that differ from prototypic opioid agonists and antagonists. Supported by R01 DA018125, K02 DA00332, and T32 DA07209.
- 475** HOMER1A IS NOT NECESSARY FOR BEHAVIORAL RESPONSIVENESS TO COCAINE
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In mammals, the Homer1 gene encodes a number of transcriptional variants of which ania-3 and Homer1a are induced in an immediate early gene (IEG)-like fashion by synaptic activity, including treatment with various drugs of abuse. Earlier work demonstrated that deletion of the entire Homer1 gene produces a cocaine "pre-sensitized" phenotype in mice that is characterized by an enhanced behavioral and neurochemical response to cocaine. To delineate the role for Homer1a induction in the cocaine phenotype of Homer1 knock-out (KO) mice, we assessed for cocaine-induced changes in behavior using a novel Homer1 mutant mouse that lacks Homer1a. When assessed in a place preference paradigm, Homer1a KO mice did not differ from their wild-type (WT) controls on all variables of interest including: basal locomotor activity, locomotor hyperactivity in response to either acute or repeated cocaine (4 X 10 mg/kg) or the increase in time spent on the cocaine-paired side. These data indicate that Homer1a is not necessary for cocaine-induced locomotor hyperactivity or conditioned reward and implicate further a down-regulation in constitutively expressed Homer proteins in determining behavioral sensitivity to cocaine, and perhaps other drugs of abuse. Supported by a NARSAD Young Investigator Award and a Faculty Career Development Award from UCSB to KKS.
- 476** NEURAL ACTIVATION DURING SMOKING SELF-CONTROL: fMRI ASSAY
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Sustained smoking cessation requires that individuals abstain even while they crave cigarettes. In order to study brain substrates relevant to this behavior, 11 acutely abstinent (overnight) cigarette smokers participated in a "self-control challenge" that utilized a specialized smoking apparatus in conjunction with fMRI. Prior to each trial, the participants watched video cues of smoking until they reported craving. Two types of trials were included: "Smoke Self-Control" trials, in which smoke was immediately available but participants were encouraged to "try not to smoke on as many of these rounds as you can manage," and "Smoke Unavailable" trials, in which access to smoke was mechanically blocked. Participants abstained from smoking on 68.5% of Smoke Self-Control trials, and rated the difficulty resisting the urge to smoke to be 6.1 + 2.1 on a 10-point scale. In the fMRI contrast comparing trials in which the participant voluntarily abstained with those in which there was no access to smoke, significant activation (Smoke Self-Control > Smoke Unavailable) was observed in a cluster encompassing portions of the dorsal anterior cingulate cortex and supplementary motor area, as well as in smaller clusters in the right dorsolateral prefrontal and in the right inferior frontal gyrus, encompassing part of the insula as well. Correlational analysis indicated greater signal change among participants who reported more difficulty abstaining during the Smoke-Self Control trials. The observed activation reflects process engaged during effortful self-control. [NIH K01 DA0051-01A1(JM), R01DA14093, TRDRP 12IT-0198 (JM)]

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477 QUALITY OF LIFE IN METHAMPHETAMINE USERS

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Methamphetamine is one of the most widely used stimulants worldwide. Although the prevalence rate of use in the United States has remained stable over the past few years, the number of methamphetamine users who meet criteria for stimulant abuse and dependence has been on the rise. Common reasons for use of the drug include efforts to improve or enhance one's life and to uplift one's mood. Nevertheless, acute effects of the drug lead to temporary improvements in mood followed by negative affect. We sought to extend this work to other aspects of mood and quality of life. Over 6000 adults completed an internet survey consisting of measurements of depression, apathy, satisfaction with life, and happiness, in addition to measures of methamphetamine use. We compared those who had used methamphetamine at least once within the past year (N=610) to those who had never used (N=6070). Participants ranged in age from 18 to 88 and came from an assortment of educational backgrounds. Methamphetamine users had significantly higher levels of depression and apathy, and lower levels of happiness and satisfaction with life than did non-users. No gender differences appeared. Methamphetamine use may decrease one's quality of life instead of enhancing it, which is contradictory to the perceptions of many users. Increasing awareness about methamphetamine's negative impact on mood and life satisfaction might help decrease prevalence of the drug's use and associated troubles.

478 REDUCING BENZODIAZEPINE CONSUMPTION IN OPIOID MAINTENANCE THERAPY PATIENTS: A CONTROLLED CLINICAL TRIAL

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Benzodiazepine (BZD) use is widespread among patients receiving opioid maintenance therapy, and is associated with behavioural problems and increased risk of overdose. Thirty-one BZD-dependent patients maintained on methadone or buprenorphine were recruited to a 12-month controlled trial assessing the efficacy of an intervention designed to reduce levels of BZD use (n=18) against a 'routine care' control group (n=13). The intervention involved replacing participants' baseline BZD use with an equivalent dose of clonazepam (a long-acting BZD), which was gradually tapered over 9 months (interrupted by 3 stable dose periods) with concomitant administration of sodium valproate to reduce withdrawal severity. Clonazepam dosing was supervised by a pharmacist together with the patient's methadone or buprenorphine dose. Patients were assessed during the trial and on completion at 12 months using self-report as well as urine and blood analyses. BZD use in the intervention group declined from 58mg to 13mg per day (mean, diazepam equivalent dose) and was significantly different from the control group (p=0.036). Of the eight participants who completed the intervention, three showed no evidence of BZD use based on analyses of blood and urine samples, three were using BZDs at therapeutic levels and two were using BZDs at levels slightly above the upper therapeutic limit. Amongst the intervention group severity of dependence scores also reduced from 10 to 3 (scale of 15 max; mean scores; p=0.001), with only one patient having a score in the significant range (i.e. 7 or more) at completion of treatment. The number of doctors accessed for BZD prescriptions also decreased (p<0.05). The results suggest that a long term intervention incorporating slow dose reduction, supervised dosing and sodium valproate co-administration was effective in reducing BZD consumption in a sample of opioid maintenance therapy patients.

479 PRENATAL EXPOSURE TO TOLUENE INDUCES LONG-TERM BEHAVIORAL DEFICITS IN MICE WHEN TESTED IN ANIMAL MODELS OF ANXIETY

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Several studies have reported that prenatal exposure to the abused solvent toluene may result in newborn adverse developmental impairment; however, few studies have analyzed the long-term impact of inhaled abuse during pregnancy on the offspring. The aim of the present study was to elucidate the long-term neurobehavioral effects of toluene prenatal exposure in the male offspring. Dams were exposed in a static exposure chamber to 8000 parts per million (ppm) toluene or air for 30 min, twice daily, from the 8th day of gestation through the 20th. After parturition, pups were tested on postnatal day 7 (PN7) and PN14 in a biobehavioral developmental test battery that included negative geotaxis, surface righting and grip strength. Prenatal exposure to toluene induced significant deficits in surface righting reflex and grip strength, but not in negative geotaxis. On PN30 and PN90, mice were tested in two animal models of anxiety: the avoidance exploratory behavior test (AEBT) and the defensive burying behavior test (BBT). In the AEBT, toluene prenatal exposure induced a decrease in the number of transitions between light/dark compartments and in the time spent in the illuminated side, in comparison with the air control group in both PN30 and PN90 mice. In the BBT no significant differences were found in parameters denoting anxiety-like behaviors; however, prenatal exposure to toluene induced a significant increase in the number of shocks that mice received during the BBT in both PN30 and PN90 mice. In order to discard non-specific effects on general activity, all mice were evaluated in the open field test finding that toluene prenatal exposure consistently decreased general activity at all ages. Finally, a record of body weight was kept all over the experiment; mice exposed in uterus to 8000 ppm toluene weighed significantly less than control mice. This research was partially supported by grants No. 43604-M (to S.L.C.) and 40895-M (to C.L-R) from Conacyt.

480 EFFECT OF MOTIVATIONAL INCENTIVES IN A COMMUNITY ADOLESCENT TREATMENT CENTER

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Numerous controlled studies have shown that motivational incentives effectively reduce drug use, but implementation in community treatment centers has been slow. This observational study examines the effect of a contingency management (CM) program on urine and attendance data in a community treatment center for adolescents. The treatment center uses offsite urine testing, and treatments include 12-step facilitation, cognitive behavioral therapy, and motivational enhancement. In the CM program, patients with negative urines or perfect attendance can earn chances each week to draw from a bag for prizes of varying value. Patients can make an increasing number of draws with consecutive negative urines. Attendance and urine data were collected for patients admitted before and after implementation of the CM program, and rates were compared using chi-square tests. For 51 patients (age 13-18) discharged before implementation of the CM program, a total of 125 urine tests were taken with 37% positive (32% cannabis, 0.8% cocaine, 6.5% amphetamine, 2.2% benzodiazepines, and 13.0% opiates). 45% of patients had positive urines at treatment entry, and of these 57% produced positive urine throughout treatment. Preliminary results with the first 7 patients enrolled in the first week of the CM program revealed no significant change in overall urine positive rates but a trend toward improved attendance, increasing from 89% total days present to 100% total days present (p<0.06). Attendance and urine data from an expected 80 additional patients will be collected and analyzed to examine the impact of the CM program on these objective measures.

481 INHALANT USE IN YOUTH: WHAT ARE THE RISKS?

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Introduction: Inhalant abuse during adolescence is associated with significant morbidity and mortality, yet there is a current paucity of services specifically targeting the needs of this group, and no consensus on appropriate clinical management. The aim of this paper is to review the current literature on inhalant use in young people, describing its epidemiology and the medical, neuropsychological, psychiatric and social correlates of use. Method: The authors conducted a comprehensive review of the inhalant literature, specifically focusing on publications related to psychiatric, neuropsychological, medical and social correlates of use. Results: Epidemiological studies to date primarily focus on experimental use alone, with little data available regarding rates of regular use or inhalant use disorders amongst young people. However, the major risk factors for inhalant use during adolescence appear to relate to peer variables and deviant behaviours, although socio-economic, school and family-related factors also seem relevant. Inhalant use is also associated with significant psychiatric and drug use morbidity, and has been suggested to be an important marker for later psychopathology, although no study has clearly identified an age or level of use that places young people at high risk. Whilst a wide array of associated toxic and medical complications have been reported in adult users and those with occupational exposure, limited research has been conducted in adolescent users. Inhalant use has also been consistently associated with neurological and cognitive deficits, with evidence of structural and functional abnormalities. Conclusions: Studies to date primarily consist of small cross-sectional studies of young people with a lifetime history of inhalant use (rather than current abuse), and typically focus on a narrow set of variables. In order to develop new treatment strategies that specifically address the needs of this population, a rigorous investigation of the impact of inhalant abuse during adolescence is urgently required.

482 REGIONAL BRAIN ACTIVATION PATTERNS DURING ACUTE MARIHUANA SMOKING: A HUMAN fMRI STUDY

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It is unclear exactly how marihuana affects brain function and behavior and so brain imaging studies will likely aid in our understanding of the neurobiological bases of marihuana abuse and contribute to the development of new medications to treat cannabis dependence. New and improved brain imaging techniques such as functional Magnetic Resonance Imaging (fMRI) offer a unique opportunity to view these subtle, yet important changes in brain function during smoking. After providing informed consent, 23 adult male and female paid volunteers, who met criteria for cannabis abuse, smoked a marihuana cigarette (3.51% delta-9-THC) via a customized smoking device during fMRI acquisition. Participants reported changes in mood state and marihuana effects via a keypad. A logarithmic polar checkerboard pattern (off-on-off-on-off, 12 sec/epoch) was presented for 60 sec, every 2.5 min to control for nonspecific changes in blood flow. Reports of "Feel Effects", "Like Drug" and "High" rapidly increased during smoking, peaked by 20 minutes and gradually declined over the next 40 min; heart rate changes paralleled this pattern. "Anxious", "Irritable" and "Crave" decreased after smoking but then gradually increased over time. Using a General Linear Model in 3 participants, changes in subjective reports of "High" were highly correlated (Bonferroni corrected $p < 0.05$) with regional increased activation in caudate, anterior cingulate and nucleus accumbens (2.8, 3.75 and 5.9% signal change, respectively). As there were no corresponding changes in visual cortex, we conclude that these effects are selective for marihuana and are not secondary to hemodynamic effects. This study is the first report of real time changes in brain activation during marihuana smoking and demonstrates that marihuana activates areas of the brain typically associated with reward. Supported by NIDA Grant DA019238 (SEL), K25DA14013 (BF), K25DA17712 (LN) and KO500343 (SEL).

483 CUE-INDUCED MARIJUANA CRAVING IN MEDICATION DEVELOPMENT: SPECIFICITY OF THE MODEL

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Craving is a phenomenon reported by most marijuana abusers and may be related both to the perpetuation of abuse and to relapse after treatment. Therefore, marijuana craving may be an important target for medication development. A laboratory model that reliably can induce and measure this difficult construct is vital for evaluating the efficacy of pharmacologic compounds in either blocking or attenuating craving for marijuana but until now has been lacking. This study tested the specificity of a cue-induction paradigm developed for potential use in evaluating medications for cannabis use disorders. Thirteen (5 male and 8 female) healthy, young adults (mean age = 28.7 ± 4.5 yrs) who met DSM-IV criteria for Cannabis Dependence but no other substance use disorder were exposed to neutral and marijuana-related tactile, visual, auditory, and olfactory cues while changes in mood, craving, and heart rate were assessed. Repeated measures ANOVAs revealed that exposure to marijuana-related cues significantly increased ratings on all VAS indices of marijuana craving ("Craving for Marijuana", "Urge for Marijuana" and "Desire for Marijuana") relative both to baseline and neutral cue exposure. Exposure to marijuana cues did not elicit craving for any other drugs including alcohol and nicotine. These findings indicate that marijuana cue reactivity is both cue and drug specific. There were no differences on any of the mood state items, or heart rate change. These findings suggest that the marijuana cue reactivity paradigm offers a strategy for assessing, under carefully controlled laboratory conditions, a medication's efficacy in attenuating craving and reactivity to marijuana-related cues. This model may provide an efficient means of identifying promising compounds for cannabis use disorders prior to undertaking expensive and time-consuming clinical trials. Supported by Grant DA019236 and Joe Young, Sr. Funds from the State of Michigan.

484 GENDER DIFFERENCES IN PATTERNS OF ADOLESCENT SMOKING: POTENTIAL EFFECTS OF SOCIAL ENVIRONMENT

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Previous studies have reported that adolescent girls may be more inclined to smoke for social reasons than boys. The purpose of this analysis was to examine real-time socio-environmental data to test whether girls were in fact more likely than boys to smoke in social situations. Adolescent smokers were prompted to report social environment and smoking behavior via electronic questionnaires at 3 time-points (early morning, after school, and bedtime), and also complete two additional self-initiated reports daily. Data from 2218 reports completed to date by 22 participants (mean age 15.8 years SD 1.2, 1 American Indian, 4 African Americans, 16 Caucasians, 1 Other) were collected. The presence of family and friends, and smokers and non-smokers and whether participants had smoked since their last entry was assessed. Linear regression analysis revealed no difference in the presence of family ($p = .946$), or smokers ($p = .702$) when smoking was reported. Boys showed a weak trend toward smoking more in the presence of friends and non-smokers ($p = .171$ and $p = .127$ respectively). Contrary to our hypothesis, data suggested that boys were more socially influenced than girls in their smoking behavior. Further analyses of social environment and gender differences in smoking behavior using larger samples and adjusting for potential confounds of level of dependence and cigarettes smoked per day are needed. Supported by NIDA Intramural Funds.

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485 ENHANCED PKA-REGULATED SIGNALING IN FEMALE RATS MAY CONTRIBUTE TO SEX DIFFERENCES IN COCAINE SELF-ADMINISTRATION

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Chronic cocaine treatment produces long-term changes in the dopamine D1-cAMP-PKA signaling pathway that are thought to underlie the development of cocaine abuse. Previous work has demonstrated sex differences in progression to cocaine abuse. We therefore examined the possibility that this pathway is differentially activated by cocaine in male and female rats. Rats were allowed to self-administer cocaine under a discrete trial procedure allowing 24-hr access to cocaine (1.5 mg/kg) or saline for 7 days. Rats were then tested under a progressive-ratio schedule following either 0 or 10 days abstinence. Western blotting was used to evaluate markers of PKA signaling including phosphorylation of dopamine and cAMP-regulated phosphoprotein of 32 kDa (DARPP-32) at Thr 34 and glutamate receptor 1 (GluR1) at Ser 845. Levels of DARPP-32, GluR1, and CDK5 in the nucleus accumbens and striatum were also examined. Phosphorylation of DARPP-32 at Thr 34 was increased in female rats compared to male rats in the striatum, particularly at baseline and after a 10-day abstinence period. Phosphorylation of GluR1 at Ser 845 in the nucleus accumbens was differentially regulated in female rats and male rats as a consequence of cocaine administration. DARPP-32 and CDK5 were increased in the striatum in both male rats and female rats after a 0-day abstinence period compared to baseline and to a 10-day abstinence period. These findings indicate sex differences in PKA-regulated signaling at baseline and as a consequence of cocaine exposure, and suggest that PKA-regulated signaling in the nucleus accumbens and striatum may contribute to sex differences in cocaine self-administration.

486 COCAINE PATIENTS HAVE MARKEDLY HIGHER RATES OF BOTH CHILDHOOD AND ADULT ADHD SYMPTOMS AS COMPARED WITH HEROIN PATIENTS AND CIGARETTE SMOKERS

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Within the general population, between 3-9% of children have ADHD, and rates of adult ADHD are estimated at <1% to 5%. Elevated rates of adult ADHD (up to 35%) are reported in substance abusers. In this group, ADHD is associated with more emotional/social problems and poor clinical outcomes. Whether the rates of "true" ADHD (i.e., ADHD that manifests in childhood prior to drug use & persists into adulthood) vary across substance abuse populations is of clinical and theoretical interest. We examined childhood and adult ADHD symptoms in 37 treatment-seeking cocaine patients, 32 methadone-maintained opiate dependent patients (MM), and 44 treatment-seeking nicotine-dependent smokers. Methods: The Brown ADD Scale (BADDS) and the Wender Utah Rating Scale (WURS) were used, respectively to assess for symptoms of adult and childhood ADHD. Validated cut-off scores were used to establish diagnoses of adult & childhood ADHD. Results: Cocaine patients had the highest incidence of childhood ADHD (38%), twice that observed in MM (19%). Similar to the general population, 5% of smokers met childhood ADHD criteria. ADHD symptoms were more prevalent in adulthood than childhood in both the cocaine and MM groups. In comparison to MM, cocaine patients had twice the incidence of adult ADHD (52% vs. 26%). No smokers met threshold for adult ADHD. Only 24% of cocaine and 6% of MM patients met criteria for "true" ADHD (both childhood and adult). Conclusion: Relative to the general population, rates of "true" ADHD were greatly elevated in cocaine patients, and four-fold higher than in MM patients. "True" comorbid ADHD may represent a unique brain vulnerability that impacts the acquisition and course of cocaine addiction and treatment response. Acknowledgments: NIDA RO1 DA-10241 (Childress), NIDA P60-DA-05186, NIDA K01 (Franklin), NIDA K23 (Langleben), Research Div., VAMC, VA VISN 4 MIRECC, and the Alexander Foundation.

487 A STUDY TO DEVELOP A NATIVE AMERICAN CURRICULUM FOR STATE-ACCREDITED, NON-TRIBAL SUBSTANCE ABUSE PROGRAMS IN SOUTH DAKOTA

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The purpose of this study was to assess and evaluate perceptions of Native American beliefs and practices among staff members of state accredited, non-tribal substance abuse programs in South Dakota. A Native American curriculum will be developed based on the survey results. The methodologies employed for this study included the development and administration of a Native American Cultural Assessment Survey (NACAS). This 165 item survey was administered to staff members of 25 state accredited, non-tribal substance abuse programs in SD. Survey results revealed that staff members possessed very little awareness/knowledge about the cultural/spiritual ways of Native Americans, yet 42% of their clients were of Native American ancestries. This data strongly suggested that staff members would benefit from a training program aiding them to become more aware of Native American cultural/spiritual ways, and increase their cultural competency levels. The impact of this curriculum effort was measured by a pre and post tests of knowledge. Pre-test score mean=56%. Post-test mean score=79%. Narrative responses on evaluations, revealed that the participants: appreciated the opportunity to learn about Native American cultural/spiritual ways; and improved their understanding levels of Native American cultural/spiritual ways. A large number of the clients served by state accredited, non-tribal programs in SD are of Native American heritages. Their counselors had very little knowledge/insights into the cultural/spiritual ways of their Native American clients. They have very little Native American cultural competency training. The Native American Cultural Assessment Survey processes, and the Native American curriculum, have the potential to serve as a model for other states to consider in the area of enhancing the "cultural competency levels" of non-tribal members, who provide substance abuse treatment services for Native Americans.

488 WITHDRAWN

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- 489** REPEATED EXPOSURE TO COCAINE ELICITS SYNAPTIC PLASTICITY IN RAT MESOLIMBIC SLICE CULTURE
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Behavioral sensitization to drug-induced locomotor stimulation is a model for drug addiction, which is characterized by progressively enhanced dopamine (DA) release in the mesolimbic system. Recent studies suggest that neural plasticity may be involved in the observed behavioral sensitization. We examined the effect of repeated exposure to cocaine (COC) on synaptic transmission and on DA release in the mesolimbic system using an organotypic slice culture. A slice of each of the medial prefrontal cortex (mPFC), the nucleus accumbens (NAc), and the ventral tegmental area of neonatal rat was arranged and maintained in a multi-electrode dish (MED) filled with culture medium. A field excitatory postsynaptic potential (fEPSP), recorded extracellularly by an MED, was evoked in the NAc of the culture by a single electrical stimulus of the mPFC. For analysis of DA release, the cultures were incubated in Krebs Ringer solution for 30 min, and the content of DA in the collected solution was determined with HPLC. The cultures were incubated in a culture medium including COC for 30 min per day for 5 consecutive days, and the amplitude of fEPSP and the content of DA were measured before and during the COC exposure. A single exposure of naive cultures to COC at 1-10 μ M attenuated the amplitude of fEPSP and augmented the content of DA in a concentration-dependent manner. Repeated exposure to 1 μ M COC, which had no significant acute effect, progressively potentiated both the depression of fEPSP and the increment of DA content during the cocaine exposure. Seven days after the cessation of the COC exposure, COC challenge reproduced the potentiation of the depression of fEPSP and of the increment of DA content. These results suggest that repeated exposure to COC sensitizes synaptic transmission to the inhibitory effect of COC in mesolimbic slice culture, which is synchronized with the potentiation of COC-induced DA release. These may be some of the synaptic mechanisms underlying behavioral sensitization involved in drug addiction.
- 490** OUTCOMES FOR BUPRENORPHINE MAINTENANCE PATIENTS IN OFFICE-BASED PRACTICE
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Background: Buprenorphine (bup) is an efficacious treatment for opioid addiction approved for use in office-based practice. Objective: To determine outcomes and correlates of outcomes for patients accepted for bup maintenance in office-based practice. Methods: Convenience sample of 6 physicians in New York City completed anonymous chart abstraction forms for all their office-based practice patients, past and current, who had been accepted for bup maintenance during 2003-2005 (N=109). The endpoint was the patient's current status or status at discharge from the index practice, presented in an intent-to-treat analysis. Results: Male, 73%; age (mean), 38 yrs; White non-Hispanic, 70%; employed FT, 49%; Hep C+, 15%; primary opioid of abuse heroin-46%, hydrocodone-29%, oxycodone-18%; abusing non-opioids at intake, 41%; completed induction, 86%; length of bup tx (mean), 9 mos; maintenance dose (mean), 18 mg; prescribed psychiatric medication during tx, 59%. The most frequent psychiatric disorders were: major depression obsessive-compulsive and other anxiety, bipolar. Prescription opioid abusers were more likely than heroin users to receive psychiatric medication ($p < .05$). At endpoint: Retained in index practice, 49%; transferred to other bup practice, 4%; transferred to methadone maintenance, 9%; transferred to other tx, 3%; lost to contact or AMA, 35%. Patients employed full-time, living in their own home and abusing prescription opioids rather than heroin, were significantly more likely to be retained in the index practice ($p < .05$). At the endpoint, known substance abuse was 25% (including opioids, 8%). Conclusions: Outcomes were positive, in that 2/3 of patients accepted for bup maintenance remained in the index practice or transferred to other treatment at the endpoint. Co-morbid psychiatric disorders and non-opioid substance abuse were common, presenting a challenge to bup maintenance in office-based settings.
- 491** MECHANISMS OF MORPHINE-INDUCED TIGHT JUNCTION MODULATION IN BRAIN MICROVASCULAR ENDOTHELIAL CELLS
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TJ disruption and breakdown of the blood brain barrier (BBB) are key features of HIV-1 encephalopathy. Tight junctions (TJ) consist of claudins, occludins and the junctional adhesion molecules. The regulatory mechanisms involved in the disruption of tight junctions during neuroinflammation are not fully understood. HIV-1 induced neuroinflammation could result in cytoskeletal changes in the tight junctions and myosin light chain phosphorylation. The signaling molecules that directly control cytoskeleton organization are of particular significance with regard to TJ function. Several studies have implicated the RhoA GTPases and myosin light-chain kinase (MLCK) protein expression in TJ regulation. The role of opiates as a co-factor in the neuropathogenesis of HIV-1 is well established; however the mechanisms by which opiates increase the neuropathogenesis of HIV-1 remain uncertain. We hypothesize that the mechanism by which morphine modulate TJ regulation involves the activation of Rho A and MLCK resulting in TJ disruption and BBB dysfunction. BMVEC were cultured with morphine for 24 hr, RNA was extracted and Rho A and MLCK gene expression was quantitated using real time PCR. Morphine (10⁻⁷-10⁻¹¹ M) significantly increased RhoA and MLCK gene expression, compared to the untreated control. Western blots results show that morphine treatment results in a significant increase in MLCK protein expression. These results suggest that the activation of the Rho GTPases and MLCK may be the signaling mechanisms that are involved in TJ modulation. Understanding the mechanism(s) of morphine induced TJ modulation may help to develop innovative strategies to prevent disruption of the TJ in opiate users.
- 492** EFFECTS OF RIVASTIGMINE TREATMENT ON INTRAVENOUS SELF-ADMINISTRATION OF METHAMPHETAMINE IN METHAMPHETAMINE-DEPENDENT VOLUNTEERS
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The development of a valid human laboratory model of intravenous methamphetamine (MA) self-administration would greatly facilitate study of MA addiction. Neurocognitive dysfunction has been associated with long-term MA exposure and is predicted to contribute to illness severity. Rivastigmine is an acetylcholinesterase inhibitor that may ameliorate cognitive dysfunction. In this study, 18 (N=6 group) non-treatment-seeking MA-dependent volunteers were randomized to receive rivastigmine (0 mg, 1.5 mg qd, or 3 mg bid) administered for 10 days. On a specified day, patients sampled MA (30 mg, IV) or placebo and these were designated as either the "green" infusion or "red" infusion. On a separate day, participants made a series of blinded choices to receive the green or red infusion either or a monetary alternative. The procedure was performed using a patient-controlled analgesia (PCA) pump. The blind has not yet been broken on the doses of rivastigmine tested, so the data are discussed in the absence of that information. In general, when patients subjectively reported that they were receiving MA, an infusion was selected if the monetary alternative was low, and dollar choices if the monetary alternative was high. When patients subjectively reported that they were receiving placebo, >95% of all choices were for money. Of interest, of the 13 individuals who have completed the protocol thus far, not one has taken all the MA that was available during a given session. In addition, in a subset of patients who self-reported a desire to abstain, or to "get clean", all available MA infusions were declined. Overall, the data reveal an orderly relationship between MA self-administration and the magnitude of available alternative reinforcers. These data also highlight similarities and differences between drug self-administration findings obtained using preclinical animal models and those obtained with human subjects. Supported by NIDA: DA-14593, DA-18185, DA-17754

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- 493 ACCESS TO HEPATITIS TREATMENT AND RISK BEHAVIORS AMONG DISENFRANCHISED DRUG USERS FROM RIO DE JANEIRO, BRAZIL**
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- BACKGROUND:** Drug users (DUs) are a marginalized population, who do not access health services on a regular basis, at high risk for viral hepatitis but low access to treatment. **METHODS:** We examined correlates of access to alcohol/drug abuse and to Hepatitis treatment, as well as the 'missed opportunities' for Hepatitis treatment among 111 DUs with HBV/HCV. Demographics, drug use and sexual behaviors, health and incarceration history data were collected. **RESULTS:** Most interviewees (84.4%) were male, of African-Brazilian descent/biracial (65.7%), had less than 4 years of education (56.8%), and lived with less than \$200 a month (76.7%). In the last 6 months, 63.3% of participants snorted cocaine, 68.4% of them snorted cocaine at least once a week, every week. High rates of unprotected sex were found: 59.7% of participants with a stable partner and 47.5% of participants with only occasional partners never/almost never use condoms. Access to alcohol/drug abuse treatment is mainly influenced by ethnicity, non-white are times less likely to access alcohol treatment (43% versus 12%, $P < 0.01$), and participants with <11 years of education are less likely to access drug treatment (42% versus 14%, $P < 0.05$). The main missed opportunities for Hepatitis treatment included lack of referral and no counseling strategies after Hepatitis diagnosis. Participants with lower chance of receiving antiviral therapy include heavy drinkers, regular users of snorted cocaine, homeless and those with no stable living, and participants with previous history of incarceration. **CONCLUSIONS:** This small sample of DUs report disquieting levels of risky sex behaviors and low access to hepatitis treatment, especially problematic among cocaine snorters. Those most in need, including participants without stable living and previously incarcerated were less likely to access treatment, calling for renewed strategies, in order to curb Hepatitis infection among impoverished drug users, their sexual partners and offspring.
- 494 THE EFFECT OF FOOD ON THE BIOAVAILABILITY OF RPR102681, A NOVEL CCK-B ANTAGONIST, IN NORMAL VOLUNTEERS**
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- BACKGROUND/AIMS:** In brain CCK is a neurotransmitter or neuromodulator involved in functions such as food consumption, stress and anxiety and possibly addiction. RPR 102681 is a potent, highly selective, orally active, non-peptide cholecystokinin-B (CCK-B) receptor antagonist being assessed for cocaine dependence. This study investigated the effects of food on the bioavailability of a single 400 mg oral dose of RPR 102681. **METHODS:** An open-label, two-way crossover, two-session (14 days apart) design with 12 healthy volunteers (3 females and 9 males, age range, 21-40) was used. The fed condition consisted of 2 eggs fried in butter, 2 strips of bacon, 2 slices of toast with butter, 4 ounces (112g) of hash brown potatoes, and 8 ounces (240ml) of whole milk. **RESULTS:** No subject discontinued because of adverse events and no significant pharmacodynamic differences between fed or fasting was observed. High fat food delayed absorption, increasing mean T_{max} in the fed state to 4.5 hours from 1.9 hours with fasting ($p = 0.006$). No difference in elimination (median $T_{1/2}$ 3.7 and 3.9 hours fed and fasting), or maximal concentration (C_{max} 415 and 401 ng/mL fed and fasting) or total exposure ($AUC(0-t)$ 1716 and 1607 ng-h/mL fed and fasting) was seen. **CONCLUSION:** Single oral doses were well tolerated. High fat food delays absorption of RPR 102681 but has no effect on maximal concentrations or total drug exposure. Supported by NIDA contract N01DA-4-8306 and NIH RR-00079 (GCRC, UCSF).
- 495 ALCOHOL USE PROBLEM SEVERITY AMONG SCHOOL-BASED YOUTHS IN THE US: THE SIGNIFICANCE OF DISTINGUISHING BETWEEN USE FREQUENCY AND CONSEQUENCES IN POPULATIONS**
B. Mancha, V. Rojas and W. W. Latimer, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
- Adolescent alcohol abuse continues to be a major public health problem in the United States. When gauging rates of problem alcohol use among population-based samples of youths, many studies have relied mainly on alcohol use frequency measures only. The present study sought to examine alcohol abuse problem severity in a school-based sample of youths using measures of alcohol-related consequences and alcohol use frequency. The present study is based on the International Longitudinal Survey of Adolescent Health, a multi-wave survey administered to school-based youth in Mexico, Puerto Rico, and the US. The present study is based on data from the survey administered to 1406 school-based youth from one middle school (grades 7-9) and one high school (grades 10-12) in the US. Twenty-two survey items addressed DSM-IV diagnostic criteria for alcohol abuse and dependence adapted from the Adolescent Diagnostic Interview (Winters & Henly, 1999). Students were categorized into 8 diagnostic groups based on their endorsement of alcohol use frequency (lifetime and past 12-month) and DSM-IV abuse/dependence criteria. In the US sample, 29.0% were classified as non-users of alcohol, 15.1% were classified as low-risk experimenters, 20.6% were classified as moderate-risk experimenters, 2.7% were high-risk experimenters, 14.3% endorsed 1-2 abuse symptoms, 6.1% endorsed 3 or more abuse symptoms, 7.5% endorsed 1-2 dependence symptoms, and 4.8% endorsed 3 or more dependence symptoms. Chi-square analyses examined rates of problem behavior among the 8 groups of school-based youths defined by their degree of alcohol problem severity. As expected, greater alcohol problem severity was generally associated with higher rates of problem behavior. In addition, greater problem behavior appeared to be associated with the number of consequences endorsed rather than the type of item (e.g., abuse versus dependence) endorsed. The study findings have significance in terms of gauging alcohol use disorder rates among US school-based youth.
- 496 DIFFERENCES IN TREATMENT OUTCOME BETWEEN MALE ALCOHOL-DEPENDENT OFFENDERS OF DOMESTIC VIOLENCE WITH AND WITHOUT ACTIVE DRUG USE**
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- This study evaluated differences between alcohol dependent offenders of intimate partner violence (IPV) with and without active drug use during 12 weeks of treatment. A secondary analysis was performed utilizing data from a randomized controlled trial, in which 85 participants were randomly assigned to manual-guided behavioral therapies (Cognitive Behavioral Therapy or Twelve Step Facilitation). Thirty-two clients (37.6%) tested positive for drug use during the 12 weeks of treatment. Active drug use was defined as testing positive for any illicit drug during the 12 week trial, while the group without active drug use was defined as having drug free urines throughout the 12 week trial ($N = 43$). Regarding baseline characteristics, participants assigned to active drug use group had significant differences across the following variables: earlier age of onset for marijuana use, earlier age of onset for cocaine use, more legal problems, more marijuana use prior to starting treatment, more years of marijuana use, more severity of problems on the ASI drug composite score, more day of alcohol use prior to starting treatment. Moreover, the active drug group had significantly more problems with anger control, at baseline compared to the participants who did not have active drug use during treatment. Regarding treatment outcome, the active drug group had significantly less sessions attended, significantly less percent days abstinent from alcohol use, significantly more total days of positive breathalyzer results, significantly less percent days of drug abstinence throughout, significantly more problems with anger control, anger expression, angry temperament, and verbal violence at the 12 week post-treatment time point. This work was supported by the following grants: The Donaghue Foundation (DF# 0026) and by NIDA grants P50-DA0924 and K12 DA00167-11 (to CJE).

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497 CATEGORICAL VERSUS DIMENSIONAL ANALYSIS OF SUBSTANCE USE SEVERITY IN INDIVIDUALS WITH CO-OCCURRING PSYCHIATRIC AND SUBSTANCE USE DISORDERS

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The study compares client and treatment characteristics of 215 individuals with co-occurring disorders using categorical versus dimensional methods. For categorical comparisons, client diagnoses from the Mini International Neuropsychiatric Interview were divided into two groups: psychotic disorders (PSY; n=42) and non-psychotic disorders (N-PSY; n=173). No group differences were found on demographic variables. At admission, the N-PSY group presented a greater history of prior detox, whereas the PSY group reported higher incidence of emergency room visits over the past year and more psychosocial problem days during the past month. No differences were found in substance use patterns between the two groups. The groups were also equivalent at discharge in completion, abstinence, employment, and AA attendance rates. Dimensional comparisons were made using cluster analysis on 9 Brief Symptom Inventory (BSI) scales, resulting in high (HI; n=60), medium (MD; n=112), and low (LO; n=43) psychiatric severity groups. On demographic and social variables, the LO group was more often White and legally involved, whereas the HI group had greater homelessness rates. Psychiatric diagnoses differed by severity; the HI and MD group displayed greater incidence of multiple diagnoses and psychotic disorders and the LC group single diagnoses of either depression or anxiety. At admission, the HI group presented a greater history of prior detox and non-detox substance abuse treatment, followed by the MD then LO groups. The HI and MD groups reported more days of primary substance use and substance use problem day relative to the LO group. At discharge, the HI group had shorter lengths of stay but did not differ on completion or AA attendance. Findings indicate a stronger association between substance use severity and psychiatric severity levels relative to diagnostic comparisons. These results highlight the importance of including problem severity measures in addition to client diagnoses when conducting assessments to inform treatment planning.

499 ALCOHOL-USE PROBLEM SEVERITY AMONG SCHOOL-BASED YOUTHS IN PUERTO RICO: THE SIGNIFICANCE OF DISTINGUISHING BETWEEN USE FREQUENCY AND CONSEQUENCES IN POPULATIONS

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Adolescent alcohol abuse continues to be a major public health problem in Puerto Rico. When gauging rates of problem alcohol use among school-based samples of youths, many studies have relied mainly on alcohol use frequency measures only. The present study sought to examine alcohol abuse problem severity in a school-based sample of youths in Puerto Rico using measures of alcohol-related consequences and alcohol use frequency. The present study is based on the International Longitudinal Survey of Adolescent Health, a multi-wave survey administered to school-based youth in Mexico, Puerto Rico, and the US. The present study is based on data from the survey administered to 972 school-based youths from one middle school (grades 7-9) and one high school (grades 10-12) in the San Juan region of Puerto Rico. Students were categorized into 8 diagnostic groups based on their endorsement of alcohol use frequency (lifetime and past 12-month) and DSM-IV abuse/dependence criteria. In the Puerto Rico sample, 32.1% were classified as non-users of alcohol, 14.7% were classified as low-risk experimenters, 32.1% were classified as moderate-risk experimenters, 5.3% were high-risk experimenters, 6.7% endorsed 1-2 abuse symptoms, 2.3% endorsed 3 or more abuse symptoms, 3.8% endorsed 1-2 dependence symptoms, and 3.0% endorsed 3 or more dependence symptoms. Chi-square analyses examined rates of problem behavior among the 8 groups of school-based youths defined by their degree of alcohol problem severity. As expected, greater alcohol problem severity was generally associated with higher rates of problem behavior. In addition, greater problem behavior appeared to be associated with the number of consequences endorsed rather than the type of item (e.g., abuse versus dependence) endorsed. The study findings have significance in terms of gauging alcohol use disorder rates among school-based youths in Puerto Rico and targeting prevention interventions to specific at-risk populations.

498 NICOTINE ALLEVIATION OF DEFICITS IN PREPULSE INHIBITION IN A RODENT MODEL OF SCHIZOPHRENIA ARE BLOCKED BY MECAMYLAMINE

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Prepulse inhibition (PPI) of the startle reflex is an operational measure of sensorimotor gating that is reduced in schizophrenia patients and in rats that have been administered drugs that activate the dopamine system. We have developed a rodent model of schizophrenia in which increases in dopamine D2 receptor sensitivity are produced through neonatal quinpirole (a dopamine D2/D3 agonist) treatment, administered from postnatal days (P)1-21. This drug treatment produces long-term increases of dopamine D2 receptor sensitivity, similar to that which occurs in human schizophrenics. In this study a total of 46 male and female Sprague-dawley rats were administered either quinpirole, a dopamine D2/D3 receptor agonist (1mg/kg), or saline from P1-21. Rats were raised to adulthood (approximately P60) and tested daily for 10 consecutive days in one of two prepulse inhibition chambers. An ambient noise of 70 dB was administered for 5 min followed by a test session consisting of the randomized presentation of 35 trials: 20 pulse trials (40 ms, 120-db pulse) and 15 prepulse trials (five each at 73, 76, and 82 db with a 20-ms prepulse given 100 ms before a 40 ms 120-db pulse). For the 73, 76, and 82 dB prepulse trials, neonatal quinpirole treatment produced a deficit in PPI, and pre-treatment with nicotine before PPI testing eliminated these deficits in D2-primed rats compared to controls. In a second experiment, we discovered that pretreatment with mecamylamine before nicotine treatment blocked nicotine alleviation of PPI deficits. These results suggest that nicotine's ability to alleviate sensorimotor gating deficits as measured by PPI is mediated by the nicotinic receptor. Support Contributed By: Res Dev Committee, ETSU

500 AN OPEN-LABEL, DOSE-RANGING TOLERABILITY STUDY OF N-ACETYL-CYSTEINE FOR THE TREATMENT OF COCAINE DEPENDENCE

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Recent preclinical studies implicate N-acetylcysteine (NAC), a cysteine pro-drug, as a potential medication for preventing relapse to cocaine use; however due to its several medical indications, NAC is given at a wide range of doses. The purpose of this pilot study was to test safety and tolerability of three different doses of NAC in cocaine dependent individuals. Twenty three treatment-seeking cocaine dependent patients participated in a 4-week medication tolerability trial and received either NAC 1200mg/day (n=8), 2400mg/day (n=9) or 3600mg/day (n=6). No serious side effects occurred and no patients were discontinued from medication due to adverse events. The proportion of people experiencing side effects in each group increased with higher dose: 37.5 % in 1200mg group, 66.6% in the 2400mg group and 83.33% in the 3600mg/day. The most prevalent side effects were headache, stomach ache and fatigue and were experienced mostly by subjects who received 2400mg and 3600mg. An additional side effect only occurred in the 3600mg group, a subject with normotensive blood pressure (BP) at baseline (mean systolic BP=129, mean diastolic BP=76) and no history of hypertension, developed higher blood pressure during treatment phase (mean systolic BP=142, mean diastolic BP=89). However, it was not clear whether the higher BP was induced by NAC, because while the BP fell to normal in the week after NAC was discontinued, it was observed again after 2 weeks while the subject was free of medication. In general, the retention rate favored the higher doses of NAC with 88% and 83% for 2400mg and 3600mg, respectively compared to 37.5% for 1200mg. Although more side effects were observed at higher doses, these side effects were generally mild. Moreover, retention was greater for higher doses. This small trial suggests that daily doses of 2400 and 3600mg are suitable dosages for future efficacy trials.

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501 12-STEP PARTICIPATION OF METHAMPHETAMINE-DEPENDENT ADULTS PREVIOUSLY PARTICIPATING IN THE METHAMPHETAMINE TREATMENT PROJECT

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The effectiveness of 12-Step programs for initiating and maintaining abstinence has been documented for a range of drugs of abuse, including alcohol, cocaine, and heroin. But in spite of increasing rates of methamphetamine (MA) use and associated problems across the U.S., the utilization and effectiveness of 12-step programs for MA dependence has not been investigated. It is unclear whether 12-step participation for MA dependence is similar to the patterns of attendance and participation seen for other drugs of abuse in terms of active participation and helpfulness as a recovery resource. Using a modified version of the Alcoholics Anonymous Involvement Scale (Tonigan et al., 1996), the current study addresses aspects of 12-Step participation in 584 MA-dependent adults participating in the longitudinal follow-up of the Methamphetamine Treatment Project (MTP). Findings document that about 85% of the sample have ever participated in any 12-Step group outside of treatment. About 55% of the sample report not attending any 12-Step meeting in the previous 6 months, although 29.2% report attending a 12-Step meeting at least once weekly, with 4.8% reporting daily attendance. Importantly, 41.9% of those who have ever attended a 12-Step meeting find these groups very helpful. Addressing active participation, 49.7% report having served the group (meeting leader, coffee maker, etc.), 5.4% serve as a sponsor, and 43.8% report celebrating a "birthday" at a 12-Step meeting. This paper presents additional findings such as the association between 12-Step participation and MA use at follow-up, and discusses the need to increase our knowledge of MA abuse, and treatment.

502 CHARACTERISTICS AND LIFE HISTORY OF OPIOID-DEPENDENT ADOLESCENTS

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The prevalence of use of heroin and other opioids among adolescents has markedly increased in the recent past. Virtually no research has been conducted to systematically characterize this growing cohort of adolescents. We conducted a detailed analysis of the characteristics and life history of opioid-dependent adolescents. Data were from the first randomized, controlled trial to evaluate combined behavioral and pharmacological treatments for opioid-dependent adolescents (ages 13-18 years eligible). Data were collected from participants (n=36) at intake into this trial using the Comprehensive Adolescent Severity Index (CASI), a structured clinical interview assessing life areas of health, stress, education, drug/alcohol use, use of free time, peer relationships, sexual behavior, family/household, legal and mental health. Results underscore a history of significant exposure to risk and high levels of risk behavior among youth. The majority of youth (93%) had a family member who drank or used drugs regularly, and 45% had a family member with significant mental health problems. Almost half of participants had experienced a significant family crisis (44%) or had someone close to them reject them (41%). Thirty-six percent had witnessed severe violence or abuse, and 31% percent of female participants reported having been raped at least once. Over half (53%) had a family member who engaged in illegal activity, and over 70% had witnessed the arrest of a friend, relative, or neighbor. The majority of youth (91%) had committed a crime, most commonly shoplifting (73%) and drug dealing (57%). Ninety-six percent of youth were sexually active and 22% reported having sex with a person they thought may have AIDS. Eighty-nine percent said they used drugs and alcohol every day in the past year. This research provides novel and clinically important empirical information about the characteristics of opioid-dependent youth.

503 MODAFINIL AND SMOKING BEHAVIOR IN ADOLESCENT AND YOUNG ADULT SMOKERS

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Modafinil is a promising pharmacologic agent for treatment of inattention and has been proposed as a potential pharmacotherapy for smoking cessation. The primary goal of this study is to examine the effects of modafinil on task performance and subjective reports of nicotine withdrawal following 24 hours of tobacco abstinence and on subsequent tobacco smoking topography as a function of the nicotine yield of a cigarette in nicotine dependent adolescent and young adult smokers. To date, 8 of 10 subjects have completed training and a 6-day protocol; subjects are required to remain abstinent from tobacco smoke for 24 hours prior to each test day (as verified via breath carbon monoxide level). The effects of modafinil (0, 200 and 400 mg) are assessed before and at 30-min intervals for three hours post dose. Assessments include cardiovascular, task performance and verbal report of drug effect and nicotine withdrawal measures. After the final assessment, subjects are allowed to smoke a single tobacco cigarette with a nicotine yield of 0 or 0.6 mg. Each dose of modafinil is tested in combination with both tobacco cigarette conditions according to a randomized double blind procedure. Preliminary analyses indicate that compared to placebo, high dose modafinil is associated with decreased craving and drowsiness and increased concentration on the Minnesota Nicotine Withdrawal Scale; decreased Hungry and Sleepy and increased Feel Drug on the Visual Analog Scales; and decreased misses on the Continuous Performance Task. In addition, there are no significant changes in smoking topography (i.e., puff number, duration, and volume). These results indicate that modafinil may aid in symptomatic relief of nicotine withdrawal in adolescents and young adults. Supported by DA15413; DA05312; M01 RR02602

504 ADVANTAGE OF A DRUG-SPECIFIC ASI DRUG COMPOSITE INDEX: VALIDITY OF AN ASI COCAINE INDEX FOR COCAINE DEPENDENCE

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The Addiction Severity Index (ASI) Drug composite index has shown considerable utility and heuristic value in studies of drug dependent patients. However, when selecting patients who all are dependent on cocaine, it is possible that modifying the composite index to reflect concerns about cocaine use might improve its ability to predict outcome from treatment. Method: Cocaine dependent patients in residential treatment (n = 163) were assessed on treatment entry for ASI, pretreatment substance use and dependence, and urge to use cocaine in the Cocaine Related Assessment of Coping Skills (CRACS). The ASI drug index questions on "drug use" were repeated for cocaine alone. At follow-up substance use was assessed with timeline Followback, urine confirmed (n = 119 at 3 months, 114 at 6 months). Results: The ASI Cocaine index showed validity in terms of significant (p < .05) correlations with number of cocaine dependence symptoms, Cocaine Negative Consequences Checklist, self-rated difficulty in quitting cocaine and urge to use cocaine (r's from .13 to .20). Discriminative validity was shown by lack of correlations with demographics and negative correlations (p < .05) with alcohol diagnosis and number of alcohol dependence symptoms. The ASI Cocaine index was significantly higher for patients who relapsed to cocaine in the first 3 months but was not related to 6 month outcome or treatment drop-out. The ASI Drug composite was not significantly related to these cocaine-specific variables and outcomes. Conclusion: Results suggest adapting the ASI Drug index to a specific drug may improve prediction of outcomes for that drug.

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505 PREFERENTIAL EFFECTS OF THE mGlu5 RECEPTOR ANTAGONIST, MTEP, ON CONDITIONED REINSTATEMENT OF COCAINE-SEEKING VS. PRIMARY REINFORCEMENT

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Metabotropic glutamate receptors (mGluRs) have been implicated in various aspects of drug addiction. This study was designed to determine whether MTEP, a potent mGlu5 antagonist, blocks reinstatement of cocaine-seeking induced by cocaine-related environmental stimuli and whether this effect extends to behavior maintained by the primary reinforcing effect of cocaine and a highly palatable conventional reward, sweetened condensed milk (SCM). Male Wistar rats were trained to associate discriminative stimuli (SD) with the availability of cocaine (S+) vs. non-reward (S-) and then placed on extinction conditions during which the reinforcer and the SD were withheld. Subsequent re-exposure to the cocaine S+ but not the non-reward S- produced recovery of responding. The data obtained show that MTEP (0-10 mg/kg, IP) administered 1 h before the onset of reinstatement sessions produced a strong reduction of S+ induced conditioned-reinstatement at doses as low as 1 mg/kg. In contrast when injected before cocaine self-administration (FR5 schedule), MTEP induced only a slight reduction of cocaine self-administration (apparent only at the highest doses 3 and 10 mg/kg) and did not alter SCM-reinforced responding. Moreover, MTEP had no effects on spontaneous locomotion. Together, these data suggest that MTEP may be more selective at blocking conditioned reinstatement of cocaine-seeking as opposed to cocaine's primary reinforcing actions, identifying the mGlu5 as a possible therapeutic target for relapse prevention. Supported by NIDA DA 07348.

506 DOPAMINE D1 RECEPTORS IN THE VENTRAL STRIATUM MEASURED WITH PET PREDICT THE CHOICE TO SELF-ADMINISTER COCAINE

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In order to investigate the effects of cocaine dependence on the D1 receptor we used PET and the radiotracer [¹¹C]NNC 112 in a group of human cocaine dependent (CD) subjects and matched healthy controls (HC). Following the PET scans, the cocaine dependent subjects underwent cocaine self-administration sessions in order to explore the association between of D1 receptor availability in cocaine seeking behavior. 25 cocaine dependent subjects (40 ± 4 yrs, 19M/6 F) and 23 matched healthy controls (38 ± 4 yrs, 19M/4F) were scanned with [¹¹C]NNC 112 on the ECAT EXACT HR+ camera for 90 minutes. The CD subjects were not treatment-seeking, had been smoking crack cocaine an average of 16.4 ± 4.5 years and spent an average of \$264 ± 118/week over the last six months. [¹¹C]NNC 112 was administered as a bolus with arterial sampling for full kinetic modeling to obtain the binding potential (BP). The regions of interest included the limbic, associative and sensori-motor striatum. During the cocaine self-administration sessions, CD subjects were given the choice to self-administer cocaine (0, 6, and 12 mg) or to receive a monetary voucher worth \$5. No difference in BP was seen between the two groups (RM ANOVA p = 0.46). However, a negative association was seen between D1 receptor BP in the limbic striatum and the choice for the 6 mg dose of cocaine (r = - 0.47, p = 0.02, corrected for age). A post-hoc analysis of the other regions showed no significance. These results do not support the hypothesis that cocaine dependence is associated with a reduced D1 receptor availability in the striatum. However, within the cocaine-dependent subjects, low D1 receptor availability in the ventral striatum was associated with the choice to self-administer cocaine, suggesting that low D1 receptor availability may be associated with an increased risk of relapse in cocaine dependence.

507 FACTORS ASSOCIATED WITH ADOLESCENT ECSTASY USE IN THE NATIONAL SURVEY OF PARENTS AND YOUTH

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Background: Suspected factors associated with ecstasy use in adolescence are understudied. Objectives: To test whether approval of drug use, other drug use, high levels of deviant behaviors, low levels of parent monitoring and high levels of sensation-seeking are associated with ecstasy use in adolescence. Method: Secondary analysis from Round 2 (2001-2002) of the National Survey of Parents and Youth public use files (n=3,363 adolescents aged 12-18 years). Data was analyzed using weighted logistic regression models. Results: More ecstasy users were in the older age group (17-18 years old), among those with lower grades in school, among those who were less religious and among those who lived with only one parent. Those that approved use of marijuana, ecstasy, inhalants and methamphetamines were more likely to be ecstasy users (aORs ≥ 15.71) and marijuana users (aORs ≥ 6.34) as compared to non-users. The associations were strongest for ecstasy use than marijuana use. Adolescents who were tobacco, alcohol and inhalant users were more likely to be ecstasy users (aORs ≥ 24.96) and marijuana users (aOR ≥ 11.52) as compared to non-users, associations were strongest for ecstasy use than marijuana use. Adolescents with higher levels of parent monitoring were less likely to be ecstasy users (aOR: 0.14) and marijuana users (aOR: 0.23) as compared to non-users, the association was strongest for ecstasy as compared to marijuana use. Those that engaged three or more times in deviant behaviors in the past year (fights, stealing and damaging property) were more likely to be ecstasy users (aORs ≥ 13.82) as compared to non-users, only stealing three or more times in the past year was associated with marijuana use (aOR: 4.41). High levels of sensation seeking were associated with marijuana use (aOR: 3.76[1.71,8.30]) and with ecstasy use (aOR: 4.38[0.77,25.07]), the estimate was less precise for the latter due to lower power. Conclusion: Approval of drug use and several risk-taking behaviors are associated with ecstasy use in adolescence and prevention strategies should target these adolescents.

508 ADULT MORTALITY AMONG MALES WITH SUBSTANCE USE DISORDERS VS. CONTROLS

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Objective. This research recognizes empirical findings regarding adult mortality among males who have been diagnosed with a DSM-III-R or DSM-IV substance use disorder (SUD). Method. The sample consisted of 768 adult males, N=337 with DSM-III-R diagnosis of SUD, N=431 controls without SUD, who participated in a longitudinal study at the Center for Education and Drug Abuse Research. Date of birth was collected for all subjects. Date of death and cause of death were collected from participating family members for each adult male that is known to have died during the past 15 years of the study. Results. The rate of mortality from all causes among adult males with SUDs was higher than the control group adult males: 4.45% vs. 1.85%, respectively (Pearson chi square = 4.384, p = .03). Also, the mean age at death for the 15 males with SUDs was 49.9 years, while the mean age at death for control group males with known dates of death was 51.1 years. Cause of death due to medical illness was identified for 13 of the 15 SUD males. These illnesses included cancer, heart attack, stroke, liver disease, kidney disease, and pneumonia resulting from Hepatitis-C. One of the SUD males was murdered, and one cause of death is unknown. Of the control group deaths, 4 causes are unknown, 2 died from medical illness, 1 committed suicide, and 1 was the victim of a hit and-run accident. Conclusions. These findings reveal higher mortality rates for adult males with SUDs than control group adult males. Almost all of the deaths in the SUD group resulted from medical illnesses.

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509 THE IMPACT OF SELF-EFFICACY, MEDICATION ATTITUDES, AND SUBSTANCE ABUSE ON HIV MEDICATION ADHERENCE

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We investigated the impact of psychological attitudes and drug abuse/dependence on HIV medication adherence. The sample was 122 HIV+ patients in medical care with a mean age of 40.4 and a 10th grade education; 61% were men, 84% were African-American, 58% were single, 48% were disabled and 30% were unemployed, and 63% were heterosexual. 25% met criteria for DSM-IV substance abuse or dependence. Primary drug of abuse included cocaine (45%) and alcohol (31%). 65% screened positive for a personality disorder on the Iowa PD screen, while 47% were positive for depression on the CESD. Most (59%) had detectable viral loads and tcells over 200 (53%). Only 2% complained of any side effects from antiretroviral medications, and most (53%) were on PI-sparing combination regimens. Non-adherence was common, with 36% not taking medications as directed, 29% taking below 95% of medications prescribed, and 44% running out of medications. Using logistic regression analysis, we identified predictors of each aspect of adherence, examining substance abuse/dependence, importance, confidence, and readiness for medication adherence, and attitudes towards HIV medications. Taking medications as directed was predicted by VAS scales (0-10) of confidence (OR=1.74, 95% CI= 1.1-2.7) and readiness (OR=1.6, CI=-2.4). Taking 95% of medications was predicted by confidence (OR=2.1, CI=1.2-3.6). Running out of medications was predicted by a higher (worse) PI attitude score (OR 1.3, CI 1-1.6). Substance abuse/dependence were not significant independent predictors of good or poor adherence, but were included in the model of running out of medications. Results indicate that interventions to improve HIV medication adherence should focus on self-efficacy and attitudes towards medication rather than substance use per se.

510 PSYCHO-PHYSIOLOGIC REACTIVITY AND CORTISOL LEVELS IN METHADONE- OR BUPRENORPHINE-MAINTAINED PATIENTS AND NON-DEPENDENT CONTROLS IN RESPONSE TO CUE EXPOSURE

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Objective: 1) To assess psycho-physiologic reactivity to opiate-related stimuli versus neutral-related stimuli in methadone- and buprenorphine-maintained patients and controls. 2) To assess cortisol levels throughout the cue exposure sessions. Methods: Three groups were selected: Methadone and Buprenorphine maintained patients and control subjects without lifetime or current dependence (except tobacco) matched for age and sex. All subjects were exposed to neutral- and opiate-related stimuli in 20-min-sessions (video and object handling) Psycho-physiologic reactivity variables were peripheral skin temperature, galvanic skin resistance and questionnaire-assessed subjective measures of opiate high, craving and withdrawal. Salivary cortisol level was measured throughout experimentation. Results: 13 patients and 13 matched controls were included. Results confirmed existence of a specific reactivity to opiate-related stimuli in the opiate dependent subjects vs. controls (no difference between methadone and buprenorphine patients). No variation of cortisol level was found in response to the opiate-related stimuli sessions for either group. However, there was an overall decrease of cortisol level throughout the sessions that was significantly less important for the opiate dependent subjects (-1.8 vs. -5 nmom/mL). Conclusion: Within this experimental study, cortisol response was not influenced by psycho-physiologic reactivity to specific stimuli. These two individual characteristics could be related to independent neurobiological characteristics (trait vs. state). Stability of individual psycho-physiologic reactivity with time needs to be studied.

511 A COMPARISON OF MEDICAL SERVICE UTILIZATION PATTERNS BETWEEN HOSPITAL AND COMMUNITY-BASED SYRINGE-EXCHANGE PROGRAM ATTENDEES

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We compared the medical service use patterns of participants randomized to one of two syringe exchange program (SEP) delivery settings: 1) hospital (n = 83); and 2) community-based (n = 83). We tested the hypothesis that participants randomized to the hospital-based SEP would use fewer medical services than those assigned to the community-based SEP. Computerized billing records were used to gather information about medical services received for the twelve-month study period. Poisson regression models were used to compare service utilization between groups controlling for demographic, psychosocial, and substance use-related characteristics. Percentages represent the percentage difference compared to the reference group. The majority was Caucasian, male, unemployed, and homeless. The mean age was 40 years (SD = 9.8). Persons who used more inpatient services were Caucasian (61.7%; p < .01), HIV positive (143%; p < .05) and had better physical (287%; p < .0001) and mental health functioning (56.2%; p < .01). Greater use of ambulatory care services was observed for the following groups: Caucasian (23.9%; p < .0001) homeless (32.5%; p < .0001), higher risky drug use (15.6%; p < .0001), HIV positive (90.6%; p < .0001), and better physical (42.9%; p < .0001) and mental health functioning (32.1%; p < .0001). Participants in the hospital-based SEP condition had 45.5% (p < .0001) fewer inpatient admissions and 18% fewer ambulatory care visits (p < .0001) than the community-based SEP. Although the hospital-based SEP group showed less inpatient and ambulatory care service use, other patient factors were also strong predictors of medical service use. Future research is needed to examine the interplay between SEP setting and patient characteristics on medical service utilization. This work was supported by NIH Grants KO1DA008408, U10DA015815, and P50DA09253

512 FACTORS RELATED TO ADOLESCENT ALCOHOL USE PROGRESSION

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Introduction: According to results from the Adolescent National Survey Monitoring the Future, 13 to 15 years old are at high risk to begin drinking. Some adolescents who consume alcohol later abuse the substance and may develop alcohol dependence. In Puerto Rico, the percentage of adolescents who drink has increased during the 1990s. A refusal of self-efficacy may predict the onset and escalation of drinking while peer and parent alcohol use appear to predict some progression beyond trial use. However, predictors of addictive drinking are not altogether clear. Identifying factors of alcohol progression is an important issue as it has substantial implications for researching and preventing adolescent alcohol use. Methods: This study uses the longitudinal data from an ongoing study in Puerto Rico on the risk and resilience to drug use among adolescent offspring of drug using and non-drug using parents. A total of 361 adolescents who completed the first one-year follow up were used in the analyses. The adolescents were between ages 13 to 16. Results: The sample is comprised of 48.5% males and 51.5% females. 61.5% of the subjects are in middle school and 32.9% in high school. 20.2% of the adolescents had started drinking by the first one-year follow up. That accounted for a net incidence of 16.3% (baseline 18.3% vs. 34.6% one-year follow up, p < .001). Linear regression analysis results indicate that mother (p = .051) and child (p = .023) depressive symptoms, adolescent involvement in violent acts (p = .002), adolescent instances of Oppositional Defiant disorder (p = .032) and adolescent access to cigarettes (p = .008) were the factors significantly associated with initiating and continuing drinking. Conclusion: The findings of this study will inform public health decision-making and improve drinking prevention strategies. We concluded that alcohol use continues to be highly prevalent among adolescents in Puerto Rico. There is an active need to develop specific proactive initiatives to address alcohol use and progression among adolescents.

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Between 9/1 and 12/9/05, 530 individuals who were displaced by Hurricanes Katrina or Rita entered treatment in publicly-funded Texas programs. Some 55% were admitted to methadone, 18% were admitted to residential, and 9% were admitted to detoxification. Admissions were statewide, with 59% in programs in the Houston area, 13% in the Beaumont area, 9% in the Austin area and another 9% in the Tyler-Longview area. Fifty-four percent of the evacuees were from outside Texas, and while the county of residence of non-Texans was not recorded, 54% had been born in New Orleans. Of the evacuees, 68% were male, average age was 37.6, 54% were Black, 40% were White, and 5% were Hispanic. In comparison, there were 20,551 individuals who were not evacuees who also entered treatment during this time period. Some 60% were male, average age was 31.7, 18% were Black, 48% were White, and 31% were Hispanic. The primary problem of the evacuees was heroin (48%), other opiates (14%), alcohol (13%), crack cocaine (9%), and marijuana (8%). The primary problem for non-evacuees was alcohol (25%), marijuana (21%), crack cocaine (15%), stimulants (14%), powder cocaine or heroin (9% each). There was no difference in the average number of months the two groups had been employed in the past year (3.8) or in their average education level (11 years); 90% of evacuees and 85% of non-evacuees had no health insurance. Some 55% of the evacuees left treatment during this time period; 33% completed treatment. In comparison, 48% of the comparison non-evacuee group left treatment in this same period and 60% completed treatment. Of the evacuees who did not complete treatment, 59% left AMA vs. 38% of non-evacuees. Thirty percent of the evacuees received no referral to other services vs. 7% of non-evacuees. These data provide insight into the characteristics of displaced substance abusers who sought treatment in Texas programs. Demographically, they differed from Texas clients, and due to the upheaval in their lives, they were less likely to complete treatment.

515 DRUG TREATMENT RESPONSE, UNMET HIV TREATMENT NEEDS, AND MORTALITY RISK OF HIV+ OPIOID-DEPENDENT PATIENTS IN A CLINICAL TRIAL IN MALAYSIA

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BACKGROUND: Heroin and injection drug use (IDU) are highly prevalent and driving the AIDS epidemic in Malaysia, accounting for 77% of AIDS cases but only a small minority (<3% in Kuala Lumpur) of patients treated for AIDS. The recent introduction of medical treatments for heroin dependence may provide an opportunity to facilitate antiretroviral treatment for HIV+ patients. **AIMS:** To evaluate the treatment response and prior HIV treatment of HIV+ heroin dependent patients. **METHODS:** We compared the treatment response of HIV+ and HIV- patients enrolled in a randomized clinical trial comparing drug counseling alone (DC; HIV+ N=4, HIV- N=35) or combined with buprenorphine (BUP+DC; HIV+ N=11, HIV- N=32) or naltrexone (NTX+DC; HIV+ N=11, HIV- N=30) and queried HIV+ patients about whether they had ever received treatment for HIV. Follow-up assessments were conducted for 18 months following treatment entry. **RESULTS:** The treatment response of HIV+ patients was comparable to the response of HIV- patients. As with the overall sample, HIV+ patients were retained in BUP+DC longer than in NTX+DC (138 vs. 90 days, $p<.05$) and achieved longer periods of consecutive abstinence (57 vs. 25 days, $p<.05$). None of the HIV+ patients reported ever being treated for HIV; all 26 had Hepatitis C, and 23% had radiologic evidence of TB. Five of the 26 HIV+ patients (but none of the HIV- patients) died after leaving the study—3 died from infections (including 1 with active TB), 1 from drug overdose (buprenorphine and benzodiazepine), and 1 from unknown causes. **CONCLUSIONS:** The findings of greater efficacy of BUP+DC support the potential role of this treatment in facilitating HIV care of heroin dependent patients with HIV, who have largely been excluded from HIV treatment in Malaysia. The findings of high mortality of HIV+ patients after leaving treatment underscore the importance of long-term maintenance treatment of heroin dependent patients and provision of HIV treatment for HIV+ patients. Supported by R01 DA14718, K24 DA000445

516 TRENDS IN NONMEDICAL USE OF PRESCRIPTION DRUGS AMONG U.S. COLLEGE STUDENTS: RESULTS FROM FOUR NATIONAL SURVEYS

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The prevalence of nonmedical use of prescription drugs (NMPD) in the U.S. is highest among individuals 18 to 25 years of age (SAMHSA, 2005). The primary aim of this study was to assess the prevalence and trends of NMPD (i.e., amphetamines, opioids, sedatives, tranquilizers) among U.S. college students between 1993 and 2001. A secondary aim was to examine whether college-level characteristics explained the variation in college-level prevalence trajectories over time. Data were collected from self-administered mail surveys, sent to independent samples of college students from a nationally representative sample of 119 four-year U.S. colleges. Participants included representative samples of 15,282, 14,428, 13,953, and 10,904 randomly selected college students at these colleges in 1993, 1997, 1999 and 2001, respectively. The results indicated that lifetime and 12-month prevalence of NMPD increased significantly between 1993 and 2001. Specific college-level characteristics were found to be positively (marijuana use) and negatively (historically black status and commuter status) correlated with NMPD, consistently across the four cross-sectional samples. Significant between-college variation in terms of trajectories in the prevalence of NMPD over time was found using hierarchical linear models, and the college-level characteristics were not found to explain all of the variation, suggesting the need for further investigation of what determines between-college variance in prevalence trends. The prevalence of NMPD among U.S. college students increased significantly between 1993 and 2001, while heavy drinking and use of illicit drugs other than marijuana remained relatively steady. The findings of this study suggest that continued monitoring of NMPD among college students is needed and collegiate substance abuse prevention programs should include efforts to reduce NMPD. This study was supported by a RWJF research grant (PI: Henry Wechsler) and a NIDA research grant DA019492 (PI: Sean Esteban McCabe).

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517 INTERACTION BETWEEN BUPRENORPHINE AND ATAZANAVIR

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Drug interactions between HIV therapeutics and opiate therapies can contribute to non-adherence and poor clinical outcomes. Co-administration of methadone with some antiretrovirals has been associated with opiate withdrawal or toxicity. Buprenorphine (BUP), a mu opioid receptor partial agonist is available as a pharmacotherapy for opioid addiction, but less is known about its interactions with HIV medications. This study determined whether a significant drug interaction occurs with simultaneous administration of BUP and atazanavir (ATV), a protease inhibitor. Method: Opioid-dependent, BUP-maintained, HIV-negative volunteers (n=9) on a stable dose of BUP for at least 2 weeks underwent blood sampling over 24 hours to determine BUP pharmacokinetics (PK). Following administration of standard clinical doses of ATV 400 mg/d for 5 days, a second PK study in which plasma concentrations of BUP and ATV was obtained. ATV PK in healthy volunteers (not receiving BUP) (n = 5) were used to determine the effect of BUP on ATV. Mini-Mental Status Examination (MMSE) was performed at baseline and following ART administration. Results: Preliminary results show that the administration of BUP significantly decreased the area under the curve (AUC₀₋₂₄) for ATV (p = 0.03), while ATV administration was associated with a significant increase in BUP C_{max} (p = 0.03) with a trend toward significant increase in BUP AUC₀₋₂₄ (p = 0.07). Additional PK analyses on a larger sample will be presented. No significant change in MMSE scores was observed and no cognitive deficits were identified. Conclusions: BUP-treated patients receiving ATV without ritonavir as part of treatment for HIV disease may need to be monitored for subtherapeutic ATV concentrations. Additional PK studies are planned to examine ATV PK with BUP and ritonavir. Increased exposure to BUP does not appear likely to be of clinical significance.

518 INTERACTIONS BETWEEN GENOTYPE AND RETROSPECTIVE ADHD SYMPTOMS PREDICT LIFETIME SMOKING RISK IN A COMMUNITY-BASED SAMPLE OF YOUNG ADULTS

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Smoking behavior is related to genetic polymorphisms associated with neurotransmitter functioning (e.g., DRD2 TaqA1) and nicotine metabolism (e.g., CYP2A6 inactive variants). While smoking rates are disproportionately high in individuals with psychiatric conditions, including attention deficit hyperactivity disorder (ADHD), the interactive effects of psychiatric comorbidities and genotypes on smoking risk have not been fully examined. In order to further evaluate associations between smoking risk, genotype and ADHD symptoms, data from Wave III from the National Longitudinal Study of Adolescent Health (AddHealth) were analyzed. Participants were 1800 unrelated individuals for whom the following genes were assayed: DAT, 5HTT, DRD2, DRD4, MAO-A, and CYP2A6. Lifetime risk of regular smoking (i.e., ever having smoked at least cigarette per day for 31 days) and retrospective ADHD inattention (IN) and hyperactivity/impulsivity (HI) symptoms were the other variables considered. Multiple logistic regression was used to predict smoking risk from ADHD and genotype after controlling for age, race, parental education and conduct disorder symptoms. MAO-A was analyzed separately for males and females. Significant DRD2 x IN (p = 0.03), MAO-A x IN (females only; p = 0.006), MAO-A x HI (females only; p = 0.008), CYP2A6 x IN (p = 6 symptoms and the risk allele. For instance, 80% of females with >= 6 IN symptoms and the MAO-A active variant had a lifetime risk of regular smoking compared with 25% with >= 6 symptoms and the inactive variant; and compared with 38% with the active variant but < 6 IN symptoms. These results from a community-based sample provide evidence that psychiatric symptoms and genetic risk factors may interact to predict smoking risk.

519 IMPROVING SIGNAL DETECTION IN HUMAN ABUSE LIABILITY STUDIES: A CASE FOR USING PRESTUDY PHARMACOLOGICAL TESTING

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In human abuse liability studies, subjects who report extensive substance use might nonetheless contribute to "failed" results because they are not able to reliably discriminate between placebo and active drug under blinded conditions. The risk of a failed study can be minimized by using pre-study pharmacological testing, an enrichment strategy designed to improve signal detection by screening out subjects with elevated placebo responses and ensuring that subjects are able to reliably detect and 'like' the subjective effects of the active drug. The recommended design for pre-study qualification is a randomized double-blinded crossover study with two treatment conditions, placebo and active positive control followed by a series of abuse potential assessments. The resulting pharmacodynamic data form the basis of the decision regarding whether the subject will be eligible for inclusion in the main study. Eligibility should be based on specific criteria to ensure that: (i) the response to the active control drug is greater than that to placebo, (ii) the overall response pattern is consistent with the expected pharmacology of the active control drug, (iii) baseline and placebo responses are acceptable, and (iv) subjects are able to tolerate the active drug. Using this type of design, we have found that at moderate to high doses of drugs from a variety of classes, approximately 40% to 50% of subjects who met drug use history criteria failed to show appropriate responses on measures of abuse potential. Examples with stimulants and sedatives will be presented. Taken together, these results provide confirmation that in human abuse liability research, substance use history alone does not ensure that subjects will be able to reliably rate their drug experiences. Studies without such pre-study pharmacological testing may therefore run a higher risk of being a "failed" study.

520 THE CHOICE FOR RAPID HIV TESTING AMONG DRUG USERS WITHIN HIV PREVENTION

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Introduction: The Rapid HIV Test uses either whole blood from a finger stick or swab of oral fluid to determine the presence of antibodies to HIV-1. The results are available in 20 minutes and the test can be performed in the field rather than a laboratory. While the advantages for HIV prevention of the Rapid HIV Test have been widely publicized, there is little empirical research on the acceptance of the Rapid HIV Test among drug users. Hypotheses: Since the Rapid Test does not require a blood draw, it is hypothesized that it would be preferred by drug users, and particularly by intravenous drug users over venipuncture. It is further hypothesized that the oral swab method would be preferred over the finger stick method. Procedures: 601 chronic drug users were enrolled in a prospective study testing the efficacy of two interventions in reducing high risk HIV behavior. At 18 month follow-up, participants are offered a choice of venipuncture, finger stick, or oral swab method to obtain a sample for HIV antibody testing. Results: Of 193 chronic drug users who have been evaluated in an on-going 18 month follow-up, 81.9% selected the oral swab method, 16.6% selected the finger stick, and 1.6% selected venipuncture. Chi square tests revealed no difference in the preference of method by type of drug user (chronic non-injection drug user, injection drug users) or gender (male, female). Interestingly, the three participants who selected venipuncture were injection drug users. Conclusions: While the overwhelming majority of both non-injection and injection drug users selected the oral swab method of testing, as little over 15% of the participants selected the finger stick method. The Rapid HIV Test is an important development to increase the acceptability of HIV testing which is recommended for HIV prevention efforts. However, it appears worthwhile to offer individuals a choice of test methods.

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521 BLOOD SHARING AND GENDER-BASED VIOLENCE AMONG IDUS IN DAR ES SALAAM, TANZANIA

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The Tanzanian AIDS Prevention Project investigates injection drug use and sexual behaviors related to HIV transmission, and safer needle use and safer sexual intentions in a sample of injection drug users (IDUs) in Dar es Salaam, Tanzania. We hypothesized that illicit injection drug use may be a significant contributor to the AIDS pandemic in sub-Saharan Africa, especially in urban areas. Procedures: As part of a mixed method study, semi-structured, face-to-face interviews (n=71) were conducted in Swahili with 30 female and 41 male IDUs between February 2003 and October 2005. These qualitative interviews elicited thick descriptions of Tanzanian IDUs' attitudes and beliefs about HIV and its relationships to other topics, most particularly intentions to safer needle and sexual practices. Verbatim transcribed interviews were analyzed in ATLAS.ti using the constant comparative method. Results: Violence against female IDUs has escalated, in a large part because of male IDUs' frustration with female IDUs' income earning abilities as sex workers. The price of heroin in Dar has doubled between 2003 and 2005 and is now adulterated. It reportedly takes twice the amount of heroin it previously did to achieve the same high. During mid 2005, giving a syringe full of the first blood withdrawn after an injection to someone unable to purchase heroin emerged as a practice to help the desperate stave off withdrawal. Gender based violence escalated during late 2005 as men began routinely accosting women in shooting galleries and stealing their blood, syringes, and money. Despite IDUs knowledge of HIV transmission, harsh economic conditions, increasing heroin prices and its reduced quality have led to the emergence of blood sharing and increased violence against women. HIV prevention and safer needle use interventions in urban Tanzania should be gender specific and include strategies that could reduce violence against women and curtail blood sharing.

522 TREATMENT OF CANNABIS-DEPENDENT TREATMENT SEEKERS: A DOUBLE-BLIND COMPARISON OF NEFAZODONE, BUPROPION AND PLACEBO

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We report the results of a 13-week double blind study comparing the efficacy of two agents, nefazodone (NEF) and bupropion-sustained release (BPR) to placebo (PBO) in treating current cannabis-dependent individuals. We hypothesized that, since cannabis withdrawal shares many similarities with Major Depression, these agents might alleviate these symptoms upon cessation and lead to a reduction in marijuana use. Individuals received manualized motivational enhancement therapy followed by cognitive behavioral treatment. The randomized sample consisted of 106 participants who were predominately male (77%) and 34% Caucasian, 28% Hispanic, 27% African American and 9% other. While there were significant differences in the gender distribution of females (PBO 7%(2), NEF 37%(15), and BPR 20% (7); $p = .009$), there were no other significant demographic differences between the three treatment groups. Forty-six patients (43%) completed the entire 13-week trial and there was no difference in retention rates based on treatment group (Log-rank = .72 $df = 2$, $p = .70$). Although mean quantitative THC levels in the NEF group were substantially lower than in the PBO or BPR group, large variances in the data may have masked a significant finding ($p = .57$). Longitudinal analyses of the proportion of subjects abstinent each week (based on urine data) revealed an increase in the abstinence rates over time for the entire sample ($p = .05$), although there were no significant treatment differences. Neither NEF nor BPR provided an advantage over PBO in reducing marijuana use among cannabis dependent individuals. However, this study demonstrates that there is a group of cannabis dependent individuals who are interested in pharmacological treatments, and that over the course of a treatment trial, such individuals tend to lessen their use of marijuana. Supported by NIDA Grant: RO1 DA13191-04

523 ACUTE AMPHETAMINE INDUCES NUCLEAR PI3-KINASE ACTIVITY AND RAPID TRANSLOCATION OF SGK1 AND AKT1 TO THE NUCLEI OF CELLS IN RAT STRIATUM

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In the nucleus, activated SGK1 and Akt1 regulate gene expression in part by inhibiting glycogen synthase kinase or apoptotic transcription factors such as Forkhead. In some cases, SGK1 and Akt1 may cooperate to promote cell survival by making a complex in the nucleus and by inducing the expression of survival genes such as P-CREB. Further, recent studies have revealed the importance of PI3-K and ERK MAP kinases in neuroplasticity; however, the details of their possible interaction and the functional consequences of PI3-K activation in neurons are not clear. In this study, we examined whether acute AMPH activates the PI3-K/Akt1/SGK1 signaling pathway in the rat striatum. We demonstrated that Akt1 and phospho-Akt1 were upregulated in the nucleus 15 min after acute AMPH whereas SGK1 and Akt1 immunoreactivity were upregulated 30 min after acute AMPH. These data suggest that Akt1 and SGK1 are translocated to the nucleus independently or that SGK1 protein levels are increased by transcription at 30 min. We also found that 15 min after acute AMPH, PI3-kinase activity (measured by γ -32P-PIP accumulation) is increased in the nucleus but not in the cytoplasm of subcellular fractionated striatal tissue. However, 30 min after AMPH, PI3-K activity is significantly decreased. PLC γ was not increased in the cytoplasm and phospho-PLC γ was undetectable in the nucleus. The rapid activation of PI3-K may underlie the immediate and transient upregulation of Akt1 and SGK1 in the nucleus, as a result of AMPH-stimulation of these kinase cascades. The effect of the PI3-K inhibitor, wortmannin, and the ERK MAP kinase inhibitor, U0126, on the translocation of SGK1 and Akt1 to the nucleus will also be presented. Supported by DA03982.

524 ADDICTION TREATMENT SERVICES AND CO-OCCURRING DISORDERS: APPLICATION OF AN INDEX TO ASSESS CHANGE IN THE DUAL DIAGNOSIS CAPABILITY OF COMMUNITY PROGRAMS

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Background. Co-occurring psychiatric disorders are common in community addiction treatment programs and associated with negative outcomes. Addiction treatment providers and systems are challenged to provide effective services, and seek practical guidance to improve care. The ASAM-PPC-2R outlines a conceptual model for program dual diagnosis capability, but operational definitions and methods to ascertain capacity levels are needed. Hypotheses. 1) Scientific methods can be applied to the ASAM model and a reliable index developed to assess program dual diagnosis capability. 2) This index can be sensitive to program change in capacity. Method. A Dual Diagnosis in Addiction Treatment (DDCAT) index was developed and tested with an initial cohort of community addiction treatment programs (n=14). The DDCAT generated 7 subscale scores and classified programs as: Addiction Only Services (AOS), Dual Diagnosis Capable (DDC) or Dual Diagnosis Enhanced (DDE). A new cohort of programs (n=16) was DDCAT assessed at baseline and 9-month follow-up. These programs received 1 of 3 enhancement strategies: assessment only (n=8), assessment + training (n=4), or assessment + training + implementation support (n=4). Results. The DDCAT exhibited operational feasibility and acceptable psychometric properties ($\alpha = .81$; $\text{intrate} = .76$; $\text{kappa} = .67$). The index was sensitive to change. All enhancement strategy groups increased dual diagnosis capability, but the assessment + treatment + implementation support condition had greater improvements (Kruskal-Wallis tests @ $p < .05$). Conclusions. Two studies with the DDCAT demonstrate its utility as an objective baseline and change measure of services for co-occurring disorders in community addiction treatment settings. Future studies will link the DDCAT with patient outcomes and be used in more experimental treatment services research.

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- 525** PREVALENCE AND PREDICTORS OF PSYCHOSIS AMONGST REGULAR METHAMPHETAMINE USERS
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Introduction: Despite reports of escalating methamphetamine use worldwide, and the documented association between its use and psychosis, there is limited information available on the prevalence of psychotic symptoms among methamphetamine users. The current study aimed to examine the prevalence of psychosis amongst a sample of regular methamphetamine users and explore relevant risk factors. Method: A cross-sectional survey of 310 methamphetamine users from Sydney, Australia. Measures of psychosis included: (a) a psychosis screening instrument derived from the Composite International Diagnostic Interview (CIDI); and (b) the Brief Psychiatric Rating Scale (BPRS) subscales of Suspiciousness, Unusual Thought Content and Hallucinations. Hostility during the worst symptom episode was measured using the Hostility subscale of the BPRS. A score of four or greater was used to define clinically significant symptoms. Dependence on methamphetamine was defined as a score of four or greater on the Severity of Dependence Scale. Results: Twenty-three per cent of participants had a clinically significant symptom of psychosis in the past year, and 13% screened positive for psychosis on the CIDI (cf. 1.2% of the Australian general population). The prevalence of clinically significant symptoms was 18% after excluding participants with a history of schizophrenia or other psychotic disorders, and was significantly higher among dependent methamphetamine users (27% vs. 8%; OR = 3.1, CI 1.6-5.9). Twenty-seven per cent of participants reported clinically significant hostility whilst psychotic. Discussion: The prevalence of psychosis in the current sample of methamphetamine users was 11 times higher than amongst the general population in Australia. Dependent methamphetamine users are a particularly high-risk group for psychosis, and improved treatment options are urgently required to reduce the risk of associated psychosis and related aggressive behaviour.
- 526** GUILT, SHAME, AND COMPROMISE OF FATHERING: A COMPARATIVE STUDY OF DRUG-ABUSING MEN
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Despite longstanding concern about guilt and shame in the lives of drug-abusing mothers, very little is known about guilt, shame, and compromise of fathering occurring in the context of chronic drug abuse. In this comparative study, data collected from an ethnically diverse sample of 229 fathers were used to document ways self-report of guilt and shame in drug-abusing men differs from that of men with no history of drug or alcohol abuse. After allowance for the potential influence of age, ethnicity, and education, the drug-abusing fathers reported significantly more guilt and more shame about failure to be a more effective parent. Moreover, unique, statistically significant relationships between chronic drug-abuse and both guilt and shame persisted even after allowance for between-group differences in personality functioning and quality of father-child relationships. Although all fathers consistently reported more guilt than shame, between-group differences in shame were much more robust than differences in guilt. The results suggest that guilt and shame are important emotions in the psychological world of drug-abusing fathers that must be addressed in parent intervention pursued with this population across systems of care. (This research was supported by National Institute on Drug Abuse Grants RO3 DA11988, P50 DA09241, and RO1 DA 20619.)
- 527** DISCRIMINATIVE STIMULUS EFFECTS OF FLUMAZENIL IN BENZODIAZEPINE-DEPENDENT MONKEYS: PHARMACOLOGIC EVALUATION UPON TEMPORARY DISCONTINUATION OF TREATMENT
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A flumazenil discriminative stimulus in diazepam (5.6 mg/kg/day)-dependent rhesus monkeys was used to compare withdrawal induced by flumazenil to withdrawal induced by temporary discontinuation of benzodiazepine treatment. Although monkeys respond on the flumazenil lever when diazepam treatment is temporarily discontinued, marked individual differences in the emergence of withdrawal over time preclude systematic investigation. To establish temporal homogeneity in the emergence of withdrawal among individuals, the shorter-acting benzodiazepine lorazepam (3.2 mg/kg/8 h) was temporarily (48 h) substituted for diazepam. Acute deprivation (11 h) of lorazepam reliably occasioned responding on the flumazenil lever in all monkeys, and these effects were attenuated by benzodiazepines (midazolam and lorazepam) and by positive GABAA modulators acting at neuroactive steroid sites (alfaxolone and pregnanolone) and barbiturate sites (pentobarbital). The potency of midazolam, lorazepam and pentobarbital to attenuate responding on the flumazenil lever was the same as their potency in substituting for a midazolam discriminative stimulus in untreated monkeys, whereas the potency of alfaxolone and pregnanolone to attenuate flumazenil-lever responding was significantly greater (5- and 10-fold, respectively) than their potency in substituting for midazolam in untreated monkeys. The flumazenil-like effects of acute lorazepam deprivation were not fully attenuated by the low efficacy positive GABAA modulators bretazenil and L-838,417, the GABAA receptor agonist muscimol, the NMDA antagonist ketamine, or the monoamine uptake blocker cocaine. Thus, positive GABAA modulators, regardless of site action, attenuate both flumazenil- and deprivation-induced benzodiazepine withdrawal, and those acting at neuroactive steroid sites are particularly effective in attenuating benzodiazepine withdrawal under both conditions. Supported by DA09157 and Senior Scientist Award DA17918 (CPF).
- 528** A MOUSE MONOCLONAL ANTIBODY BLOCKS RECOVERY OF (+)-METHAMPHETAMINE SELF-ADMINISTRATION IN AN ANIMAL MODEL OF RELAPSE
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Rats were trained to self-administer 0.016 and 0.024 mg/kg (free base) doses of METH under a fixed-interval (FI) 1-min schedule of drug presentation. After responding stabilized, saline was substituted for METH to partially extinguish responding. Subsequently METH was made available again under the FI schedule to measure the rate of recovery of METH self-administration. Once METH self-administration stabilized a second time, the saline extinction was repeated. Finally, an anti-METH mouse monoclonal antibody mAb911 (affinity for METH of 41 nM) was given intravenously (600 mg/kg) and on the next day measurement of recovery of METH self-administration was repeated. Without mAb911, METH self-administration recovery approached pre-extinction levels during the first self-administration session. After mAb911 administration, METH self-administration remained at the saline-extinction level for 3 to 4 days. Thus, the anti-METH monoclonal antibody blocked the recovery of METH self-administration for several days in this animal model of relapse. Supported by NIDA Grants DA14362, DA05477 and DA11560.

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529 A LONGITUDINAL INVESTIGATION OF INTIMATE PARTNER VIOLENCE AMONG MOTHERS WITH CO-OCCURRING MENTAL ILLNESS AND SUBSTANCE ABUSE DISORDERS

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Objective: Severe mental illness (SMI), substance use, and intimate partner violence (IPV) have emerged as major intersecting public health problems that adversely and disproportionately impact the lives of women in the U.S. This longitudinal study investigated the demographic and clinical correlates of IPV in a sample of 379 mothers with severe mental illness. Methods: We conducted a secondary analysis of longitudinal data using multiple logistic regression. Participants were part of a longitudinal, community-based study of mothers with severe mental illness. The women were interviewed initially in 1995-1996 (T1) and then about 20 months later in 1997-1998 (T2). Results: Multiple logistic regression analyses shows a significant positive relationship between alcohol and drug misuse and IPV at T2, indicating that women with the co-occurring diagnosis of substance misuse (dual diagnosis) are more likely than others to report IPV. The number of lifetime psychiatric hospitalizations and the number of symptoms related to psychiatric disability exhibited at the time of interview are positively associated with IPV, and age is inversely associated with IPV. Conclusions: Mental health professionals servicing mothers with mental health problems need to be aware and prepared to assess the significant correlation among these intersecting public health problems in order to affect successful interventions. Particular attention must be given to the special treatment needs related to dual diagnosis and victimization and its impact on this vulnerable population.

530 A COMPARISON OF COCAINE- AND MARIJUANA-DEPENDENT SUBJECTS PRESENTING FOR MEDICATION TREATMENT TRIALS

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Evaluation of the characteristics of individuals presenting for substance abuse treatment can provide important information to help focus treatment services. In the present study, demographic and clinical characteristics of individuals presenting for medication trials for the treatment of cocaine (n=170) or marijuana dependence (n=35) were compared. Chi-square or nonparametric (Wilcoxon rank sum) tests were used to detect statistically significant differences between dependence groups. Marijuana-dependent (MD) subjects were more likely to be Caucasian (91%) than cocaine-dependent (CD) subjects (43%) (p<.0001), and MD subjects presenting for treatment were younger than CD subjects (mean(sd)=31.6(8.7) years vs. mean(sd)=35.4(7.2) years, p<.005). MD subjects were also more likely to have completed more than 12 years of education than CD subjects (83% vs. 25%, p<.0001). No differences in marital status were seen between the two groups. CD subjects were more likely to report anxiety symptoms than MD subjects (38% vs. 11%, p<.005). TimeLine FollowBack data from the 30 days prior to study entry found that CD subjects were abstinent from use approximately mean(sd)=18.5(8.3) days while MD subjects were abstinent approximately mean(sd)=5.4(5.5) days (p<.0001). No difference in number of cigarettes smoked in the previous 30 days between MD and CD subjects was found. Both studies had high drop-out rates, with approximately 40% of subjects discontinuing prior to randomization or not returning for at least one visit after receiving medication. Subjects are continuing to be recruited for the marijuana treatment trial; data from the expanded sample will be presented as well as data on additional measures. In this preliminary analysis, with the exception of binge (cocaine) and daily (marijuana) use patterns and some demographic characteristics, the groups were similar. Supported by NIDA grant K23DA15440.

531 BUPRENORPHINE METABOLISM BY PRETERM HUMAN PLACENTAS

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Methadone maintenance programs are considered the standard of care for treatment of the pregnant opiate addict. Methadone is currently the only drug approved for treatment of this patient population in the U.S. Buprenorphine (BUP), a partial μ opioid-agonist is used in several countries for treatment of this patient population and is in phase II clinical trials in the U.S. Reports indicate that both drugs improve maternal and neonatal outcome but that they were also associated with neonatal abstinence syndrome (NAS). Our hypothesis is that placental disposition of BUP during pregnancy might affect the concentration of an opioid in the fetal circulation and hence could affect the incidence and intensity of NAS. Recent reports from our laboratory indicate that the transplacental transfer of BUP is lower than that for methadone and that term placental aromatase is the major enzyme responsible for the metabolism of BUP to norBUP and methadone to EDDP. However, the structure and functions of preterm placentas are different. Therefore, the goal of this investigation was to determine the kinetics of BUP metabolism by human placentas obtained from preterm deliveries. Placentas were divided according to their gestational age at parturition into three groups: Late second trimester (17-26 weeks), early 3rd trimester (27-33) and late 3rd trimester (34-40). In all placentas, BUP was metabolized by its N-dealkylation to norBUP as revealed by HPLC/UV and HPLC/MS. The activity of the enzyme metabolizing BUP in placentas from early third trimester was 0.85 ± 0.16 pmol/mgP.min which is lower than that from term placentas 2.5 ± 0.4 pmol/mgP.min. The identification of the enzyme catalyzing the reaction as well as its kinetics is currently underway. Supported by grant from NIDA to MSA.

532 A PROSPECTIVE FRENCH MULTICENTER OBSERVATIONAL STUDY ON COMPLIANCE TO HEPATITIS C TREATMENTS CHARACTERISTICS OF SUBPOPULATION OF PATIENTS WHO ACQUIRED HCV INFECTION VIA DRUG

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Objective: To analyze the baseline profile of HCV-infected patients who have an ongoing drug addiction compared with those with a former drug addiction and those with no drug addiction. Patients and Methods: From January, 2003 to December, 2004, 1,945 chronic HCV-infected patients were included in the CHEOBS study. Three groups were identified: A: 257 (13%) present drug users, among which 35 (2%) used drugs only and 222 (11%) were in a drug substitution program [76/222 (34%) used methadone, 146/222 (66%) high dose buprenorphine], B: 601 (31%) former drug users; C: 1,087 (56%) patients who had no history of drug abuse. Results: The drug abusers compared to patients who had no history of drug abuse were more frequently male (A 82%, B 74%, C 50%; p<0.001), younger (A 37, B 42, C 52 years; p<0.001), alcohol abusers (A 7%, B 6%, C 2%; p<0.001) and HIV coinfectd (A 7%, B 7%, C 1%; p<0.001). These patients lived more frequently in poor socio-economic conditions (A 30%, B 17%, C 10%; p<0.001), had higher levels of past anxiety-depression (A 41%, B 30%, C 18% (p<0.001), which led frequently to a suicide attempt (A 20%, B 8%, C 3%; p<0.001). They had a shorter duration of HCV infection (A 14.6, B 19.5, C 23.3 years). The distribution of genotypes (G) was significantly different (p<0.001): G1 (A 46%, B 47%, C 62%); G2 (A 1.6%, B 3.6%, C 16.6%); G3 (A 43.8%, B 39.5%, C 12.7%); G4 (A 8%, B 9.6%, C 6%); other genotypes (A 0.4%, B 0.2%, C 2.8%). Severe liver fibrosis (F3/F4) was less frequent in the present drug users group (24.5% vs 33.8% vs 38.1%; p=0.001). Conclusion: In clinical practice, patients who start HCV treatment are frequently present or former drug abusers. The former drug abusers showed an intermediate profile between the two other groups.

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533 ELECTRONIC BUCCAL DRUG DELIVERY SYSTEM TO TREAT ADDICTION AND CHRONIC DISEASES: A PORCINE STUDY IN THE FRAME OF "INTELLIDRUG" PROJECT

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Objectives: A basic requirement in medication delivery technologies is to get the desired therapeutic effect with minimum side effects and as controlled as possible. Our purpose is to investigate whether the oral cavity can provide access to efficient and non-invasive drug delivery using an electronic and software driven system. Such an automatically operated system may be particularly advantageous if fixed in the oral cavity of drug addicts to ensure their compliance with intake of anti-opiate medication. In the present study the effectiveness of an electronic buccal delivery system delivering naltrexone was evaluated on pigs, as part of the development of a self-contained intra-oral miniature drug delivery device. **Methods:** The system consists of an extra-oral component (containing a drug reservoir, an actuation mechanism to push the drug solution, a flow sensor, power source and software) and an intra-oral outlet system mounted on a dental prop. The system was tested on 12 pigs in a controlled study over 6 experimental session days. The anti-opiate drug naltrexone, in various doses, was delivered by the system to the buccal mucosa during 10 minutes or was injected i. v. and its blood levels assessed during 6 hours. **Results:** Administration of i. v. naltrexone induced a sharp increase in blood levels after 5 minutes, and then a steep decrease. In contrast, transmucosal delivery resulted in a gradual increase in blood naltrexone levels, reaching its peak after 90 minutes, and followed by a slow decrease. After 6 hours the blood levels of naltrexone delivered to the buccal mucosa were higher compared to i. v. administration. **Conclusions:** The results suggest that buccal delivery by an electronic system has the potential to cause long-lasting and controlled blood levels of naltrexone and other medications. The IntelliDrug research project was supported by the European Commission under the Sixth Framework (Project no. 002243 IST)

534 INTERACTIONS OF GENDER AND MENSTRUAL CYCLE PHASE WITH PROGRESSIVE RATIO MEASURES OF COCAINE SELF-ADMINISTRATION IN CYNOMOLGUS MONKEYS

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Clinical and preclinical data suggest that fluctuations in ovarian steroid hormones across the menstrual/estrous cycle influence the behavioral and abuse-related effects of cocaine in females (see Mello & Mendelson, 2002; Lynch et al., 2002). The effects of gender, menstrual cycle phase, and ovarian hormone fluctuations on cocaine-maintained responding (0.032 mg/kg/inj) under a progressive-ratio schedule were investigated in four female and two male cynomolgus monkeys. Females were studied across 32 menstrual cycles, and ovulatory cycles were defined by luteal phase elevations in progesterone. Data were analyzed for the early and mid-follicular phase and the mid- and late-luteal phase of the menstrual cycle. Progressive-ratio break points for cocaine were significantly higher in females than in males ($p < 0.0001$), and these gender differences were greatest during the early ($p < 0.001$) and mid-follicular phases ($p < 0.01$) of the menstrual cycle. Progressive-ratio break points did not vary consistently as a function of menstrual cycle phase during ovulatory cycles, and there were no systematic patterns of progressive ratio break points during anovulatory menstrual cycles. There were no significant differences in progressive ratio breakpoints between ovulatory and anovulatory cycles. Although changes in ovarian steroid hormones may influence cocaine intake under some conditions, consistent patterns of responding for 0.032 mg/kg/inj cocaine were not detected during ovulatory menstrual cycles in cynomolgus monkeys. Lower doses of cocaine (0.01 and 0.0032 mg/kg/inj) are currently being examined under the same conditions. This research was supported by grants R01-DA14670, K05-DA00101 and K05-DA00064 from NIDA, NIH.

535 A COMPARISON OF 8-HETERO TROPANES: INHIBITION OF MONOAMINE UPTAKE SYSTEMS

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The class of 3-aryltropans has been widely explored for potential medications for remediation of cocaine abuse. Research has focused predominantly on 3-azatropans and it is now well recognized that these compounds can be designed to manifest varied selectivity and potency for inhibition of the dopamine (DAT), serotonin (SERT) and norepinephrine (NET) uptake systems. We had also reported that the 8-nitrogen atom present in the 3-aryltropans is not essential for these 8-azabicyclo[3.2.1]octanes to bind to monoamine uptake systems. Indeed, we had demonstrated that compounds in which the amine (8-N) had been exchanged for an ether (8-O) or a methylene (8-CH₂) retained potency and selectivity. More recently, we reported the synthesis and biological activity of a new class of unsaturated 8-thia-3-aryl-bicyclo[3.2.1]oct-2-enes, which exhibit nanomolar inhibitory potency at the DAT, with substantial selectivity versus SERT inhibition. We now report an elaboration of this class to include the 3- α -(boat)-aryl and 3- β -(chair)-aryl-8-thiatropans. A comparison of these new compounds with 8-oxa- and 8-aza-tropans confirms that potency and selectivity can be strongly influenced by the orientation of the C3-aryl ring. Thus, in a comparison of 3-(3,4-dichlorophenyl) substituted compounds, the 8-thia-3- β -aryl compound inhibits the DAT with an IC₅₀=5.7nM and SERT=8.0nM; in contrast, the 8-thia-3- α -aryl compound inhibits the DAT IC₅₀=6.9nM and SERT IC₅₀=99nM. This relative potency and selectivity pertains for the 8-oxa analogs. Thus, the 8-oxa-3- β -aryl compound manifests a DAT IC₅₀=3.3nM and SERT IC₅₀=6.5nM, while the 8-thia-3- α -aryl compound inhibits the DAT IC₅₀=3.1nM and SERT IC₅₀=65nM. These new compounds provide further support for our contention that topology may play as strong a role as functionality in the determination of biological activity within the class of 8-hetero-substituted 3-aryl-bicyclo[3.2.1]octanes.

536 COMPARISON OF THE EFFECTS OF BINGE SMOKING OF LOW- AND HIGH-NICOTINE CIGARETTES ON HYPOTHALAMIC-PITUITARY-ADRENAL AXIS HORMONES AND MOOD IN MEN

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Twenty-four men who met DSM-IV criteria for nicotine dependence provided informed consent for participation in studies designed to compare the effects of smoking three low or high nicotine cigarettes on hormonal, cardiovascular and mood measures. Cigarettes were smoked at one hour intervals and subjects took one 5 sec puff every 30 sec for 4 minutes. Plasma nicotine levels increased significantly within 8 min after smoking the first high nicotine cigarette and within 4 min after smoking the second and third cigarette. There were no significant increases in plasma nicotine levels after smoking a low nicotine cigarette. Cardiovascular, hormonal and VAS ratings of positive subjective effects (high, rush, stimulated) increased significantly after each high nicotine cigarette, but the magnitude of the increase diminished with repeated cigarette smoking. After low nicotine cigarettes, there were no significant increases in ACTH; cortisol and DHEA decreased progressively after each cigarette and increases in positive subjective effect ratings were not sustained. VAS ratings of negative subjective effects (sick, dizzy, jittery, bad feeling) did not increase after high or low nicotine cigarettes. Ratings of "craving" decreased significantly during smoking, but the decrease was greater after high nicotine cigarettes. These data are consistent with reports that the first cigarette of the day is most salient, and suggest that tolerance to nicotine develops quite rapidly during repeated cigarette smoking. These findings are also consistent with the hypothesis that stimulation of the HPA axis may be one important aspect of the abuse-related effects of cigarette smoking. This research was supported by grants R01-DA15067, P01-DA14528, T32-DA07252, K05-DA00064 and K05-DA00101 from the National Institute on Drug Abuse, NIH.

537 SINGLE-DOSE METHAMPHETAMINE RESERPINE INTERACTIONS

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BACKGROUND: Reserpine, an extract of Indian Snakeroot (*Rauwolfia serpentina*), irreversibly inhibits the action of the vesicular monoamine transporter producing a depletion of neuronal monoamines and decreased CNS sympathetic activity similar to chronic methamphetamine abuse. Reserpine is being evaluated as a pharmacotherapy for methamphetamine (MA) addiction. Although sustained reserpine dosing depletes CNS monoamines the first dose of reserpine can increase neurotransmitter levels. If reserpine and MA both increase CNS monoamine levels a larger pharmacodynamic response than predicted for either drug alone could occur. This study tested acute single dose interactions between reserpine and MA. **METHODS:** Interactions between 15 mg iv MA given 60 hours before and 12 hours after a single oral dose of reserpine (0.5 or 1.0 mg) or placebo were assessed in 30 MA using subjects using a double-blind, parallel-group, placebo-controlled inpatient design. Subjective effects were assessed with visual analog scales and cardiovascular function was assessed with non-invasive measures of heart rate and blood pressure. **RESULTS:** Methamphetamine increased mean peak heart rate (24.6 ± 10.8 , 20.5 ± 13.1 and 16.9 ± 15.7 beats per min in the placebo, reserpine 0.5 and 1.0 mg conditions respectively) and reserpine blunted this response (21.6 ± 12.4 , 11.5 ± 8 and 8.9 ± 7.5 in the placebo, reserpine 0.5 and 1.0 mg groups). No significant changes were seen with other measures. **CONCLUSIONS:** The first dose of reserpine does not increase the pharmacodynamic effects of MA but single low doses of reserpine attenuate the heart rate response to MA. Supported by NIDA contract N01DA-4-8306 and NIH RR-00079 (GCRC, UCSF).

538 THE RELATIVE ACTIVITY OF OPIOIDS AS P-GLYCOPROTEIN SUBSTRATES

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Chronic clinical pain remains poorly treated. The use of mu opioid analgesics such as morphine can treat the pain, but the rapid development of tolerance to the analgesic effects necessitates ever increasing doses to be administered. Unfortunately, tolerance to the constipatory effects occurs at a slower rate, a condition we refer to as differential tolerance. As the dose of morphine is increased to overcome the tolerance to the analgesic effects, the effects at the gut increase, leading to severe, often life threatening, constipation. As such, there is a great need to develop opioids to which differential tolerance does not develop in order to reduce the severity of constipation. Our hypothesis is that the efflux transporter, P-glycoprotein (Pgp), contributes to the development of central tolerance by actively pumping morphine out of the CNS. Pgp is present at the blood-brain barrier (BBB), morphine is a known Pgp substrate, and Pgp has been shown to be upregulated in morphine tolerant animals. As analgesia is primarily central and constipation is primarily peripheral, up-regulation of Pgp would be expected to lead to lower brain concentrations of morphine comparative to naive animals, and therefore contribute to tolerance to the analgesic effects. We have validated Pgp assays using morphine, codeine, oxycodone and methadone to confirm that these opioids are Pgp substrates with efflux ratios of 2.3, 1.90, 2.06 and 3.4, respectively. These studies were conducted in the presence of Pgp inhibitors (verapamil and GF120918) to confirm Pgp mediated effects. As such, methadone (efflux ratio = 3.4) possessed the greatest activity as a Pgp substrate, while codeine (efflux ratio = 1.90) possessed the least activity as a Pgp substrate from this group. Based on these in vitro results, it appears that Pgp may be involved in the BBB transport of a wide variety of opioid analgesics.

539 INFLUENCES OF SUBSTANCE ABUSE AND MENTAL ILLNESS ON INCIDENTS OF VIOLENCE AND VICTIMIZATION

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This study examined differences in violent incidents perpetrated and experienced by individuals with substance use disorders only (SDO), mental disorders only (MDO), and co-occurring substance use and mental disorders (COD). A total of 419 subjects (Ss) recruited from mental health and substance abuse treatment settings indicated whether they had experienced acts of violence in the past 30 days. For each act they had perpetrated or experienced, Ss were asked where the incident took place, who was involved, whether individuals were injured, and whether alcohol or drugs were used before the incident. We examined distributions of violence characteristics among diagnostic groups and used logistic regression analyses controlling for demographic characteristics and adjusting for clusters of incidents involving the same individual to test differences among Ss with single disorders (SDO or MDO) vs co-occurring disorders. Approximately 41% (n=171) of Ss were involved in at least one incident of violence as a perpetrator or victim, generating a total of 379 incidents. More incidents of violence involved victimization (62%) than perpetration (38%). Perpetration incidents involving SDO Ss were significantly more likely to involve bruises and cuts (OR=6.16, p=.005), take place outdoors (OR=3.04, p=.047) and involve alcohol (OR=8.52, p=.001). Perpetration incidents involving MDO Ss were significantly more likely to involve bruises and cuts (OR=12.80, p=.007) and take place within a residence (OR=8.47, p=.024). Victimization incidents involving SDO Ss were significantly more likely to involve using drugs (OR no drug use=0.27, p=.007). Despite common stereotypes of individuals with substance use and mental disorders, more incidents involved victimization than perpetration. With respect to incidents of perpetration, type of disorder was the strongest predictor of type of injury, location, and the use of alcohol. With respect to victimization, type of disorder only predicted the use of drugs prior to the incident.

540 MARIJUANA USE AND EXPECTANCIES' ASSOCIATION WITH RISK TAKING

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Marijuana users are at increased risk for health and behavioral problems associated with risk taking (Sussman & Stacy, 1996). Chronic users have shown increased risk taking on the Bechara Gambling Task (Whitlow et al, 2004), but such laboratory research is scarce. Furthermore, marijuana users who have more positive marijuana outcome expectancies (Schafer & Brown, 1991) may be more vulnerable to risk taking. The present study examined the relation between marijuana use, expectancies and risk taking, as measured by a laboratory Balloon Analogue Risk Task (BART, Lejuez et al, 2002). The BART has been shown to differentiate cigarette smokers from nonsmokers but has not been explored with marijuana users. Data were collected from a sample of 113 college student tobacco smokers (59% male, 86% Caucasian, 12 cigarettes/day on average). Marijuana expectancies and risk taking propensity were examined within non-users (n = 34), infrequent (n = 40; 5 days/month on average), and frequent marijuana users (n = 39; 23 days/month on average). Results indicated that frequent users reported lower expectations of cognitive-behavioral impairment and negative effects of marijuana, and higher expectations of relaxation/tension reduction and social/sexual facilitation. While behavior on the BART was correlated with marijuana expectancies (r = .31, p < .01), it did not differentiate the three marijuana use groups. Regression analyses showed that individuals with more positive marijuana expectancies (specifically for craving/physical effects) evidenced increased risk taking on the BART (B = .25, R² = .10, p < .05). Findings indicate that risk taking propensity in marijuana users is related to greater expectation of positive reinforcement from marijuana and not simply to frequency of use. Placebo-controlled research examining effects of acute marijuana smoking on risk taking propensity is needed to make the causal connection between marijuana use and risk taking and to differentiate drug effects from expectancy effects.

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- 541 WHICH SMOKING CESSATION INTERVENTION WORKS FOR SMOKERS WITH AN ALCOHOL ADDICTION?**
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Background: In Germany about 75% to 95% of alcohol dependent patients in residential treatment after detoxification are smokers. Smoking cessation interventions for these smokers show an unsatisfying effectiveness. Allocating patients to different interventions may be an effective strategy to optimize smoking cessation interventions. Aim: Optimizing treatment for alcohol dependent smokers in residential treatment for substance abuse treatment. Hypotheses: (1) A cognitive-behavioral and a motivational smoking cessation intervention show the same acceptance in process evaluation. (2) Both interventions show the same effectiveness. (3) Smokers low in motivation will benefit more from a motivational intervention. Smokers low in self-efficacy will benefit more from a cognitive-behavioral intervention. Methods: In a randomised controlled trial 663 alcohol dependent smokers were assigned to a motivational (MT) or a cognitive-behavioral treatment (CBT). Data were collected before treatment, at the end of intervention, at 3, 6 and 12 months follow-up. Binary logistic regressions were used for statistical analyses. Results: Both interventions showed a good acceptance. At 12 months follow-up abstinence rates of CBT were 6.9%, of MT 9.0%. There were no significant differences in abstinence rates between treatment conditions. Data showed a high variance of abstinence rates from 0 to 22% between centers. No matching effect could be detected. Conclusions: Before exploring for whom interventions work (moderator effects), researcher should have a closer look on how smoking cessation interventions work (mediator effects). The effects of smoking cessation may be optimized by implementing a restrictive tobacco control policy in residential treatment for alcohol dependence. Acknowledgement: Funding through grant by the German Federal Ministry of Education and Research (BMBF, Funding number: 01EB0141).
- 542 DIFFERENCES AMONG INBRED RAT STRAINS IN NOVELTY SEEKING, LOCOMOTOR ACTIVITY AND AMPHETAMINE SELF-ADMINISTRATION**
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Previous research indicates that individual differences in response to novelty predict the rewarding effect of psychostimulant drugs. Using different inbred rat strains, the current study examined if the link between response to novelty and response to amphetamine (AMPH) is heritable. Toward this goal, an initial experiment was conducted using outbred Sprague-Dawley rats to determine if reliable acquisition of AMPH self-administration is obtained using an autoshaping procedure. The procedure consisted of 5 daily 60-min autoshaping sessions where non-contingent AMPH infusions (0.1 mg/kg/infusion) were given paired with a light cue. This was followed 30 min later by a 60-min AMPH self-administration session in which the light cue and AMPH infusion were contingent on a lever press using a fixed ratio 1 (FR 1) schedule of reinforcement. During this phase (5 days), rats were under food restriction (20g per day). Subsequent sessions consisted of only the 60-min self-administration session, and the FR value was increased incrementally from 1 to 5 every three days, without food restriction. Results demonstrated that the autoshaping procedure yielded a reliable acquisition curve, followed by stable responding. In a subsequent experiment, various commercially available strains of inbred rats (ACI; BDIX (BD9); Brown Norway (BN); Buffalo (Buf); Dahl salt sensitive (DSS); Fischer (F344); Lewis (LEW); Spontaneous hypersensitive rat (SHR); Wistar Kyoto (WKY)) were assessed for response to novelty and acquisition of AMPH self-administration using the autoshaping procedure. Differences among strains in locomotor activity in an escapable novel environment and novelty place preference were obtained. Differences in acquisition of AMPH self-administration were also observed among strains. By elucidating behavioral differences seen among strains, further insight into genetic variables underlying the link between novelty seeking and drug reward may be obtained. (Supported by USPHS grant DA 05312).
- 543 CHILDHOOD ABUSE, SUBSTANCE USE DISORDER, AND PREGNANCY PROBLEMS IN YOUNG ADULT WOMEN**
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This study aimed at determining the moderating role of current substance use disorder (SUD) in the association between severity of childhood abuse (physical, emotional, and sexual) and pregnancy problems (abortions, miscarriages, complications during pregnancy and delivery/PREG/PROB) in young adult women (age 19-23) who participated in a prospective longitudinal study since they were adolescents (age 14-18). The sample was composed of young adult women who at age 14-18 met criteria for a DSM-III-R diagnosis of SUD (n=146) and controls (n=26). The average age was 21.9 years (sd=1.69). Fifty eight percent were Caucasians, 35% were African Americans and 6% belonged to other ethnic background. The educational level was 12.68 (sd=1.57) and the level of socioeconomic status according to Hollingshead criterion was 33.30 (sd=10.96). The results of the correlational analyses showed that physical ($r=.20, p=.01$), emotional ($r=.14, p=.06$), and sexual ($r=.18, p=.02$) abuse were correlated with PREG-PROB at age 19-23. Also, current SUD was correlated with childhood physical ($r=.32, p=.000$), emotional ($r=.27, p=.000$), and sexual ($r=.28, p=.000$) abuse. The results of the moderation analysis revealed that childhood physical abuse (Beta=.47, $p<.01$) and the interaction between physical abuse and SUD (Beta=-.43, $p<.05$) were associated with PREG/PROB ($R^2=.08, F=2.5, p=.02$). Also, history of childhood emotional abuse (Beta=.37, $p=.01$), SUD severity (Beta=.27, $p=.04$) and the interaction between emotional abuse and SUD were related PREG/PROB ($R^2=.11, F=3.42, p=.003$). The results of the analysis testing the moderating role of SUD in the association between sexual abuse and PREG/PROB were not significant. The data underscore the long lasting impact of childhood physical and emotional abuse in interaction with current SUD on young adult women's reproductive system.
- 544 HEALTHY LIFESTYLES: A PSYCHO-EDUCATIONAL GROUP PROGRAM FOR WOMEN WITH SUBSTANCE USE DISORDERS**
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Research indicates that achieving and maintaining a healthy lifestyle, including substance free activities, can decrease the probability of a relapse back to substance use, yet women in substance abuse treatment do not have time or do not take the time to take care of themselves and prepare for a substance free lifestyle. The purpose of this project was to offer women a weekly psycho-educational group program to provide them with the tools necessary to live a substance free, healthy lifestyle. The program consists of twelve modules designed to promote a substance free lifestyle and enhance physical and mental health. Healthy Lifestyles utilizes a holistic approach, emphasizing healthy eating, exercising and relaxing, maintaining sobriety, enhancing healthy leisure activities, and initiating pro-social contacts for the women and their children. Topics addressed in the program include: physical activity, food and nutrition, wellness (medical and dental care), the science of substance abuse, recreation and hobbies, sexuality, mental health, social support networks, healthy parenting, sustaining a healthy lifestyle and relapse prevention. Each module of the program is two hours in length and involves 30 minutes of yoga training. Women in outpatient treatment for substance use were recruited from two Iowa substance abuse treatment centers to participate in the Healthy Lifestyles program. This program has been successfully implemented several times in two Iowa substance abuse treatment centers. Qualitative data suggests that participants utilized the information to develop healthier substance free lifestyles. Participants indicate that the program fostered the development of stronger support systems which assists with recovery. However, the success was confounded by poverty issues, such as inability to have appropriate exercise clothes, and limited resources to obtain healthy food options. Future research will be conducted to examine the effectiveness of the program in terms of leading a substance free lifestyle six months after program completion.

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- 545 USING NONLINEAR MIXED MODELS TO ANALYZE DISCOUNTING BEHAVIOR IN ADOLESCENT SUBSTANCE USERS AND CONTROLS**
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INTRODUCTION: By estimating rates from exponential and hyperbolic models, studies have shown that substance using (SU) adults discount delayed rewards more rapidly than controls, but rates and other aspects of discounting (large vs. small, real vs. hypothetical, and delayed vs. probabilistic rewards) have not been systematically examined in adolescents. **AIM:** Develop and utilize a nonlinear mixed model (NMM) statistical approach to determine the best-fitting models (evaluating different functions and inclusion of random effects) and test between-group and within-subject differences in aspects of discounting. **HYPOTHESES:** SU adolescents will discount delayed and probabilistic rewards more rapidly than controls, and this effect will be more pronounced for large hypothetical and small real rewards. **METHODS:** 40 SU and 40 control adolescents (mean 16 yr, 46% Caucasian) completed a 50 minute discounting task assessing delay (1 to 260 weeks) and probabilistic (10 to 95%) outcomes for \$40 real, and \$40 and \$500 hypothetical rewards. NMMs of different functions were evaluated for fit to mean indifference points. **RESULTS:** Exponential and simple hyperbolic functions indicated that SU adolescents discounted delayed rewards more rapidly than controls ($p < .05$) but complex hyperbolic functions fit these data better based on likelihood-based selection criteria and indicated no group differences in rates. With all fixed effect models, as delay to reward increased, SU adolescents chose significantly smaller rewards than controls ($p < .05$); however, for \$40 real and \$40 hypothetical rewards, proper inclusion of a random subject effect negated this group difference. Using the NMM approach, probabilistic rewards will be compared between groups and aspects of discounting will be compared within subjects. **CONCLUSIONS:** Choice of nonlinear function and inclusion of random subject effects can affect conclusions regarding differences in discounting behavior and the NMM provides a useful method for evaluating different models. Grant Support: NIDA DA-009842, 011015, 012845
- 546 DELAYED EFFECTS OF CM BEHAVIORAL DAY TREATMENT COMPARED TO CM ONLY ON LONG-TERM ABSTINENCE**
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Contingency management (CM) for housing, and work therapy with behavioral day treatment (BDT), reduces substance abuse, days homeless and unemployed, for cocaine dependent homeless. But whether CMBDT reduces substance use beyond CM alone is unknown. This randomized controlled trial compared abstinence outcomes between contingency-managed housing and work only (CM Only, $n=103$), and CM with daily BDT (CM+, $n=103$) to answer this. Subjects were provided a furnished apartment starting week 1. In week 2, a drug-free urine test permitted subjects to remain in housing and work therapy. Subjects were moved from housing to a shelter within 6 hrs. of a drug positive urine, and returned after 3 consecutive negative tests. CM Only received these 2 interventions for 24 weeks, while CM+ additionally received BDT in weeks 1-8, and aftercare weeks 9-24. Urine was tested MWF for cocaine, marijuana and alcohol through 6 months, and randomly 1/wk, months 7-12. Intention-to-treat analyses assessed overall and sustained abstinence. Mean abstinence across weeks 1-52 was .43, $SE=.031$ for CM Only and .54, $SE=.035$ for CM+, ($p=0.0217$). Mean consecutive weeks abstinent was 10.77, $SE=.79$ for CM Only, versus 13.89, $SE=.93$ for CM+, ($p=0.0113$). GEE analysis of abstinence as a function of treatment, study phase, and their interaction, found an overall difference between groups ($p > 0.014$). Abstinence across wks 1-8, 9-24, and 25-52 was for CM Only 73%, 58% and 34%, and for CM+ was 79%, 64% and 49%, significantly different for wks 25-52, ($p > 0.0001$). Results are consistent with prior trials showing benefit of CM when added to day treatment. Findings suggest that CM+ confers marginal initial benefit beyond CM housing and work during and soon after treatment. But a CM+ impact may be on long term and sustained abstinence. Long term effects on housing and employment await further analyses. Supported by NIDA RO1 DA11789-04
- 547 RISKY BUSINESS: SEXUAL BEHAVIORS, DRUG USE AND VIOLENCE AMONG SEX-TRADING WOMEN IN ST. LOUIS**
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To gain insight into behaviors prevalent among sex traders, such as high risk sexual behaviors, drug use, victimization, and street violence, women in the City of St. Louis Medium Security Institution (MSI) were interviewed between May and September 2005, for a series of focus groups. Eligible women included those with an arrest history who appeared in the St. Louis City or Missouri State Drug Courts. The sample of 30 was 70% African-American, ranging in age from 19 to 48 (mean=35.9). In accordance with focus group methodology, content of the groups varied depending on participant interest and input; however, several salient themes emerged. Participants noted that oral sex was the most common sex trade activity, and that they were paid not only to provide but also to receive oral sex. Rates charged by sex act varied widely but were often as low as a few dollars. Regular customers typically received 'discounts', and activity was reported highest around the first of the month, when customers were likely to have cash. Consistent with the literature, condom usage was described as irregular. In terms of drug use, participants reported that crack cocaine was most commonly used, with binges often lasting for several days. Regarding victimization, women frequently reported sexual abuse in childhood, and some described abusive relationships as adults, including one woman with visible scars resulting from being stabbed 47 times. Participants also reported being beaten and raped by customers, which led to their carrying weapons, ranging from knives to razors under the tongue, and sometimes perpetrating violence, including murder, as protection against further violence. These findings, already utilized to inform our current interview and HIV prevention intervention, will be described in greater detail to confirm the vulnerability of this population of women. These results suggest that more effective interventions are needed to assist this incarcerated population in making lifestyle changes beginning during incarceration and continuing after release.
- 548 COOPERATION AND DEFECTIONS AMONG OPIOID-DEPENDENT PATIENTS AND COLLEGE STUDENTS**
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Opiate users may not be sensitive to contingencies of punishment, and the Iterated Prisoner's Dilemma Game (IPG) is one mechanism in which this may be assessed. Fifty six treatment-seeking opiate dependents during intake for a buprenorphine treatment study and thirty one undergraduates at the University of Vermont participated in this study. Participants played a 60-trial IPG versus a computer opponent applying a tit-for-tat strategy. Percent cooperation was determined in the IPG in the first and last half of each session for all participants. The purpose of this study was to identify if, and to what extent strategies during the second half of an IPG changed from the first half for college students and for opiate users. For the college students, percent cooperation in the second half of the 60 trials was 14% ($SD=19\%$) greater than percent cooperation in the first half ($p=0.0004$) whereas for opiate users percent cooperation in the second half decreased 1% ($SD=18\%$) from that of the first half ($p=0.6749$). College students learned to cooperate over the 60 trials while opiate users did not; this may have been based on delayed reinforcement for cooperation and delayed punishment for defection. This suggests that drug dependents do not learn the contingencies of punishment. These findings are consistent with those obtained using a Gambling Task.

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549 HAND-IN-HAND PROGRAM: A PSYCHO-EDUCATIONAL GROUP PROGRAM FOR WOMEN WITH SUBSTANCE USE AND CO-OCCURRING MENTAL HEALTH DISORDERS

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Forty to sixty percent of women in substance abuse treatment also have co-occurring mental health disorders. Women's understanding of their mental health and substance use disorders is limited, which impacts their recovery, medical compliance, and ability to manage both disorders. The purpose of this psycho-educational group program is to increase knowledge about substance use and co-occurring mental health problems in order to bring about a substance free lifestyle, increase medical compliance, and enhance physical and mental health for women with substance use disorders. The Hand-in-Hand program was developed by Prairielands ATTC staff, and incorporates a combination of motivational interviewing and cognitive behavioral techniques to assist clients in achieving their goals. This program consists of fourteen modules which teach clients specific strategies to attain and maintain mental health, including exercise, nutrition, physical self-care and how to be their own advocate for health through healthier communication with their family members, physicians, and psychiatrists. Specific areas addressed in the program include: Family Relationships, Mental Health Promotion, Substance Abuse Continuum, Anxiety Disorders, Post Traumatic Stress Disorder, Coping with Grief, Depression, Bipolar Disorder, Schizophrenia, and Eating Disorders. Eight women from a community based substance abuse treatment center in Iowa were recruited to this program. Pre and post tests were developed to assess change in knowledge of substance use and mental health, and evaluate treatment compliance. Qualitative data suggest that clients believed the program will help them achieve and maintain a successful recovery, and assist them in attaining medical compliance. Future research will be conducted to examine the effectiveness of the program in terms of general knowledge of mental health disorders and substance use disorders, communication skills, self-care, medical compliance, and recovery.

551 FACTORS ASSOCIATED WITH HEALTH STATUS—10-YEAR FOLLOW-UP OF PRENATAL COCAINE/POLYDRUG USE

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Drug use during pregnancy may indicate risk for poor health outcomes. The relationship of demographic, pre and postnatal maternal drug use and partner violence with perceived health was evaluated. 184 (87 cocaine (C+); 97 non cocaine (C-)) urban, low SES women were recruited at infant birth and assessed after 10 years. The Medical Outcomes Study Short Form (SF-36 V2) and Conflict Tactics Scales-Revised (CTS-R) were used to assess eight physical and mental health domains, two health summary scores (physical functioning, role limitation due to physical and emotional problems, bodily pain, general health perceptions, vitality, social functioning, mental health and mental and physical health summary) and partner violence. Multiple regression analyses were used to evaluate the association between perceived health, substance use, and partner violence. Clinically elevated SF-36 scores were compared by cocaine status using Chi-square analyses. Prenatal cocaine use was associated with more bodily pain ($p < .02$), poorer general health ($p < .0002$), social functioning ($p < .02$), and mental health (summary score) ($p < .02$). Prenatal alcohol use was associated with role limitation due to emotional problems ($p < .002$) and current use of alcohol ($p < .009$) was associated with poor mental health ($p < .03$). Prenatal tobacco use was associated with lower vitality ($p < .009$) and current tobacco use was associated with poorer mental health ($p < .05$). Greater partner abuse was associated with lower general health ($p < .03$), less vitality ($p < .02$), more bodily pain ($p < .05$) and poorer mental health ratings ($p < .01$). The effects of prenatal cocaine use, current tobacco and alcohol use on lower mental health ratings were mediated by partner abuse. C+ women had a higher percentage of scores $< 1SD$ below the mean in physical functioning, bodily pain, general health, social functioning, role restriction due to emotional problems, mental health and physical health summary (p 's $< .05$). Cocaine use prenatally, ongoing drug use, and partner violence are associated with poorer health outcomes in high risk women.

550 TRAUMA, POST TRAUMATIC STRESS DISORDER, AND SUBSTANCE USE DISORDERS: FINDINGS FROM THE AUSTRALIAN NATIONAL SURVEY OF MENTAL HEALTH AND WELLBEING

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The aim of the present study was to examine the association between trauma and post traumatic stress disorder (PTSD) and substance use disorders (SUDs) and to examine the correlates of SUD+PTSD comorbidity in the Australian general population. Data were collected from a stratified sample of 10,641 participants as part of the Australian National Survey of Mental Health and Wellbeing (NSMHWB). A modified version of the Composite International Diagnostic Interview was used to determine the presence of DSM-IV anxiety, affective, and substance use disorders, and ICD-10 personality disorders. SUD+PTSD was experienced by a significant minority of the Australian general population (0.5%). Among those with PTSD the most common SUD was an alcohol use disorder (24.1%), while among those with a SUD, PTSD was most common among individuals with an opioid use disorder (33.2%). Consistent with the clinical literature from the United States, individuals with SUD+PTSD experienced significantly poorer physical and mental health, and greater disability compared to those with a SUD alone. In contrast, individuals with PTSD alone and those with SUD+PTSD shared a remarkably similar clinical profile. It is important that individuals entering treatment for SUD or PTSD be assessed for this comorbidity. The addition of either disorder may present complications which need to be considered for the provision of appropriate treatment. Further research is necessary to ascertain which treatments are most effective in treating comorbid SUD+PTSD.

552 CLINICAL CORRELATES OF ACCELERATED AGING: MULTIPLE STEM CELL LINEAGE DEPRESSION IN ADDICTION

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Previous clinical studies at our centre are consistent with accelerated aging occurring in addicts in the brain, dental tissues and hair. We have previously shown that mental index (MI) was statistically associated with dental index (DI). It was therefore of interest to determine if there was a statistical association between MI and DI on the one hand, and hair greying index (GI) or the other. Results from our recent surveys were combined. Complete data sets were available on 86 drug addicts (DA) and 9 general medical (GM) patients. There was no sex difference in the two groups. Age range was restricted to 19-45 years and the mean age was similar in all groups. Specific indices and between group differences of drug exposure have been previously described. Significant correlations between age and DI and GI were noted in both DA and GM. DI was associated with MI in addicts ($P=0.0089$) and with temporal greying in GM ($P=0.028$). MI tended to be associated with temporal greying in DA ($P=0.106$) and with vertex greying ($P=0.107$) in all patients. Temporal greying was associated with vertex greying in both DA and GM ($P < 0.000001$). Other associations were not significant. In DA the lifetime alcohol consumption and temporal GI were both significant on multivariate regression. These results in these limited numbers indicate that there is a relatively weak association between DI and MI and hair greying, but remain consistent with a deleterious effect on accelerated aging in all tissue beds. This data clearly calls for further investigation in larger case matched samples, and also indicate a basic sciences investigation of the likely effects of addiction to accelerate aging. Based on other data pro-apoptotic, stem cell inhibitory and disordered mechanisms of DNA repair may be implicated.

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553 CHANGES IN FUNCTIONS OF GLUTAMATE RECEPTOR AND ITS MODULATORS IN THE SPINAL CORD OBTAINED FROM ETHANOL-DEPENDENT RATS WITH PAINFUL NEUROPATHY

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Chronic ethanol consumption produces a painful peripheral neuropathy. However, central mechanisms underlying the development of neuropathic pain-like state induced by chronic ethanol treatment are unknown. Rats were treated with control diet and ethanol diet (1.25-5 w/v% of liquid diet) for 72 days. Mechanical hyperalgesia was clearly observed during ethanol consumption ($p < 0.001$ vs. control group) and even after ethanol withdrawal in rats, and it lasted for 14 weeks. It is of interest to note that this hyperalgesia was significantly attenuated by repeated i.p. injection of ifenprodil, a selective NR2B-containing NMDA receptor antagonist ($p < 0.001$ vs. control group). At 24 days after ethanol withdrawal, immunohistochemical study showed an increase in phosphorylated-NR1 and mGluR5-like immunoreactivities in the superficial dorsal horn of the spinal cord from chronic ethanol fed-rats. Furthermore, Western blot analysis revealed that the level of phosphorylated-cPKC was significantly increased by chronic ethanol treatment ($p < 0.001$ vs. control group). Immunohistochemical study revealed that the phosphorylated-cPKC-like immunoreactivity was clearly increased in the superficial dorsal horn of the spinal cord from ethanol-fed rats. In addition, double immunostaining revealed that the increased p-cPKC-IR was almost overlapped with NR2B-containing NMDA receptors in the superficial dorsal horn of the spinal cord from ethanol-fed rats. These findings provide evidence for a substantial role of the enhanced cPKC-dependent glutamate receptor functions in the development or/and maintenance of the ethanol-dependent neuropathic pain-like state in rats.

554 MATERNAL SEPARATION CAUSES CHANGES IN COCAINE SELF-ADMINISTRATION IN DAMS AND TREATED PUPS AS ADULTS

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Repeated maternal separation (MS) of pups from dams is often used as an early life stressor (PN2-15) that causes profound neurochemical, neuroendocrine and behavioral changes in the pups that persist into adulthood. To examine the effects of MS on cocaine self-administration, four separation conditions were used: 15 or 180 minute separation (MS15 and MS180), brief handling without separation (MS0) and a non-handled group (NH). Dams were allowed to self-administer cocaine (0.25 mg/kg/infusion) during daily 2 hour sessions for one week after weaning. There was an overall significant effect of maternal separation on the cocaine self-administration of the dams however; the length of separation appeared not to affect the dams' behavior. The dams whose pups were handled in their presence (MS0) averaged more infusions per session during the first week than the NH group. The acquisition of cocaine self-administration (0.0625-1.0 mg/kg/infusion) was evaluated in the treated pups as adults. While the MS180s acquired at the lowest dose, the MS15s did not respond for cocaine at rates greater than that seen with saline administration. The NH group received the greatest number of infusions and intake at the highest doses. Following self-administration, no differences were observed between groups in activity of two liver carboxylesterases involved in the inactivation of cocaine, ES10 and ES4; suggesting that any differences in pharmacokinetics are not responsible for the behavioral differences observed. This data suggests that in addition to the profound changes that occur in pups as result of maternal separation, the dams are also susceptible to alterations in behaviors. NIH grants RR00165, DA00418 and DA015040.

555 OPIUM AND HEROIN DEPENDENCE IN IRAN: ONE OR TWO EPIDEMICS?

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With an estimated 2-4 million opioid dependent individuals, Iran is experiencing severe problems associated with drug dependence. Opium use (by smoking or ingestion) has a long history in Iran, but heroin, often used by injection, has emerged more recently as a major problem and now accounts for approximately 1/4 of opioid dependent individuals. It is not known, however, whether opium users and heroin users represent separate populations with different backgrounds, drug use histories and treatment needs. Consequently, we compared demographic and drug use characteristics of subjects reporting primarily opium (N=36) or heroin (N=81) use entering a clinical trial of buprenorphine and naltrexone treatment in Tehran. Of the opium users, 14/36 reported lifetime use of heroin; 3 were currently using heroin regularly in addition to opium, and 11 reported no or infrequent current heroin use. Of the heroin users, 65/81 reported lifetime opium use, including 41 who used opium before starting heroin. Opium and heroin users were similar on most demographic features, including age, education, marital status, employment. Opium users reported significantly longer duration of opioid use (9.7 vs. 5.7 years, $p < .05$) but less time incarcerated (2.4 vs. 9.4 months). Heroin users had a higher prevalence of injection drug use (66% vs. 22%), were less likely to use condoms consistently (24% vs. 38%), and had a higher prevalence of hepatitis C (19% vs. 6%). The study findings suggest that opium users are at risk for transitioning to heroin dependence and that heroin dependence is linked with imprisonment, injection drug use, inconsistent condom use, and an increased risk of Hepatitis C. Supported by R01 DA14718 and 2 K24 DA000445

556 GENDER DIFFERENCES IN RATES OF POSITIVE URINE DRUG TESTS FOR OPIATE, COCAINE, AND MARIJUANA USE AMONG SOUTH AFRICAN DRUG USERS

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The present study sought to examine gender differences in recent use of opiates, cocaine, and marijuana as assessed by a positive urine drug test using gas chromatography/mass spectrometry methods. This study is based on data from the International Neurobehavioral HIV Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of HIV, and Hepatitis A, B, and C in the U.S, South Africa, and Russia. The present study is based on the South Africa sample comprised of 144 drug users between 18 and 50 years of age in the Pretoria region. The Pretoria baseline sample was 91% Black and 65.3% male with 33.3% of the baseline sample testing positive for HIV. Multinomial logistic regression indicated that females (OR = 3.29; 95% CI = 1.59; 6.80) were significantly more likely than males to test positive for cocaine while controlling for age. Specifically, 60% of females in the sample tested positive for cocaine compared to 33.0% of males. Multinomial logistic regression indicated that males (OR = 4.79; 95% CI = 1.83; 12.57) were significantly more likely than females to test positive for marijuana while controlling for age. Specifically, 90.4% of males in the sample tested positive for marijuana compared to 70.0% of females. There was no gender difference in rates testing positive for opiate use with 64.0% of females and 59.6% of males testing positive. There is a lack of research elucidating risk factors associated with drug use in South Africa. Improving our understanding of drug use risk factors may be central to efforts to prevent HIV and other diseases, such as Hepatitis B and C, given substantiated relationships between drug use and disease status.

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557 DELAY DISCOUNTING BASED ON ACTIVATION IN THE VENTRAL STRIATUM

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One way impulsivity has been operationalized is as the tendency to devalue reward as a function of delay ("delay discounting"). In humans, delay discounting is inferred from expressed preferences for alternatives that differ in amount and immediacy. A participant's preferences may not directly reflect discounted value, however, since they may be influenced by mechanisms of self-control. The goal of the present study was to evaluate delay discounting without relying on preference, by inferring reward from change in activity within the ventral striatum when a research participant won rewards in a test situation. Eight smokers, abstinent for 12 h, performed a card task in conjunction with functional magnetic resonance imaging (fMRI). At the onset of each of 48 trials in the task, the participant was informed of the possible reward. The task was performed on two separate occasions; during one session, the reward on each trial was either 25 or 50 cents, to be received either immediately after the task or in 1 week; and during the other session, the reward on each trial was either 1/2 or 1 full drag of cigarette smoke to be received either immediately after the task or in the midst of a similar session 1 week later. In preliminary analyses, significant activation was observed on winning trials relative to rest in the ventral striatum (VS), as well as in clusters in the prefrontal and parietal cortices. Region of interest analysis of the VS indicated that activation was significantly greater during winning trials in which the amounts were larger, and in trials in which the reward was immediate. Ongoing analyses will compare signal change across reward types (cigarette smoke versus money), and examine the relationship between these data and delay discounting based on participants expressed preferences. These data support the feasibility of using fMRI signal change in the VS to infer level of delay discounting. [NIH K01 DA0051-01A1(JM), NIH 3R01DA015179-02S1 (EL)]

558 MARIJUANA USE AND TOBACCO SMOKING TRAJECTORY: ASSOCIATED ETHNIC AND GENDER DIFFERENCES AMONG ADOLESCENT SMOKERS

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Previous research has suggested ethnic and gender differences in first substance use, including more frequent use of marijuana (MJ) prior to first use of tobacco among African Americans (AA) compared to European Americans (EA). Blunt (guttled cigar filled with MJ) smoking combines the intake of tobacco and MJ. Our objective here was to examine ethnic and gender differences in cigarette consumption as a function of sequence of MJ or tobacco smoking initiation among adolescent smokers applying for tobacco cessation treatment. Three hundred and forty-one adolescent smokers [means (SD), 16.1 (1.2) years, 60% girls, 47% African-American, cigarettes smoked per day 15.6 (9.8)] completed a telephone interview as part of pre-eligibility screening for a smoking cessation trial. Substance use trajectory data included age at first cigarette puff and its temporal relationship to first MJ use, first cigarette type (menthol vs non), daily smoking, and number of currently smoked cigarettes per day (CPD). Sixty-six percent of adolescents reported current MJ use, and 45% of MJ users reported they had initiated MJ use before tobacco cigarettes. Eighty percent of MJ users reported smoking blunts. Analyses using independent t test showed that EA teens smoked more cigarettes than AA teens (17.8 vs 13.3; $p < 0.001$). EA boys reported smoking five more CPD, on average, than EA girls ($p < 0.001$). Among MJ users, AA who used MJ before tobacco reported smoking fewer cigarettes (14.8 vs 11.2; $p = 0.046$), while there was no significant differences in EA adolescents based on order of substance use initiation. AA were also more likely than EA to report that their first cigarette was a menthol (88% vs 68%; $p < 0.001$). Further identification of ethnic and gender differences in relationships among smoked substance use trajectory might inform culturally- and developmentally-tailored interventions to reduce youth substance use.

559 ACTIVATION OF SINGLE NEURONS IN THE ORBITOFRONTAL CORTEX DURING COCAINE SELF-ADMINISTRATION

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Studies across species have reliably demonstrated the important role that the orbitofrontal cortex (OFC) plays in evaluating rewards and guiding reward-driven behaviors. A number of studies have also implicated the OFC in mediating behaviors related to drug rewards. For example, imaging studies have shown activation of the OFC during drug craving and consumption in addicted human subjects. To date, however, no study has examined the activation of individual OFC neurons during drug self-administration: an analysis that is critical in order to understand what role the area plays in compulsive drug use. To address this issue, we implanted arrays of 16 microwires bilaterally in the OFCs of five rats. The rats were then trained to self-administer cocaine (0.75 mg/kg, IV; FR1) for 3 hours every day for approximately two weeks, until responding was stable. Following training, we recorded from single neurons during a final cocaine self-administration session. Our results support the hypothesis that neurons in the OFC are strongly modulated during performance of drug seeking and taking. Of the 296 recorded neurons, approximately 75% exhibited significant phasic modulations during short epochs (5 sec, 0.25 msec bins) preceding, following, or surrounding the operant response for cocaine. Of these neurons, approximately 60% displayed phasic activations and approximately 40% displayed phasic inhibitions. Furthermore, around 70% of the 296 recorded neurons exhibited significant tonic modulations, resulting in either enhanced (~50%) or decreased (~50%) firing during the self-administration session as compared to firing during a pre-session baseline. Finally, slightly more than 50% of the 296 neurons exhibited both phasic and tonic modulations, suggesting that the activity of many neurons signals cues for or behavior related to drug reward across multiple timeframes. We will consider the implications of these results and address the apparent role of the OFC in psychostimulant self-administration behavior.

560 LIFE AREAS WITH MORE NECESSITY OF CHANGE FOR THE IMPROVEMENT OF QUALITY OF LIFE AMONG COCAINE USERS

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Introduction: Treatment programs must be made available based on the needs that patients report in order to improve their quality of life. Generally, drug users are not asked about what is important to them and their contributions to public health programs have been minimal. Objectives: To explore the lifestyle areas that are most significant and require change in order to improve the quality of life of cocaine users. Methods: Sample: cocaine users who in the last 6 months had been attending substance-abuse programs ($n = 120$), $x = 32$ years ($DS = 6.7$), and with a mean of 11 years of drug use ($DS = 6.2$). Descriptive analysis and data frequencies were obtained using the Drug User Quality of Life Scale (DUQOL-1), adapted to Spanish and in a non-injecting population according to the Injection Drug Use Quality of Life Scale (IDUQOL). Results: Among 22 lifestyle areas, the areas most commonly selected as important were: health (96.7%), family (96.7%), feeling good about yourself (90.8%), having sense of the future (85.8%), and drug and alcohol treatment (85%). The less selected areas were: drug and alcohol use (41.7%), spirituality (45%), neighborhood safety (50%), transportation (50.8%), harm reduction and having community resources (51.7%). The areas with more necessity of changing to improve the quality of current life were: Consumption of drugs and alcohol (75.8%), Health (60.8%), Money, Leisure Activities, and to Feel good about yourself (57.5%). Conclusions: In addition to drug use treatment and health improvement, cocaine users, by majority, point to the need to improve their self-esteem, and change the activities they engaged in during their free time to improve their quality of life. It is important to consider these needs when establishing therapeutic programs among this type of population. Supported by Centro Superior de Investigación en Salud Pública, Generalitat Valenciana

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561 PERSISTENT CHANGES IN MEDIAL PREFRONTAL CORTEX mRNA LEVELS FOLLOWING BINGE COCAINE SELF-ADMINISTRATION AND VARYING DURATIONS OF ABSTINENCE

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Previous studies have demonstrated that binge patterns of cocaine self-administration can produce differential behavioral profiles depending on the length of the abstinence period. For example, breakpoints maintained by cocaine on a progressive ratio schedule are increased following a 10-day deprivation period, but not following one day of abstinence. Similarly, studies have shown that there is a time-dependent increase in the magnitude of reinstated responding following extended-access conditions of cocaine self-administration (i.e. "incubation of craving"). In the present study, whole genome expression profiles (33,840 genes) were analyzed from the medial prefrontal cortex of rats. Rats self-administered cocaine on a discrete-trials schedule of reinforcement (DT4) for 10 days, which was followed by increasing durations of a drug-free period (1 to 100 days), or were drug-naïve at the time of sacrifice. 17,470 genes were found to be present in the analysis, and 222 probes were differentially expressed at some time point. Quantitative PCR confirmation of the array data confirmed that Arc, NGFI-A, NGFI-B, and c-fos were significantly decreased at 1 day of abstinence, and remained decreased for up to 100 days of a drug-free period. D5 receptor and hippocampin 4 mRNA levels were increased at 100 days of abstinence. These persistent changes in mRNA expression may contribute to the long-lasting behavioral alterations following binge cocaine self-administration and abstinence, and may be associated with clinical findings of high levels of relapse to drug use, even following extended periods of abstinence.

562 NMDA ANTAGONIST INTERACTIONS WITH OPIOIDS IN MODELS OF TOLERANCE AND ACUTE DEPENDENCE

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Opioid agonists are some of the most effective analgesics in clinical use however, these compounds have several disadvantages including the development of tolerance to their analgesic effects and physical dependence. N-methyl-D-aspartate (NMDA) receptor antagonists have been shown to modify development of opioid tolerance and dependence, which could prove clinically useful. To further investigate the interaction of the NMDA and opioid systems we tested the effects of opioid agonist/NMDA antagonist drug combinations in two behavioral procedures in male Sprague Dawley rats. In the first study, we examined if the low affinity NMDA antagonist, memantine, would block morphine tolerance in the warm water tail withdrawal measure of antinociception (N=14). Tests were done both before and after chronic opioid dosing. Percent maximum possible effect, ED50's, potency ratios, and 95% confidence intervals were generated in each experiment. When administered chronically in combination with 10 mg/kg morphine, memantine at 3 mg/kg, but not 10 mg/kg, prevented tolerance development to morphine's antinociceptive effects. In the second study, memantine and the potent NMDA antagonist MK-801 were assessed for their ability to prevent acute opioid dependence using an acute opioid antagonist sensitization (AOAS) operant procedure. Morphine pretreatment alone produced acute sensitization to the operant rate depressing effects of naltrexone (N=17). Both memantine (1-10 mg/kg; N=8) and MK-801 (0.03-0.1 mg/kg; N=9) failed to block morphine induced sensitization to naltrexone. In addition, MK-801 alone (0.01-0.1 mg/kg; N=8) did not produce any sensitization to naltrexone. Overall the results of these studies support previous findings that drugs with NMDA antagonist activity will block tolerance development to opioids. Conversely, thus far, uncompetitive NMDA antagonists appear ineffective at blocking AOAS. Further testing is needed to determine if other glutamatergic drugs can block AOAS. NIDA DA-01442 and DA-13609.

563 THE ROLE OF ON-SITE 12-STEP MEETING DURING TREATMENT AS A PREDICTOR OF FUTURE 12-STEP ATTENDANCE AND SUPPORT FOR ABSTINENCE

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Post-treatment 12-step (12SG) affiliation is useful in maintaining treatment gains and enhances support for abstinence, a critical predictor of positive outcome; however, not all clients attend and many disaffiliate quickly after treatment ends. This study compares the outcomes of clients who attended a program with and without an onsite 12SG to assesses (1) the role on having an onsite 12SG meeting at drug treatment programs on post-treatment 12SG participation, and (2) the influence on 12SG participation on support for abstinence. Hypotheses – (HO1) Onsite 12SG significantly increases the likelihood of post treatment 12SG attendance; (HO2) 12SG attendance significantly increases subsequent support for abstinence. Methods – Outpatient treatment clients recruited at two publicly funded programs in NYC, one with (n=111) and one without (n=139) an on-site 12SG; interviewed at treatment admission, discharge, 3- and 6-months post discharge. Participants are mostly ethnic minorities, poly-substance users with crack as primary substance. Results – (HO1) Participants in the program with an on-site 12SG were 1.83 times more likely to have attended at least one 12SG between discharge and 3 month follow-up, 1.96 times more likely to have attended at least one 12SG between 3 month and 6 month follow-up, and 2.43 times more likely to have attended at least one 12SG at any point in the 6 months post-discharge. (HO2) 12SG attendance in the 3 months post-discharge significantly predicted a higher degree of support for abstinence in the subsequent period, and 12SG attendance between 3- and 6-month follow-up also predicted higher support at 6 month follow-up. Conclusions – Holding an on-site 12SG appears to be an effective and cost-effective strategy to increase the likelihood of 12SG attendance and support after treatment ends. Funded by National Institutes on Drug Abuse Grant R01 DA015133.

564 INSTITUTIONALIZATION MASKS OUTCOMES AND BIASES TREATMENT EFFECT ESTIMATES

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Institutionalization, or spending time in a controlled environment, can produce a misleading appearance of improvement in treatment outcome studies, because it leads to reductions in drug use, crime, and other behaviors of interest. Substance abuse treatment clients are, moreover, at particularly high risk for institutionalization. In recent large-scale treatment outcome studies, 40% or more of treated samples were institutionalized for a portion of their follow-up periods (see, for instance, DATOS, DATOS-A, NTIES, and ATM). Typically, however, outcome analyses have not accounted for the effects of institutionalization on outcome measures, an omission that can produce biased treatment effect estimates that conflate treatment effects on institutionalization with treatment effects on other outcomes. In this report, we describe the strengths and weaknesses of four standard approaches for dealing with this institutionalization confound, and discuss these in the context of a rigorous theory of causal effects. We show that the standard approaches all provide biased estimates of treatment effects except under strenuous assumptions. We illustrate these biases using a case study of the effects of treatment modality on drug use severity using a large sample of adolescent substance abuse treatment clients (n=1256), over 40 percent of whom were institutionalized at follow-up. In this study the effects of residential care on drug use severity 12-months after program entry ranged from significant and beneficial to significant and detrimental depending on the approach used to account for institutionalization. This research was supported by NIDA Grants R01 DA015697, R01 DA016722 and R01 DA017507.

565 DEVELOPING A MULTI-PROBLEM SCREENING SYSTEM FOR YOUTH

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The AMA Guidelines for Adolescent Prevention Services (GAPS) state youth should be screened annually for eating disorders, sexual activity, alcohol and other drug use, tobacco use, abuse, school performance, depression, and suicide risk. GAPS also recommends screening for comorbid risk behaviors in these domains. Despite the emphasis on screening, many providers do not routinely screen for risk behaviors that affect youth. The lack of age-appropriate and efficient tools for identifying problem behaviors is a barrier to screening youth. The optimal screening tool should be brief and able to identify youth with multiple risk behaviors. In Phase I, a multi-domain screening system for youth (11 to 19 yrs) was developed to determine clients' risk behaviors and problems within 10 life domains including: alcohol, tobacco, and drug use; school problems; abuse victimization; emotional distress and suicide risk; sexual behaviors; family functioning; violent behavior; unhealthy weight control; physical activity; behaviors related to motor vehicle occupant injuries; and peer relations and social skills. The screening tool was piloted with nine youth prevention and intervention professionals. In Phase II, Danya finalized the screening tool, including brief intervention protocols for instrument administrators based on motivational messages that provide customized responses to youth and a prioritization matrix to highlight issues youth would most like to discuss. The screening instrument was then programmed for use on a CD-Rom. Additionally, Danya is conducting a full-scale psychometric evaluation of the screening tool. This presentation discusses the development and refinement of the screening tool, as well as the psychometric evaluation in progress in Phase II of the project.

567 EQUIVALENCE LEARNING IN COCAINE-DEPENDENT INDIVIDUALS

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Objective: The purpose of this study was to examine the ability of cocaine dependent individuals to procedurally learn equivalence relationships between stimuli and to generalize such learning when stimuli are presented in novel recombinations. **Participants and Methods:** Twenty-two active cocaine users (20 male and 2 female) and 21 age-matched healthy control participants (10 male and 11 female) completed a computerized acquired equivalence task. The task consisted of four phases: (1) initial shaping of antecedent-consequent stimuli pairs, (2) training of equivalence between initial and novel antecedents, (3) shaping of new consequents to initial antecedents, and (4) a test of the generalization of phase 3 learning to the novel antecedents trained in phase 2. Performance in phases 1-3 is thought to be dependent on intact basal ganglia function, and performance in phase 4 is thought to be dependent on intact hippocampal function. The number of errors made during each of four phases of the task was the primary outcome measure. **Results:** Cocaine users performed similarly to controls when learning simple antecedent-consequent pairings (phases 1 and 2), but made significantly more errors than controls ($F_{1,40} = 4.87$, $p < 0.05$). **Conclusions:** Cocaine users had more difficulty than controls in learning stimuli relationships under conflicting response demands, but had no difficulty generalizing this learning once they achieved criterion. The dissociation of performance between these specific learning demands is qualitatively similar to the performance pattern seen in Parkinson's patients, and is consistent with other evidence of abnormal striatal dopamine transmission in chronic cocaine abusers.

566 SALVINORIN A: UNUSUAL INTERACTIONS AT THE MU OPIOID RECEPTOR

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Background. Salvinorin A (SA) is a non-nitrogenous neoclerodane diterpene that is a selective and potent kappa opioid receptor agonist. Initial experiments conducted in our lab showed that SA partially inhibits mu receptor binding. **Hypothesis.** SA will interact with mu opioid receptors in a manner inconsistent with simple competitive kinetics. **Methods.** Opioid binding assays were conducted using various radioligands, membranes prepared from CHO cells expressing the cloned human mu receptor ("mu cells") or rat brain, using established methods. Binding data were fit to the 3 parameter logistic equation, as well as one- and two-site binding models, using MLAB-PC. **Results.** SA inhibited [3H]DAMGO binding with clearly discernable plateaus. The best fit parameter estimates of the logistic equation for 0.5, 2.0 and 8.0 nM [3H]DAMGO were: $IC_{50} = 465, 592, 1750$ nM, $N = 0.86, 0.59, 0.30$ and $A = 13\%, 27\%, 36\%$. "A" is the extrapolated plateau (% of control). SA inhibited [3H]diprenorphine binding with clearly discernable plateaus. The best fit parameter estimates of the logistic equation for 0.02, 0.1 and 0.5 nM [3H]DIP were: $IC_{50} = 631, 356, 7200$ nM, $N = 0.57, 0.51, 0.26$ and $A = 24\%, 27\%, 28\%$. SA inhibited [125I]JIOXY (0.01 nM) binding with a plateau: $IC_{50} = 525$ nM, $N = 1.1$, $A = 53\%$. Binding surface analysis showed that SA decreased the B_{max} of mu binding sites labeled with [3H]DAMGO. Additional data will be presented at the meeting. **Conclusion.** SA may allosterically modulate mu receptor binding. **Acknowledgement.** This research was supported in part by the Intramural Research Program of the NIH, NIDA and NIDA grant DA018151-01A2

568 METHAMPHETAMINE DIFFERENTIALLY MODULATES RANTES AND ITS VARIANT ALLELE (IN1.1C) GENE EXPRESSION IN HIV-1

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Chemokines and chemokine receptors are involved in binding and entry of HIV-1 into the host cells. RANTES (regulated on activation, normally T cell-expressed and -secreted) is a critical chemokine that competitively inhibits HIV-1 by binding to its main receptor CCR5, whereas the variant allele of RANTES, In1.1C has been associated with accelerated HIV-1 disease progression. Recent studies have indicated an entangled epidemic of HIV-1 infection and drug abuse, particularly with methamphetamine (Meth). Dendritic cells (DC) are the first line of defence against HIV-1 infection. However, the role of Meth on the expression of total RANTES or its variant allele (In1.1C) by DC has not been studied yet. We hypothesize that Meth, down-regulates the gene expression of total RANTES and up-regulates RANTES variant allele In1.1C leading to rapid progression to AIDS. Mature dendritic cells (MDC) and immature dendritic cells (IDC) from normal subjects (~ 5X10⁵ cell/ml) were cultured with Meth (10, 100 & 250 uM) for 24 hr. RNA was extracted, DNA free RNA was reverse transcribed followed by quantitative real time PCR for total RANTES, RANTES variant allele In1.1C and house keeping gene beta-actin. Our results showed that Meth significantly inhibited total RANTES with a reciprocal upregulation of RANTES variant In1.1C gene expression by DC from normal subjects. Results from HIV-1 infected subjects, showed lower levels of RANTES gene expression compared to normal controls, while the RANTES variant allele In1.1C gene expression was significantly higher in the HIV-1 infected subjects compared to normal controls. We believe that, this is the first report showing the effect of Meth on RANTES and the RANTES variant allele and support the premise that Meth plays a significant role in HIV-1 disease progression, potentially by downregulating total RANTES and upregulating RANTES variant allele In1.1C.

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- 569** CHRONIC DISORDER OF MENTAL HEALTH AND SOCIAL LIFE DUE TO METHAMPHETAMINE ABUSE
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Methamphetamine (METH) abuse has been one of the most severe problems in Japan since 1945. As a result, psychiatric medical service in Japan has a long history of treatment of METH psychosis. Based on this, we know long-term METH abuse induces chronic disorder of mental health and social life. This is demonstrated in this study. The Research Group of Information on Drug Dependence, which is assigned epidemic monitoring of drug abuse by the Japan Ministry of Health, Labour and Welfare, gathered 3418 case reports of METH abusers from approximately 150 mental hospitals for 12 years between 1991 and 2002. We studied these case reports. The format of the case reports includes 30 survey items to determine the social background, length, frequency and method of abuse, and the severity of disorder due to abuse in each case. We examined the relationship between each parameter and the periods and recent frequency of abuse by t-test. In the cases in which the abuse began more than 10 years prior to the study, the following features showed a significantly higher rate than the other cases: the existence of paranoia and hallucination, severe dysfunction in occupation or academic work, being an elementary or junior high school student before the abuse occurred, being jobless or being a gangster after the abuse occurred. Similar results were obtained from the cases in which the abuse had not occurred for a month period of a month or more prior to the study. Such cases can be defined as the cases of chronic mental disorder. These include 661 cases (19.1% of all the cases) showing existence of paranoia and hallucination. Based on this, the following three conclusions can be made: [1] Long-term METH abuse causes prolonged psychosis and dysfunction of social life. [2] The existence of paranoia and hallucination that persists even for one month after cessation of METH use is demonstrated. [3] METH abuse beginning at early adolescence contributes to prolonged abuse and mental disorder.
- 570** CHANGES IN CORTICAL Γ -AMINO BUTYRIC-ACID-ERGIC SYSTEM UNDER A NEUROPATHIC PAIN-LIKE STATE IN MICE
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Clinically, it has been reported that chronic pain induces sleep disorder, leading to depression, anxiety and reduced quality of life. Furthermore, it is considerable in clinic that sedative drugs are less potent hypnotic efficacy in patients with chronic pain. Consistent with clinical reports, we found here that the onset time of sleep induced by a full benzodiazepine receptor agonist midazolam (56, 75, 100 mg/kg, i.p.), which shows physical dependence, was significantly prolonged in mice with sciatic nerve ligation (pA receptor, could affect the onset time of sleep and the sleep time in mice with sciatic nerve ligation. We found that the onset time of sleep and the sleep time induced by propofol was not affected in mice with sciatic nerve ligation. Under these conditions, pretreatment with an antiepileptic drug valproate (40 mg/kg, s.c.), which increases the level of endogenous GABA, with midazolam (56 mg/kg, i.p.) in mice with nerve injury reversed the onset time to the normal level. These findings suggest that chronic pain may decrease the released level of GABA and the efficiency of GABAergic neurotransmission in the brain, so that the hypnotic effect of midazolam was suppressed in mice with sciatic nerve ligation.
- 571** TRANSFER OF METHADONE ACROSS PRETERM PLACENTAS AND THE ROLE OF THE EFFLUX TRANSPORTER P-GLYCOPROTEIN
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Methadone is the therapeutic agent of choice for treatment of the pregnant opiate addict. The disposition of methadone by the placenta is one of the factors affecting its concentration in the fetal circulation. Accordingly, placental transfer and metabolism of methadone during gestation could affect the incidence and intensity of Neonatal Abstinence Syndrome (NAS). However, the structure and functions of human placenta changes during gestation thus affecting the transfer of methadone to the fetal circulation. Therefore, the goal of this investigation was to determine the effect of gestational age (GA) on transplacental transfer of methadone. The ex-vivo technique of dual perfusion of placental lobule was utilized to determine its transfer across placentas obtained between 27 and 34 weeks of gestation. The fetal transfer rates for methadone, normalized to that for the marker compound antipyrine, were as follows: Preterm placentas, $19.5 \pm 4\%$; term, $29.4 \pm 4\%$ ($p < 0.05$). The clearance index for methadone was 0.56 ± 0.1 for preterm placentas and 0.83 ± 0.1 ($p < 0.05$) for term, respectively. These data indicate that the transfer of methadone across preterm placentas was 30% less than that in term placentas. This could be attributed to the significantly higher expression of the efflux transporter P-glycoprotein (P-gp) in preterm placentas. If the above conclusion, based on in vitro data, is true in vivo then the concentration of methadone in the fetal circulation during early gestation is likely to be less than at term and the activity of P-gp might be one of the factors affecting the concentration of methadone in the fetal circulation and consequently the incidence and intensity NAS. Supported by a grant from NIDA to MSA.
- 572** IMPLICATION OF SRC FAMILY KINASE-DEPENDENT TYROSINE PHOSPHORYLATION OF NR2B SUBUNIT-CONTAINING NMDA RECEPTOR IN THE REWARDING EFFECT OF MORPHINE
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We demonstrated previously that N-methyl-D-aspartate (NMDA) receptors, particularly NR2B subunit-containing NMDA receptor, are critical for the rewarding effects induced by morphine in mice. In addition, it has been widely accepted that tyrosine phosphorylation of the NMDA receptor potentiates its receptor function. Therefore, the present study was undertaken to clarify the role of tyrosine phosphorylation of NR2B subunit-containing NMDA receptor through activation of Src family kinase in the development of morphine-induced rewarding effect in mice. The phospho-Tyr-1472 NR2B subunit protein was significantly increased in the mouse lower midbrain containing the ventral tegmental area (VTA) of mice that had shown the morphine (5 mg/kg, s.c.)-induced rewarding effect ($p < 0.001$ vs. saline-conditioned group). We also found that in vitro treatment of newborn mouse midbrain neuron/glia cocultures with morphine (10 μ M) for 3 days caused a significant increase in levels of neural phospho-Tyr-1472 NR2B subunit- and phospho-Tyr-416 Src family kinase-like immunoreactivities ($p < 0.01$ vs. control cells). These increases in levels of immunoreactivities were reversed by co-treatment with a Src family kinase inhibitor PP2 (1 and 10 μ M). These findings suggest that Tyr-1472 phosphorylation of NR2B subunit-containing NMDA receptor via activation of Src family kinases in the midbrain may be involved in the development of morphine-induced rewarding effect.

573 CHALLENGES OF RECRUITING HIGH-RISK DRUG-USING WOMEN FOR A HIV VACCINE TRIAL

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Recruitment of women at the highest risk of HIV acquisition is necessary for clinical trials research testing HIV vaccines among high-risk populations. We use a community-based recruitment approach in order to target women who engage in risky drug-using and sex behaviors that increase their risk of HIV. However, recruitment of high-risk women presents several challenges given that this population tends to be difficult to track, prone to incarcerations and distrustful of government-sponsored research. Our recruitment approach is a multi-stage process involving ethnography, the use of a mobile assessment unit (van), and referral of eligibles to the research office for comprehensive medical screening and HIV testing. Four hundred sixty-one women in the Philadelphia metro area have been prescreened since August 2005. The mean age of these women was 36; 74% were non-Hispanic African-American, 20% non-Hispanic white and 6% were Latino. In the three months prior to screening, 80% reported using crack cocaine, 47% reported injecting drugs, 65% reported exchanging sex for money or drugs, 26% reported having unprotected vaginal or anal intercourse with an IDU. Two hundred thirty-four women prescreened eligible to participate in the HIV vaccine trial but only 73 have been screened in the office and 29 have enrolled to date. Of those who have completed medical screening 20% were determined to be HIV positive. Community-based recruitment strategies have successfully identified and enrolled women at the highest risk of HIV. However, major barriers exist in facilitating the linkage of eligible women from the community to the research office. While we continue to examine the barriers to participation, it is likely that clinical trials for HIV vaccines will need to become more deeply embedded in the communities from which potential participants are initially recruited.

574 WITHDRAWAL-ASSOCIATED INCREASES IN OPIATE REINFORCEMENT: EFFECTS OF CANDIDATE ANTI-RELAPSE MEDICATIONS

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Opiate dependence and withdrawal may increase the relative reinforcing effects of opiate agonists and contribute to relapse. Drugs that attenuate withdrawal-associated increases in opiate reinforcement may help prevent relapse. In the present study, rhesus monkeys were trained under a concurrent-choice schedule of heroin and food availability. Choice sessions were conducted daily from 11am-1pm and consisted of 5 components. During each component, responding on one key (FR10) produced heroin injections (0-0.1 mg/kg/inj), and responding on a second key (FR100) produced 1 gm food pellets. Increasing heroin doses were available during successive components to permit determination of a full heroin-choice dose-effect curve during each session. Heroin (0.1 mg/kg/inj) was also available under a FR 10/TO 15 min schedule during a daily, 21-hr supplemental heroin self-administration session from 1pm -10am. Under these conditions, heroin maintained a dose-dependent increase in heroin choice during the choice session (total intake approximately 1 mg/kg/day), and subjects also self-administered approximately 4 mg/kg/day heroin during the supplemental session. Termination of access to supplemental heroin produced overt withdrawal signs and leftward shifts in the heroin choice dose-effect curve, indicative of a withdrawal-associated increase in the relative reinforcing effects of heroin. Test drugs were evaluated for their ability to prevent withdrawal signs and/or withdrawal-associated increases in heroin choice. The relatively high-efficacy mu opioid agonists methadone and morphine dose-dependently and completely prevented both withdrawal signs and withdrawal-associated increases in heroin choice, whereas the intermediate-efficacy mu agonist buprenorphine was less effective. The alpha-2 adrenergic receptor agonist clonidine, the monoamine releaser amphetamine and the kappa opioid receptor antagonist 5'-guanidinonaltrindole (GNTI) were ineffective. Further studies with other candidate anti-relapse medications are ongoing. Supported by P01-DA14528 and R01-DA02519 from NIDA, NIH.

575 AN ADAPTIVE STEPPED-CARE APPROACH FOR REDUCING MARIJUANA USE IN METHADONE MAINTENANCE PATIENTS

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This study evaluated the effectiveness of an adaptive stepped care model on reducing cannabis use in methadone maintenance patients. Subjects submitting cannabis-positive urine samples were advanced to increased counseling (up to 9 hours per week) until producing 4 consecutive weeks of cannabis and other drug-negative urine samples. Continuation of routine treatment, including access to uninterrupted methadone delivery, was contingent upon attending scheduled counseling and achieving abstinence. Weekly urine samples were collected using a random schedule; subjects were followed for one year. 18% (n=57) of the treatment program's census tested cannabis-positive during the six months prior to implementing this intervention. Data from patients who submitted only cannabis-positive urine samples during this baseline period (n=15; mean=61% cannabis-positive urine samples) are included in this report. Most subjects (66%) discontinued cannabis use prior to the intervention and remained at reduced levels of treatment throughout the follow-up. Subjects who advanced (n=5) to higher steps of care had a greater percent of cannabis-positive urine samples during the 6-month baseline period (100% vs. 42%). Subjects were exposed to a mean 20.6 weeks of intensified care (range=13-31); 86% of all scheduled individual and group sessions were attended. Four of these 5 subjects (80%) discontinued cannabis use during the 12-month follow-up period. One subject elected to continue using cannabis and left the treatment program against medical advice. The results show that cannabis use in treatment programs using methadone can be modified with adaptive stepped care approaches, combined with clinic-based behavioral incentives. This combination treatment approach appeared to operate as an avoidance paradigm for low-rate cannabis users, and as a platform for delivering intensive schedules of counseling over an extended duration for high-rate users. ACKNOWLEDGEMENT: Supported by NIDA Grants R01DA12040 and R01DA016375

576 REPEATED NICOTINE AND MECAMYLAMINE ON METHAMPHETAMINE SELF-ADMINISTRATION AND REINSTATEMENT IN RATS

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Research has indicated a high correlation between psychostimulant use and tobacco cigarette smoking in human substance abusers. The objective of the current study was to examine the effects of repeated nicotine (NIC) administration (0.4 mg/kg, SC) and a nicotinic receptor antagonist (mecamylamine, 3 mg/kg, SC) on acquisition of methamphetamine (METH; 0.03 mg/kg/infusion) self-administration in rats. In addition, the potential of NIC and mecamylamine to induce reinstatement of previously extinguished drug-taking behavior was assessed. Mecamylamine pretreatment did not block acquisition of METH self-administration nor did it reinstate METH-seeking. NIC reinstated METH-seeking, but only in rats previously administered NIC. One mechanism by which NIC may reinstate METH self-administration is by acting as a conditioned stimulus for the availability of drug due to its association with METH during the acquisition phase. Thus, in another experiment, this mechanism was explored by examining the effects of repeated NIC (0.2 mg/kg) administration given in an unpaired manner from the METH self-administration sessions during acquisition. NIC-induced reinstatement of METH-seeking behavior and NIC sensitized locomotor hyperactivity were also assessed in these animals. Unpaired NIC administration did not persistently alter responding during the acquisition of METH self-administration. However, following extinction, NIC administration reinstated METH-seeking behavior in this group. NIC-induced reinstatement was independent of whether previous repeated NIC administration was temporally paired with the METH self-administration session. Furthermore, expression of locomotor sensitization to NIC was associated with significant NIC-induced reinstatement of METH-seeking behavior. Thus, although blockade of mecamylamine-sensitive nicotinic receptors did not alter METH self-administration, stimulation of nicotinic receptors produces a nonassociative change in the neural systems involved in METH reinstatement. Supported by USPHS grants DA12964, DA17548, and T32 DA07304.

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577 DRINKING AND DRUG-USE PATTERNS AND DISORDERS IN ISRAEL: RESULTS OF A NATIONAL HOUSEHOLD SURVEY

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Purpose: Patterns of alcohol drinking and drug-use and prevalence of past-year and lifetime disorders were assessed in a national sample of Israeli residents, and compared with other countries participating in the WHO World Mental Health Survey initiative. Methods: A CAPI version of the Composite International Diagnostic Interview (WMH-CIDI) was administered to a nationally representative sample of 4,859 non-institutionalized adult men and women. Response rates were 73% and 88% respectively in Jewish and Arab localities, and 70% among immigrants from the former Soviet Union (FSU). Overall refusal was 14%. Results: Lifetime abstinence was reported by 41% of respondents. Among past-year drinkers, 61.7% consumed a single drink per drinking occasion, and 93.4% consumed <4 drinks per occasion (mean =1.8; SD=1.9). Just over a quarter of the total sample (28%) were referred to the diagnostics questions, and 3.9% of the total sample met DSM-IV criteria for abuse and 1.1% for dependence. Among alcohol abusers, 36.4% consumed a single drink/occasion, and 78% consumed <4 (mean=2.8; SD=3.0). The most common abuse criteria endorsed were 'endangered self while drunk' (58.5% of abusers), and 'hangover interfered with daily activities' (50.7%). Drinking patterns and disorder rates in sub-populations (e.g., FSU immigrants) are also addressed. Ever-use of any illicit drug (or nonmedical use of sedatives/tranquilizers) was reported by 12.8% of respondents - 16.4% of men and 9.5% of women. Cannabis use accounted for the vast majority of this use. Criteria for a diagnosis of abuse (lifetime) were met by 1.4% of respondents; virtually none (n=12) met dependence criteria. Conclusions: Rates of lifetime and past-year alcohol abuse are similar to those observed in other countries despite relatively light drinking patterns, possibly supporting the hypothesis of a heightened biological sensitivity to alcohol among Jews. Illicit drug use is still uncommon in mainstream Israel society.

578 MENSTRUAL CYCLE PHASE MODULATES PHENCYCLIDINE (PCP) SELF-ADMINISTRATION IN MONKEYS

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Clinical and preclinical data indicate there are sexually dimorphic patterns of drug abuse and these differences are attributable to gonadal hormones. In humans, the positive subject-rated effects of drugs such as cocaine and amphetamine are more pronounced during the follicular phase of the menstrual cycle, which is characterized by elevated estrogen and low levels of progesterone. During the luteal phase, characterized by increased levels of progesterone and moderate estrogen levels, human subjects report diminished positive effects. The purpose of the present study was to determine the effect of menstrual cycle phase on oral PCP self-administration in female monkeys. Three adult female rhesus monkeys (*M. mulatta*) trained to self-administer PCP served as subjects. Menstrual cycle phase was confirmed by presence of epithelial cells characteristic of follicular and luteal phases collected by vaginal swabbing. Amounts of PCP self-administered were examined during the mid-follicular phase (days 7-10 from menses onset) and mid-luteal phase (days 20-23 from menses onset). Monkeys self-administered PCP concentrations of 0.125, 0.25, and 0.5 mg/ml and water under concurrent FR 16 schedules of reinforcement across several months/cycles. Levels of PCP self-administration were concentration- and menstrual phase-dependent. The concentration response curve was shifted upward during the luteal phase. Numbers of deliveries were significantly greater during the luteal phase than the follicular phase for the 0.25 and 0.5 mg/ml PCP concentrations. The 0.125 mg/ml PCP concentration maintained the greatest number of deliveries and increasing the concentration produced significant decreases in deliveries at 0.25 and 0.5 mg/ml. The results from the present study suggest that menstrual cycle phase modulates PCP self-administration in female rhesus monkeys. Elevated PCP self-administration during the luteal phase may reflect a compensatory increase to overcome progesterone's negative effects. Supported by NIDA grants R01 DA02486-26 and K05 DA15267-04 (MEC) and T32-DA07097 (JLN)

579 METHAMPHETAMINE- OR COCAINE-INDUCED CRAVING: CAUSE OR CONSEQUENCE OF FREQUENT DRUG USE?

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Most theories of addiction seek to account for drug-seeking behavior motivated by exposure to unconditioned stimuli, such as drugs. In this study, we examined factors associated with methamphetamine (MA)-induced craving. 18 non-treatment-seeking MA-dependent volunteers participated. Several days following admission to the clinical research center, participants completed craving ratings using visual analogue scales before and after receiving an acute infusion of MA (30 mg, IV). MA-induced craving was not related to demographic variables (age, gender, ethnicity), and was not associated with baseline levels of apathy ($p=0.14$), depression ($p=0.24$), or years of MA use ($p=0.86$). MA-induced craving was, however, strongly associated with the frequency of MA use in the 30 days prior to assessment ($F_{1,15}=10.74$, $p=0.005$). These data are similar to those obtained in a previously published study in cocaine-dependent participants. In that study, 15 non-treatment-seeking cocaine-dependent volunteers completed craving ratings using visual analogue scales before and after receiving an acute infusion of cocaine (40 mg, IV). As reported previously, cocaine-induced craving was associated with baseline levels of apathy ($p<0.05$), but was not related to demographic variables, and was not associated with baseline levels of depression ($p=0.49$) or years of cocaine use ($p=0.13$). We now report that cocaine-induced craving was also associated with frequency of cocaine use in the 30 days prior to assessment ($F_{1,13}=7.27$, $p=0.018$). Taken together, these data suggest that frequency of use accounts for the magnitude of stimulant-induced craving, or alternatively that the magnitude of stimulant-induced craving accounts for frequency of drug use. In either case, the relationship between use and drug-induced craving deserves additional investigation. Supported by NIDA: DA-14593, DA-18185, DA-17754

580 PSYCHIATRIC SYMPTOMS MAY INFLUENCE THE PERFORMANCE OF COCAINE-DEPENDENT SUBJECTS IN A NEW NEUROPSYCHOLOGICAL BATTERY SENSITIVE TO PREFRONTAL FUNCTIONS

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Introduction: There is accumulating evidence that cocaine dependent subjects have deficits in cognitive functioning. Psychiatric comorbidity is common among substance abusing populations, and may be an important confounding factor in neuropsychological evaluation. The aim of the present work is to examine the influence of psychiatric symptoms on the performance of cocaine dependent individuals in frontal lobe functions. Methods: The Frontal Assessment Battery (FAB) consists of 6 subtests which explore abstraction, cognitive flexibility, motor programming, sensitivity to interference, inhibitory control and environmental autonomy. Its administration takes about 10 minutes. The Self Reported Questionnaire (SRQ) was used to evaluate psychiatric symptoms. This instrument was designed to study mental illness in primary care settings in developing countries, and consists of 20 "yes or no" questions covering anxiety and depressive disorders; 4 further questions investigate psychosis. Twenty eight cocaine dependent men participated in the study. They were recruited from an inpatient substance abuse program, after at least one week of abstinence. Statistical analysis was performed using Spearman correlation coefficient. Results: FAB scores were negatively correlated with SRQ scores ($r = -.462$; $p < .05$), suggesting that higher levels of psychiatric symptoms impaired the performance on executive function tests. Conclusion: This result suggests that deficits in cognitive functioning of cocaine dependents may be at least in part mediated by psychiatric symptoms. Further investigation is needed in order to elucidate this association.

- 581** COMPARISON OF CONDITIONED PLACE PREFERENCE PRODUCED BY KETAMINE IN ADOLESCENT VERSUS ADULT RATS
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Drug abuse often begins during adolescence yet limited preclinical research has been conducted in adolescent subjects. The effects of ketamine in adolescent rats were compared to those in adults to determine if there was a difference in abuse-related effects between the age groups. Ketamine, a "club drug", is known to be abused in adolescents and young adults. In addition, its behavioral effects are mediated by NMDA receptors which undergo considerable modification during the adolescent period. The conditioned place preference (CPP) procedure was used to measure the reinforcing effects of ketamine (1, 3 and 10 mg/kg, i.p.), 15 mg/kg, i.p. cocaine (positive control) and saline (negative control) in adolescent [post natal day (PND) 28-40; N=40] and adult [PND 75; N=40] rats. Animals were conditioned twice daily using a standard 2-compartment place conditioning chamber, pairing either drug or saline each for 4 sessions. A biased procedure was utilized with the drug paired with the initially less preferred side. For the adult rats, cocaine produced a significant increase in time spent on the drug-paired side, relative to the saline group. Ketamine 1 and 10 mg/kg failed to produce any change in time spent in either environment whereas 3 mg/kg ketamine produced a significant decrease in time spent in the drug-paired environment. The adolescents demonstrated a reversal of side bias after the conditioning sessions therefore all treatment conditions, including the saline control, showed increases in time spent on the drug-paired side. Only ketamine 3 mg/kg produced a greater increase in time spent in the drug-paired environment relative to saline in adolescent rats. Overall, 15 mg/kg cocaine produced CPP in the adult rats whereas 3 mg/kg ketamine produced a place aversion. Conversely, in adolescent rats, 3 mg/kg ketamine produced the largest increase in time spent in the drug paired environment suggesting a dichotomy in the reinforcing potential of ketamine between the two ages groups. Additional testing in an unbiased procedure is ongoing.
- 582** BOLD IMAGING OF THE ACUTE EFFECTS OF MARIHUANA SMOKING: ASSESSING POSSIBLE CONFOUNDS DUE TO SMOKING AND GLOBAL BLOOD FLOW CHANGES
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Blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI) is a new tool for the study of the acute effects of drugs. While fMRI offers excellent temporal and spatial resolution, it may be confounded by non-specific changes in BOLD signal that arise from drug effects on the cardiovascular system. These effects may obscure regional changes in neural activity due to the subjective and/or reinforcing effects of the drug. Imaging the effects of smoked marihuana (MH) is particularly challenging due to smoking-induced subject motion, changes in respiration, and MH-induced tachycardia that may affect the global BOLD signal. To assess global changes in CBF, we measured perfusion using arterial spin labeling (ASL) before, and at 15 and 40 minutes after MH smoking. We also assessed changes in BOLD signal during a visual stimulation task (VS: 2 epochs, 12s checkerboard alternated with 12 s fixation point) every 2.5 min. We used the ASL measurements to validate the use of the VS task, which can be interleaved into the study without interruption (ASL has poor temporal resolution (5 min) and interrupts the BOLD measurements). Two MH-dependent subjects were imaged during MH smoking; ratings of drug effects and mood state were assessed by visual analog scales (every 2.5 min, alternated with VS) before, during and after smoking a MH cigarette (3.51% delta-9-THC) via a customized smoking device. Contrasts between baseline runs and post smoking runs showed no statistically significant differences, even at very low thresholds ($p < 0.1$), indicating no changes in global BOLD signal, although there was a trend towards reduced activation during (but not after) smoking. These results are in agreement with the ASL measurements that revealed no differences between pre-smoking, 15 min, and 40 min post-smoking and further suggest that these analytical techniques can be applied to reduce the impact of confounding factors and advance our understanding of the neurobiology of smoked MH. NIDA DA017712 (LN), DA14013, DA03994, DA019238, DA00343.
- 583** SUPPRESSION OF MORPHINE-INDUCED REWARDING EFFECT UNDER THE NEUROPATHIC PAIN LIKE STATE IS ASSOCIATED WITH CONCOMITANT ACTIVATION OF B-ENDORPHIN-CONTAINING NEURONS
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The present study was undertaken to investigate the mechanism of the suppression of the morphine-induced rewarding effect under a neuropathic pain-like state. Here, we found that the suppression of the μ agonist-induced place preference with sciatic nerve ligation was reversed by pre-microinjection of a specific antibody to β -endorphin into the ventral tegmental area. At 1 day after sciatic nerve ligation, mRNA level of pro-opiomelanocortin (POMC) was significantly increased in the hypothalamus ($p < 0.001$ vs. 1 day after sham-operation), whereas the expression of POMC mRNA was decreased in the hypothalamus at 7 days after sciatic nerve ligation ($p < 0.001$ vs. 7 days after sham-operation). In consistent with these results, the immunoreactivity for β -endorphin (β -endorphin-IR) was decreased in the arcuate nucleus (ARC) at 7 days after sciatic nerve ligation. Interestingly, sciatic nerve ligation produced a marked increase in the immunoreactivity for Δ fosB (Δ fosB-IR), an excitatory neuronal marker, compared with that in sham-operated rats. The Δ fosB-IR was overlapped with β -endorphin-IR-positive neurons in the ARC. These data indicate that sciatic nerve ligation increases the synthesis of β -endorphin in the hypothalamic neurons projecting to the VTA in the early process of the development of a neuropathic pain-like state in response to the excitatory input and then eventually causes results in the depletion of β -endorphin at 7 days after sciatic nerve ligation. These results suggest that under a neuropathic pain like state, β -endorphin production was increased and the β -endorphin-containing neuron was continuously activated and released, resulting in the long-lasting down-regulation of μ -opioid-receptors. This phenomenon could lead to the suppression of the morphine-induced rewarding effect under a neuropathic pain-like state.
- 584** SERVICE NEEDS, UTILIZATION, AND OUTCOMES OF WOMEN IN WOMEN-ONLY AND MIXED-GENDER DRUG ABUSE TREATMENT PROGRAMS
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Substance abuse treatment programs specialized for women have been developed over the past two decades; however, there is little research examining the effectiveness of such programs. This prospective longitudinal study compared service needs, utilization, and outcomes for 189 women in women-only (WO) programs to those for 871 women in mixed-gender (MG) programs in California. Data were collected at intake and at 3 months and 9 months following admission into treatment. The Addiction Severity Index (ASI) was administered to assess client's problem severity at both intake and the 9-month follow-up interview, and the Treatment Service Review was used to measure service utilization at the 3-month interview. Arrest records were also obtained from the Department of Justice. Results show that compared to women in MG programs, women in WO programs at baseline were less educated and more likely to be white, physically abused in the past 30 days, and receiving residential treatment (as opposed to outpatient treatment). Women in WO programs had greater problem severity in a number of domains including alcohol, drug, family, medical, and mental health. At the 3-month follow-up, more women in WO programs received employment, medical, parenting, and HIV services than did women in MG programs. They also reported receiving a greater number of alcohol, drug, and psychiatric services than did women in MG programs. Hierarchical linear models were applied to examine the effects of program characteristics (e.g., WO vs. MG, treatment modality) and client characteristics (e.g., demographic variables, primary drug, and baseline problem severity) on multiple outcomes (seven domains of the ASI and number of arrests). Controlling for other program characteristics and baseline client characteristics, WO programs demonstrated more favorable outcomes in drug use ($\beta = -1.22$) and arrests (OR = .63, 95%CI = .99) at the 9-month follow-up. The two groups did not differ in other ASI domains. Implications for service improvement will be discussed.

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585 WHY DO CANNABIS USERS QUIT? RESULTS OF A PILOT STUDY IN 20 GERMAN OUTPATIENT TREATMENT FACILITIES

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Introduction: Many studies have shown that in treatment of substance disorders it is highly important to identify individual reasons for quitting and for using cannabis in order to stimulate patients motivation to change. Until now, little is known whether self-referred or coerced patients differ in reasons of quitting cannabis use. Aims: To investigate if cannabis users who seek help on their own report significantly different reasons for quitting as patients who were sent to an outpatient treatment facilities. Methods: In a pilot study of "CANDIS - Targeted Treatment for Cannabis Disorders" the questionnaire "Reasons for Quitting" (McBride et al., 1994) was translated into german language culturally adapted and extended. Differences in reasons for quitting were examined in patients with cannabis disorders of outpatient treatment centres in the district of Dresden/Germany in 2005. They were asked to assess 47 reasons on Likert-scale from 0 (not important) to 9 (very important). Group differences were assessed by t-test for independent samples. Results: Significant differences in ratings for reasons for quitting between groups (self-referred, N=8 vs. coerced N=18) were found with regard to: productivity (M=8.50 vs. M=5.32) and cognitive abilities (M=8.25 vs. M=4.95) as well as joy in recreational activities (M=6.5 vs. M=2.63) and negative mood (M=8.13 vs. M=3.58), feelings of isolation (M=7.38 vs. M=1.26) and lowered self-confidence (M=7.50 vs. M=2.89). No significant differences between these two groups were found: self-control (M=5.50 vs. M=6.00), health-concerns (M=4.13 vs. M=3.00), social influences (M=3.25 vs. M=4.42) and saving money (M=6.50 vs. M=5.79). Conclusions: Self-referred patients reveal a substantial different pattern of reason for quitting cannabis use compared to patients that were coerced to enter a treatment. Further analyses in this pilot study suggest that the RfQ might be a powerful tool to predict outcome.

586 A CHIMERIC HUMAN ANTI-COCAINE MONOCLONAL ANTIBODY ALTERS THE DISTRIBUTION BUT NOT THE METABOLISM OF COCAINE IN MICE

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The concentration of cocaine in the brain is a critical determinant of the probability of reinstating self-administration behavior. Anti-cocaine antibodies that decrease brain concentrations of cocaine by sequestering it in the peripheral circulation would be expected to decrease the probability of relapse. A predominantly human sequence monoclonal antibody, 2E2, with high affinity ($K_d = 4$ nM) and specificity for cocaine over its metabolites was tested for its ability to alter the pharmacokinetics of cocaine. Mice received an i.v. infusion of 2E2 (120 mg/kg) or vehicle. One hour later the mice received an i.v. bolus injection of an equimolar dose of cocaine HCl (0.56 mg/kg) and 400 units/kg of heparin. At times ranging from 0.75 to 60 min after the cocaine injection blood samples and the brain were collected from individual mice and their cocaine concentrations were then measured using GC/MS. Brain concentrations were corrected for the residual cocaine in intracerebral blood. In the absence of 2E2, cocaine rapidly distributed from plasma with an initial $t_{1/2}$ of 1.9 min followed by a slower terminal elimination phase with a $t_{1/2}$ of 26 min. In contrast, there was no cocaine distribution phase from the plasma in the presence of 2E2, but cocaine was still rapidly eliminated with a $t_{1/2}$ of 17 min. Importantly, 2E2 produced a 26-fold increase in the area under the cocaine concentration-time curve (AUC) in plasma and a concomitant 4.5-fold (78 %) decrease in the cocaine AUC in the brain. The calculated volume of distribution of cocaine in these mice was 6.0 l/kg and 0.14 l/kg in the absence and presence of 2E2 respectively. Therefore, 2E2 restricted cocaine to the plasma compartment thereby limiting its distribution to the brain but did not prevent cocaine's normal rapid metabolism. Thus, 2E2 has in vivo effects that would predict significant clinical efficacy for reducing the probability of relapse in cocaine abusers.

587 DOPAMINE RECEPTOR ANTAGONISTS ACCELERATE COCAINE SELF-ADMINISTRATION BY RAISING THE SATIETY THRESHOLD

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Dopamine receptor antagonists increase the rate of cocaine self-administration. However, in terms of reinforcement theory this effect is paradoxical as antagonists of reinforcement should decrease the rate of responding. According to our pharmacological model of maintained self-administration, the rate of responding at a given unit dose of cocaine is determined by the magnitudes of the satiety threshold and the elimination $t_{1/2}$ of cocaine. We investigated whether the D1 and D2 dopamine receptor antagonists SCH23390 and (-)-eticlopride altered these parameters. Rats were implanted with a jugular and a femoral catheter and cocaine was continuously infused for 7.3 hours at rates of 1, 2 or 4 $\mu\text{g}/\text{kg}/\text{sec}$. At 90 min, and then hourly, a sample of blood was withdrawn via the second catheter. After the third sample the rats were injected with SCH23390 (15 nmol/kg i.v.), blood samples were taken 20 min later and then hourly. SCH23390 had no effect on the plasma steady state concentration of cocaine and, therefore, did not change the $t_{1/2}$ of cocaine. In a separate experiment, rats self-administered cocaine at a unit dose of 1 mg/kg i.v. and after 2 hours of a stable rate of self-administration, a continuous non-contingent infusion of cocaine was started at a rate (2.0 - 4.8 $\mu\text{g}/\text{kg}/\text{sec}$) that maintained steady state concentrations above the satiety threshold, which stopped self-administration. The i.v. injection (20 nmol/kg) of SCH23390 or (-)-eticlopride, but not vehicle, reinstated self-administration despite the continuous cocaine infusion. It is concluded that these antagonists raised the satiety threshold above the steady state level produced by the continuous infusion. The antagonist-induced increase in the rate of cocaine self-administration is because at the higher concentrations the rate of cocaine elimination is increased, as dictated by first order kinetics. This explanation based on a PK/PD interaction does not produce the paradox inherent in the reinforcement theory of maintained self-administration.

588 HCV RISK FACTORS AMONG STREET-RECRUITED SUBSTANCE-ABUSING WOMEN

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Hepatitis C virus (HCV) infection is one of the most frequent chronic blood-borne infections in the US, causing significant morbidity and mortality. Among the risk factors associated with the HCV infection, drug injection remains a predominate route of transmission. Sexual transmission of HCV is possible but much less efficient as compared to hepatitis B virus or HIV. Other routes of transmission including tattoos, piercing, and drug preparation equipment have been proposed. A limited number of epidemiological studies have examined the risk factors associated with the HCV transmission in women, particularly in minorities. We examined the HCV associated risk factors in substance abusing females involved in NIAAA and NIDA funded HIV prevention studies of street recruited women. As a part of the 12 month follow-up, participants were interviewed about drug equipment sharing practices, tattoos, body piercing, and blood transfusions and sharing of the personal hygiene equipment. Among 782 predominantly African American women, 152 tested positive for HCV antibody and had completed the 12 month follow-up. HCV positive women, compared to HCV negative women, had significantly higher lifetime rates of drug injection (60% vs. 6 %); HCV positive drug injectors were more likely than HCV negative drug injectors to report reusing needles and syringes as well as other drug preparation equipment used by someone else (60% vs. 38% and 49% vs. 30% respectively). Although cocaine use was highly prevalent in the entire sample (70.2%), HCV positive women were more likely to smoke crack cocaine (95% vs. 71%). Among cocaine users, HCV positive women were more likely to reuse related equipment (79% vs. 65%). HCV positive women were also more likely than HCV negative women to have a tattoo (36% vs. 25%) or receive a blood transfusion (33% vs. 17%). No differences were observed related to body piercing or sharing of the personal hygiene equipment. To identify if other than parenteral routes of transmission play a role in HCV acquisition, multivariate logistic regression analysis will be applied to these data.

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589 HORMONE INJECTION AMONG PERSONS WHO TRANSFORM THEIR GENDER

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The subcutaneous injection of female hormones by persons who transform their gender from male to female is cited as a risk factor for HIV and other blood-borne infections, but the prevalence and predictors of this unique risk behavior are poorly understood. Initial findings on hormone injection and its correlates are presented from an on-going study of this population in the New York Metropolitan Area. Baseline data are available for 73 respondents. The current sample reflects diversity with regard to age (range of 19 to 71 with a mean of 43) and ethnicity [overall Hispanic identification = 24.6%; category breakdowns (including Hispanic): White=69.9%; Black=12.3%; other=17.8%]. Hormone Use and Injection: Over half (58.9%) of the respondents had previously taken some type of female hormone supplement, with 37% of them reporting a lifetime history of hormone injection. Total years of hormone use ranged from <1 to 37 (mean= 5.5) with total years of hormone injection ranging from <1 to 20 (mean=4.4). The age during which hormones were first used ranged from 9 to 63 (mean=35). Age Differences in Hormone Use and Injection: Current age was strongly associated with the age during which hormones were first used ($r=.70$; $p=.00$) (i.e. younger respondents started using hormones earlier). Among the hormone users ($n=44$), Current age was moderately associated with hormone injection ($r=-.29$; $p=.05$) (i.e. younger respondents were more likely to inject). Conclusions: The injection of hormones is relatively common among persons who transform their gender from male to female. Age differences in the prevalence of hormone injection, and the age of first injecting, point to generational differences in this phenomenon. Hormone injection may become significant as a risk factor for blood-borne infections in this population. Support by grant 1 R01 DA91797-01A0 from NIDA Key words: transgender, female hormones

590 THE AFFECTIVE PROPERTIES OF NICOTINE WITHDRAWAL ARE DIMINISHED IN ADOLESCENT VERSUS ADULT RATS

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Our previous work demonstrated that adolescent rats display fewer physical signs of nicotine withdrawal relative to their adult counterparts. This study compared the affective properties of nicotine withdrawal in adolescent and adult rats using the place aversion paradigm. Male Wistar rats ($n=5-6$ per group) were tested for their initial preference for either of two distinct compartments of a conditioning apparatus. Rats were then prepared with subcutaneous (sc) pumps that delivered either saline or a dose of nicotine that produces equivalent nicotine levels (13.5 mg/kg/day in adolescents; 9.0 mg/kg/day in adults; salt) for 14 days. In order to ensure nicotine dependence, conditioning began six days after pump implantation. Conditioning was conducted over the subsequent eight days, and consisted of four two-day conditioning trials. On one day, rats received mecamylamine (1.5 mg/kg, sc) to precipitate nicotine withdrawal in their initially preferred compartment. On alternate days, rats received saline in their non-preferred compartment. Rats were then re-tested for their preference for each compartment. A subsequent study examined potential age-related differences in learning the association between environmental cues and aversive stimuli. Adult and adolescents ($n=8$ per group) received lithium chloride (LiCl; an aversive stimulus) using similar conditioning procedures. Adult rats displayed a significant place aversion produced by nicotine withdrawal; however, adolescents did not display this effect. Our results appear to be specific to nicotine withdrawal and not developmental differences in learning, since there were no differences between these age groups in learning place aversion to LiCl. The present findings displaying reduced effects of nicotine withdrawal, taken together with studies demonstrating enhanced sensitivity to reinforcing effects of nicotine, could constitute a powerful basis for increased vulnerability to nicotine dependence during adolescence. (Supported by National Science Foundation Grant DUE 04-26266).

591 A DOUBLE-BLIND, PLACEBO-CONTROLLED ASSESSMENT OF POTENTIAL INTERACTIONS BETWEEN INTRAVENOUS METHAMPHETAMINE AND RIVASTIGMINE: CARDIOVASCULAR AND SUBJECTIVE EFFECTS

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The purpose of this study was to assess the effects of rivastigmine (Exelon®), an acetylcholinesterase inhibitor and cognition-enhancer, which is approved for the treatment of dementia of the Alzheimer's type, in volunteers with methamphetamine (MA) dependence. Cortical acetylcholine is critical to cognitive processing and there is a large body of evidence for the role of cholinergic drugs in improving experimentally induced memory impairment, even when the experimental toxin is MA. These putative mechanisms make rivastigmine an attractive potential candidate for MA dependence treatment. The study design was a double-blind placebo-controlled safety/interaction study that evaluated rivastigmine (1.5 mg, qd and 1.5 mg, bid) versus placebo on responses produced by experimental administration of MA (0, 15 and 30 mg, IV). This design was selected to provide for an assessment of the effects of rivastigmine, compared to placebo, on (1) the cardiovascular and subjective effects produced by MA, and (2) the reinforcing effects produced by MA. For this study, the final sample will consist of 18 MA-dependent non-treatment-seeking volunteers, randomized to receive rivastigmine or placebo. To date, 15 patients have completed the entire protocol. The data include comprehensive assessments of cardiovascular measures (heart rate, blood pressure), and subjective effects (e.g., High, Desire). Additional safety data, including adverse events will also be presented. These data will provide preliminary evidence of the safety and potential efficacy of Rivastigmine for MA dependence. A medication that is effective at reducing neurocognitive deficits associated with MA dependence is predicted to assist individuals in treatment to make use of counseling strategies and effect behavioral change. Supported by NIDA: DA-14593, DA-18185, DA-17754

592 AGE-DEPENDENT DECREASES IN BRAIN GLUTAMATE AND GABA AFTER ACUTE TOLUENE IN JUVENILE AND ADOLESCENT RATS BY HIGH-RESOLUTION MRS

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The neurobiological consequences of inhalants remain unclear. We compared the neurochemical effects of toluene in rats exposed on PN21 or PN35 to 0, 8000, or 12,000 ppm toluene in 2 15-min exposures, 2 hrs apart. Immediately after the 2nd exposure, brains were harvested and ~5-mg punches taken from frontal cortex, dorsal hippocampus and anterior striatum. Using ex vivo high-resolution magic angle spinning 1H magnetic resonance spectroscopy at 11.7-T, glutamate (GLU), glutamine (GLN), GABA, and glycine (GLY), as well as NAA, lactate, myo-inositol were quantified. There were significant developmental changes in most metabolites, e.g., increases in GABA and GLN in striatum and hippocampus between PN21 and PN35. There were no significant toluene-induced changes in GABA, GLU, GLN or GLY at either age in cortex or striatum, except for a small reduction in GABA in cortex at PN35 (not PN21) after 8000 (not 12,000) ppm toluene. In hippocampus at PN21 GABA was significantly decreased after either dose, whereas hippocampal GLU was decreased only after 12,000 ppm toluene. By adolescence (PN35), changes in hippocampal GABA or GLU were not significant. Elevations in GLN were limited to striatum at PN21. Toluene also elevated alanine in cortex and striatum at both ages. Toluene increased lactate in cortex at both ages and in striatum at PN21. These results reveal substantial, localized, age-related effects of toluene on the MR-visible neurochemical profile and suggest that MR-based neuroimaging may be of diagnostic value in cases of inhalant-induced neurotoxicity. Compared to younger rats, adolescent rats appear more sensitive to decreases in cortical GABA and less sensitive to decreases in hippocampal GABA and GLU after acute exposures to high-levels of toluene that mimic patterns of binge exposure. (Supported by R21-DA019151 to SEB and R01-DA-16736 to MPG).

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593 THE PERTH NALTREXONE IMPLANT SERVICE; AN OVERVIEW OF THE FIRST FIVE YEARS

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A total of 1575 patients were treated with naltrexone implants over a 5 year period (August 2000 to December 2005). These sustained-release implants (Go Medical Implants) have previously been described by Hulse and O'Neil (Addiction Biology 2004) and deliver naltrexone for approximately twelve months with blood levels maintained above 1ng/mL for 272 days. Forty percent of the patients presented for a repeat implant but this figure would rise to 42% when for the estimated 180 new patients who received their first implant recently and have not yet returned for follow up treatment. Patients returned for a second implant treatment a mean of 353 days after their first implant. In addition, 263 of 623 patients (42%) presented for further implants after their second implant. Approximately 40% presented again for their 4th implant, and 40% of that group for their 5th implant. This trend of approximately 40-50% returning for subsequent implants is consistent with some of the treatment programs using short acting implants. The naltrexone levels recorded are usually above 4ng/mL for the first 180 days and above 1ng/mL for the first 270 days. Abstinence from opiates is virtually complete in the first 90 days (3/830 urines were positive) with opiate use usually delayed until the blood level falls below 2ng/ml and often until it falls below 1ng/mL. It is common to see opiate use recommence for a short time (usually less than 3 weeks) prior to the second implant. Most patients represent for their second implant with a history of being drug free for 6-9 months with many having a short relapse almost electively prior to their second implant.

594 PREDICTORS AND CORRELATES OF THE HAZARDOUS USE SUBTYPE OF DSM-IV CANNABIS ABUSE

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AIMS: There are four criteria for DSM-IV cannabis abuse, endorsing any one of which leads to a diagnosis of abuse. Our analyses show that 51% of Americans with lifetime cannabis abuse endorsed hazardous use and no other criterion. There has been some debate over whether individuals who are diagnosed based on endorsement of this criterion alone suffer from a true psychiatric disorder. Using nationally representative survey data, we investigated clinical and use-related correlates of the hazardous use only (HU) subtype of DSM-IV cannabis abuse by comparing these subjects to all others who received a diagnosis of abuse by meeting one or more of the other criteria. METHODS: 2,851 respondents to the National Epidemiologic Survey of Alcohol and Related Conditions (N=43,093) were diagnosed with lifetime cannabis abuse. Odds ratios and 95% confidence intervals comparing individuals with HU only to those with all other forms of cannabis abuse were calculated using SUDAAN. Continuous measures were dichotomized at the median. RESULTS: While the HU subtype was associated with increased frequency of use (OR 1.37, CI 1.11-1.69 for frequency of use during period of heaviest use) and younger age of onset of use (OR 1.69, CI 1.41-2.03), it was also associated with lower number of joints usually smoked (OR 0.62, CI 0.51-0.76), fewer criteria of cannabis dependence endorsed (OR 0.46, CI 0.39-0.55), and fewer episodes of abuse (OR 0.79, CI 0.64-0.98). Subjects with the HU subtype were dramatically less likely to have sought treatment for any drug use disorder (OR 0.18, CI 0.13-0.27). They were also less likely to have a history of other drug use disorders (OR 0.57, CI 0.47-0.68), mood disorders (OR 0.70, CI 0.57-0.85), or personality disorders (OR 0.75, CI 0.61-0.91). CONCLUSIONS: Lower associations with many clinical conditions and indicators of a drug use disorder demonstrate that HU may be distinct from other subtypes of abuse. Our results suggest that HU could be a measure of frequency of use rather than the psychiatric disorder delineated by other abuse subtypes.

595 EFFECT LAAM DOSE AND REDUCING CONTINGENCY MANAGEMENT REWARDS ON ILLICIT DRUG USE IN OPIOID-DEPENDENT COCAINE ABUSERS

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In order to examine the effect of altering contingencies on illicit drug use in opioid-dependent cocaine abusers maintained on different LAAM dose regimens, we conducted secondary analyses of data from a 24-week, randomized clinical trial, in which 140 opioid-dependent cocaine abusers (95M/45F; 39AA/10H/91C) were assigned to receive one of the following: low-dose LAAM (30,30,39 mg/MWF) with adjunct contingency management procedures (LC); low-dose LAAM (30,30,39 mg/MWF) without contingency management procedures (LY); high-dose LAAM (100,100,130 mg/MWF) with adjunct contingency management procedures (HC); and high-dose LAAM (100,100,130 mg/MWF) without contingency management procedures (HY). Urine samples were collected thrice weekly. For those in the HC and LC group, each urine negative for both opioids and cocaine resulted in a voucher worth a certain monetary value that increased for consecutively drug-free urines (wks 1-12) or a voucher with a low fixed value (wks 13-24). Subjects in the HY and LY group received vouchers according to a yoked-control schedule. Vouchers were exchanged for mutually agreed upon goods and services. Groups did not differ on retention and baseline characteristics. Preliminary analyses based on piecewise hierarchical linear modeling indicate that, during wk 1-12, opioid use declined most rapidly in HC and HY groups relative to LC and LY groups and, during wk 13-24, the decline in opioid use was maintained in all groups with no further reductions seen. During wk 1-12, cocaine use decreased over time least rapidly in the HY group. Of the other 3 groups, the slope of the decline in cocaine use differed significantly from horizontal in HC and LY groups only. During wk 13-24, cocaine use did not decline further in any group. These results suggest that initial declines in drug use were maintained when the value of the reward was reduced, regardless of opioid maintenance dose. (Supported by NIDA grants DA50853 and DA05626.)

596 AVAILABILITY AND USE OF CLUB DRUGS IN NEW YORK CITY NEIGHBORHOODS

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Objective: Data are sparse on availability and use of club drugs among urban, economically-disadvantaged, racially diverse populations. We aimed to investigate club drug use (CDU) and availability in 36 ethnographically defined neighborhoods in 12 community districts of New York City. Methods: A community-based sample of non-drug users, former drug users, non-injection drug users and injection drug users aged ≥ 18 years were recruited from target neighborhoods. Availability and use of club drugs (defined as ecstasy, LSD, PCP, GHB, ketamine and methamphetamine) was assessed through an interviewer-administered questionnaire. Results: To date, of 405 people recruited, 50.6% were Hispanic, 39.0% were Black and 10.3% were White mixed or other race. The sample was mostly male (70.6%); median age was 37 (range 18-64). In terms of lifetime CDU, PCP was the most frequently reported club drug (39.3%), followed by LSD (30.6%), ecstasy (20.7%), ketamine (6.4%), methamphetamine (4.7%) and GHB (2.5%). CDU in the last 6 months was reported by 76 (18.8%), with PCP (6.4%), ecstasy (5.4%), and LSD (3.0%) reported most frequently. When asked about availability in neighborhood of residence: PCP was the most frequently reported (16.5%) followed by ecstasy (15.1%), LSD (8.6%), and methamphetamine (4.9%). Those who reported living in neighborhoods where club drugs were available were significantly more likely to have used (43.0 vs. 10.8 %, $p < 0.001$). Among club drug users, there were no significant differences in terms of age, race/ethnicity, gender, education and sexual identity among those who reported club drug availability in their neighborhood versus those who did not. Conclusions: These preliminary data suggest that club drugs are available in a variety of New York City neighborhoods. Despite increasing concerns about methamphetamines, availability and use have remained relatively low.

597 LEVERAGING TECHNOLOGY: EVALUATION OF A COMPUTER-BASED BRIEF INTERVENTION FOR POSTPARTUM DRUG USE AND A DYNAMIC PREDICTOR OF TREATMENT RESPONSE

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The present study is an examination of the response of postpartum women with histories of drug use to a single-session computer-based motivational intervention. This study also evaluated the ability of changes in within-intervention state motivation ratings to predict intervention outcome. A total of 107 postpartum women who reported drug use in the month prior to pregnancy were recruited prior to leaving the hospital, and randomly assigned to 20-minute computerized intervention vs. control conditions. The primary intervention consisted of three separate components presented in counterbalanced order; participants completed visual analogue scale ratings of intention to quit, problem recognition, and treatment readiness at baseline and after each of the three intervention components. Primary outcomes included changes in self-reported drug use and drug use as confirmed by urinalysis, both measured at 3-month follow-up. Intervention effects on changes in drug use were significant for drug use frequency averaged across all substances ($p = .042$, Mann Whitney U test; Cohen's $d = .46$) and for illicit drugs other than marijuana ($p = .032$, Mann Whitney U test; $d = .40$), but not for marijuana alone ($p = .202$, Mann Whitney U test; $d = .39$). Intervention effects for dichotomous outcomes (yes/no for marijuana use, drug use other than marijuana, and any drug use) were not significant, but yielded similar effect sizes. Regarding dynamic prediction of intervention effects, intervention-associated decreases in self-reported drug use intention (vs. ratings made immediately prior to the intervention) were predictive of use of drugs other than marijuana ($p = .045$ but not of marijuana use. These results suggest that brief computer-based interventions can be efficacious. These results also suggest that within-intervention predictors of intervention response, used as proxy outcomes, may facilitate rapid intervention development and optimization.

598 KNOWLEDGE OF HEPATITIS AMONG RURAL FELONY PROBATIONERS

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Background: Drug users under community supervision are at high risk for contracting and transmitting infectious diseases, including Hepatitis and HIV, through unsafe injection practices and unprotected sexual encounters. However, there are no known studies examining Hepatitis and HIV knowledge among injecting drug users (IDUs) and non-injecting drug users (Non-IDUs) in rural America. Methods: Participants were enrolled in a HIV intervention study for rural ($n=800$) felony probationers in Appalachian Kentucky. Data pertaining to demographic characteristics, drug use, sexual activity, infectious diseases, and HIV/Hepatitis knowledge were collected using an interviewer-administered questionnaire. Bivariate analyses distinguished differences between IDUs ($n=179$) and Non-IDUs ($n=621$), while negative binomial regression was used to assess the independent correlates of Hepatitis knowledge. Results: Participants were primarily white (95%), male (67%), and mean age was 34 years. While IDU/Non-IDU participants did not differ on most demographic characteristics, IDUs had more extensive criminal histories. IDUs were more likely to have overdosed, used variety of illicit substances in the past 30 days, and participated in substance abuse treatment. In addition, IDUs had engaged in more transactional sex and oral sex within the last six months. The prevalence of Hepatitis B, Hepatitis C, and other sexually transmitted infections was higher among IDUs. Injectors scored significantly higher on the HIV Risk Behavior Knowledge Test, but there was no difference on the Hepatitis Knowledge Test. Results from the negative binomial regression indicated that having been tested for HIV and HIV knowledge significantly promoted probationers' score on the Hepatitis Knowledge Test. Conclusions: Rural probationers have a relatively good understanding of HIV and Hepatitis treatment and prevention; however, both injectors and non-injectors are still engaging in high risk behaviors. Community supervision is an opportune time to for the delivery of behavioral health interventions to hard-to-reach, high-risk rural populations.

599 INCIDENCE AND PREDICTORS OF DRUG INJECTION AMONG YOUNG NON-INJECTING HEROIN USERS IN CHICAGO

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Objectives: To examine transitions from non-injecting heroin use to drug injection, subsequent risk practices, and infection with HIV and HCV. Methods: Non-injecting heroin users (NIHU) 16-30 years old were recruited in Chicago through street outreach and respondent-driven sampling and followed at 6 month intervals. Computerized self-administered interviews and serological data were collected at each visit. Results: Of 668 participants, 603 (90%) were eligible for a 12-month follow-up: 55% were African-American, 21% non-Hispanic white, 64% male, and median age was 26. At baseline, 18% had ever injected, though not in the prior 6 months. HIV and HCV seroprevalence was 3.6% and 2.5%, respectively. At 12-month follow-up, recent drug injection was reported by 26% ($n=29$) of former injectors and 11% ($n=42$) of those with no history of injection. In multivariate analysis, those who had injected for the first time ($n=42$) were more likely to be white than African-American ($p=0.016$) and younger than 25 years ($p=0.038$). First-ever injectors often receptively shared needles (46%), cookers (40%), cotton (28%), and water (29%), and 39% reported being injected by someone else. Former injectors who remained noninjectors were more likely to be African-American than white (48% vs 28%, $p=0.134$), report no chance of injecting in the future ($p=0.030$) and to have used heroin daily ($p=0.010$). During follow-up 3 HCV seroconversions were observed, of which one was a first-ever injector. Conclusion: NIHU who were white and those under 25 years of age were significantly more likely to initiate injection within one year of baseline. High-risk injection practices were common at initiation.

600 THE INCREMENTAL INPATIENT HEALTH SERVICE COSTS ASSOCIATED WITH MARIJUANA COMORBIDITY

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In this paper, we examine the relationship between marijuana use and health service utilization in the United States by considering the incremental effect on inpatient hospital service utilization of marijuana dependence/abuse for patients being admitted with non-marijuana related primary diagnoses. Using data from the 1993-2000 National Hospital Discharge Survey (NHDS) we begin by aggregating the primary ICD-9-CM codes into clinically homogenous aggregate illnesses and conditions based on a single-level diagnosis classification developed by the Agency for Health Research and Quality. We focus our attention on diseases/conditions that the literature identified as plausibly linked to cannabis use (Hall and Pacula, 2003; Hall and Babor, 2000) but also typically involve a toxicology screen, specifically alcohol problem disorders, mood disorders and thought disorders. Our results consistently show a positive association between marijuana co-morbidity and length of stay as well as charges for inpatients suffering from alcohol problems as their primary indication. In addition, we find evidence of a positive association between average charges and marijuana co-morbidities for mood disorders. Our estimation of the economic cost of marijuana use due to increased inpatient utilization associated with just these two conditions falls within the range of \$7.2 to \$16.6 million annually.

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601 A DOUBLE-BLIND, PLACEBO-CONTROLLED ASSESSMENT OF TOPIRAMATE EFFECTS ON CIGARETTE CRAVING AND REWARD

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Topiramate is an FDA approved medication for the treatment of seizure disorder. Topiramate inhibits neural activity by elevating cerebral GABA levels and blocking the AMPA glutamate receptor, and has been shown to be efficacious in the treatment of cocaine and alcohol dependence. In the latter study, cigarette smoking was also found to be reduced by topiramate. To investigate its effects in cigarette smokers, we are conducting a double-blind clinical pharmacology study assessing the effects of topiramate (75 – 150 mg/day) on cigarette craving and reward. Cue testing involves handling and smelling cigarettes, lighting a cigarette and viewing a video depicting people smoking cigarettes. Following the cues, subjects smoke one cigarette in puff-volume apparatus. Cue and cigarette testing is performed on the 9th and 15th day of treatment. Patients include non-treatment seeking cigarette smokers. Preliminary analysis (n = 25) of the data confirms that cigarette cues elicit a reliable craving and withdrawal response, and that the smoked cigarette elicits a reliable reward and satiety response. Treatment data indicate that topiramate attenuates cue induced total craving and withdrawal sub scores, and reduces cigarette smoking satiation and reward in a dose related manner. The effects of topiramate on 3 hour abstinence-based craving and withdrawal, ad lib smoking, and the physiological response to cues and a smoked cigarette will also be presented. The data from this study provide preliminary evidence that topiramate may be a useful treatment medication for managing cigarette craving.

602 PSYCHOMETRIC PROPERTIES OF THE COCAINE CRAVING QUESTIONNAIRE (LONG AND BRIEF) AND RELATIONSHIP TO COCAINE RELAPSE OUTCOMES

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Objective: This study examined the psychometric properties of the Cocaine Craving Questionnaire (CCQ – Long and Brief) in an inpatient sample of cocaine abusers and examined its relationship to cocaine relapse measures after discharge from inpatient treatment. Method: Cocaine dependent individuals (n = 115) participating in inpatient treatment for cocaine dependence were assessed on cocaine craving using the long and brief versions of the Cocaine Craving Questionnaire (CCQ), and prospectively followed for 90 days after discharge from inpatient treatment. Reliability, internal consistency and concurrent validity of both the long and brief versions of the CCQ were examined. The predictive validity was examined by assessing its relationship to time to initial cocaine relapse and drug use escalation after relapse (frequency and amount of cocaine used upon relapse) using Cox proportional hazards regression and multiple regression analyses respectively. Factor analysis was conducted to obtain a shorter, one-dimensional craving scale. Results: Patients with higher craving scores at intake (long and brief versions) were at significantly higher risk of relapse than subjects with lower craving scores. Baseline craving did not predict frequency and amount of cocaine use after relapse. Factor analyses resulted in a 5-item one-dimensional craving scale, which was significantly associated with risk of relapse. CCQ scores were also significantly associated with stress and drug cue-induced craving in the laboratory. Conclusions: Although both the long and brief versions of the CCQ were reliable and valid in this sample, these findings support the use of the brief version of the CCQ in studies of both the cocaine dependence etiology and treatment outcome (Supported by P50-DA16556 and K02-DA17232).

603 COLLEGE DRUG USE: PREVALENCE, PATTERNS, AND INTEREST IN INTERVENTIONS

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Drug use among college students has continued to increase in the past decade (Mohler-Kuo, Eun Lee & Wechsler, 2003; McCabe, Knight, Teter, & Wechsler, 2005). Although the majority of students do not meet criteria for abuse or dependence, use of alcohol, drugs or the combination often leads to an increase in risky behavior and negative consequences. The current study assessed patterns of alcohol, drug (street and prescription), gambling, and cigarette use as well as students' interest in various types of interventions. Participants were 399 college students, 50% male and 19 (S.D. = 1.8) years old. The ethnicity of the sample was 75% Caucasian, 15% African American, 4% Hispanic, and 5% Multiethnic or Other. The majority of participants reported using marijuana in their lifetime (60%), and used an average of 5.5 (SD= 10) days in the past month. The majority (63%) reported experiencing one negative consequence and averaged five (M=5.2, SD=7.2) due to their drug use. Preliminary analyses indicated students were interested in attending a variety of workshops; including sexual risk (37.3%), drug use (31%), alcohol (34%), and prescription drug use (28%). Students reported less interest in workshops on gambling, and tobacco with 20% expressing interest. Students were asked hypothetically if they were concerned about their use, what interventions they would be interested in receiving, participants reported interest in brief feedback/counseling with a counselor unaffiliated with the college (28%), a web-based program about alcohol or drugs (27%), or a confidential conversation via the telephone (26%). Additional analyses will include an evaluation of the relationship between students' drug use, number of negative consequences due to their use, and level of interest in an intervention and modality. A better understanding of which intervention modalities are most appealing to students will assist in the process of developing effective interventions. This research was supported by the National Institute on Drug Abuse, grant #: P50 DA 09241.

604 CLINICIAN ADHERENCE TO COUNSELING MANUALS DURING OFFICE-BASED BUPRENORPHINE MAINTENANCE

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We assessed treatment adherence among nurses administering counseling during office-based buprenorphine maintenance and evaluated the degree to which specific counseling components were associated with outcomes using the Medical Management Adherence & Competence Scale. This scale was used by independent, trained raters to rate audiotaped Standard Medical Management (SMM; medically-focused counseling with minimal psychosocial counseling) and Enhanced Medical Management (EMM; integrated medically- and psychosocially-focused counseling) sessions, which had been offered as part of randomized controlled trial of buprenorphine maintenance in a primary care clinic. Based on a randomly selected sample of counseling session tapes (N=320), nurses in both SMM and EMM briefly administered many of the techniques they were trained to implement (mean adherence (frequency) = 2.33/7) and did so with good competence (mean competence=3.54/7). As predicted, EMM sessions were significantly longer than SMM sessions (43.25 vs. 23.23 min.; p<.01). Further, nurses utilized the psychosocial counseling components significantly more frequently in EMM vs. SMM sessions. The above suggests that SMM and EMM were implemented with good adherence. Preliminary analyses also reveal that RN competence discussing medical complications of opiate use (both SMM & EMM) and RN completion of educational handouts on warning signs of relapse and social support for abstinence (EMM only) were correlated with mean weeks of opiate negative urine toxicology tests (r's=.52, .45, .41; p's<.05), and that competence discussing medical complications of opiate use and describing key aspects of the 12-steps were associated with treatment weeks completed (r's=.55 & .47; p's<.05). Findings may assist with developing guidelines for the training, supervision, and monitoring of primary care-based staff offering counseling to the buprenorphine-maintained patient. Supported by R01DA09803 & K24DA000445 (RSS) & K23DA15144 (MVP)

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605 STATISTICAL AND SPATIAL ANALYSIS OF HIGH-RISK BEHAVIORS AMONG HIV-POSITIVES IN NEW YORK CITY

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BACKGROUND: This study examined high-risk sexual and drug use behaviors among HIV seropositives and the relationship between services in a geographic locale and the concentration of HIV positives who continue to engage in risky behaviors. **METHODS:** Logistic regression models examined the influence of individual characteristics (health status, demographics, service utilization) and social contexts (neighborhood poverty rate, density of HIV service providers) as predictors of risky behaviors (unprotected sex, IDU sexual partner, current drug use and exchange of sex for money or drugs) among a probability sample of HIV positive adults living in NYC (N=651), 1998-1999. Geographic distributions of service and residence locations at the health district level were analyzed spatially. **RESULTS:** Gender was an important predictor of unprotected sex, exchanging sex for money or drugs, and having an IDU sexual partner. Participants with unstable housing were more likely to have an IDU sexual partner, exchange sex for money for drugs or to have recently used drugs. However, persons who received housing support (OR: .339, CI .189-.610) were less likely to have used drugs in the last six months. Participants who lived in poor neighborhoods (OR: 2.24, CI .430-1.07) or had a case manager (OR: 1.91, CI 1.10-3.33) were more likely to have an IDU sexual partner. Also, participants from poor neighborhoods were at increasing risk for having used drugs in the last six months. Seropositives with a regular sexual partner were more likely to have unprotected sex. Density of service providers in the neighborhood was not strongly associated with high risk behaviors. **CONCLUSION:** Contextual (poverty level) as well as individual (demographic, unstable housing) client characteristics are important factors influencing risky sexual and drug behaviors among HIV positives. Further research is needed to disaggregate both the possible influence of different services within the residential context and the impact of structural factors on risky sexual and drug use behaviors.

606 NOVEL TRIVALENT ANTAGONISTS WITH SELECTIVITY FOR ALPHA7 NICOTINIC ACETYLCHOLINE RECEPTORS

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Neuronal nicotinic acetylcholine receptors (nAChR) are the primary substrate for nicotine dependence, and are recognized as potential therapeutic targets for indications ranging from Alzheimer's disease and schizophrenia to analgesia. Multiple subtypes of nAChR are present in brain, presenting both a challenge and an opportunity to selectively target particular subtypes for specific indications. The alpha7 nAChR is of interest as a therapeutic target, since it has been implicated as a mediator of both cognition and neuroprotection. Previously characterized bis-quaternary ammonium and piperidinyll compounds showed relatively little activity as antagonists of alpha7 nAChRs compared to the numerous beta subunit-containing subtypes. We now report the synthesis and functional characterization of a series of tris-quaternary ammonium salts. Compounds were tested for inhibition of ACh-evoked responses of rat alpha4beta2, alpha3beta2, alpha3beta4 or alpha7 nAChR subunits expressed in *Xenopus* oocytes. Results show that GZ551A (1,3,5-tri-[pent-1-ynyl-5-(3-n-butyl-pyridinium)]-benzene tribromide), GZ551B (1,3,5-tri-[pent-1-ynyl-5-(3-n-butyl-pyridinium)]-benzene tribromide) and GZ558C (1,3,5-tri-[pent-1-ynyl-5-(3-n-butyl-pyridinium)]-benzene tribromide) were relatively selective for inhibiting alpha7 nAChR responses compared to those of other subtypes tested. The most potent and selective compound was GZ551A, which produced noncompetitive inhibition of the alpha7 response (IC50 of 130 ± 20 nM), while IC50 values for inhibition of alpha4beta2, alpha3beta2 and alpha3beta4 nAChRs were 7.0 ± 2.3 , 11 ± 3 and 2.4 ± 0.5 microM, respectively. Our results indicate that these compounds are of significant value for preclinical studies relating nAChR subtypes to specific effects of nicotine in vivo and in vitro, and ultimately may be of value for therapeutic development. Supported by U19DA017548.

607 RAPID ASSESSMENT OF DRUG USE AND SEXUAL HIV RISK PATTERNS IN VULNERABLE POPULATIONS IN DURBAN, PRETORIA AND CAPE TOWN, SOUTH AFRICA

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The rapid assessment explored the linkage of drug abuse and HIV/AIDS among vulnerable drug using populations that could contribute to South Africa's heterosexually transmitted HIV epidemic. A cross-sectional, descriptive study was undertaken using observation, mapping, key informant interviews and focus groups in known "hotspots" for drug use and risky sexual behaviour in Cape Town, Durban and Pretoria. Focus group interviews included injecting and non-injecting drug users, commercial street sex workers (CSWs) and men who have sex with men (MSM) who also use drugs. Key informant interviews included the former together with service providers. Purposive snowball sampling and street intercepts were used to recruit adult drug users. Data were collected over a four-week period. Interviews and focus groups were facilitated and audio-recorded by a team of two trained fieldworkers. Key informant interviewees were offered free Voluntary Counseling and Testing (VCT) using the SmartCheck Rapid HIV-1 Antibody (finger-prick) Test in a non-clinic (private) field setting. Across sites 168 interviews were undertaken, including 146 key informant and 22 focus group interviews. Over a quarter of participants agreeing to be tested were positive for HIV. Female CSWs, followed by MSM appear to be most at risk for drug-related risky sexual practices. Injecting drug users also reported engaging in numerous behaviors that put them at risk for contracting (and transmitting) HIV. Across the various groups there is a lack of awareness about where to access HIV treatment and preventive services, and barriers to accessing appropriate HIV and drug-intervention services were reported. Female CSWs were less well informed about HIV preventive services than other groups and were also less empowered to access services in general. Strategies for introducing or scaling up sustainable interventions to reach drug-using populations especially vulnerable to HIV will be presented.

608 DELAY DISCOUNTING AND TEEN SMOKING

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Delay discounting is considered an index of impulsive choice. Several studies have shown adult smokers discount more (perform more impulsively) than nonsmokers; however, only one published study has compared teen smokers and nonsmokers (Reynolds et al., 2003). Inconsistent with adult findings, teen smokers did not discount more than teen nonsmokers. The current study replicated the earlier teen-smoking study and included a new real-time measure of discounting and a self-report survey of impulsivity. It was expected teen smokers would again not discount more than nonsmokers; however, smokers were expected to score higher on the self-report survey of impulsivity. Twenty nonsmokers (10 females) and 17 smokers (8 females) between 14 and 16 years of age completed a question-based measure of delay discounting (DDQ), the Experiential Discounting Task (EDT), and the Barratt Impulsiveness Scale-11-Adolescent (BIS-11-A) in a single laboratory session. Smoking status was verified from breath carbon-monoxide levels. Smokers did not differ from nonsmokers on the DDQ or EDT; however, smokers were more impulsive on the BIS-11-A, $t(36) = 2.72$, $p = .005$ (one-tail test). Self reports of alcohol, marijuana, and caffeine use also were collected, and the teen smokers reported significantly more alcohol and marijuana use than the nonsmokers. Smokers and nonsmokers did not differ in caffeine use. Combining the smokers and nonsmokers, the BIS-11-A and EDT were significantly correlated with alcohol use: $r = .30$, $p = .043$ (one-tail test) and $r = .58$, $p = .002$ (one-tail test), respectively. Greater impulsivity on these measures was associated with more alcohol consumption. To conclude, the current findings corroborate an earlier finding that teen smokers do not discount more than teen nonsmokers, even though these groups did differ on a survey measure of impulsivity. This discounting finding is inconsistent with findings between adult smokers and nonsmokers and poses important developmental questions about the relation between impulsive discounting and cigarette smoking (e.g., causal versus. consequent).

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609 ASSOCIATION BETWEEN PLATELET SEROTONIN TRANSPORTER AVAILABILITY, PROLACTIN RESPONSE TO META-CHLOROPHENYLPYPERAZINE AND TREATMENT OUTCOME IN COCAINE
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Background: While chronic cocaine exposure is found to alter platelet serotonin transporter (5-HTT) availability, and prolactin (PRL) response to meta-Chlorophenylpiperazine (m-CPP), the relationship between the two measures and their clinical implications are not fully studied. Objective First, we examined the relationship between platelet 5-HTT availability, a presynaptic 5-HT measure, and PRL response to m-CPP, a marker of postsynaptic 5-HT activity in cocaine dependent individuals. Second, we investigated whether such alterations are associated with measures of treatment-outcome. Methods: Platelet [3H] paroxetine binding sites were assayed and m-CPP challenge was performed in 35 African American cocaine dependent individuals at admission to an outpatient treatment program and 33 matching controls. Outcome measures included negative urine drug screens and treatment retention. Results: Confirming our previous results, cocaine subjects showed reduced Bmax of [3H] paroxetine ($t=4.67$, $p < 0.01$) and blunted PRL response to m-CPP ($F=21.86$, $p < 0.01$) compared to controls. There was a significant positive correlation between Bmax and delta PRL[peak - baseline PRL] ($r = 0.47$, $p < 0.01$). No association between the 2 measures was found in controls ($r = 0.14$). While significant main effects of Bmax on treatment retention were observed ($p < 0.01$), there were no significant main effects of delta PRL or any interaction effects on outcome measures. Conclusions: It appears that pre and postsynaptic alterations in 5-HT activity may be associated in cocaine dependence. Whether there is a causal association between the two measures, or cocaine has separate and independent pre- and post-synaptic effects needs to be clarified. Although the combined influence of the two 5-HT measures on treatment-outcome was not observed, in view of the small sample size, this issue deserves further study. Funding: grants DA00340 and DA015504 to AAP from the National Institute on Drug Abuse

610 BRAZILIAN FEMALE CRACK USERS SHOW HIGH SERUM ALUMINUM LEVELS
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Introduction: there is knowledge of the damage produced by crack smoking, but there is no information on its impact by using crushed aluminum cans as makeshift pipes, which is common in southern Brazil. Chronic aluminum intake is associated with neurological damage. We describe the impact of such form of use in serum aluminum levels (SALs) of crack smokers. Method: 76 current (30 days) female crack smokers were enrolled in the study by chain referral and snowballing. Their mean age was 28.4 (+/-7.8). They provided information on their drug use, and blood for SAL. Three SALs could not be used due to hemolysis. Results: respondents smoked on average 49 rocks per month (interquartile range from 16 to 90); 58 (79%) smoked from crushed can pipes, while 15 (21%) reported other forms of crack smoking with indirect aluminum contact (aluminum foil on top of glass pipes). Of the 73 subjects, 53 (72.6%) had a SAL at the 2 µg/l level and 13 (17.8%) had a SAL at the 6 µg/l cut-off point, which is above the maximum reference value. When these subjects were compared to a sample of non-drug users matched by mean age, we found similar median values and interquartile ranges for SAL between groups (3.2 - 4.6) for crack smokers; 2.9 (1.6-4.1) for controls, but with different means and standard deviations (4.7 +/- 4.9 for crack smokers; 2.9 +/- 1.7 for controls ($p = 0.059$, Mann-Whitney's test). Discussion: these crack smokers - either using or not crushed aluminum can pipes - have high proportions of SAL. Further studies are needed to elucidate and replicate these findings. If proven true in future research, preventive measures must be discussed for these high risk subjects.

611 ASSOCIATION BETWEEN DRUG ABUSE AND SPONTANEOUS OR THREATENED MISCARRIAGE IN PSYCHIATRICALY ILL WOMEN
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From a large dataset of patients, we examined medication use and drug abuse across pregnancy in a low SES population of pregnant women who had a psychiatric illness. We examined significant associations between drug dependence and threatened or completed miscarriage. The data consisted of 121 pregnant women who were receiving prenatal care over a two year period. Information on age, diagnoses, prescriptions, type, dose and quantity of medications are included. Almost 20% of the women were diagnosed with drug dependency or abuse and 8% had toxic blood levels of psychotropic medication that required hospitalization. Sixty-two percent of the women had a primary diagnosis of Bipolar Disorder. The pregnant women had multiple health problems coded on Axis III: 58% had a pain diagnosis and 40% had infection and were prescribed various types of medications. A majority of the prescribed medications were antimicrobial, opiate analgesics or for treatment of psychiatric illness. Nine women had spontaneous abortions and 31 had a threatened spontaneous abortion. Spontaneous abortion was significantly associated with a diagnosis of Bipolar Disorder and multiple medication use during the first trimester. Both threatened abortion and completed miscarriage were associated with Polydrug Dependence (Chi-Square=9.329; $p = 0.01$). We will present a multivariate model of predictors of miscarriage and threatened miscarriage. Conclusions: by diagnostic codes, none of the pregnant women were treated for their substance abuse or dependence. Bipolar pregnant women are at risk for miscarriage for multiple reasons. Reasonable treatments for drug dependence should be part of the risk to benefit assessment after women with psychiatric illness become pregnant. Funding: grants DA00340 and DA015504 to AAP from the National Institute on Drug Abuse

612 TRAUMATIC EVENTS, PTSD, AND GENDER DIFFERENCES OVER TIME IN SYRINGE-EXCHANGE PARTICIPANTS

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Few longitudinal studies have assessed ongoing exposure to traumatic events and posttraumatic stress disorder (PTSD) symptoms in out-of-treatment substance dependent people. The present study examines changes in traumatic event exposure and PTSD symptoms among male and female syringe exchange participants in Baltimore. Preliminary analyses include 162 participants; a larger sample will be available for presentation. Most (70%) participants are male, minority (75%), and unmarried (57%); average age is 41 years. A majority completed high school (58%), although only 18% are employed. Women were less likely than men to be employed (6% vs. 23%; $p < 0.01$), but no other demographic differences emerged. Participants completed measures of lifetime traumatic event exposure and current PTSD symptoms at study intake and were followed for up to 16 months. Participants were asked monthly about traumatic event exposure in the preceding month; current symptoms of PTSD (Posttraumatic Stress Scale; Falsetti et al., 1993) were assessed at 4, 8, and 12 months. Data from the first 6 months are reported in these preliminary analyses. At each monthly follow-up, about half of the sample reported exposure to a traumatic event in the preceding month. Women were more likely than men to report traumatic event exposure at nearly every monthly follow-up. At Month 1, for example, 69% of women reported a traumatic event exposure compared to 41% of men ($p < 0.01$). PTSD symptom severity was moderate at baseline (mean \pm SD: 24 \pm 28) and failed to change appreciably over time to the Month 4 follow-up (20 \pm 22). Women reported greater symptom severity than men at both baseline (41 \pm 36 vs. 18 \pm 21; $p < 0.0001$) and Month 4 (28 \pm 23 vs. 17 \pm 21; $p < 0.05$). The high rate of new exposures to traumatic events and the largely unabated severity of PTSD symptoms in this sample, especially women, underscores the vulnerability of this population and the need to improve access to and motivation for treatment. Study supported by NIH-NIDA grants: K23DA15739 & R01DA12347.

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613 PREDICTORS FOR LONG-TERM RETENTION IN METHADONE MAINTENANCE TREATMENT CLINIC LOCATED IN 2 DIFFERENT COUNTRIES

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Aims: To compare predictors for long term retention between two MMT clinics, one in the USA and the other in Israel. **Methods:** The study included 302 patients admitted to the Las Vegas Adelson MMT Clinic (1/February/2000 25/April/2004) and 492 patients admitted to the Tel-Aviv (25/June/1993 24/June/2003) Adelson MMT Clinic. Drug abuse during the first month and during the 13th month in treatment (or last month if patient stayed >3 months but less than 12 months) was studied and defined positive if at least one urine result during that month was positive. Kaplan Meier analyses and Cox models for multivariate analyses were used for cumulative retention. **Results:** The Las-Vegas patients were older than the Tel Aviv patients (43.4±9.4y vs. 36.7±8.5y), and had a higher proportion of sera-positive hepatitis C (83.4% vs. 56.9%) and a higher abuse of cocaine (52.3% vs. 13.7%) and amphetamines (15.6% vs 9.2%) on admission, but fewer were parents (46.3% vs. 63.8%). Cumulative retention and one year retention was higher in Tel-Aviv (73.6% vs. 61.6% p=100mg/day) while in Las-Vegas predictors were being sera-positive hepatitis C, no amphetamines abuse on admission and a high methadone dose. In a common model, being from Tel-Aviv, having a high methadone dose, using no amphetamines on admission, being older on admission and using no opiates after one year predicted longer retention. **Conclusions:** Although Tel-Aviv had a higher retention rate, both clinics had similarly high proportions of patients who stopped illicit opiate use after one year in treatment and in both a high methadone dose was a predictor for cumulative retention. Difference in retention may reflect differences in patient characteristics and environment.

615 OPIOIDS MODULATE SUBSTANCE P EXPRESSION

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Background: Both opioids and neuropeptide substance P (SP) function as potent neurotransmitters and modulators of neuroimmunoregulation. Our earlier studies showed that morphine upregulates SP expression in human immune cells in vitro. The present study was undertaken to determine the in vivo effects of opioids and opioid withdrawal on SP expression. **Methods:** Using EIA and real time RT-PCR assay, we analyzed plasma SP levels and SP gene expression in peripheral mononuclear cells (PBMCs) isolated from opioid dependent subjects either on methadone maintenance or undergoing opioid withdrawal (gradual decrease of methadone dose) during a 10-day detoxification treatment course. **Results:** The levels of SP in plasma and PBMCs isolated from 48 opioid dependent subjects on methadone maintenance were significantly higher than 29 normal control subjects. There was no correlation of SP levels with age, gender, and race in the study subjects. In contrast, SP mRNA levels in PBMCs from 50 Chinese opioid dependent subjects decreased during the course of opioid withdrawal. **Conclusion:** Since SP is implicated in depression, anxiety, and stress, our data suggest a possible cellular mechanism responsible for psychiatric disorders often seen in opioid dependent individuals. In addition, these data suggest that SP may serve as a cellular marker of opioid abuse. Further, our study provides compelling evidence to support future investigations on therapeutic approaches of using SP antagonists for the treatment of opioid abuse-mediated psychiatric disorders.

614 BUPROPION REDUCES SOME OF THE SYMPTOMS OF MARIHUANA WITHDRAWAL IN CHRONIC MARIHUANA USERS

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There are currently no approved pharmacotherapies for treating cannabis dependence. Despite prior negative results in another laboratory, we have had encouraging pilot results and so designed a double-blind, placebo-controlled study to test the effectiveness of bupropion (Zyban® SR) to reduce withdrawal symptoms in chronic, heavy marijuana users. Presently, 11 men and 4 women have been randomized and 9 subjects (6 men, 3 women) have completed 21 days of medication. Bupropion was used in the method currently recommended for tobacco cessation: 150 mg (or placebo) taken once a day for days 1-3 and then taken twice a day (total dose of 300 mg/day) for the remainder of the study. Subjects maintained their usual marijuana intake until Quit Day (day 8), after which they were required to cease intake of THC products for the remaining 14 days. Dependent measures included daily completion of a 28-item adjective check list, a sleep log, and a computerized performance assessment battery (for logical reasoning, memory, reaction time, and sustained attention). A Withdrawal Discomfort Score, based on a subset of 10 adjectives, revealed that for 7 days immediately following cessation, placebo-treated subjects reported more symptoms than bupropion-treated subjects. Bupropion did not affect craving for marijuana: Both groups reported similar increases during the cessation period. However, those randomized to the bupropion treatment arm were more likely to complete the study than those randomized to the placebo arm (83% completion for bupropion vs. 44% completion for placebo). Bupropion increased subjective ratings of sleepiness on the Stanford Sleepiness Scale and caused poorer performance on the sustained attention task. Other measures of sleep and performance were not different between the two groups. These results suggest that bupropion may be useful for alleviating marijuana withdrawal symptoms and be useful in subject retention during long-term cessation programs. Supported by NIDA Grants DA017275 (DP) and DA000343 (SEL).

616 GAMMA-VINYL GABA INHIBITS COCAINE-PRIMED RELAPSE BY A DA-INDEPENDENT MECHANISM IN RATS

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Previous studies demonstrate that gamma-vinyl GABA (GVG), an irreversible GABA transaminase inhibitor, inhibits the acute rewarding effects of cocaine and other drugs of abuse. In the present study, we investigated whether and how GVG inhibits cocaine-primed relapse in laboratory rats. We found that systemic administration of GVG (25-300 mg/kg i.p.) dose-dependently inhibited cocaine-induced reinstatement (relapse) of extinguished drug-seeking behavior in rats. However, the mechanism appears to be dopamine (DA)-independent, because the same doses of GVG failed to alter cocaine-induced increase in extracellular DA in the nucleus accumbens (NAc) in rats during reinstatement testing or in naïve rats. Similarly, GVG alone, when administered systemically or locally into the NAc, also failed to alter the basal levels of extracellular DA. In contrast, GVG pretreatment produced an additive or synergistic effect on cocaine-induced increases in extracellular glutamate, whereas GVG alone mildly elevated extracellular glutamate. Finally, cocaine priming did not significantly alter extracellular GABA levels in the NAc, while GVG dose-dependently elevated extracellular GABA levels, when administered systemically or locally into the NAc. Such an increase in GABA appears to be derived predominantly from reversal of GABA transport, because blockade of type 1 GABA transporters by SKF89976A prevented, but blockade of voltage-dependent sodium channels by tetrodotoxin failed to alter GVG-induced increases in extracellular GABA levels. Together, the present study, for the first time, suggests that GVG dose-dependently inhibits cocaine-primed relapse by a mechanism correlated to GVG-induced increase in GABA and/or glutamate, but not to a decrease in cocaine-induced increase in DA in the NAc.

617 VACCINATION AGAINST NICOTINE DOES NOT PREVENT NICOTINE-INDUCED CHANGES IN FETAL NICOTINIC RECEPTOR BINDING AND C-FOS mRNA EXPRESSION

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Gestational exposure of rats to nicotine produces long-lasting alterations in brain development. Vaccination of adult female rats against nicotine has been shown to reduce the distribution of maternally administered nicotine to fetal brain. In the current study, the effects of vaccination on nicotine-induced changes in fetal 3H-epibatidine binding and c-fos mRNA expression were evaluated using tissue from a previous pharmacokinetic study of vaccination. A nicotine dosing regimen designed to resemble nicotine intake in a smoker (0.03 mg/kg i.v. every 14 minutes for 16 h/day, total dose 2 mg/kg/d of the base) was administered from GD1-20. Nicotine levels in fetal brain 25 min after a nicotine dose were substantially reduced by vaccination, whereas the chronic accumulation of nicotine in fetal brain was not. Gestational nicotine exposure increased fetal 3H-epibatidine binding on GD20 by 83% in whole brain and 84% in spinal cord, and decreased c-fos mRNA expression by 44-62% in various fetal brain regions and lung. Vaccination did not alter these effects. These data suggest that nicotine dosing, using a clinically relevant intermittent bolus dose regimen, produces substantial changes in fetal nicotinic receptor and c-fos mRNA expression. The decrease in c-fos mRNA expression contrasts with previously reported increases, and suggests that the nicotine dosing regimen used may influence its effects. The lack of effect of vaccination suggests that the cumulative exposure of fetal tissues to nicotine may influence the measured parameters to a greater extent than peak exposure levels. Supported by grants DA015668, DA10618 and P50-DA13333

618 THE DIFFERENTIAL NEUROPLASTICITY HYPOTHESES OF DRUG ADDICTION: THE HYPOTHESES AND ELECTROPHYSIOLOGICAL EVIDENCE

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Drug addiction is characterized by differential changes in motivated behavior. As drug seeking and taking increase and become compulsive, other motivated behaviors show signs of weakening. Drug addiction is caused by drug-induced neuroplasticity. However, drug-directed behaviors and other motivated behaviors are mediated by overlapping neuronal circuits. One must therefore ask how chronic drug effects might lead to differential changes in behavior that define addiction. The Differential Neuroplasticity hypothesis provides a theoretical framework that may be helpful in addressing this question. It is hypothesized that neurons that contribute to drug-directed behavior and neurons that do not are differentially activated during drug taking and that the associated differences in patterns and rates of firing make the two groups of neurons differentially susceptible to activity-dependent acute effects of drug. The differential acute effects of drug, in turn, contribute to differential long-lasting plasticity. The differential plasticity is proposed to contribute to a lasting facilitation of drug-related neural signals and suppression of signals related to behaviors other than drug seeking and taking. This differential change in signaling is expected to lead to a selective strengthening of drug-directed behaviors and a general weakening of other motivated behaviors. Initial electrophysiological investigations of this hypothesis in animals self-administering cocaine suggest that accumbal neurons that exhibit phasic and tonic excitatory responses during the drug session are less sensitive to the acute inhibitory effects of cocaine than are other neurons. Additional evidence indicates that the two groups of neurons also undergo distinct changes in basal firing across a 30-day regimen of cocaine self-administration. Neurons that are responsive to drug-related events show either no change or an increase in basal firing; whereas, other neurons show a significant decrease. These findings are consistent with basic predictions of the hypothesis.

619 EFFECTS OF THE DELTA OPIOID RECEPTOR AGONIST SNC80 ON INTRACRANIAL SELF-STIMULATION IN RATS

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Central administration of peptidic delta opioid agonists has been reported to produce reinforcing effects in preclinical assays of drug self-administration, conditioned place preference and facilitation of intracranial self-stimulation (ICSS) in rodents. Conversely, we have shown that intravenous administration of the systemically active, non-peptidic delta opioid agonist SNC80 does not maintain drug self-administration in non-human primates across a broad range of conditions. To extend this line of investigation, the present study assessed the effects of SNC80 on ICSS in rodents. Sprague Dawley rats implanted with electrodes in the lateral hypothalamus were tested on a FR1 schedule of reinforcement to respond for electrical stimulation. Response rates were measured across a descending series of 15 current frequencies, and rate-frequency curves were determined under baseline conditions and after treatment with SNC80 (0.1-10 mg/kg, s.c.), amphetamine (0.1-1.0 mg/kg, i.p.) or the kappa agonist U69593 (0.1-0.56 mg/kg, i.p.). As reported previously, amphetamine produced leftward shifts in rate-frequency curves and decreased ICSS thresholds, whereas U69593 produced rightward shifts in rate-frequency curves and increased ICSS thresholds. In comparison, SNC80 did not produce lateral shifts in rate-frequency curves or alter ICSS thresholds, suggesting that it does not produce abuse-related effects in this procedure. However, the highest dose of SNC80 significantly decreased rates of responding. Peak effects of SNC80 were obtained within the first 15 min and had subsided by 45 min post-injection. The potency and time course of SNC80 are consistent with results from earlier studies in rodents and non-human primates. Taken together, these findings suggest that systemically administered SNC80 fails to produce abuse-related effects in rats as well as in non-human primates. (Supported in part by R01-DA11460 from NIDA, NIH).

620 10-YEARS' COURSE OF ALCOHOL USE AND ALCOHOL DEPENDENCE FROM ADOLESCENCE TO ADULTHOOD: FINDINGS ON ONSET AND STABILITY FROM A PROSPECTIVE COMMUNITY STUDY

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Objectives: To estimate 10 years incidence and stability of alcohol use and DSM-IV alcohol dependence and to examine factors influencing onset and stability between adolescence and adulthood. Methods: Data from the 10 years follow-up of the prospective longitudinal EDSP-study were used. This epidemiological study is based on a randomly drawn community sample of adolescents and young adults (N=3021) from Munich, Germany. The DSM-IV version of the Munich Composite International Diagnostic Interview was used to assess alcohol use and diagnostic status at baseline and follow-up. Results: At baseline 81.9% had used alcohol more than twelve times. Occasional use was most frequent (39.7%) followed by regular use (31.4%). The proportion of lifetime hazardous users was 5.3%, and of lifetime alcohol dependence 5.6%. 10-years incidence rates of regular use (49%) did not differ across age groups but incidence rates of hazardous use (7.0% vs. 6.2%) and dependence diagnoses (9.8% vs. 4.6%) were higher in younger age-cohorts. About 50% of those with a hazardous use pattern or DSM-IV dependence at baseline also fulfilled dependence criteria or had a hazardous use pattern in the twelve month before the follow-up investigation. Transitions from occasional or regular use to hazardous use or dependence were predicted by depressive disorders (ORs of 1.7-3.3). Nicotine dependence (OR=2.1; 95%CI 1.4-3.1) and regular cannabis use (OR=2.0; 95%CI 1.3-3.1) reduplicated risk. However, stability was solely predicted by social phobia (OR=8.2; 95%CI 2.3-29.1) and a higher quantity and frequency of use (OR=2.8; 95%CI 1.1-7.7). Conclusions: Incidence of alcohol use and dependence seems to rise in younger age cohorts. The onset of hazardous use and dependence between adolescence and adulthood seems to be affected by nicotine dependence and cannabis use, yet, stability is lower compared to findings among adults from other studies.

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- 621 NICOTINE SENSITIZATION IN A RODENT MODEL OF PSYCHOSIS: A COMPARISON OF BDNF IN THE NUCLEUS ACCUMBENS OF ADULT AND ADOLESCENT RATS**
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Perna, M.K. Maple, A.M., Correll, J. A., Brown, R.W. Dept. of Psychology, East Tennessee State University, Johnson City, TN 37614. We have demonstrated that neonatal quinpirole (D2/D3 receptor agonist) treatment to rats produces long-term priming of the dopamine (DA) D2 receptor that persists throughout the animal's lifetime. In Experiment 1, the offspring of six male-female Sprague-dawley (SD) rat breeder pairs were administered one daily i.p. injection of quinpirole (1mg/kg) or saline from postnatal days 1-21 (P1-21) and raised to adolescence. Beginning on P31 all animals were administered one i.p. injection of 0.5 mg/kg free base nicotine tartarate every other day for three weeks. Results showed that D2-primed adolescent rats did not demonstrate nicotine-induced hypoactivity early in training as controls administered nicotine demonstrated equivalent levels of sensitization as compared to controls administered nicotine by the end of training. In Experiment 2, offspring of seven breeder pairs were given the identical neonatal drug treatment as in Experiment 1 but raised to adulthood (P60). Although initial hypoactivity did not differ across groups, D2-primed rats given nicotine demonstrated significantly more robust sensitization than controls given nicotine. One day after testing, brain tissue was taken and the nucleus accumbens and frontal cortex were dissected away from the rest of the brain. Although frontal cortex is yet to be analyzed, we found that neonatal quinpirole treatment produced a significant decrease in nucleus accumbens BDNF in both adolescent and adult rats that was alleviated by nicotine. This is similar to past work from our laboratory that has shown nicotine alleviated significant decreases of hippocampal BDNF produced by neonatal quinpirole treatment. These results suggest that sensitization to nicotine in D2-primed rats is dependent upon age, and nicotine alleviates the decreases in neurotrophins produced by neonatal quinpirole treatment in a brain area associated with addiction.
- 622 PHOSPHORYLATION OF AKT IS DECREASED IN THE NUCLEUS ACCUMBENS OF RATS TREATED ACUTELY WITH COCAINE IN A BINGE-PATTERN**
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Akt signaling has been suggested to act as a regulator of dopamine-mediated behaviors in addition to its classical role as a growth-promoting serine/threonine kinase. Here we tested the ability of cocaine to regulate Akt phosphorylation in the striatum of rats. Animals were injected with cocaine or saline in a binge-pattern, which consisted of 3 daily injections of 15 mg/kg cocaine or 1 ml/kg saline spaced one hour apart, for 1, 3 or 14 days. Animals were killed 30 minutes following the last injection. Nucleus accumbens and caudate putamen were rapidly dissected and tissues were prepared for Western blot analysis of phosphorylated and total Akt protein levels. Phosphorylation of Akt on the threonine308 residue was significantly reduced in the nucleus accumbens, but not the caudate putamen, in response to 1-day binge-pattern administration of cocaine. Time course data show that this effect was not present after 3 or 14 days of cocaine administration. No changes in total Akt protein levels were observed in any treatment group. These data show that acute cocaine exposure influences Akt phosphorylation and, hence, activity. Further studies are underway to identify down-stream targets of Akt that are in turn modulated by cocaine. [This work was supported by grants from NIDA/NIH: DA009580 (EMU) and DA018326 (EMU).]
- 623 REINSTATEMENT OF COCAINE-SEEKING BEHAVIOR IN RATS SELECTED FOR HIGH OR LOW IMPULSIVITY OR SACCHARIN INTAKE: SEX DIFFERENCES**
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Rats selected for high (HiI) impulsivity and those selectively bred for high (HiS) saccharin intake acquired cocaine self-administration faster than their low-responding (LoI, LoS) counterparts. This study extended these findings to the reinstatement phase and added a male/female comparison. Eight groups were compared: HiI Females (HiIF), LoIF, HiI Males (HiIM), LoIM, HiSF, LoSF, HiSM, and LoSM. HiI and LoI rats were selected based on performance on a delay discounting task for food that offered a choice of a small immediate or large delayed reward with a delay that increased after responses on the delay lever and decreased after responses on the immediate lever. A mean adjusted delay (MAD) was calculated for each session/rat, and this value was used to categorize rats. HiS and LoS groups were based on selective breeding. Rats were implanted with an i.v. catheter and trained to lever press under a fixed ratio (FR) 1 schedule for 0.4 mg/kg cocaine in 2 h sessions for a 10-day maintenance phase. Next, cocaine was replaced by saline for 14 days (extinction). Saline- and cocaine- (5, 10, and 15 mg/kg, i.p.) induced reinstatement of drug-seeking behavior was then measured over 6 days with saline and cocaine given on alternate days. HiIM and F and LoIM and F rat showed similar patterns of cocaine maintenance and extinction. In contrast HiSM and F rats self-administered significantly more cocaine than LoSM and I rats during the maintenance phase, and they were slower to extinguish lever press responses when cocaine was replaced by saline. Both HiI and HiS male and female rats had significantly greater reinstatement of drug-seeking behavior following the 15 mg/kg cocaine priming injection than LoI and LoS rats. High levels of impulsivity and saccharin consumption predicted greater reinstatement of drug-seeking behavior. Females exceeded males in maintenance, extinction, and reinstatement. Male/Female, HiI/LoI, and HiS/LoS rats are useful models for studying vulnerability to drug abuse. Supported by R01 DA03240 and K05 DA15267 (MEC).
- 624 TREATMENT GOALS INDICATE MOTIVATION**
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Motivation to change is typically assessed with either a measure of when one plans to change (e.g., Stage of Change) or a measure of strength of motivation (e.g., Contemplation Ladder). Another possible measure is smoking goal (e.g., abstinence vs. reduction). We recruited 188 tobacco smokers to a natural history study in which they reported cigarettes per day daily for 28 days via phone. We selected 37 smokers with a goal to quit abruptly, 43 with a goal to quit gradually, 43 with a goal to reduce only and 65 who planned to not change over the next month. Outcomes were the incidence of quit attempts (> 24 hours of abstinence) and reduction (> 25% from baseline cigarettes per day). Participants with a goal to quit abruptly were most likely to quit or reduce (57%), followed by those with a goal to quit gradually (44%), followed by those with a goal to reduce only (37%), followed by those with a goal to not change (10%) (Bartholomew's test for trend, $p < 0.0001$). Similar results occurred when only quit attempts were examined: 43% vs. 21% vs. 14% vs. 5% ($p < 0.0001$). Although half (50%) of smokers who planned to change did quit or reduce, few met their exact goal: 29% of those with a goal to quit abruptly did so, 16% of those with a goal to quit gradually did so and 23% with a goal to reduce only did so. The major liabilities of the study were a small, volunteer sample and absence of data on long-term success. Our results suggest goals for change indicate strength of motivation to change; i.e., those who planned to quit abruptly appeared to be the most motivated. These results are consistent with the clinical notion that drug users with a goal to reduce first are less motivated to quit. They are also similar to prior studies on "commitment" to abstinence among alcohol, cocaine, and opiate users (Hall et al., JCCP 58: 175).

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625 MALE-FEMALE DIFFERENCE IN RISK OF RAPID TRANSITION TO DEPENDENCE AMONG RECENT ONSET TOBACCO AND ALCOHOL USERS IN PERU

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BACKGROUND & AIMS: In this work we seek to estimate possible male-female differences in risk of developing a dependence syndrome soon after onset of tobacco smoking and alcohol beverage consumption (i.e., within 24 months of starting use). For this purpose, we adapt epidemiologic survey methods now widely used in the USA. **METHODS:** The study data are from the Peruvian National Household Survey on Drug Abuse we conducted during 2002, with a representative sample of urban residents 12-64 years (n=4,850). **RESULTS:** A total of 472 respondents had just started to smoke tobacco; among these, an estimated 8% developed the tobacco dependence syndrome within 24 months of first use. The risk of rapid transition to dependence was 3 times greater for male smokers, as compared to female smokers ($p < 0.01$). Regarding alcohol, 654 respondents had just started to drink alcohol, of whom 3%-4% made a rapid transition to alcohol dependence (within 24 months of onset), again with three-fold excess risk for males ($p < 0.05$). **DISCUSSION:** These new findings from Peru are both convergent with recent evidence from the USA (e.g., for male excess in alcohol dependence, see Wagner & Anthony, under review) and non-convergent (e.g., for no male excess in tobacco dependence, see Storr et al., 2004). Aspects of traditional culture and gender-specific roles may continue to protect Peruvian women from rapid-onset tobacco dependence whereas this appears no longer to be the case in the USA. **SUPPORT:** DEVIDA –Belgian Technical Cooperation, Lima, Peru.

626 ALCOHOL USE AND BODY IMAGE AMONG ADOLESCENT EXPERIMENTAL SMOKERS

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Greater emphasis has been placed on adult than youth smokers in the literature. Likewise, more work has been focused on regular than experimental or light smokers. The current pilot study examined alcohol use and body image among 29 smoking teens (mean = 18 cigarettes per week, SD = 28) who enrolled in an intervention program to prevent nicotine dependence in Richmond, Virginia. We have a small, yet rich, dataset and plan to achieve a sample size of at least 40 by June, 2006. The sample is 55% male, 55% African-American, and 31% Caucasian, with a mean age of 15.6 (SD = 1.7) years. Participants started using alcohol (86%) when they were 13.7 (2.3) years old and tobacco when they were 13.9 (1.9) years old. Teens noted an average of five alcohol-related problems when drinking heavily (e.g., vomiting, hangovers, regretted actions, trouble with parents). Participants reported a body mass index of 23.4 (6.3), which is in the high-normal range, and desired a BMI of 19.5 (5.5), which would be in the low-normal range. They reported being moderately satisfied with their bodies and that they sometime use smoking for weight management. Thinner teens and those with a better body image initiated alcohol use earlier ($r = .43, p < .05$). Those who used smoking as a weight management strategy were more frequent users of alcohol and experienced more alcohol-related problems ($r = .41, p < .05$). These data point to a connection between body image issues and drug use in teens. The results are of particular interest given the diversity of the sample and the similarity between the genders on relevant variables. Further analyses are planned to explore the full dataset in more detail (e.g., regressions). Research and clinical implications will be discussed.

627 US TRENDS IN AMBULATORY-CARE-OPIOID PRESCRIBING FROM 1993-2003

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BACKGROUND: Prescription opioid misuse has increased rapidly during the last decade. Opioid prescribing may contribute to the supply of abusable opioids, but little is known about how opioid prescribing patterns have changed during this time. **METHODS:** We used 11 years of survey data from the National Ambulatory Medical Care Survey, a nationally representative stratified cluster sample of ~30,000 physician office visits per year, to estimate how many US office visits included prescription of an opioid medication (an "opioid visit") to persons aged 12+ during 1993-2003, calculated rates using US Census denominators, and categorized opioid visits by type of opioid in order to explain overall trends. Linear time trends were estimated taking into account the survey design. **RESULTS:** Among 272,983 visit observations, we identified 11,327 opioid visits, representing ~32 million office opioid visits/year in the US, an average rate of .142 opioid visits per person per year (95%CI: .134-.149). Two pronounced time trends were evident: a significant increase in the opioid visit rate over the decade (.126 in 1993 to .166 in 2003, a 32% increase, $p < .001$ for trend) and a large shift in the types of opioids prescribed. Whereas codeine and propoxyphene visit rates declined (40% and 28%), visit rates for higher potency opioids such as hydrocodone and oxycodone increased (115% and 156%). Most of the opioid visit trend was explained by hydrocodone visits, which increased at a rate of ~1 million additional visits per year from 1993-2003 up to a total of 18 million hydrocodone visits in 2003 (95%CI: 14-22 million, 45% of all 2003 opioid visits). **CONCLUSIONS:** Opioid prescribing patterns in ambulatory care have changed markedly in the last decade. Co-occurring increases in opioid abuse and prescribing suggest that office visit prescribing may be one channel for the supply of abused opioids in the US.

628 METHAMPHETAMINE INJECTION IS INDEPENDENTLY ASSOCIATED WITH RECEPTIVE NEEDLE SHARING AMONG INJECTION DRUG USERS IN TIJUANA, MEXICO

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Objectives: Tijuana has the highest rate of illicit drug use in Mexico and injection drug use is a growing problem. We examined factors associated with receptive needle sharing among injection drug users (IDUs) to inform HIV prevention interventions. **Methods:** In 2005, IDUs >18 years old who injected in the last month underwent antibody testing for HIV, HCV and syphilis and an interviewer-administered survey. Multiple logistic regression identified factors associated with self-reported receptive needle sharing during the past 6 months. **Results:** Of 220 IDUs, 91% were male; median age and age at first injection were 34 and 19 years. Prevalence of HIV, HCV and syphilis was 2.8%, 95% and 14.1%, respectively. Drugs injected most were heroin alone (98%) methamphetamine alone (43%) and heroin and methamphetamine combined (64%); fewer (28%) injected cocaine. Non-injected methamphetamine (48%), heroin (49%) and tranquilizers (32%) were also common. Three quarters (77%) reported receptive needle sharing in the last 6 months, a practice independently associated with injecting methamphetamine (AOR: 2.52; 95% CI: 1.17, 5.39), shooting gallery attendance (AOR=2.73; 95% CI: 1.25, 5.94), injecting in the street (AOR: 2.87; 95% CI: 1.20, 6.93), ever being arrested for carrying used needles (AOR: 2.97; 95% CI: 1.36, 6.46), and ever receiving drug treatment (AOR=2.76; 95% CI: 1.28, 5.93). **Conclusions:** Receptive needle sharing was common in Tijuana, especially among methamphetamine injectors and IDUs who inject in shooting galleries or public places. Our data suggest policing policies in Tijuana may contribute to high risk injection behaviors and that interventions with police are needed. The association between drug treatment and needle sharing may be explained by the fact that existing programs are typically abstinence-based – only two methadone maintenance programs exist. Expanded access to sterile syringes and substitution therapies are greatly needed in Tijuana.

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- 629** ABSTINENCE FROM COCAINE DOES NOT MODIFY THE CEREBRAL METABOLIC EFFECTS OF COCAINE SELF-ADMINISTRATION IN THE PREFRONTAL CORTEX OF NONHUMAN L. Porrino, T. J. Beveridge, H. R. Smith and M. A. Nader, Wake Forest University Health Sciences, Winston Salem, NC
- The pattern of changes in cerebral metabolism associated with cocaine administration is dependent on the extent and magnitude of previous cocaine exposures. We have shown that alterations in metabolic activity accompanying cocaine administration within the prefrontal cortex of monkeys, as measured with the quantitative 2-[14C]deoxyglucose (2DG) method, shift from widespread activation following administration to drug naïve animals to a more restricted pattern including only limited medial and orbital cortical areas after chronic self-administration. However, the functional response of these brain regions following abstinence and then re-exposure to a single session of cocaine self-administration has not been described in this model. In the present study monkeys self-administered cocaine (0.3 mg/kg/infusion under a fixed-interval schedule) for a period of 100 days followed by either 1 (n=4) or 3 (n=3) months of abstinence and were compared to food-reinforced controls whose responding had been maintained by food under identical schedules (n=4) and had undergone similar abstinence. Following abstinence animals were exposed to a single session of cocaine or food self-administration in which all monkeys acquired the full number of available reinforcers. Immediately following the final reinforcer, local cerebral glucose metabolism was assessed via the 2DG method. Following both 1 and 3 months of abstinence cocaine produced significant decrements in metabolic activity throughout both the medial and orbital cortex extending rostrally from Area 10 caudally to the anterior insula. This response, although equivalent in magnitude to the changes in functional activity observed after 100 days of exposure to self-administration with no abstinence, involved a wider regional extent. These data suggest that even prolonged abstinence does not ameliorate the neuroadaptations associated with chronic cocaine exposure, at least those critical for the functional response to this drug. Supported by DA09085 and DA06634
- 630** IMPROVING TREATMENT PARTICIPATION ON PAROLE: THE CJ-DATS TRANSITIONAL CASE MANAGEMENT STUDY
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- A major obstacle to the effectiveness of post-prison treatment for substance-abusing offenders is low treatment engagement: the failure of parolees to show up for scheduled treatment and, if they do show up, their tendency to drop out early. At the systems level, there is a need to improve the transition process between prison treatment and community treatment to increase the likelihood that participants in prison treatment, supervised community correctional treatment, or work release treatment programs successfully enter their assigned community treatment placement upon release and remain engaged in treatment for a reasonable length of time. Successful re-entry also depends on parolees' identifying needs and obtaining needed services in the community. In order to address this re-entry problem, the Transitional Case Management (TCM) study seeks to test whether a strengths-based case management intervention offered during an offender's transition from incarceration to the community increases participation in community substance abuse treatment, enhances access to needed services, and improves outcomes (e.g., drug use, crime, employment). The study is part of NIDA's Criminal Justice Drug Abuse Treatment Studies (CJ-DATS) and involves the participation of five Research Centers. Two hundred inmates from each Center are being randomly assigned to the TCM group or to a Standard Referral group. Study participants are assessed at baseline (during incarceration) and at 3 and 9 months following release to the community. The study also includes an economic component that will assess the benefits and costs of the TCM model relative to standard parole services. Funded by NIDA Grant U01DA16211
- 631** MODELING PLEIOTROPY FOR FAMILY STUDY DATA: SUBSTANCE CONSUMPTION COMORBIDITY USING GEE-2 LINKAGE/ASSOCIATION JOINT ANALYSIS
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- Background: Identifying genetic variants and environmental factors of etiological importance for co-occurring substance abuse remains a difficult challenge. We previously demonstrated the utility of generalized estimation equations covariance modeling (GEE-2) for joint linkage/association analysis of single phenotypes in family data. Advantages of GEE-2 include the ability to model pleiotropy- a single genetic variant affecting multiple phenotypes - and GxE interactions. Using family data and incorporating linkage evidence reduces the likelihood of spurious association of putative genetic variants due to population stratification. Objective: To model jointly the association of single genetic variants and environmental covariates with, and the linkage of single genetic variants to, the co-occurrence of alcohol and nicotine consumption phenotypes. Method: Using the National Longitudinal Study of Adolescent Health (Add Health) Wave I data, the two phenotypes are the typical number of alcoholic drinks consumed in the past year, and the typical number of cigarettes smoked per day in the past month. DAT1, DRD4, 5HTT, CYP2A6, DRD2 are successively included in the GEE-2 models along with demographic, environmental and psychiatric symptoms. Results: So far, there are trends toward evidence of positive linkage for alcohol consumption, but negative linkage for cigarette smoking and cross-product covariance for DAT1, which is shown to have a positive ($p < .05$) pleiotropic association with the two phenotypes after controlling for significant phenotype-specific demographics. Conclusion: GEE-2 linkage/association joint analysis is a flexible method to model complex pathways leading to multiple substance abuse when putative genetic variants are already implicated, although it does not help explain biological mechanisms per se (supported by NIDA DA00221, DA016314, DA020922).
- 632** COCAINE ALTERS HIPPOCAMPAL AND STRIATAL PROGESTERONE AND ALLOPROGESTERONE LEVELS IN BOTH MALE AND FEMALE RATS
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- Acute and chronic cocaine administration increases plasma levels of progesterone in both male and female rats. This study aims to determine whether progesterone and its bioactive metabolite, allopregesterone (ALLOP), are altered in the hippocampus and striatum (areas known to modulate cocaine induced behavioral responses) after acute cocaine administration. To this end, intact male and female rats were administered 20 or 5 mg/kg of cocaine respectively. Thirty minutes after drug treatment rats were decapitated, brain removed and analyzed for progesterone and ALLOP using HPLC. In both sexes, progesterone levels in the hippocampus and striatum were increased after cocaine administration. In saline treated controls, female rats have overall higher levels of ALLOP in the striatum and hippocampus than male rats. After cocaine administration, no significant alterations were observed in the ALLOP levels in the hippocampus or striatum. These results demonstrate for the first time similarly to previously reports in progesterone serum, cocaine also increases progesterone levels in the brain. Moreover, due to the bioactive role of ALLOP, because females have higher overall levels of ALLOP in the striatum, sexual dimorphic pattern in ALLOP concentration levels may have important consequences in the known sex differences to cocaine. This work was supported in part by SCORE 506-GM60654 and SNRP NF 39534.

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633 MODERATE MARIJUANA USE EXTENDS RETENTION IN A CLINICAL TRIAL OF BEHAVIORAL NALTREXONE THERAPY FOR HEROIN DEPENDENCE

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The relationship between marijuana use and treatment outcome among participants completing an inpatient detox and initiating naltrexone use as part of a clinical trial comparing Behavioral Naltrexone Therapy (BNT, n=31) against Compliance Enhancement (CE; n=32) was investigated. Participants were 52 men (82.5%) and 11 women (17.5%). Approximately 30% were Hispanic (n = 19), 16% African-American (n = 10), and 54% Caucasian (n = 34). The average age was of 35.5 years (SD = 9.2). Marijuana use was quantified as the percent of urine samples testing positive for THC. Marijuana use was not related to the percent of opiate free urines or the number of days in treatment in the full sample. However, these relationships differed across treatment groups. Marijuana use was associated with a greater percentage of opiate negative urines ($r = 0.40, p = 0.24$) in the BNT group and a lower percent of opiate negative urines ($r = -.412, p = 0.18$) in the CE group. Marijuana use was not significantly related to the number of days in treatment in either treatment condition. Survival analyses (Kaplan-Meier method) testing the relationship between marijuana use (no use (0% urines positive for THC), intermittent use (1% to 79% of urines positive for THC), and consistent use (>79% of the urines testing positive for THC)) indicated the survival curves differed among the three marijuana use groups (Log rank = 12.2(df = 2), $p = 0.002$). Median survival times were 35 days, 133 days, and 35 days for the no use, intermittent use, and consistent use groups, respectively. Results indicate marijuana use is associated with opiate use and with treatment retention among opiate dependent patients seeking an outpatient Naltrexone based treatment program. However, the direction of these associations is moderated by the type of psychosocial treatment provided. Possible mechanisms will be discussed.

634 HIGH-RISK DRINKING, SUBSTANCE USE, AND RISK BEHAVIOR AMONG COLLEGE STUDENTS: A PRELIMINARY INVESTIGATION

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We compared high-risk drinking, substance use, and other risk behavior among a random sample of Greek affiliated (n=183) and non-Greek affiliated (n=642) college students. Hypothesis. We hypothesized that gender, age, number of sexual partners, experience of sexual coercion, and Greek membership would be associated with high-risk drinking, substance use, unprotected sex, and experience of violence. Procedures. The 44-item anonymous survey to assess health behaviors, which had a 40% return rate, was mailed to a random sample (N=825) of college students in 2002. Analyses. Descriptive and multivariate analyses were conducted to examine the variables of interest. Binge drinking was defined as 5 or more drinks in one sitting for males and 4 or more drinks for females. Results. Results from the descriptive analysis (which will be examined further using multivariate methods) indicate that among the total sample, there were no differences in gender with respect to high-risk drinking or sexual experience (i.e., being sexually active). However, males were more likely to experience violence shortly after consuming alcohol or other drugs, whereas females were more likely to experience forced sexual touching. Binge drinking was associated with substance use in the past year and month. Binge drinking, Greek membership, greater perceived personal HIV risk and lower perception of others' HIV risk were associated with having multiple sexual partners. These findings were significant after controlling for race, age, and gender. Implications. Educational and prevention programs that are gender specific, target psychosocial factors associated with binge drinking, as well as consider the cultural and normative behaviors that are associated with Greek affiliation and that facilitate risk behavior are likely to be effective in changing short- and long-term behavior among college students.

635 EFFECTS OF NOVEL N,N'-DODECANE-1,12-DIYL-BIS-3-PICOLINIUM DIBROMIDE ON NUCLEUS ACCUMBENS DOPAMINE RELEASE IN RATS SENSITIZED TO NICOTINE

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The mesolimbic dopamine (DA) system has been implicated in the rewarding effects of many drugs of abuse, including nicotine (NIC). We have shown that the novel nAChR antagonist N,N'-dodecane-1,12-diyl-bis-3-picolinium dibromide (bPiDDB) reduces intravenous NIC self-administration in rats and inhibits acute NIC-induced DA release and DA metabolites in the rat nucleus accumbens (nACB). The present study examined the effects of bPiDDB after repeated NIC treatment on nACB DA release in Sprague-Dawley rats, using in vivo microdialysis with HPLC-EC. Rats were pretreated with daily injections of NIC (0.4 mg/kg, once daily sc) or saline for 5 days and then were challenged with 0.4 mg/kg NIC or saline. Measurements of DA release were performed approximately 24 hr after the last injection of NIC. Results revealed increased basal levels of DA in the nACB dialysate following repeated NIC, compared to saline. The NIC challenge increased DA release in nACB, and the NIC-induced effect was blocked by pretreatment (15 min prior to NIC challenge) with the non-selective nAChR antagonist mecamylamine (4 mg/kg, sc). Similarly, pretreatment (15 min prior to NIC injection) with the novel nAChR antagonist bPiDDB (1 or 3 mg/kg, sc) dose-dependently attenuated the NIC-induced DA release in nACB. These results indicate that repeated pretreatment with NIC enhances basal DA levels in microdialysate from nACB, and bPiDDB likely acts as an antagonist at neuronal nAChRs to inhibit the effect of NIC in nACB. The ability of bPiDDB to inhibit the effect of NIC in nACB in rats previously sensitized to NIC and provides further support for bPiDDB as a lead compound with potential utility for the treatment of NIC dependence. (Supported by U19 DA 017548).

636 IMPULSIVITY AND TREATMENTS FOR SMOKING: A LABORATORY MODEL

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The present study investigated the relationship between a behavioral measure of impulsivity and the effects of a nicotine patch and voucher reinforcement in smokers. Smokers were randomly assigned to a 14-mg transdermal nicotine patch (n = 15) or a placebo patch (n = 15) group. All subjects attended three, 2 hr sessions in counterbalanced order: 1) low voucher magnitude, 2) high voucher magnitude and 3) control. Before each session, participants completed a behavioral task involving choices between small, immediate amounts of money (\$0.05 after 1-sec) and a larger, progressively increasing delayed amount of money (\$0.10 after 1, 30, 60, 90 and 120-sec). Then, participants were exposed to 4, 10-minute blocks, each separated by a 20-min cigarette free period. During each 10-min block, participants could earn money for each 30-second period that they did not take a puff from a cigarette. A standard ascending schedule of reinforcement, including a reset contingency, was used. The value of the high magnitude condition was 4 times the value of the low magnitude condition. During the control session, participants earned money regardless of whether they took a puff. Participants in both groups showed large reductions in the number of puffs taken when vouchers were introduced [$F(3,29)=32.509, p<.001$]. Active patch participants showed greater reductions in the number of puffs taken than placebo patch participants across all three conditions, although the difference was not statistically significant. There was a positive correlation between the total number of impulsive choices (i.e., small, immediate consequence) and the total number of puffs taken [$r(28)=0.41, p<.05$] and a negative correlation between the total number of impulsive choices and latency to the first puff [$r(28)=-0.46, p<.05$] during the high magnitude condition. These findings suggest that individual differences in the effects of voucher reinforcement may be related to individual differences in participant impulsive choice.

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637 DOES WORKING INCREASE THE RISK OF ADOLESCENT TOBACCO USE? AN EPIDEMIOLOGIC INVESTIGATION

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The links between adolescent work and substance use have been investigated by researchers using a variety of samples and statistical methods. However, little is known about whether these associations exist among youth in urban areas or whether going to work actually increases the risk for initiating substance-using behaviors. In the current study, data from the Secenc Generation of the Johns Hopkins University Prevention Intervention Research Center (JHU PIRC) Preventive Intervention Trials, a urban-based community cohort of approximately 800 youth followed since the first grade, is analyzed to investigate the specific links between adolescent work and tobacco-using behaviors. When at or around the tenth grade, young people who spend more than 10 hours per week working for pay are twice as likely to report using tobacco in the past 30 days than non-workers (Odds Ratio (OR)=2.2, 95% Confidence Interval (CI)=1.1, 4.3). This association holds even after adjustment for potential selection-effects, such as early externalizing behaviors, academic performance, peer affiliations, and parent monitoring. On the other hand, survival analysis indicates that youth who work more than 10 hours per week at wave 10 are more likely to initiate tobacco use earlier than youth who do not work or work less than 10 hours per week (Hazards Ratio (HR)=1.3, 95% CI=1.0, 1.8). Furthermore, among youth who have not yet used tobacco by the tenth grade, those who transition from not working in grade 10 to working in grade 11 have 8-times the risk of starting to use tobacco than youth who do not work in either wave (Relative Risk (RR)=8.0, 95% CI=2.8, 22.9). These results indicate a strong link between working and tobacco use. Researchers and policy makers should begin to look at the types of jobs youth hold and at workplace tobacco policies to ensure young peoples' early experiences working are beneficial to the personal development of these youth. Acknowledgements: DA018013, DA11796, MH57005.

638 PROXIMAL DEPRESSION SYMPTOMS, NOT DIAGNOSIS, PREDICTS CONTEXT OF RELAPSE AMONG SUBSTANCE-ABUSING YOUTH WITH AND WITHOUT COMORBID DEPRESSION

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The Youth Addiction Relapse Model suggests that affective disturbance will make substance use disordered (SUD) youth vulnerable to relapse in specific contexts after treatment. While diagnoses of internalizing and externalizing disorders do not appear to be related to relapse contexts, depression (DEP) symptoms experienced closer in time to first use after treatment are associated with relapse in negative intrapersonal contexts (e.g., coping with frustration/anger/boredom). This study compared contexts of SU relapse between SUD-only and comorbid (SUD/DEP) teens after inpatient treatment. Hypotheses were that DEP diagnosis would not be associated with relapse in specific contexts but that proximal DEP symptoms would be associated with relapse in negative intrapersonal, negative physiological (e.g., coping with pain, illness), and interpersonal (e.g., feeling criticized or rejected) states. Subjects were 174 SUD youth (45% female; mean age = 15.8 (SD = 1.2), 33% also had a lifetime DEP diagnosis. Youth and their parents signed consent and were interviewed separately while teens received inpatient SUD and psychiatric treatment, and again 6 mos and 1 yr posttreatment to gather detailed information about teen first relapse episodes. Hierarchical multiple logistic regression analyses were used to test five models predicting contexts according to Marlatt and Gordon's (1985) classification (negative intrapersonal, negative physiological, other intrapersonal, interpersonal, and social pressure situations). As predicted, a diagnosis of DEP was not associated with relapse in any of the five contexts. Youth who experienced posttreatment depressive symptoms were more likely to relapse in negative intrapersonal contexts (OR = 3.6, $p < .001$), and interpersonal contexts (OR = 3.1, $p = .001$) than their peers. Findings indicate that relapse prevention efforts should be targeted at reducing affective distress after treatment to reduce likelihood of relapse in common high-risk situations.

639 SEXUAL ABUSE AND DRUG INVOLVEMENT AMONG MIDDLE SCHOOL STUDENTS IN MEXICO CITY

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Exposure to violence is associated with drug involvement among adolescents. However, several questions remain to be answered, including: Is there a particular form of violence that has a greater effect on the risk of drug involvement and in the use of particular drugs? Do effects of violent victimization vary by gender? The present study is aimed at exploring one form of violence, sexual abuse, in relation with the use of tobacco, alcohol, marijuana, cocaine, inhalants, and psychotherapeutic drugs in a population of students of two middle schools located in downtown Mexico City. Methods. A total of 936 young participants (508 men, 428 women, mean age of 13.7 years), responded a self-administered questionnaire. Exposure to sexual abuse was assessed using an adapted question from a national student survey that specifically asked about lifetime sexual abuse. Drug use was assessed by asking if participants had used tobacco, alcohol, marijuana, cocaine, inhalant drugs, and psychotherapeutic drugs. Analyses were stratified by gender. GEE models will analyze profile responses of drug involvement. Results. An estimated 12% of the girls and 4% of the boys reported sexual abuse by a person at least five years older than them ($\chi^2 = 22.2, p < .001$). Males who were sexually abused had higher rates of alcohol use than those who had not been abused (83.3% vs. 59.5%, $p < .05$), inhalants (31.6% vs. 5.4%, $p < .001$) and cocaine (16.7% vs. 4.7%, $p < .05$). Females who suffered sexual abuse had higher rates of use of tobacco (42.0% vs. 27.1%, $p < .05$), alcohol (74.5% vs. 56.1%, $p < .001$), tranquilizers (20.0% vs. 6.9%, $p < .01$) and amphetamines (10.0% vs. 3.3%, $p < .05$). Comment. Limitations considered, these results can be useful to illuminate the discussion of the relationship between sexual abuse and drug involvement. Acknowledgement. CONACYT, Mexico, grant 25902H, NIDA, grant, DA12390, and NCMHHD, grant MD002217.

640 GENETIC INFLUENCES ON THE RELATIVE REINFORCING VALUE OF NICOTINE

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This pharmacogenetic investigation examined the effects of naltrexone, a mu opioid receptor antagonist medication, and the functional mu opioid receptor (OPRM1) A118G polymorphism on the relative reinforcing value of nicotine. In a within-subject, double-blind study design, 30 smokers of each OPRM1 genotype (A/A vs A/G or G/G) participated in two experimental sessions following 4 days of naltrexone vs. placebo. On day 4, Participants were tested for the relative reinforcing value of nicotine using a cigarette choice paradigm that evaluates choice of 0.6mg vs. 0.05mg Quest cigarettes after a brief period (2hr) of nicotine abstinence. The main finding of this study was a significant gender by OPRM1 interaction; among females, the G allele was associated with a reduced relative reinforcing value of nicotine and among males there was no effect of OPRM1. The effect of medication phase was not significant. We subsequently genotyped our sample for a common functional Val108Met polymorphism that influences levels of COMT (catechol o-methyl transferase) enzyme, which degrades dopamine and metabolizes estrogen. We observed a significant COMT by gender interaction in the hypothesized direction; among females (n=21), the low activity Met/Met genotype was associated with a lower relative reinforcing value of nicotine. In a post-hoc analysis, women with the Met/Met genotype showed a further reduction in nicotine choices while on naltrexone as compared to placebo treatment. THIS RESEARCH WAS FUNDED BY A TRANSDISCIPLINARY TOBACCO USE RESEARCH CENTER NCI/NIDA P5084718 AND RO1 DA-017555-03.

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641 MARIJUANA ARRESTS: INFLUENCES OF ETHNICITY, GENDER, BLUNTS VS. JOINTS, AND MARIJUANA ETIQUETTE

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Problem: Thousands of persons, mainly young adults, are stopped and arrested annually for marijuana smoking and possession in New York City. Substantial racial disparities are evident. **Background:** The blunts (marijuana in a cigar shell) subculture is popular among African-American and Latino males young adults. Joint subculture participants are typically older whites, females, employed, and endorse marijuana etiquettes. **Hypothesis:** The ethnic disparities in police stops or arrests for marijuana violations are mediated in part by blunts smoking and endorsement of marijuana etiquette items. **Methods:** A peer group questionnaire was completed by groups of youths where one was a marijuana user. Marijuana users (N=514) were classified as: 1) blunts users (40%)—prefer and regularly smoked marijuana as blunts and seldom use joints/pipes. 2) joints users (25%)—prefer and regularly smoke marijuana as joints and rarely use blunts. 3) mixed users (35%)—report using marijuana as joints and blunts. **Findings:** African-Americans and Latinos and blunts users were most likely to be stopped/arrested. Females and those endorsing marijuana etiquette items had low police contacts. **Logistic regression:** Female marijuana users are less likely than males to be stopped (Odds Ratios ~ .38) or arrested (OR ~ .25). Likewise, blunts users are significantly more likely than joints users to be stopped (OR ~ 2.4, 3.3) and to be arrested (OR ~ 5.0, 5.3)—even after controlling for gender, ethnicity, and age. Latinos are more likely than whites to be stopped in the past year (OR ~ 4.0) and arrested (OR ~ 3.5, 6.0); blacks are somewhat more likely than whites to be arrested (OR ~ 2.4, 3.9). The mediating influence of etiquettes was small. **Conclusions:** A neglected lifestyle factor—being a blunts (or mixed) user—is more important than ethnicity in the risk of a marijuana-related arrest among these respondents. Ethnic disparities are not eliminated and only modestly reduced.

642 EXTRACELLULAR PROCESSING OF BETA-ENDORPHIN IN THE RAT STRIATUM AND CEREBROSPINAL FLUID: EVIDENCE FOR THE EXTRACELLULAR ACTIVITY OF INSULIN-DEGRADING ENZYME

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Beta-endorphin (BEND), an endogenous opioid peptide with high affinity for the mu opioid receptor, has been shown to be involved in drug reward. The potential for in vivo biotransformation of BEND in the extracellular space following release has not been previously directly addressed. We have extended our recent studies of BEND extracellular processing, using antibody-directed immunoprecipitation studies and kinetics studies to support the notion that insulin-degrading enzyme (IDE) is directly involved in β -endorphin processing. Utilizing microinfusion/microdialysis and MALDI mass spectrometry, we studied BEND biotransformation in the striatum of Fischer rats, we observed rapid cleavage resulting in BEND (1-18), as well as several fragments resulting from further N-terminal degradation. Further, incubation of BEND with the wash fluid of isolated striatal slices in vitro resulted in several BEND fragments, including BEND (1-18), (1-17), (2-18), (2-17), (18-31), (19-31), and (20-31). Addition of bestatin, an aminopeptidase inhibitor, prevented observation of BEND (20-31), (2-17) and (2-18). A metal chelator, 1,10-phenanthroline, inhibited all observed cleavage of BEND. Studies of rat cerebrospinal fluid (CSF) revealed enzymatic cleavage of full-length BEND, resulting in BEND (1-17), (1-18), (18-31), and (19-31). Co-incubation with bestatin had no effect on the observed cleavage pattern, whereas 1,10-phenanthroline inhibited cleavage. The observed pattern of cleavage sites (Leu17-Phe18 and Phe18-Lys19) is consistent with published in vitro studies of purified IDE cleavage of BEND. The enzyme inhibitor susceptibility of the CSF enzyme activity is also consistent with that of IDE. Using a monoclonal antibody directed against IDE, we were able to immunoprecipitate enzyme activity present in CSF. An extracellular localization of functional IDE in the brain has not been prior established. Support: DA00049, DA05130 (MJK), NCRR Grant RR00862 (BTC)

643 CLUB DRUG FOCUS GROUPS: TALES FROM THREE CITIES

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This presentation highlights findings from fifteen focus groups conducted with adolescent and young adult Club-drug users in St. Louis, Miami, and Sydney. The focus groups were conducted as part of a NIDA funded Tri-City study examining the diagnostic nosology of Ecstasy (MDMA), Ketamine, GHB, and Rohypnol. The characteristics of the sample of 71 were: 70% male, 62% white, and 68% were 15-25 years old. A number of themes emerged from this data noting similarities and differences between sites. Ecstasy was the most popular club drug reported at all three sites, although there were differences in the way the drug was perceived. Ecstasy use was positively regarded by all users. Specifically, focus-group participants described an emotional closeness with others while on the drug, as well as experiencing feelings of trust from which one could tell another person one's true feelings. While all participants described heightened physical sensations and feelings of connectedness to other users, St. Louis users framed these experiences as having a spiritual nature producing altered states of consciousness much as has been described for LSD in the 60s. Participants from Sydney described similar sensations but did not equate them with any spiritual experience, and even downplayed feelings of emotional closeness described in St. Louis. Another difference involved the description of the low feeling following the high of taking Ecstasy. Occurring approximately 24 to 48 hours post use, St. Louis users described this low as "Suicide Tuesday." As a combination of lethargy, depression, and low energy participants at all three sites described different ways of dealing with these negative feelings. For example, some users relied on using Prozac, or other drugs, to overcome this low while other users simply slept the whole day. Importantly, all users were largely incapacitated by this state, unable to maintain normal roles and responsibilities. This paper will outline these and other differences in the perceptions and experiences of Ecstasy users, as well as describe how these findings can inform the nosology of Ecstasy (MDMA) use.

644 A DOUBLE-BLIND, PLACEBO-CONTROLLED ASSESSMENT OF ARIPIPRAZOLE EFFECTS ON METHAMPHETAMINE CRAVING: INPATIENT LONGITUDINAL AND CUE REACTIVITY STUDIES

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According to the dual-deficit model, withdrawal from prolonged exposure to stimulants (cocaine, methamphetamine) results in synaptic deficits of dopamine and serotonin. This model predicts that pharmacotherapies that correct these neurochemical deficits will be effective in treating stimulant addiction. Aripiprazole, an antipsychotic agent acting on both dopamine and serotonin systems, may have potential as a treatment for methamphetamine addiction. To investigate this, we have recently completed a double-blind inpatient clinical pharmacology study assessing interactions between intravenous methamphetamine (15 mg and 30 mg i.v) and oral aripiprazole (15 mg). In addition to these stimulant interactions, the effects of aripiprazole treatment or abstinence related craving and methamphetamine cue reactivity were evaluated. Cue testing involved handling methamphetamine smoking and injecting paraphernalia and viewing a video depicting methamphetamine abuse. Cue testing was performed at baseline and on the 9th day of treatment. Patient included non-treatment seeking, methamphetamine abusers (N=16), 18-45 years of age, with active drug abuse habits. Abstinence related craving, assessed every other day of the inpatient stay with the Brief Substance Craving Scale, demonstrated a moderate reduction in the aripiprazole group after the first week of treatment. Cue-induced methamphetamine craving, desire to use now, and nervousness ratings were also moderately reduced by aripiprazole treatment. The effects of aripiprazole on related measures of mood (POMS, BDI) and the psychiatric side effects of treatment will also be presented. The data from this study provide preliminary evidence that aripiprazole may be a useful medication for managing methamphetamine craving. Support Contributed By: N01DA-2-RFP-8838 and NIH NCRR MO1 RR00096

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- 645** PREMATURE DISCHARGE FROM OPIOID TREATMENT PROGRAMS: PATIENTS' PERSPECTIVES
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Length of stay in opioid treatment programs (OTP) is a strong predictor of positive treatment outcomes. Nevertheless, many patients leave treatment prematurely before achieving their treatment goals. To further understand premature OTP discharge in the context of a larger study on entry and retention in treatment, qualitative interviews were conducted with 17 patients who were discharged within 6 months of admission, 64.7% of whom were discharged within 90 days. In addition, program discharge summaries (n=14) were collected and compared to the patient explanations for no longer attending treatment. Based on analysis of patient interviews and program records several patterns emerged. From a program perspective, reasons for discharge included referral to another program (3; 21.4%), non-compliance with program rules (1; 7.1%), leaving program before completion of treatment plan (4; 28.6%), and incarceration (6; 42.9%). Patient reasons for no longer attending the program were more complicated and varied. Two patients left treatment after a life even that disrupted their routine. Four patients had a conflict with the OTP staff about program rules and regulations. Four patients no longer wanted to be on methadone. Of these four patients, two specifically stated they felt methadone "controlled" them in ways similar to heroin and they did not want to be "controlled" by any drug. One of the four went to a drug-free program for detoxification and remained drug free three months later. The most common reason for OTP discharge was incarceration (7; 41.2%). Implications of the patients' reasons for leaving treatment are discussed. Acknowledgements: NIDA DA 015842 and T32 DA07292.
- 646** POLYDRUG USE AS A RISK FACTOR FOR ATTEMPTED SUICIDE AMONG ADOLESCENTS IN PUERTO RICO
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Introduction. Suicide is a tragic and potentially preventable public health problem. Much of the research on suicide behavior has focused on adolescent depression and alcohol use, with less attention on illegal drug use and specifically polydrug use. The objective of this research was to determine the association between suicidal attempts and polydrug use among Puerto Rican adolescents. Methods. The study sample was comprised of 691 adolescents (12 to 15 years old) and their parents (n=940). This sample was selected from poor neighborhoods with one or more copping areas operating within them. Parents and their offspring were interviewed in their homes, utilizing a computer-assisted personal interviewing program. The Spanish version of the Composite International Diagnostic Interview (CIDI) assessed substance abuse and depression. Drug use was corroborated through saliva tests. Results. Of the 691 adolescents, 339 (49.1%) were males and 352 (50.9%) were females. Almost 50% of the sample was 14 to 15 years old (49.2%) and more than 50% were between seven and eight grade (52.6%). The overall suicide attempt prevalence was 4.7%. Multiple logistic regression analysis revealed that females (OR=2.9, p=0.022) those who met criteria for depression (OR=7.5, p<0.001) and those who use alcohol (OR=4.1, p=0.002) were more likely to be suicidal attempters. Polydrug users (OR=16.1, p<0.001) who use alcohol and other illegal substances simultaneously (marihuana, cocaine and/or heroin) were significantly more likely to attempt suicide. Parent substance use was not statistically associated with the suicidal attempt of their offspring. Conclusions. Results of this study show a positive association between polydrug use and suicidal attempts among Puerto Rican adolescents, suggesting that Hispanic youth who use multiple substances may be at higher risk for a suicidal attempt independently of their depression condition.
- 647** QUESTION-BASED ASSESSMENTS OF DELAY DISCOUNTING: DO RESPONDENTS SPONTANEOUSLY INCORPORATE UNCERTAINTY INTO THEIR VALUATIONS FOR DELAYED REWARDS?
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Delay discounting is an index of impulsive choice, and numerous studies have shown addicted populations (e.g., alcohol, smoking, gambling) discount more (perform more impulsively) than never-addicted control participants (Bickel & Marsch, 2001). Delay discounting is typically assessed in humans with question-based measures in which respondents choose between delayed and immediate monetary amounts. These measures are believed to assess the extent to which subjective value for rewards is discounted specifically as a function of delay. However, delayed rewards are also uncertain. No research has examined the extent to which participants judge delayed rewards as also uncertain when completing delay-discounting measures. Thirty seven (18 females) participants between 14 and 16 years of age completed a delay-discounting measure, and immediately following answered questions (DDCQ questionnaire) about their certainty of receiving the delayed rewards if chosen. Delay-discounting and DDCQ data were analyzed using an area-under-the-curve method. It was hypothesized participants would rate the delayed rewards as increasingly uncertain with increasing delay to receipt, and that these certainty ratings would be correlated with rate of delay discounting. Self reports of alcohol, marijuana, and caffeine use also were collected. Results showed respondents did increasingly rate the delayed rewards as uncertain with increasing delay, and certainty ratings were correlated with delay discounting, $r(36) = .347, p = .04$ (one-tail test). Also, DDCQ ratings were correlated with self-reported alcohol use, $r(36) = -.280, p = .05$ (one-tail test). No other relations were significant. These results suggest respondents judge delayed rewards both in terms of delay and certainty when completing measures of delay discounting. This finding holds important implications for future addiction research in interpreting why addicted persons often discount more than non-addicted controls, i.e., delay to reward or uncertainty about delayed rewards?
- 648** PROTEOMIC ANALYSES OF HEROIN-INDUCED DIFFERENTIAL PROTEIN EXPRESSION BY NORMAL HUMAN ASTROCYTES
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The US is currently experiencing an epidemic of heroin use entangled with HIV-1 infection. The CNS is a common target for both HIV-1 and heroin. Astrocytes, integral components of the CNS, are reported to be susceptible to HIV-1 infection. Upon activation, astrocytes release a number of immunoregulatory products or modulate the expression of a number of proteins that foster the immunopathogenesis of HIV-1 infection. However, the role of heroin on the expression of the proteome of normal human astrocytes (NHA) has not been elucidated. We hypothesize that heroin modulates the expression of a number of proteins by NHA that foster the immunopathogenesis of HIV-1 infection. We utilized the proteomic method of difference gel electrophoresis (DIGE) combined with protein identification through high performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Our results show that heroin significantly (Student's t-test) dysregulates the expression of a number of proteins in NHA such as tryptophan 5-monooxygenase activation protein, cathepsin D preproprotein, reticulocalbin 1 precursor and ATP synthase. Several of these differentially expressed proteins were confirmed by western blot and their respective genes by real-time, quantitative PCR (Q-PCR) analysis. Identification of unique, heroin-induced proteins may help to develop novel markers for diagnostic, preventative and therapeutic targeting in heroin using subjects.

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649 TOWARD A BETTER UNDERSTANDING OF THE RELATIONSHIP BETWEEN GENDER AND CRACK/COCAINE USE

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Emerging literature suggests that inner-city substance-misusing women are more likely to use crack/cocaine than any other drug, yet little theoretical or empirical work addresses mediators of this relationship. To address this gap in the literature, the current study examined the role of theoretically relevant personality (i.e., negative emotionality, and impulsivity) and environmental (history of sexual abuse) variables as potential underlying mechanisms (i.e., mediators) of the relationship between gender and drug choice among 152 (37% female) patients receiving treatment for substance use in an inner-city residential treatment program. Results indicated that women were significantly more likely to use crack/cocaine than any other drug, and further were more likely to use crack/cocaine than men across current use and dependence status as well as lifetime use. Surprisingly, women evidenced higher levels of impulsivity than men. When considering lifetime drug choice, impulsivity mediated the relationship between gender and crack/cocaine use, yet mediation by impulsivity (or any other individual difference variable utilized) was not evident when considering current drug use and dependence. Negative emotionality and history of sexual abuse were related at a univariate level but not found to be mediators in any case. Together, these results suggest that impulsivity may underlie the choice of women to choose crack/cocaine when considered over their lifetime, and also suggest the need for the exploration of additional variables such as social context variables to account for current drug choice. Additionally, these findings raise important questions as to why women in this treatment setting would be more impulsive than men.

650 GENETIC AND ENVIRONMENTAL VULNERABILITIES UNDERLYING ADOLESCENT SUBSTANCE USE AND PROBLEM USE: GENERAL OR SPECIFIC?

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Are genetic and environmental risks for adolescent substance use specific to individual substances or general across substance classes? We examined this question in 645 monozygotic twin pairs, 702 dizygotic twin pairs, 429 biological sibling pairs, and 96 adoptive (biologically unrelated) sibling pairs ascertained from community-based samples, and ranging in age from 12-18 years. Substance use patterns and symptoms were assessed using structured psychiatric interviews. Biometrical model fitting was carried out using age- and sex-specific thresholds for (a) repeated use and (b) problem use, defined as one or more DSM-IV symptoms of abuse or dependence. We hypothesized that problem use would be more heritable than use in adolescence, and that both genetic and environmental risks underlying tobacco, alcohol, and marijuana use and problem use would be significantly correlated. Results of univariate analyses suggested significant heritable factors for use and problem use for all substances with the exception of alcohol use. Shared environmental factors were important in all cases and special twin environmental factors were significant for tobacco use, tobacco problem use, and alcohol use. Multivariate analyses yielded significant genetic correlations between each of the substances (for both levels studied), and significant shared environmental correlations among use variables only. Our results suggest that tobacco, alcohol, and marijuana problem use are mediated by common genetic influences, but shared environmental influences may be more substance-specific for problem use. Supported by NIH grants DA-13956, DA-12845, DA-11015, DA-05131, MH-01865, MH-43899, and HD-10333.

651 BUPRENORPHINE-ASSISTED TREATMENT IN A DRUG COURT PROGRAM

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The Detroit-Wayne County Buprenorphine assisted Drug Court treatment program was initiated in May 2005. It is ongoing. This poster presentation details the rationale for Buprenorphine therapy in a drug court program. Also presented are participant characteristics, assessment procedures, treatment methods and preliminary outcome data. Traditionally, Drug Court treatment programs are "drug-free", creating an initial problem for successful involvement of opiate-dependent drug court participants. Participants in this program are maintained on Buprenorphine for a maximum of nine months. Retention and engagement in treatment have been reliable predictors of positive treatment outcomes. It was believed that the use of Buprenorphine would have a direct impact on those outcomes as it has in other substance abusing populations. Also, the provision of psychiatric care for co-occurring disorders has been shown to improve treatment response. This program provides psychiatric care for co-occurring disorders. At induction, all participants are given a baseline diagnostic evaluation using the Structured Clinical Interview of DSM-IV Disorder (SCID), Addiction Severity Index (ASI), Millon Clinical Multiaxial Inventory - Third Edition (MCMI-III), Brief Symptom Inventory (BSI), Quality of Life Inventory (QOLI), and High Risk Behavior Scale (HRBS). Weekly urine drug screens are also collected. Participants with DSM Axis I diagnoses are provided psychiatric care. All participants attend weekly individual and weekly group therapy. Preliminary data collected during the first program year will be presented.

652 VARIABILITY OF ENDOGENOUS GHB CONCENTRATION IN TWO POPULATIONS

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Gamma-hydroxybutyrate (GHB) is a structural analog and a metabolite of gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the central nervous system. Originally used as a therapeutic agent, the molecule was gradually withdrawn from therapeutic use and mainly associated with other psycho-active substances in rave parties. Determination of GHB levels was carried out in non clinical and clinical studies but higher levels than those usually reported as physiological ones were described in forensic experts and then considered by toxicologists. In addition, the possibility of an endogenous GHB post-mortem production was advanced and was highlighted. Aim: To develop a reproducible, sensitive and specific method to determine endogenous levels of GHB in different samples. We present a GC-MS analytical method to quantify GHB in a local representative population (healthy volunteers, n=50) and outpatients in a "Methadone Unit" (n=14). Results: First data show that the analytical method by GC-MS used to analyse forensic sample cannot determine endogenous concentrations of GHB in this two populations. Confirmation is necessary but these preliminary data are in agreement with the possibility of a post mortem increase of this neurotransmitter. GHB analysis is easy but estimating it appears difficult to determine endogenous or exogenous origin. We will also present some GHB threshold values in healthy volunteers. 1. CPPD 2004. D. RICHARD and all. GHB and metabolites in post mortem tissues

653 THE BED NUCLEUS OF STRIA TERMINALIS AS A NEURAL SUBSTRATE FOR MEDIATING OPIATE WITHDRAWAL IN NEONATAL RATS

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It is believed that the bed nucleus of stria terminalis (BNST) is an important site for the actions of norepinephrine during opiate withdrawal (OW). We are investigating the involvement of the BNST and the influence of the noradrenergic system on the infant rat during OW. We hypothesized that clonidine, in combination with tapered opiate doses would be more effective than morphine alone in attenuating behavioral OW symptoms and decreasing activated neurons in the BNST of newborn rats. Osmotic minipumps containing methadone (14mg/kg/day) or saline were placed in dams (n=8) on gestation day 15. At postnatal days (P)2 and 8, methadone or saline-exposed pups were cross-fostered onto naïve dams. At P3-5, 10-12 and P 17-19, methadone-exposed pups were treated with tapering doses (twice daily at 10, 8, and 6mg/kg, respectively) of morphine+clonidine (0.2mg/kg/day; MORPH+CLON; n= 18; or morphine (MORPH; n=18). Pups prenatally exposed to saline were injected with clonidine (0.2mg/kg/day; SAL+CLON; n=18) or an equal volume of saline (SAL; n=18). OW symptoms were precipitated by naloxone (0.1mg/kg) at P6, 13 and 20 and behavioral symptoms were scored. Opiate dependence in P6, 13 and P20 pups was evidenced by an increase in OW behaviors and a reduction in quiet-alert state (ANOVA $p<0.05$, Tukey $p<0.05$) versus saline-treated. The OW behaviors that were affected by the different treatment regimens varied with age. Immunohistochemistry for c-Fos increased in the BNST of P6, 13 and P20 pups. MORPH+CLON attenuated OW behaviors and reduced the number of activated neurons (ANOVA $p<0.05$, Tukey $p<0.05$) for all ages. Western Blot hybridization data showed an increase in c-Fos in the BNST for P13 MORPH group (34% increase) and P20 (212% increase) morphine vs. saline-exposed pups (P6 data being evaluated). These data suggest a correlation between behavioral and cellular markers of OW in the BNST of infant rats and suggests that clonidine is effective in reducing OW symptoms in opiate-dependent newborn rats.

654 PRIOR EXPOSURE TO A NEUROTOXIC REGIMEN OF METHAMPHETAMINE REVEALS THE EXISTENCE OF DOPAMINERGIC NEURONS RESISTANT TO FURTHER EFFECTS OF METHAMPHETAMINE TREATMENT

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Multiple high-dose administrations of methamphetamine (METH) cause persistent striatal dopaminergic deficits, as evidenced by findings that high-dose METH treatment results in decreases in dopamine (DA) content, tyrosine hydroxylase activity, and vesicular monoamine transporter-2 (VMAT-2) activity that persist weeks to months after treatment. METH treatment also causes an acute decrease in VMAT-2 function, as assessed in a sub-population of vesicles purified from treated rats, that may contribute to increased cytosolic DA concentrations and ultimately the persistent dopaminergic deficits caused by the stimulant. Interestingly, results from the present study suggest that some dopaminergic neurons may be resistant to the long-term effects of METH under certain conditions. In particular, a challenge high-dose, neurotoxic METH regimen did not further decrease striatal VMAT-2 activity or DA content in rats exposed 7 or 30 d previously to a neurotoxic regimen of METH, as assessed 7 d after administration of the second METH regimen. Moreover, the challenge with a neurotoxic METH regimen did not further decrease VMAT-2 activity acutely in rats exposed 7 d previously to a neurotoxic regimen of METH, as assessed 1 h after administration of the second METH regimen. These data suggest that the resistance of dopaminergic neurons to a subsequent neurotoxic METH administration may be associated with a lack of an acute effect of METH on VMAT-2 function in these neurons. (Supported by DA00869, DA11389, DA04222, DA000369, DA13367, DA019447)

655 INHALANT USE-RELATED DISORDERS: RELIABILITY AND CO-OCCURRING DRUG DISORDERS

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Inhalants are perhaps the most lethal class of drugs of abuse, especially among drugs that tend to be initiated at younger ages. However, little research addresses inhalant abuse or etiology. Inhalant use is rarely evaluated in addiction treatment. Inhalant users were studied to estimate the (a) reliability of DSM-IV inhalant diagnoses for 4 types of inhalants and aggregated diagnoses and (b) co-occurrence of disorders related to alcohol, tobacco, and cannabis use. A total of 162 adolescent and young adult inhalant users (mean age=20.38 yrs) were recruited from the St. Louis area using community flyers (n=131) or friend referrals (n=27) and from addiction treatment settings (n=4). Data were collected using a modified Substance Abuse Module (SAM), adapted for in-depth interviewing of inhalants use. Of all participants, 2/3 were male and 83.3% were Caucasian. Participants had used a wide range of inhalants 5 or more times: 84.5% used nitrous oxide, 41.3% used a gas (e.g., ether or helium), 37.4% used computer duster, 27.1% used paint-related inhalants, 25.2% used glue or toluene, 23.9% used markers or white out, and 8.4% used amyl nitrites. Kappa estimates of one-week test-retest reliabilities for having any diagnosis were excellent to fair: 0.81 for gases (24.1% met criteria), 0.72 for aerosols (17.3% met criteria), 0.66 for nitrites (3.7% met criteria), and 0.43 for solvents (13.6% met criteria). Kappa for aggregated diagnoses (criteria could be met regarding use of any inhalant) was excellent 0.75 (40.2% met criteria). Results for specific criteria and associations between use and diagnoses for types of inhalants will be presented. A greater proportion of inhalant users with an inhalant-related diagnosis met criteria for tobacco dependence and cannabis-related disorders compared to other inhalant users; the two types of inhalant users did not differ on alcohol-related diagnoses. These results suggest the SAM inhalants interview provides reliable diagnoses for separate types of inhalants as well as aggregated inhalants diagnoses.

656 GENDER DIFFERENCES BETWEEN OUT-OF-TREATMENT INJECTORS

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This study compared demographics, drug use, mental health status and HIV risk behaviors between male and female out-of-treatment injection drug users (IDUs) in Denver, Colorado. Between November 2000 and 2004, we recruited 802 participants through street outreach and conducted structured interviews examining a range of variables. The average age of participants was 39 years and 28% were female. Additionally, 50% were Caucasian, 21% African American, 20% Latino, and 9% of another ethnicity. Significant gender baseline differences were found. Female injectors were younger, had less education and were less likely to be employed, ever arrested or homeless as compared to male injectors. While male injectors had been injecting longer, female injectors reported injecting more amphetamines. Females had significantly higher rates of lifetime and current emotional, physical and sexual abuse as well as higher lifetime and current symptoms of depression, anxiety and suicidal ideation. Females had a higher perceived chance of getting HIV and reported engaging in risk behaviors that supported this perception. Almost half (40%) of female injectors reported using dirty syringes without bleaching, compared to 33% of males. In addition, 63% of females engaged in unprotected anal or vaginal sex in the last 30 days as compared to 43% of male injectors. Over half (59%) of the females had an IDU sex partner and 43% reported trading sex for drugs in their lifetime compared to 36% of males who had an IDU sex partner and 18% who traded sex for drugs. Results from this study show that female out-of-treatment IDUs engage in higher HIV risk behaviors than men. In addition, they appear to have many co-occurring issues that need to be better understood in order to develop effective outreach and intervention techniques. Supported by the National Institute on Drug Abuse DA09832.

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657 RISK OF SEDATIVE-HYPNOTIC PROBLEMS SOON AFTER ONSET OF EXTRA-MEDICAL USE: UNITED STATES, 2001—2003

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BACKGROUND & AIMS: Analyzing the most recently available epidemiological data for the United States (US), we estimate risk of developing a dependence-related syndrome of sedative-hypnotic (SH) problems among persons with recent-onset and extra-medical SH use (i.e., within 24 months after first SH use). Besides estimating risk of developing this syndrome, we investigate characteristics that might signal greater risk. **METHODS:** The study estimates are based on data from the National Surveys on Drug Use and Health (NSDUH) conducted in 2001-2003, with a nationally representative sample (n=164,870) and standardized assessments. The SH dependence-associated syndrome encompasses clinical features of SH dependence, as well as SH-associated socially maladaptive behavior (e.g., family, work, or school difficulties secondary to SH use). Analysis methods for estimation were appropriate for the complex probability sample surveys. **RESULTS:** A total of 353 respondents, 0.2% of the sample, were found to be recent-onset SH users. An estimated 13% developed this SH dependence-associated syndrome within 24 months after onset of use. Excess risk of the SH dependence-associated syndrome was found in relation to earlier onset of SH use (RR~7; p<0.05), but not independently with sociodemographic or sociodemographic characteristics. **DISCUSSION:** Roughly 1 in 7 extra-medical SH users developed a dependence-associated syndrome within 24 months after onset of use, and there is greater risk when onset occurs before mid-adolescence. These results set the stage for more probing prospective studies of the problems associated drug dependence and drug-related social maladaptation that is occurring secondary to the extra-medical use of these drugs. **SUPPORT:** NIH/NIDA/FIC D43TW05819; T32DA07292, K05DA015799.

658 PTSD-OPIATE ABUSE COMORBIDITY: APPLYING EVOLUTIONARY APPROACHES TO THE LIFE HISTORY MILESTONES OF INDIVIDUALS

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Background: Comorbidity of substance abuse and post-traumatic disorder (PTSD) is well documented. Widely used classification analysis such as latent transition analysis may not capture sufficient details of multiple pathways over-time to delineate the nature of psychiatric and substance abuse comorbidity. **Objective:** To analyze the pathways involving trauma, opiate use and abuse, and PTSD. **Method:** As a part of a longitudinal cohort of Vietnam veterans followed-up over 30 years, the sample (n=642) for this study was drawn from the third wave of the surveys conducted in 1996-7. The sample originated in 1972 and was a general sample of Vietnam veteran returnees plus an over sample of those returnees who had tested positive for drug use. Measures include timing of opiate use, abuse and dependence from the 1972, 1974 and 1996-97 surveys together with retrospective timing of lifetime trauma and DSM-IV PTSD symptoms and diagnoses obtained in 1996-7. We employ classification and regression trees (CART) as implemented in S-Plus as well as cladistic and dendrogram (clustering) techniques currently used in evolutionary molecular genetics. **Results:** For predicting opiate abuse or dependence among those who ever used, a PTSD diagnosis was the primary predictive factor. However, among those without a PTSD diagnosis, the order of exposure was important. Having used opiates before or concurrent with trauma was a predictor for developing abuse or dependence. Opiate use before or concurrent with trauma tended to increase the duration of PTSD symptomatology. It also tended to increase the length of opiate use, unless the originating trauma occurred very early. **Conclusion:** CART results help identify major differences in multiple pathways. Dendograms using other covariates will further confirm the CART results with the use of nested significance tests (supported by MH060961, DA14632, DA020922).

659 A SYSTEMATIC REVIEW OF HARM REDUCTION

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A comprehensive approach to drug control policy involves a mix of law enforcement, treatment, prevention and harm reduction approaches. This paper present the results of a systematic review of harm reduction. Harm reduction was defined as those policies and interventions aimed at reducing harm, and excluded those interventions that reduce use (and hence harm). Therefore, the review considered the following as harm reduction interventions: needle syringe programs; supervised injecting facilities; non-injecting routes of administration; outreach; HIV education and information and HIV testing and counselling; brief interventions; and overdose prevention interventions. A comprehensive search strategy identified a total of 1,361 research reports concerned with injecting drug use, harms and harm reduction interventions. Half of this literature (n=681) was descriptive in nature. The other half of the literature concerned harm reduction interventions (n=680). The largest intervention type to be reported on was needle syringe programs (NSP) (n=344). The results of the review revealed that there is significant support for the efficacy, effectiveness and cost-effectiveness of NSP. Despite the substantial evidence-base for NSP, they cannot be considered a stand-alone strategy. To date there is a very limited evidence-base upon which to judge efficacy or effectiveness of supervised injecting facilities. Non-injecting routes of administration appears to be a promising harm reduction avenue, worthy of further exploration. We found reasonable evidentiary support for outreach. Brief interventions have received minimal attention as harm reduction interventions. Most recent attention in overdose prevention has focussed on naloxone distribution to injecting drug users. It remains an untested but theoretically promising harm reduction intervention. Education and information are intuitively appealing harm reduction interventions, and are likely to be among the less costly interventions. Unfortunately these positive aspects are not matched by effectiveness.

660 RATS EXHIBITING ACUTE BEHAVIORAL TOLERANCE TO NICOTINE SHOW EVIDENCE OF NICOTINIC CHOLINERGIC RECEPTOR (nAChR) DESENSITIZATION

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Individuals vary in susceptibility to nicotine addiction. However, there is little evidence that behavioral sensitivity to nicotine is dependent upon the functional state of nAChRs. In order to determine the relationship between behavioral desensitization (in other words, acute tolerance) and in vitro desensitization of nAChRs, the desensitization of nicotine-stimulated 86Rb+efflux was studied in the thalamus of individual male Sprague-Dawley rats trained to discriminate nicotine. Acute tolerance was assessed as follows. Rats were injected with nicotine (0.4 mg/kg free base, s.c.), tested for nicotine discrimination for 2 min, then injected with the same dose of nicotine 90 min, 180 min, and 270 min after the first injection and tested for nicotine discrimination after each injection. The susceptibility of nAChRs of individual rats (n = 16) to desensitization was assessed by use of a synaptosomal 86Rb+ efflux assay. Synaptosomes were perfused with low concentrations of nicotine (0.005, 0.01, 0.02, and 0.03 μ M) for 6 min prior to stimulation of 86Rb+ efflux with nicotine (10 μ M). The slopes of lines fit to the behavioral desensitization were plotted as a function of the decline of nicotine-stimulated 86Rb+ efflux following in vitro desensitization of synaptosomes prepared from individual subjects. A significant correlation was observed between the in vitro desensitization of synaptosomal 86Rb+ efflux and the extent of behavioral desensitization of individual rats ($r=0.671$, $p = 0.0044$). These findings are consistent with the idea that production of acute behavioral tolerance by nicotine is related to its ability to induce nAChR desensitization at the cellular level. These findings also support the suggestion that humans who choose to use tobacco products do so because they possess nAChRs that differ in susceptibility to desensitization. (This work was supported by the Philip Morris External Research Program.)

661 GENDER DIFFERENCES IN SEXUAL RISK BEHAVIORS AND SEROPOSITIVITY AMONG YOUNG NON-INJECTION HEROIN USERS

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Introduction: Despite the understanding shown in clinical trials that there are health and socio-psychological problems related to increased poly-substance use, researchers continue to study a single substance. The fact is that patients who exclusively abuse a single substance are unrepresentative of the population of substance abusers. This study aims to understand how gender plays a role in the prevalence of poly-substance use and its relation to HIV risk among each drug use combination. **Method:** The sample consists of 332 young males and 71 females. An office interview was used to collect the data. Participants received serum testing for the HIV antibody. **Results:** Nearly eighty-nine percent (88.6.0%) reported regular poly-substance use. Near equal rates of poly-substance use were observed by gender (males-89.5% vs. females-84.5%). Marijuana, cocaine and crack were the most prevalent drugs mixed. Females reported more co-use of crack (42.3% vs. 23.2%, $p=.002$) and males reported more co-use of marijuana (55.1% vs. 39.4%, $p=.018$). Non-significant differences were observed in the co-use of cocaine (males 27.7% vs. females 19.7%, $p=.184$). Poly-substance female users were more likely to report sexual assault (38.3% vs. 3.4%, $p<.001$), experience anxiety symptoms (38.3 vs. 17.5, $p=.001$), engage in commercial sex (21.7% vs. 5.4%, $p<.001$), have an IDU sex partner (10.0% vs. 1.7%, $p=.004$) and STDs (26.7% vs. 3.4%, $p<.001$). Poly-substance male users were more likely to report physically violent encounters (69.4% vs. 55.0%, $p=.036$) and have a supportive peer (95.3% vs. 83.3%, $p=.002$). Non-significant differences were observed regarding HIV status by gender, however females showed a higher percent of HIV+ than males (3.5% vs. 0.3%, $p=.072$). **Conclusion:** High rates of poly-substance use were observed in male and female young adult non-injectors of heroin. Poly-substance use needs to be an area of research in future HIV/AIDS trials, particularly in addressing HIV prevention/intervention for female poly-substance users.

662 PREDICTORS OF HEROIN SEEKING, PURCHASING AND CONSUMPTION

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Results from a semi-structured interview were analyzed for variables that link or separate the behavioral domains of heroin seeking, purchasing and consumption. Participants reported using heroin for an average of 20 years and urine samples were available for 90 of the 100 respondents. Urinalysis reflected poly-drug use with 50% testing positive for cocaine, 15% positive for marijuana and 9% positive for benzodiazepines. Regression analysis was used to identify significant ($p<.05$) predictors of past-month heroin seeking, purchasing and consumption. The number of daily bags of heroin consumed (mean=4.5) was significantly predicted by the primary route of heroin use (0=intranasal $n=37$), 1=parenteral ($n=58$, $B=.214$), bag unit cost ($B=-.384$, mean=\$10.71) and total monthly income ($B=.589$, mean=\$1663). The number of weekly heroin purchasing episodes (mean=13.9) was significantly predicted by distance to supplier ($B=-.287$, median= 1-2 mile), total monthly income ($B=.310$) and number of suppliers ($B=.282$, mean=3.5). Percent of income spent on heroin (mean=72%) was significantly predicted by greater IV heroin use ($B=.214$) and use of non-heroin opiates ($B=-.246$). Unit purchase amount (number of \$10 bags per episode) was significantly predicted by distance to supplier ($B=.294$). Factor analysis of all measures extracted 4 components, explaining 64% of the variance, which meaningfully separated consumption, purchasing and seeking measures (as the above analyses suggest). Cluster analysis identified two subgroups. Cluster 1 ($n=89$) included individuals with lower monthly incomes (\$1368), who spent 75% of their income on heroin, consumed 4 bags/day, were more likely to snort and less likely to use other opiates. Cluster 2 ($n=11$) had much higher income (\$4146), spent 50% of this income on heroin, consumed 7 bags/day, were more likely to inject and more likely to use some other opiates. These analyses suggest meaningful differences among the behaviors of seeking, purchasing and using heroin. Clusters suggest meaningful subgroup differences between users according to income and route of administration. Supported by NIH/NIDA DA15462.

663 NEURAL SUBSTRATES OF RELAPSE TO HEROIN-SEEKING USING A REINSTATEMENT MODEL IN RATS

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Although much is known about the neurocircuitry of relapse to cocaine-seeking using the reinstatement model, relapse triggered by other drugs of abuse, including opiates, is less clear. We hypothesized that the circuitry underlying reinstatement in heroin-trained animals would show overlapping, yet distinct differences from cocaine-trained animals. To test this idea, we examined the neural substrates of reinstatement of heroin-seeking produced by heroin-paired cues, or heroin itself. Male, Sprague-Dawley rats were trained to lever press on a FR1 schedule for heroin (25 $\mu\text{g}/50 \mu\text{l}$ i.v. infusion) paired with presentations of a light-tone conditioned stimulus (CS) during daily 3-hr sessions. Following chronic heroin self-administration (2 weeks), extinction of lever responding was conducted in daily sessions prior to reinstatement testing. Using a within-subjects design, rats received 4 reinstatement tests, in which heroin-seeking behavior was measured as lever responding in the absence of contingent heroin reinforcement. The first set of reinstatement tests involved response-contingent CS presentations following bilateral intracranial infusion of either a GABA agonist mixture (baclofen-muscimol (B/M) 0.3/0.03 nmole/side) or vehicle into one of several different brain regions, including subregions of the amygdala, nucleus accumbens, prefrontal cortex, and other areas. The second set of reinstatement tests involved a priming injection of heroin (0.25 mg/kg, s.c.) following either B/M or vehicle infusions. Results showed that vehicle infused animals reinstated to both CS presentations and a priming injection of heroin. B/M inactivation of several areas critical for the reinstatement of cocaine-seeking also reduced heroin-seeking behavior to CS presentations and/or a priming dose of heroin; however, as predicted, additional areas were involved in mediating relapse to heroin-seeking. Comparison and implications of these differences for understanding the neurocircuitry of relapse will be discussed. Supported by NIH Grant DA015369

664 EFFECTS OF ABSTINENCE REINFORCEMENT ON THE FREQUENCY AND ENJOYABILITY OF PLEASANT ACTIVITIES DURING TREATMENT FOR COCAINE DEPENDENCE

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Drug dependence is a condition wherein the behavioral repertoire of the user is monopolized by drug use to the exclusion of participation in alternative, healthier activities. In the present study, the Pleasant Events Schedule (PES) was used to examine changes in the frequency and enjoyability of engaging in everyday activities across a one-year treatment period. The PES lists 320 activities organized into 10 empirically derived subscales, including social, solitary, and outdoor activities. Subjects were 78 methadone-maintenance patients enrolled in a randomized clinical trial on treatments for cocaine abuse (Silverman et al., 2004). Subjects were randomly assigned to one of 3 treatment conditions: condition THM+V in which they received methadone take-home privileges plus vouchers contingent upon negative cocaine and opiate urine screens, condition THM in which they received methadone take-home privileges contingent upon negative cocaine and opiate urine screens, and condition UC in which they received usual-care. Subjects completed the PES pre-, mid-, and post-treatment. During the 52-week treatment period, patients in the THM+V condition achieved the greatest abstinence from cocaine and opiate abuse (57% negative screens) and reported significant increases in frequency across 9 of the 10 PES subscales, with no significant changes in enjoyability ratings. Patients in the THM and UC conditions achieved significantly less abstinence (34% and 14% negative screens, respectively) and reported no significant increases in frequency on any of the subscales. Enjoyability ratings did not change significantly in the THM condition but decreased significantly on 7 of the 10 subscales in the UC condition across the one-year study period. These results show that reinforcement contingencies that increase cocaine and opiate abstinence can concurrently increase the frequency of everyday pleasant activities, and that ongoing abuse may diminish enjoyability of these same activities.

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- 665 GROOMING THE NEXT GENERATION OF SUBSTANCE ABUSE CLINICIANS: CURRICULAR CHECKLIST TO HELP EDUCATORS INFUSE EVIDENCE-BASED PRACTICES INTO UNDERGRAD AND GRADUATE COURSEWORK**
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Kerner, et al., (2005) advocated that the link between the dissemination of evidence-based and the public's welfare is vital. Nevertheless, as late as 2002, Mc Gynn found that individuals with alcohol dependence disorders received evidence-based treatment less than 10.5% of the time. Federal entities and professional groups have allocated funds and resources to develop new evidence-based treatments and to help clinicians adopt evidence-based practices. However, less attention has been paid to changing academic courses for clinicians. Teaching evidence-based practices during a clinician's academic career is an effective way of ensuring a clinician's practice aligns with current research. In fact, Jackson (1999) found that clinicians' tended to adhere to practices they were taught while in college. Experts in training clinicians and disseminating evidence-based practices (Miller, et al, 2006, Edmundson, et al, 2004, Roget, et al, 2004, and Rawson, et al 2002), have called for a new emphasis on teaching evidence-based practices during a clinician's "formative years" (Crane and Hafin 2002). The difficulty for educators lies in discerning which evidence-based practices to teach especially when Davis, et al, (2004) reported that more than 400,000 articles are added to the biomedical literature every year. The Mountain West Addiction Technology Transfer Center (ATTC) in conjunction with other ATTCs, researchers, and addiction educators has developed an evidence-based curricular checklist. This presentation will review the process used to develop the checklist, the curricular checklist, references used to build the checklist, and recommendations for undergraduate and graduate as well as generalists' and specialists' courses. Finally, while Miller, et al (2006) cautioned against developing a definitive list of evidence-based practices, a collaborative effort between researchers, educators, and ATTCs was utilized to generate the first draft to give educators a place to start.
- 666 DOES BEHAVIORAL INHIBITION INCREASE THE RISK OF SUBSTANCE USE DISORDERS?**
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Background: Behavioral Inhibition (BI) refers to a temperamental tendency of children to consistently react with initial fear and distress to unfamiliar events. A number of studies reported associations between BI and several mental disorders. We investigated longitudinal associations between BI and the subsequent onset of several substance use disorders (SUD) in a representative community sample. Method: The data come from the baseline and three follow-up waves of the Early Developmental Stages of Psychopathology (EDSP) Study, a 10-yr longitudinal general population survey of adolescents and young adults in Munich (Germany). Preliminary data were drawn from a population of 2,206 individuals who completed the last follow-up. BI was retrospectively assessed using the RSRI and its two subscales "social/school" and "fear/illness"; assessment of SUD was based on the M-CIDI according to DSM-IV. Results: Associations between prior BI and subsequent onset of dependence from alcohol, nicotine, cannabis and other illicit substances were found. The results show that the BI factor "fear/illness" mainly predicted an increased level of risk for the onset of the above mentioned disorders. The largest difference between the two subscales was found for cannabis dependence. The increase of one standard deviation concerning the "fear/illness" score predicted a 1.70-fold odds ratio (95% CI = 1.35-2.13), whereas the odds ratio obtained considering the social factor was only 1.08 (95% CI = 0.84-1.39). Conclusion: Prospective analysis revealed a relationship between childhood BI and subsequent increased level of risk for dependence of nicotine, alcohol and illicit substances, especially cannabis. These associations can be mainly attributed to the subscale "fear/illness", indicating that general fear and somatic disturbances seem to play an important role in the development of SUD. Whether BI can be considered as a risk factor or as a mediator, e.g. within the relationship between anxiety disorders and subsequent SUD should be examined in further analysis.
- 667 COCAINE CRAVING EARLY IN RESIDENTIAL TREATMENT AS PREDICTOR OF TREATMENT ATTRITION AND COCAINE USE OUTCOMES**
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Craving (urge to use) is central to many models of relapse but it is not clear whether craving is an important predictor of treatment response in its own right or is an epiphenomenon secondary to pretreatment drug use severity. This predictor study investigated two questions about cocaine urges in simulated high-risk situations early in treatment: (1) which pretreatment cocaine use measures predict greater urge, and (2) does urge to use cocaine predict treatment attrition and outcome. Method: Cocaine dependent patients (n = 163) in residential treatment (median = 30 days) were assessed during the first week of treatment for pretreatment substance use and dependence and urge to use cocaine in the Cocaine Related Assessment of Coping Skills (CRACS). At follow-up substance use was assessed with timeline Followback, urine confirmed (n = 119 at 3 months, 114 at 6 months). Results: Level of cocaine urge in the CRACS in treatment was unrelated to sex, race, age, income, other substance use, route, years used, pretreatment percent days using cocaine, and expected effects or number of negative consequences from cocaine. However urge was higher for those who spent more money on cocaine. Urge in the CRACS did not predict drop out from treatment but significantly predicted frequency of cocaine use during the first 3 months, even after covarying pretreatment cocaine use frequency or amount spent on cocaine. It did not predict 3-6 month use. Conclusion: Results suggest that urge to use cocaine early in treatment does predict early outcomes above variance shared with pretreatment cocaine use severity.
- 668 NICOTINE-SPECIFIC MONOCLONAL ANTIBODY (Nic311) PHARMACOKINETICS IN RATS**
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Passive immunization against nicotine with nicotine-specific monoclonal antibodies may hold therapeutic potential for treating nicotine addiction. Recent studies have begun to characterize the effects of passive immunization on nicotine pharmacokinetics, especially the distribution of nicotine to the brain. Obtaining estimates of the pharmacokinetic parameters for these antibodies is important for determining effective antibody dosing, and for determining their relationship to therapeutic efficacy. In this study male rats (n = 7) were administered Nic311 (30 mg/kg i.v.) and blood samples collected over 70 days for analysis of serum IgG levels by quantitative ELISA. Individual pharmacokinetic parameters were estimated from serum concentration-time data using noncompartmental methods. The volume of distribution at steady state, total clearance, and terminal half-life were 190±29 ml/kg, 0.6±0.03 ml/hr•kg, and 9.8±1.3 days, respectively. Two animals exhibited a marked increase in total antibody clearance starting on day 5-8, possibly due to the presence of rat-anti mouse antibodies. These pharmacokinetic parameter estimates for Nic311 correlate well with previously reported values for nonspecific mouse IgG in rat. Future studies using Nic311 in rats will need to assess for the presence of unusually high antibody clearance as an experimental confounder. Supported by NIDA grants DA10714 and T32-DA07097.

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- 669** ALCOHOL-USE PROBLEM SEVERITY AMONG SCHOOL-BASED YOUTHS IN MEXICO: THE SIGNIFICANCE OF DISTINGUISHING BETWEEN USE FREQUENCY AND CONSEQUENCES IN SCHOOL-BASED YOUTHS
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The present study examined alcohol abuse problem severity in a school-based sample of youths in Mexico using measures of alcohol-related consequences and alcohol use frequency. The study is based on data from the International Longitudinal Survey of Adolescent Health, a multi-wave survey administered to school-based youths in Mexico, Puerto Rico, and the US. The results are based on data from the survey administered to 1,229 school-based youths from one middle school (grades 7-9) and one high school (grades 10-12) in Mexico. Twenty-two survey items addressing DSM-IV diagnostic criteria for alcohol abuse and dependence were adapted from the Adolescent Diagnostic Interview (Winters & Henly, 1999). Youths were categorized into 8 diagnostic groups based on their endorsement of alcohol use frequency (lifetime and past 12-month) and DSM-IV abuse/dependence criteria. In the Mexico sample, 39.8% were classified as non-users of alcohol, 18.0% were classified as low-risk experimenters, 24.6% were classified as moderate-risk experimenters, 2.2% were high-risk experimenters, 8.0% endorsed 1-2 abuse symptoms, 2.8% endorsed 3 or more abuse symptoms, 2.5% endorsed 1-2 dependence symptoms, and 2.2% endorsed 3 or more dependence symptoms. Chi-square analyses examined rates of problem behavior among the 8 groups of school-based youths defined by their degree of alcohol problem severity. Results indicated that greater alcohol problem severity was generally associated with higher rates of problem behavior. In addition, greater problem behavior appeared to be associated with the number of consequences endorsed rather than the type of item (e.g., abuse versus dependence) endorsed. Extant school-based studies have generally sought to define alcohol problem severity based on use frequency only. The present study findings have significance when seeking to provide a more detailed understanding of variations in alcohol abuse problem severity related to consequences.

- 670** ACQUISITION OF DRUG-INDUCED CONDITIONED PLACE PREFERENCE IN FISCHER AND LEWIS RATS

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Simpson and Riley (2005) recently reported that animals with a history of morphine acquired a conditioned place preference (CPP) to morphine significantly faster than those without a history. This difference was not seen in asymptotic performance, but rather in the more rapid acquisition of CPP, suggesting that the acquisition procedure may be a more sensitive assay of differences between groups than just asymptotic conditioning. We and others have used CPP with Fischer and Lewis rats to explore genetic factors in drug abuse vulnerability. Although these strains reportedly differ in their responses to morphine-induced CPP at 4 mg/kg (Lewis > Fischer), their CPP responses have not been fully described. To determine whether strain differences in morphine CPP are also evident at a lower dose, adult male Fischer and Lewis rats were subcutaneously injected with 1 g/kg morphine (n = 12 per strain) or equivalent saline (n = 12 per strain) over four conditioning cycles using a biased design in a biased smooth vs. textured apparatus. Each conditioning cycle was separated by a CPP test in order to assess acquisition, ending with a final CPP test to assess asymptotic performance. A 5 (trial) x 2 (strain) x 2 (dose) repeated-measures ANOVA on time spent in the drug-paired chamber yielded a significant interaction among all three factors [$F(4,176) = 8.93$, $p = .446$]. These data support the use of CPP acquisition to more fully characterize drug-seeking behavior, and given the development of CPP at this low dose in only the Fischer animals, further suggest that the "addiction-prone" Lewis vs. "addiction-resistant" Fischer dichotomy typically ascribed to the Fischer-Lewis model may need reevaluation.

- 671** IMPROVED ADHERENCE TO ANTIRETROVIRAL MEDICATION WITH ELECTRONIC MONITORING AND CONTINGENCY MANAGEMENT

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HYPOTHESIS: In a 16-week randomized clinical trial, a contingency management (CM) based intervention will be associated with higher adherence than an intervention providing non-specific support for participants' own adherence efforts. **METHODS:** Participants prescribed antiretroviral medication with histories of substance use used and sub-optimal adherence during a baseline assessment were randomly assigned to 16-weeks of weekly CM-based or supportive counseling, followed by 16 additional weeks of data collection and feedback to providers. The CM intervention involved review of data generated by electronic pillcaps that record bottle opening (MEMS) and brief substance abuse counseling. CM participants were reinforced for MEMS-measured adherence with draws for prizes and bonus draws for consecutive weeks of perfect adherence. Potential total earnings averaged \$800. MEMS-measured adherence was analyzed using SAS PROC MIXED. **RESULTS:** Altogether, 56 participants were randomized to CM (n=28) or support (n=28). MEMS-measured adherence to the reinforced medication was significantly higher in the CM group relative to the supportive counseling group ($p < .05$) during the 16-week treatment phase. Adherence drifted downward after the intervention was discontinued. A continuous measure of viral load was significantly lower in the CM group, although categorical measures of improvement did not differ. Proportions of positive urine toxicology tests did not differ significantly between the two groups. **CONCLUSIONS:** A brief CM-based intervention was associated with significantly higher adherence and lower viral loads. However, there was considerable room for greater short-term benefit and better retention of benefits. Supported by R01 DA15215, P50 DA09241, VISN 1 MIRECC, M01RR06192.

- 672** PSYCHOSOCIAL BENEFITS ASSOCIATED WITH PARTICIPATION IN A SELF-HELP GROUP FOR PATIENTS WITH COMORBIDITY

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Background: A supportive social network can facilitate recovery from substance abuse and mental illness. **Objective:** To implement a consumer-led, voluntary, dual-focus 12-step group (Double Trouble in Recovery, DTR) within a psychiatric day-treatment facility, document DTR participation rates, and determine psychosocial benefits associated with DTR attendance. **Methods:** Newly admitted psychiatric outpatients (n=78) were recruited from May 2004-2005 and encouraged to attend a weekly DTR group facilitated by an experienced DTR member. Six month outcome measures included positive affect, social support for abstinence, and frequency of attendance at traditional 12-step groups (e.g., AA, NA). Multiple regression was used to examine the relationship between DTR attendance and 6-month outcomes; the baseline equivalent of each outcome was entered as a covariate. **Results:** The majority of subjects were male (63%) and minority (45% Black, 33% Hispanic); mean age was 40 years; and 72% had used cocaine or other drugs (by self-report or hair/urine tests) in the month before treatment. The mean number of DTR groups attended was 4.9 (sd=7.7, range 0-34); 60% attended at least one DTR group. At 6-month follow-up DTR attendance was significantly associated ($p < .05$) with higher positive affect (sd. beta=.23), higher social support for abstinence (sd. beta=.47), and, among subjects with recent drug use, increased traditional 12-step attendance (sd. beta=.28). **Conclusion:** Introducing a dual-focus self-help group in an outpatient treatment setting results in moderate participation rates and is associated with important psychosocial aspects of recovery for persons with co-morbid disorders. [NIDA grant R01-DA015912]

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673 HOW PATTERNS OF ALCOHOL USE IMPACT PHYSICAL AND MENTAL HEALTH IN HIV-POSITIVE INDIVIDUALS

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Background: People with alcohol problems approach drinking in different ways. Some drink a few drinks daily, others binge on weekends, while others are consistently heavy drinkers. How these patterns differentially relate to health is understudied. Methods: In a sample of 312 HIV-positive people with alcohol problems, levels of alcohol use were collected using Time Line Follow Back method on a 30 day calendar. All drinks were converted into standard drinks and calculations were made to determine 1) total number of standard drinks in past 30 days, 2) number of drinking days in past 30 days, and 3) number of heavy drinking days in past 30 days (defined by NIAAA as 5 or more drinks for men and 4 or more drinks for women on one occasion). These three measures of alcohol use were correlated with HIV health, HIV medication adherence (sample was all taking antiretroviral medication), readiness for change, depression, and anxiety. Findings: Having been diagnosed with AIDS correlated with number of drinking days, but not binge days or total number of drinks. Adherence to HIV medication correlated with total number of drinks, but not with drink days or binge days. Anxiety correlated with all three measures of alcohol use. Depression correlated with total number of standard drinks, but not with drink days or binge days. Readiness for change correlated with number of drinking days and number of binge days but not with total number of drinks. Conclusion: Multiple measures of alcohol use is important to determine level of risk for physical and mental health. Understanding differential risk for drinking patterns can inform treatment approaches. As disease models and abstinence-based treatment programs make room for motivational treatment and harm reduction approaches, informing clients of the risks of their chosen goals is an important responsibility of the treatment provider.

674 SELECTIVE ANTAGONISM OF DOPAMINE D3 RECEPTORS BY SB-277011A ATTENUATES THE REINFORCING EFFICACY OF NICOTINE AS MEASURED BY A PROGRESSIVE-RATIO SCHEDULE IN RATS

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Because the dopamine (DA) D3 receptor is primarily localized within the mesocorticolimbic system, it may have potential as a pharmacotherapeutic target for the treatment of drug dependence. Consistent with this view, studies have shown that the selective DA D3 receptor antagonist SB-277011A is efficacious in animal models of cocaine-, nicotine-, alcohol-, and heroin-seeking behaviours. Previous studies have also shown that a commonality shared by selective DA D3 receptor antagonists is that they significantly reduce cocaine self-administration only when the workload imposed upon the animal is increased either in terms of progressive-ratio (PR) break-point or in the transition from low fixed-ratio (FR) (e.g. FR1-FR2) to high FR (e.g. FR10) schedules of reinforcement, or when the unit dose of cocaine is lowered. The purpose of the present study was to further examine the effects of a broad range of doses of SB-277011A on nicotine self-administration (NSA) in rats under a PR schedule, which imposes relatively high response requirements for nicotine. Two groups of rats were trained to respond under a PR schedule of either nicotine or food reinforcement. Once responding was stable, SB-277011A (3-56 mg/kg i.p.) or vehicle was administered one hour prior to the operant session. In the NSA group, the highest dose tested significantly decreased the mean number of reinforcers and mean response rates. In contrast, SB-277011A had no effect on either the mean number of reinforcers or response rate in the food maintained group. These data further support the idea that the DA D3 receptor plays a role in the reinforcing efficacy of nicotine and that selective DA D3 antagonists may have clinical utility in the treatment of nicotine dependence. Supported by contract #4500035291 from GlaxoSmithKline.

675 THE IMPACT OF HIV+ PARENTS' DRUG USE ON THEIR ADOLESCENT CHILDREN

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Hypothesis: The impact of parental substance use on the adjustment of their adolescent children was examined over time. We anticipated that parental substance use would influence children in two major areas: increasing mental health symptoms and problem behaviors. Procedures and Subjects: A representative sample of 220 HIV+ parents and 329 adolescent children in New York City were repeatedly assessed over 5 years. Some parents never used hard drugs over the 5 years (nonusers). Among hard drug users, parents who used hard drugs during a specific 3-month period were classified as "active users" and those who abstained from drug use were classified as "inactive users." Statistical Analyses: Multivariate regression analyses were used to analyze the impact of patterns of substance use over time. Results: During periods when parents were active users, adolescents' emotional distress, depression, anxiety, and trouble with peers significantly increased. However, when parents were inactive users, adolescents' responses were similar to youth whose parents were nonusers over the 5 years. Parental use of alcohol or marijuana had few effects on adolescent emotional distress; adolescent marijuana use was higher when parents used marijuana. Conclusions: Even time-limited reductions in parents' substance abuse can have a significant positive impact on their adolescent children's adjustment.

676 ASSESSING ORGANIZATIONAL NEEDS AND READINESS FOR INNOVATION TRAINING

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Assessments of training needs, training preferences, and barriers to training should improve evaluations of program and treatment staff responses to training activities and help develop more effective methods for transferring evidence-based technologies into clinical practice. The TCU Program Training Needs Survey (PTN) was developed in collaboration with several regional Addiction Technology Training Centers (ATTCs) to identify and prioritize training needs and preferences of treatment programs. The instrument consists of 54 items organized to measure seven domains: Facilities and Climate, Computer Resources, Staff Training Needs, Preferences for Training Content, Preferences for Training Strategy, Barriers to Training, and Satisfaction with Training. This study describes the psychometric properties and structure of the PTN survey instrument using data collected between 2000 and 2004. The data were collected from 589 treatment personnel representing approximately 195 treatment programs. The TCU Organizational Readiness for Change (ORC) instrument was also collected for each treatment agency. The PTN was found to be psychometrically sound and results of a validity analysis using the PTN and ORC revealed that programs with better organizational climate scores (higher OCI index scores) had significantly higher facilities and climate scores (indicating more resources), reported significantly fewer barriers to training, and reported significantly more satisfaction with the training they received. Changes in the PTN domains over regularly scheduled intervals are also presented as a method to evaluate training efforts as well as monitor changes in needs and important resources. Results indicate that the PTN provides a useful means of identifying treatment issues that program staff and management believe should be addressed and helps gauge program needs and interests for training. Collectively, this type of information can be used to guide overall training efforts as well as predict the types of innovations that participating programs are likely to seek out and adopt.

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677 GABA_A RECEPTOR SUBTYPES AND CLINICALLY RELEVANT EFFECTS OF BENZODIAZEPINES: ANTI-CONFLICT AND REINFORCING EFFECTS OF L-696 IN PRIMATES

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Benzodiazepines (BZs) exert their effects by binding to multiple subtypes of the gamma-aminobutyric acid type A (GABA_A) receptor, more specifically those that contain alpha-1, alpha-2, alpha-3 and alpha-5 subunits. To understand the potentially different roles of these subtypes in the therapeutic and side effects of BZs, we evaluated GABA_A receptor subtype-preferring compounds in rhesus monkey models predictive of anxiolytic and reinforcing effects of BZs. These compounds included zolpidem, which exhibits preferential binding at GABA_A receptors containing alpha-1 subunits and L-696, which exhibits higher efficacy in potentiating GABA-induced chloride conductance at alpha-3 subunit-containing receptors (approximately 50% increase in a GABA EC₂₀-induced current) compared to alpha-1, alpha-2, and alpha-5 subunit-containing receptors (approximately 20%). Zolpidem was ineffective in a conflict model of the anxiolytic effects of BZs, whereas L-696 increased rates of responding suppressed by mild shock without altering rates of non-suppressed responding. Under a progressive-ratio schedule of i.v. methohexital injection, both zolpidem and L-696 maintained injections/session above vehicle levels, with zolpidem self-administered to a higher degree than L-696. Overall, these results raise the possibility that the alpha-3 subunit-containing GABA_A receptor may play a role in the anxiolytic properties of BZ-type drugs. However, alpha-3 subunit-containing GABA_A receptors also may play a role in abuse potential of BZ-type compounds, although the binding and efficacy profile of L-696 may confer reduced abuse potential compared to compounds that bind to alpha-1 subunit-containing GABA_A receptors. Supported by DA11792 and RR00168.

678 TOBACCO AND MARIJUANA BLUNT SMOKING EFFECTS ON SPIROMETRIC MEASURES; PRELIMINARY FINDINGS

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Both tobacco and marijuana smoking are known to impact respiratory function. Our aim was to determine whether blunts (guttated cigars filled with marijuana) combine both these effects. Within an adolescent smoking cessation trial, we investigated the influence of smoke exposure from cigarette smoking on pulmonary function in adolescents with and without a history of blunt marijuana use. Seventeen teenage smokers (mean age 15.4 SD 1.3 years, 59% female, 71% Caucasian, mean years smoking 3.0 SD 1.8, mean Fagerström Test for Nicotine Dependence 6.1 SD 2.0, mean cigarettes per day 15.9 SD 6.7) performed a pulmonary function test prior to and immediately after smoking a single cigarette for a puff topography experiment. As compared to non-blunt users, T-tests revealed that blunt use during the last 14 days, was associated with a less severe reduction in forced expiratory volume in one second (FEV₁) (p = .024) and peak expiratory flow (PEF) (p = .036) following the acute tobacco exposure. Contrary to our expectations, these findings suggest a potential training effect of marijuana blunt smoking that competes with the chronic effects of smoke exposure. These preliminary findings warrant confirmation through prospective studies that further test the spirometric effects of concurrent marijuana and tobacco smoking.

679 CEREBRAL METABOLISM IN COCAINE DEPENDENCE WITH COMORBID MAJOR DEPRESSION

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Cocaine dependence (CD) is often accompanied by major depressive disorder (MDD) as a comorbid condition (CD+MDD); moreover, transient depressive symptoms may occur during cocaine abstinence in natural settings. We used FDG-PET imaging to explore the neural basis for such associations between CD and depressive symptoms. Participants were treatment-seeking outpatients with CD (n=12; no mood disorder), MDD (n=13; all in episode) and CD+MDD (n=12; met DSM-IV criteria for both CD and current MDD). Normal controls (NC; n=12) were also imaged. CD and CD+MDD participants had equivalent cocaine histories; all were abstinent for 3 days (inpatient) before PET with no worsening of mood. All participants were imaged medication-free at rest. Normalized cerebral metabolic rate (nCMR, regional/whole brain counts) was compared by t-test across groups in template-defined regions of interest (ROIs). Compared to CD and MDD as separate disorders, CD+MDD displayed shared and unique metabolic features. Significant nCMR decreases were seen in dorsal prefrontal and perigenual cingulate (CD+MDD=CD > CD=MDD=NC), left striatum (CD+MDD=CD > MDD=NC) and cerebellum (CD+MDD > CD=MDD=NC). Prefrontal and anterior cingulate hypometabolism found in CD+MDD is consistent with prior studies of MDD in non-drug using samples. Overall the findings suggest a functional anatomy for CD+MDD that shares features with MDD and CD alone, but that also involves functional contributions from posterior cingulate, lateral temporal lobe and cerebellum. The notion of CD+MDD as a phenotype with a unique neural substrate has implications for understanding the pathophysiology and treatment of this comorbid condition. Support: NIH DA12271, DA000288, RR00645.

680 STRUCTURE-ACTIVITY STUDIES ON JD_TIC: FUNCTIONAL ANALYSIS AND ANTIDIURETIC ACTIVITY

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It is now well established that a vast array of biological events can be mediated through three distinct opioid receptor subtypes. An integral part of the effort to characterize the mu, delta, and kappa receptor subtypes has been the discovery of selective opioid receptor antagonists. The discovery of trans-3,4-dimethyl-4-(3-hydroxyphenyl)piperidines by Zimmerman et al. introduced a new and structurally unique class of opioid antagonists. Since it has long been thought that opioid receptor antagonists may be utilized as medications for individuals suffering from opiate abuse we have developed (3R)-7-hydroxy-N-((1S)-1-(((3R,4R)-4-(3-hydroxyphenyl)-3,4-dimethyl-1-piperidinyl)methyl)-2-methylpropyl)-1,2,3,4-tetrahydro-3-isoquinolinecarboxamide (JD_Tic); a selective kappa antagonist. In order to better understand the key features essential to opioid receptor activity and selectivity we have undertaken a SAR study of the tetrahydroisoquinoline moiety on JD_Tic. We have synthesized and evaluated enantiomerically pure analogs that substitute carbon, oxygen, sulfur, sulfoxide, and sulfone for the isoquinoline nitrogen. The functional activity of each compound was assessed using [³⁵S]GTPgammaS. The carbon analog had a K_e of 0.17 nM and dose dependently reduced U50-488 induced diuresis. We have determined the presence of an isoquinoline nitrogen is not essential for potency but plays a significant role in selectivity. Further study of this structural class may lead to more potent and selective kappa antagonists for the treatment of opioid addiction. Acknowledgment: This research was supported by NIDA Grant DA09045

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681 ATOMOXETINE FOR COCAINE DEPENDENCE

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d-Amphetamine may be effective for cocaine (COC) dependence. However, identifying novel agonist replacement therapies is important because clinicians may be reluctant to use d-amphetamine because of its abuse potential. The aim of this study is to determine the cardiovascular and behavioral effects of acute intranasal cocaine doses during chronic atomoxetine treatment. Atomoxetine was chosen because its pharmacological and behavioral effects overlap to some extent with those of prototypical stimulants, but it has less abuse potential. We hypothesized that COC would be well tolerated during atomoxetine maintenance. We further hypothesized that atomoxetine would attenuate some of the subjective effects of COC. This study consists of 5 atomoxetine maintenance conditions, which are completed in fixed order (0, 20, 40, 80 and 0 mg/day). After 3-5 days of atomoxetine maintenance, volunteers are administered ascending doses of intranasal COC (4, 20, 40 and 60 mg) within a single experimental session. COC administrations are separated by 90 minutes. Repeated measures analysis of variance will be used to analyze the data. Two volunteers have completed the study, 2 are currently enrolled, and 2-4 will participate during the next 3 months. COC alone (i.e., during placebo atomoxetine maintenance) produced prototypical cardiovascular and subjective effects (e.g., increased heart rate, blood pressure, and ratings of like drug). The cardiovascular effects of COC alone were not clinically significant. During maintenance on the highest dose of atomoxetine, the heart rate increasing effects of COC were larger in magnitude than observed during placebo maintenance. However, these effects were not clinically significant, and no adverse events were observed. During atomoxetine maintenance the blood pressure effects of COC were similar to those observed during placebo maintenance. Atomoxetine dose-dependently attenuated some of the subjective effects of COC (e.g., Drug Liking). These preliminary results suggest that COC is well tolerated during atomoxetine maintenance.

682 MORPHINE NON-COMPETITIVELY INHIBITS [3H]DADL BINDING IN CHO CELLS CO-EXPRESSING MU AND DELTA RECEPTORS

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Background. Based on non-competitive binding interactions we suggested that mu and delta receptors associate as a mu-delta receptor complex in rat brain. Hypothesis. The same non-competitive binding interactions observed in rat brain will be seen in CHO cells that co-express mu and delta receptors, but not in cells that express mu or delta receptors. Methods. We used CHO cells expressing the cloned human mu (mu cell), cloned human delta (delta cell), or cloned mouse delta/human mu (dimer cell) in [3H]DADL binding assays. In most cases, intact cells were treated with 100 nM SUPERFIT, and, after washing three times, cell membranes were prepared. [3H]DADL binding assays followed published procedures and were conducted in 10 mM TRIS-HCL, pH 7.4, 100 mM NaCl, 3 mM MnCl₂, 2 μM GTP. Results. The double receptor expression was confirmed by both western blots and receptor binding. Treatment of dimer cells SUPERFIT decreased [3H]DADL binding to delta receptors by ~75% and to mu receptors by ~30%. SUPERFIT treatment did not decrease [3H]DADL binding to mu cells. The IC₅₀ values for inhibition of [3H]DADL binding to SUPERFIT-treated dimer cells were: DPDPE (66 nM) and morphine (410 nM). [3H]DADL saturation binding experiments with SUPERFIT-treated dimer cells showed that DPDPE (65 nM) increased the K_d (2.4 to 12.1 nM) without changing the B_{max} (464 to 587 fmol/mg protein). In contrast, morphine (400 nM) lowered the B_{max} to 301, a 35% decrease, without changing the K_d. Both DPDPE and morphine were competitive inhibitors of [3H]DADL binding to SUPERFIT-treated mu cells. Conclusion. The mu-delta opioid receptor complex defined on the basis of non-competitive binding interactions in rat brain over 20 years ago likely occurs as a consequence of the formation of mu-delta heterodimers. SUPERFIT treated dimer cells may provide a useful model to study the properties of mu-delta heterodimers. Acknowledgement. This research was supported in part by the Intramural Research Program of the NIH, NIDA.

683 THE IMPORTANCE OF EARLY PROGRESS IN TREATMENT FOR FEMALE SUBSTANCE ABUSERS

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The present study examines the causal modeling of treatment dynamics & change during treatment the context of a women's residential Therapeutic Community program with an enhanced trauma intervention. The research is guided by the TCU Treatment Process Model for understanding the full range of client & programmatic factors that affect in-treatment change & post-treatment outcomes. This study of female substance abusers predicts that therapeutic relationship variables, along with program participation variables, have effects on retention in the program and, in the longer term, on post-treatment outcomes. The study hypothesizes that: (1) Individual change in early engagement (i.e., therapeutic alliance and satisfaction with program) will relate positively to treatment retention and progress in treatment; & (2) Retention & progress in treatment will relate positively to post-treatment outcomes. The study participants (n=260) are women, homeless or living doubled up & at risk for homelessness, who have substance abuse disorders & who are head of household with dependent child(ren). The core investigation uses a quasi-experimental, non-equivalent control group design (women enter either a TC with enhanced trauma services or a standard TC), with prospective, longitudinal repeated measures, intent-to-treat analyses and four assessment points: baseline (program entry), 3-months, 9-months and 15-months post-baseline. Treatment process measures were obtained at 1-month, 3-months and 6-months during treatment. Results: Causal modeling indicates the importance of (a) external circumstances impacting the client at program entry, (b) early therapeutic engagement, (c) personal progress in treatment, which are all related to (d) retention in treatment and successful exit, which, in turn, are related as predicted to reduction in trauma symptomatology at 15-month follow-up. The results of the present study will augment our understanding of treatment dynamics and progress for women in residential substance abuse treatment programs and has important implications for enhancing treatment engagement and retention for that population.

684 ENHANCING TREATMENT ADHERENCE IN COMORBID BIPOLAR AND ADDICTIVE DISORDERS: TREATMENT DEVELOPMENT AND PILOT TESTING

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Treatment adherence is a major clinical problem associated with comorbid substance use and bipolar disorders. The aim of this study is to describe the theoretical bases, treatment development and application of a counseling approach aimed at enhancing treatment adherence for patients with bipolar and substance use disorders. This individual therapy model integrates counseling methods developed for alcoholism and other addictions, such as motivational enhancement therapy and relapse prevention, with educational and relapse prevention therapies proven efficacious in bipolar disorder. The feasibility, acceptability, and utility of this model were tested through three pilot studies. During the first pilot study, patients had a median attendance of 7 out of the 8 weeks of the study (mean=6.2, SD=2.1), and 89% (8/9) of the sample completed four of the eight weeks of treatment. The second pilot was a 12 week study. Five (62%) of the eight subjects who met inclusion criteria completed that study and had 100% attendance rates. One subject was referred to higher levels of care who attended 100% of scheduled sessions prior to referral. Only two (25%) subjects dropped out between week 4 and 6. The third pilot work included five subjects. Of the 40 sessions scheduled in that study, only three were missed (92.5% attendance rate). The therapy was well accepted by patients and was found easy to administer by therapists. These results support the utility of this model in enhancing treatment adherence. Testing this model in larger randomized trials is warranted. Supported USPHS Grants R21 AA 014396 and in part by R01 AA11929; R29 AA10523; R01 DA019992; R01 DA-019142, R01AA13370, NIDA CTN; & VA MIRECC grant.

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685 CORRELATES OF SUBSTANCE USE AMONG HOMELESS YOUTH IN EIGHT CITIES

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Introduction: Little is known about correlates of drug use among homeless youth. Understanding such correlates may be helpful for designing interventions targeting homeless youth. Methods: In 8 cities, 684 homeless youth completed an anonymous survey to assess substance use and related risk factors. Analyses were conducted for youth ages 14-17 (n=181) and 18-24 (n=503). Number of substances ever used (lifetime) and used in the past 30 days (recent) were tested for association with the following predictors: gender, ethnicity, sexual orientation, living status, suicide attempt, onset of substance use, family history of a substance problem, used substances with parent, and survival sex. Significant variables were entered in forward multiple regressions to assess their joint association with lifetime and recent use. Results: For ages 18-24, 35% of the variability in lifetime use and 19% of the variability in recent use was explained by using with a parent, early onset of use, being white, having a family history of a substance problem, being male, and identifying as lesbian, gay, or bisexual (LGB) (F6,363=33.48, $p<0.0005$ and F6,363=15.82, $p<0.0005$, respectively). For ages 14-17, 47% of the variability in lifetime use and 40% of the variability in recent use was explained by using with a parent, ever attempting suicide, being white, early onset of use, and having a family history of a substance problem (F5,125=23.75, $p<0.0005$ and F5,125=18.59, $p<0.0005$, respectively). Conclusions: Discovering these correlates may aid providers in identifying homeless youth who are at greatest risk of substance abuse. Similar correlates of substance use were found for both groups, however for older youth, being male and identifying as LGB were related to greater lifetime and recent use. For those under 18, ever attempting suicide was related to greater lifetime and recent use. For homeless youth providers, it may be useful to screen for suicidality in young homeless youth who are using. Supported by NIDA RO1 DA015522

686 CURRENT MAJOR DEPRESSION IN FORMER CANNABIS USERS

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BACKGROUND. The association between cannabis dependence and major depression is often understood as misdiagnosed expected effects of heavy cannabis use mistaken for depressive syndromes. To investigate whether this could account for the entire relationship, the association of past cannabis dependence with past-year DSM-IV major depression (ie, non-overlapping time frames) was investigated in individuals who no longer use drugs and who drank no more than small amounts. We conducted the study using data from the National Epidemiologic Survey on Alcohol and Related Conditions, a representative sample. METHODS. Former cannabis users who did not use drugs in the last 12 months and who drank no more than 12 drinks in the last 12 months (n=1,887) were divided into those with (n=170) and without (n=1,717) past cannabis dependence. Logistic regression was used to test the association between prior cannabis dependence and current major depression, controlling for demographic characteristics. RESULTS. Past cannabis dependence significantly increased the risk of current major depressive disorder (OR=1.93, CI, 1.16-3.21). This relationship was not attenuated by control variables. CONCLUSION. The strong association between past cannabis dependence and past-year major depression is not entirely an artifact of misdiagnosed expected effects of heavy use. These findings provide important prevention and treatment implications for individuals with cannabis dependence.

687 PREVALENCE OF HEPATITIS C AMONG A COHORT OF HISPANIC INJECTION DRUG USERS

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Although HCV is a serious health problem among injection drug users that require special attention, sparse information is available on the prevalence of HCV among Hispanic IDUs. This paper assesses the prevalence of HCV and related factors within a non-institutional sample of Hispanic IDUs recruited in the streets of Miami-Dade County, Florida. This study started fieldwork in February 2005 and is still being carried out. Participants recruited through street outreach were eligible if they reported injecting drugs on a weekly basis during the previous 6 months, were 18 years of age or older, and were of Hispanic origin. Among the 113 respondents already enrolled in the study, 84.1% tested positive for HCV. Among those who tested positive for HCV, 13.6% also tested positive for HIV. Almost 92% of the Hispanic IDUs who tested positive for HCV reported injecting and consuming alcohol on a daily basis for the last three months. More than half (54.7%) also reported sharing syringes, needles and/or other injection paraphernalia. More than two-thirds (67.4%) reported having had one or more sexual partners in the last three months but only 12.6% reported having protected sex on a regular basis. Among the respondents who tested positive for HCV, half of them (50.5%) reported having fair or poor health and 38.9% needed care in the last 3 months however, only 24.2% had health insurance. Almost two-thirds (62%) of those who tested positive for HCV reported having ever received a positive Hepatitis C test result. Despite the serious public health threat that HCV poses among injection drug users and those who engage in drug use and sex with them, there seems to be a lack of effective prevention efforts among injection drug users regarding the risks of becoming HCV positive, the need for preventing further harm to the liver if they are HCV positive, and how to reduce risks for transmitting HCV to others.

688 IMPACT OF GROUP MOTIVATIONAL INTERVIEWING ON STAGES OF CHANGE IN DUALY DIAGNOSED INPATIENTS

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Motivation to change predicts not only patient engagement and retention in substance related treatment but also treatment outcome and is a dynamic process that may be enhanced. The purpose of this study was to examine whether adding motivational interviewing in a group format (GMI) to the standard treatment program (ST) of an inpatient psychiatric hospital for 101 dually diagnosed patients would move patients in early stages of change for alcohol and drug dependence to later stages. We hypothesized that participants who received GMI would endorse being in the action or maintenance stages for substance use by the 3-month follow-up compared to those receiving ST. Using logistic regression, progress was defined as being in a more advanced stage of change at either the 1 or 3-month follow-up compared to baseline, and the final stage being either 'action' or 'maintenance' according to data derived from the stage-of-change algorithm for alcohol and illicit drugs. Participants already in maintenance at baseline were excluded from these analyses. At the 1-month follow-up, multivariate logistic regression revealed no significant predictors. In contrast, at the 3-month follow-up, treatment group served as a significant predictor ($p = .005$). Participants in GMI were significantly more likely to be in the action or maintenance stages than participants in ST for changing their alcohol use. However, no significant predictors for being in the action or maintenance stage in terms of changing drug use were found at the 3-month follow-up, although results approached significance ($p = .06$). These results support the hypothesis that group motivational interviewing enhances stage of change among dually diagnosed patients with alcohol dependence, but that maintenance strategies (e.g., booster sessions) may be needed to significantly enhance stage of change for patients with drug dependence. Clinical implications and future research directions are discussed. This work was supported by Grant 1 R03 DA016747-01 to E.J. Santa Ana.

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- 689 RISK BEHAVIORS OF OUT-OF-TREATMENT COCAINE BASE PASTE AND COCAINE HYDROCHLORIDE USERS: ONE-YEAR FOLLOW-UP**
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Background: We previously communicated a high frequency of risk behavior of out-of-treatment Cocaine Base Paste users (CPDD, 2002, 2004). Aim: To compare risk behaviors of out-of-treatment CBP users and Cocaine Hydrochloride (CH) users by means of Privileged Access Interviewing in a one-year cohort study. Material and methods: Twenty eight privileged access interviewers were trained to recruit and administer a questionnaire about substance use pattern and related risk behaviors at the intake, six months and 12 months follow up assessments. Recruitment was carried out in the four districts of Santiago of Chile with the highest PBC and CH use prevalence. Inclusion criteria were: at least one CBP (group 1) or CH (group 2) use in the last month, predominant current use of CBP (group 1) or CH (group 2), and without treatment for substance abuse in the last six months (both groups). Generalized Estimating Equations (GEE) were employed to compare risk behaviors through the follow-up. Results: 402 of 467 subjects (86.1%) were followed-up for one year. CBP users (n=204) reported greater frequency than CH users (n=198) of: sexual risk behavior [Odds Ratio (OR): 1.61 (95%CI: 1.16-2.24)]; self inflicted injuries [OR: 2.39 (95%CI: 1.45-3.95)]; suicide attempt [OR: 4.92 (95%CI: 2.11-11.42)]; carrying of weapons [OR: 1.55 (95%CI: 1.11-2.18)]; commission of offenses [OR: 1.72 (95%CI: 1.23-2.40)]. Conclusions: CBP users showed a greater frequency of risk behaviors than CH users during this cohort study. This profile confirm the high vulnerability of CBP users and should encourage further research and outreach interventions particularly focused in this group. Acknowledgement: This research was funded by FONDECYT (Grant 1030431)
- 690 THE RELATIONSHIP BETWEEN DISTRESS TOLERANCE AND ANTISOCIAL PERSONALITY DISORDER AMONG MALE INNER-CITY RESIDENTIAL TREATMENT-SEEKING SUBSTANCE USERS**
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Individuals with co-morbid Antisocial Personality Disorder (APD) and SUD are characterized by aggression, violence, and criminal behavior, and are at an increased risk for poor substance use treatment outcomes. Unfortunately there is an absence of evidence for the effective treatment of APD, highlighting the need for an increased understanding of the mechanisms underlying the development of this disorder. One construct that has been addressed in the literature for understanding vulnerability for substance use is distress tolerance, defined as the ability to persist through emotional distress. Evidence indicates that low distress tolerance is significantly related to the engagement in substance use, inability to sustain an abstinence attempt, and inability to remain in residential substance abuse treatment. In sum, distress tolerance is hypothesized to underlie maladaptive behavioral responses to emotional distress. Similar processes may be occurring among individuals with APD, such that when faced with emotional distress, these individuals are at an increased risk of turning to violence and aggression to alleviate their negative emotions. Thus, we hypothesized that individuals with APD would evidence significantly lower levels of distress tolerance than individuals without APD. As such, we assessed 127 inner-city males receiving residential substance abuse treatment for distress tolerance with two computerized laboratory measures. The mean age of the sample was 40.1 years (SD = 9.8) and 88.2% were African American. As expected, multivariate logistic regression analyses indicated that low distress tolerance significantly predicted the presence of an APD diagnosis, above and beyond demographics, substance use severity, and diagnostic status ($\chi^2(3) = 16.39, p < .01$), suggesting that low levels of distress tolerance may be a key factor in understanding the development of APD, thereby setting the stage for future studies and the development of appropriate interventions for this at-risk group.
- 691 CANNABIS-USING SCHIZOPHRENIA PATIENTS TREATED WITH ATYPICAL NEUROLEPTICS: DO THEIR SYMPTOMS DIFFER FROM THAT OF CANNABIS ABSTAINERS?**
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PURPOSE: Most studies investigating the influence of cannabis use on schizophrenia symptom patterns have been performed in patients treated with typical neuroleptics (TN). Since a cannabis-TN combination might be particularly disadvantageous, this study examined schizophrenia symptoms in a group of cannabis using schizophrenia outpatients treated with atypical antipsychotics. SAMPLE: Forty-three schizophrenia patients treated with atypical neuroleptics on an outpatient basis. Patients were divided into three groups: Cannabis abstainers, moderate users, and daily users. METHODS: All patients completed a questionnaire assessing demographic and drug use characteristics. Next, patients were interviewed by the semi-standardised Positive and Negative Syndrome Scale (PANSS). Cannabis use was assessed by self-declaration. RESULTS: No differences were found between the abstainers, the moderately, and the daily cannabis using schizophrenia patients on the PANSS scores. CONCLUSION: Cannabis use had no influence on symptom patterns in schizophrenia patients treated with atypical neuroleptics.
- 692 PREDICTORS OF RETENTION IN AN ADOLESCENT AND YOUNG ADULT SMOKING-CESSATION TRIAL**
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Attrition rates in smoking cessation programs for youth are high, and cessation rates appear to correlate with the amount of treatment received. Thus, it is important to examine the characteristics of early dropouts to foster increased adherence to treatment and cessation rates. We examined data on 52 adolescents and young adults (mean age = 20.9 years, SD = 3.20; 51.9% female) in a smoking cessation trial to determine which personal variables are associated with early dropout. Subjects were screened using the Structured Clinical Interview for DSM-IV Axis I Disorders, the Kiddie-SADS Present and Lifetime Version, and the Family History-Research Diagnostic Criteria interview. In addition, subjects completed a 7-item impulsivity questionnaire and the self-report Social Support Questionnaire. Subjects smoked at least 10 cigarettes daily for the 3 months before entering the 10-week treatment. Analysis was done using the general linear model for the variables of interest, with treatment length as the dependent measure. A history of a depressive disorder ($F = 4.28, p = .04$) or non-nicotine substance use disorder (SUD; $F = 5.31, p = .03$) were significant predictors of early dropout. Gender had a trend towards predictive power ($F = 3.01, p = .09$), with males receiving more treatment than females. There was also an interaction between gender and SUD, wherein females with SUD history had a tendency to drop out earlier from treatment than their male counterparts ($F = 2.57, p = .07$). The level of social support, impulsivity, history of disruptive behavioral disorders and familial psychiatric or SUD diagnosis were not predictors of retention in treatment. Because nicotine dependence may further exacerbate depressive and SUD symptoms and increase morbidity, these findings highlight the need to develop effective methods to engage these youth in smoking cessation programs. Supported by DA15131 and a Children's Medical Center Foundation grant.

693 IMAGING CHANGES IN BRAIN FUNCTION AND STRUCTURE IN AN ANIMAL MODEL OF INHALANT ABUSE

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Neurological function can be impaired from chronic toluene abuse and neuroimaging studies provide evidence of white matter disease. Therefore, we combined PET and MRI in adolescent rats to test the hypotheses that (1) reinforcing doses of inhaled toluene produce changes in FDG uptake and (2) these metabolic alterations relate to toluene-induced changes in white matter. Adolescent male Sprague Dawley rats received FDG and 11C-toluene PET scans followed by MRI scans using a magnetization transfer (MT) contrast (n=16; microPET R4, CTI; MRI: 9.4T 21-cm horizontal, Magnex Scientific). Animals were then conditioned with 2000 or 5000 ppm inhaled toluene in a modified conditioned place preference (CPP) chamber. Following 12 exposures, animals again received FDG PET and MRI MT scans. Their brains were then stained for myelin using the Weil method. A separate group of adolescent animals (n=8) were scanned again 2 mos later to examine recovery of brain function following toluene cessation. All data were spatially pre-processed, normalized to stereotaxic space and segmented. PET and MRI images were globally normalized to the mean voxel value and the same ROI template was applied to all scans. Regional changes in brain function relative to the conditioned response were made using Statistical Parametric Mapping (SPM) t-maps and region of interest (ROI) analyses. 2000 ppm toluene produced a stronger CPP than 5000 ppm. Locomotor activity decreased with increasing toluene exposures. 11C-Toluene uptake was highest in pons, colliculi and the internal capsule. These regions also showed the largest decrease in MT ratio, whereas the most significant changes in FDG occurred in cortical areas. Histological data supported the decline in MTR signal. Whole brain FDG uptake decreased although there was a significant rebound following toluene cessation. Correlations between the change in MTR and the change in FDG ($R^2 = 0.76$) suggest that a distinct functional versus anatomical profile characterizes the detrimental effects of toluene abuse.

694 GENDER DIFFERENCES IN IMPROVEMENT IN READINESS TO CHANGE CRACK COCAINE USE: COMPARING PEER-ENHANCED VERSUS STANDARD HIV PREVENTION INTERVENTIONS

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For over 25 years researchers have studied behavior change and addiction using the Transtheoretical Model. Research on the impact of intervention type as well as gender on readiness to change is scarce. EachOneTeachOne, a NIDA-funded HIV prevention study, aimed to reduce HIV risk behaviors among out-of-treatment drug abusers. It provided the opportunity to evaluate readiness to change cocaine use by intervention type (standard HIV education versus peer-enhanced) and gender using intent to treat analyses. Of the 929 crack cocaine users who completed a 3-month follow-up, 384 individuals (153 women, 231 men) were in the standard and 545 (241 women, 304 men) were in the peer-enhanced intervention. Four levels of crack cocaine use characterized users' days used in the past 30 days: none (0), low (1-5), moderate (6-14), and high (15-30). A continuous readiness score (Diclemente et al., 2004) was used to detect improvement in readiness to change cocaine use on three levels: precontemplation, contemplation, and preparation/action. As expected, there were no differences between intervention groups on readiness at baseline. Most participants were in contemplation (87% at baseline, 88% at follow-up). In terms of crack cocaine use, 54% were 'high' level users at baseline, with more women at this level (58%) than men (51%). Over time, frequency of crack cocaine use decreased from baseline (66% improved), with the peer-enhanced group showing greater improvement than the standard (70% vs. 61%). Among women in the standard intervention who improved in readiness score, 88% reported reduced frequency of crack cocaine use. The high numbers of individuals who remain in contemplation at baseline and follow-up suggests the need to refine the continuous readiness scoring algorithm or to better understand the impact of our intervention. Further analyses will examine both readiness score cutoff points as well as other explanations for findings.

695 RANDOMIZED CONTROLLED TRIAL OF LEVODOPA-CARBIDOPA AND BEHAVIOR THERAPY FOR COCAINE-DEPENDENT OUTPATIENTS

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Levodopa-carbidopa has been considered as a potential cocaine pharmacotherapy on the premise that this dopamine precursor may help to restore natural dopamine levels following cocaine discontinuation. In early feasibility and dose-ranging studies, we found l-dopa to have a favorable safety profile but only a weak efficacy signal. To enhance effectiveness, l-dopa was examined in combination with the behavioral intervention of contingency management (CM). The design was a 12-week randomized, double-blind, outpatient clinical trial. Participants (N=152) were assigned to one of two medication conditions: l-dopa/carbidopa (800/200) or placebo; crossed with one of three therapy conditions: clinical management, cognitive behavioral therapy, or CM (vouchers contingent on cocaine-negative urine tests). Outcome data were analyzed by generalized estimating equation (GEE) models for repeated-measures. Treatment retention was highest in the l-dopa + CM group (45%) compared to all other treatment groups (mean = 15%). A significant medication main effect for proportion of benzoyllecognine (BE)-negative urines emerged, favoring l-dopa (64%) treatment over placebo (49%). Adding CM therapy to l-dopa treatment significantly increased the rate of sustained cocaine abstinence with 41% of the subjects in the l-dopa + CM group achieving 3 consecutive weeks of BE-negative urines, compared to less than 15% of the subjects in the other treatment groups. L-dopa was well tolerated and good levels of medication compliance were obtained. Future studies examining an agonist approach for cocaine dependence should consider the joint application of pharmacological and behavioral "replacement" interventions.

696 ACAMPROSATE DECREASES THE SEVERITY AND DURATION OF RELAPSE AND AIDS IN POST-RELAPSE RECOVERY OF ABSTINENCE IN ALCOHOL-DEPENDENT PATIENTS

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Background: A major goal of alcohol dependence treatment is relapse prevention. Acamprosate, with psychosocial support, is effective in helping alcohol-dependent patients maintain abstinence and regain abstinence following relapse. In the current analysis, we examined the effect of acamprosate on relapse severity in patients who returned to drinking, and assessed their post-relapse recovery. Methods: The intent-to-treat (ITT) population from three double-blind, placebo-controlled, multicenter, pivotal trials (13-, 48-, and 52-weeks) in which patients received acamprosate 1998 mg/day (n=372) or placebo (n=375), in combination with psychosocial therapy, was evaluated for the quantity of alcohol consumption during relapse (at Day 0, 30, 60, 90, last visit). Weekly frequency of alcohol consumption (13-week) and duration of individual relapse episodes (48-week) were also reported. In an ITT population subset with ≥ 1 documented relapse before last study visit, rate of complete abstinence, percent days abstinent, and time to first drink were analyzed on abstinence periods post-relapse. Results: Of 747 patients, 616 relapsed over the study course (placebo, 89%; acamprosate, 76%). Post-relapse recovery was evaluated in patients who relapsed before last study visit (n=587). Pooled data show a significantly smaller proportion of acamprosate- than placebo-treated patients reported consuming >5 standard drinks/day during the interval preceding Day 30, 60, 90 and last study visit ($p < 0.01$). Acamprosate was statistically superior to placebo ($p < 0.05$) for the frequency of alcohol consumption during relapse (13-week) and relapse duration (48-week). A significantly greater proportion of acamprosate- vs. placebo-treated patients regained abstinence following initial relapse and maintained it for the trial remainder (13% vs. 5%, respectively; $p < 0.001$). Conclusions: In addition to helping alcohol-dependent patients maintain abstinence, acamprosate reduces relapse severity in patients who return to drinking and aids in abstinence recovery.

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697 PRESCRIPTION DRUG ABUSERS: ABUSE IS NOT ABUSE IS NOT ABUSE

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Prescription drug abuse has been increasing over the past 10 years (DAWN, NSDUH, MTF). These increases have warranted concern by the FDA, DEA, clinicians, congress and others resulting in requests to develop risk management plans (RMP) designed specifically to track problems of abuse and diversion of newly marketed controlled substances. The RMPs are designed to not only monitor for abuse and diversion, but characterize the nature and extent of the problem, and guide the implementation of interventions to control or reduce these problems. Interventions become difficult when the various types of prescription drug abusers and diverters are considered. These include: health care professionals; hard core opioid addicts (heroin); hard core opioid addicts (prescription drugs); polydrug abusers; rave abusers; inexperienced (casual) abusers; patient abusers/addicts; patient diverters; entrepreneur/pill brokers and sham patients. Each of these types of abusers present unique characteristics that make a single approach to monitoring and reducing abuse and diversion difficult since the various types of abusers may be present in different localities, i.e. heroin addicts in urban areas and primary prescription abusers in rural areas and obtain the drugs through different means. In addition, media responses to abuse by these different populations is variable with much more attention given to the inexperienced abuser and diverters than to the hardcore abusers. Descriptions of each of these types of abusers and diverters will be presented along with approaches that may be used to monitor and reduce this abuse and diversion.

699 EFFECTIVE USE OF MOTIVATIONAL SKILLS BY THERAPISTS IMPROVES CLIENT MENTAL HEALTH AND SUBSTANCE USE STATUS

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This study tested the hypothesis that therapy of clients with co-occurring mental health and substance use disorders (COD) using Motivational Interviewing (MI) would yield significantly better outcomes than usual treatment and that this would reflect model-consistent changes in therapist behavior. After a control period, clinicians received MI training and then employed MI in all individual therapy sessions. Using an interrupted time series design, we studied 10 therapists and 18 clients from two mental health clinics. Therapists received MI training in a 2-day workshop with demonstrations and role-play of MI skills, plus 8 bi-weekly MI coaching sessions. All therapy sessions were audio taped and randomly selected tapes were analyzed for MI skill performance. Clients completed surveys after each session, including Brief Symptom Inventory, Readiness to Change algorithm, Substance Use Questions, and Working Alliance Inventory. A three level Hierarchical Linear Model was used to examine impact of therapist training on clients' global BSI, RTC, substance use, and WAI. For each clinician-client dyad, MI fidelity measures were averaged and included in the second level of the HLM model. Client impact variables were examined as a function of key MI skills performance. Following therapist training there was a significant reduction in Global BSI and significant increases in RTC Medication Use, Client and Therapist WAI. Post training changes in these client variables were related to therapist improvement in specific MI skills. For example, BSI changes were associated with a reduction in the number of therapists' Closed Questions and an increase in clients' Self Motivational Statements (SMS). Post training decrease in client Drug Use was related to more frequent SMS and a reduction in Closed Questions. The acquisition and effective use of MI skills by mental health therapists for treatment of COD yields significant improvement in client mental health and substance abuse. Specific changes in client variables are related to enhancement of MI consistent behavior.

698 THE COLORADO WOMEN'S PRISON PROJECT: PRELIMINARY FINDINGS AT BASELINE - SUBSTANCE ABUSE BEHAVIORS, HISTORIES, AND SERVICE NEEDS/UTILIZATION OF YOUNG AND MATURE FEMALE OFFENDERS

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CO-WPP is a 5-year NIDA sponsored study whose purpose is to compare the effectiveness of 2 prison-based SA treatment models for female offenders, a Therapeutic Community and an Intensive Outpatient Program. Preliminary data is based on an initial cohort of 523 female offenders admitted to the Denver Women's Correctional Facility (DWCF) between Feb. 2002 and October 2005. Little is known about treatment for the female offender population in our prisons and even less is known about the profiles and needs of the aging female offender. In this poster, we compare the demographic profiles, substance abuse (SA), criminal justice involvement, and other risk behavior histories prior to the present incarceration of Young (less than age 40), n=377, 72%, and Mature (age 40+), n=146, 28%, female offenders recommended for intensive SA treatment during their present incarceration term. We further identify the 2 age cohorts' self-reported service needs 6 mo. prior to the present incarceration and subsequent service utilization while in prison. The total female offender cohort is predominantly Caucasian, under-educated, and unmarried; more than 1/3 had been unemployed in the year prior to their current arrest; the median age is 35. The women in the study have an extensive LT arrest history. Over 3/4 of them are parents, with an average of 3 children. While none of the services offered are age-specific, the 2 age cohorts utilized the services offered at DWCF at similar proportions. The profiles and behavior histories of the 2 age cohorts will be examined to identify and suggest more age-appropriate services for incarcerated female offenders.

700 RANDOMIZED, DOUBLE BLIND COMPARISON OF DRUG COUNSELING COMBINED WITH BUPRENORPHINE, NALTREXONE OR PLACEBO FOR TREATING OPIOID DEPENDENCE AND REDUCING HIV RISK IN MALAYSIA

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BACKGROUND: Injection drug use (IDU) and heroin dependence are driving the HIV/AIDS epidemic in many Asian countries, including Malaysia, where drug treatment has not been available. SPECIFIC AIMS: To introduce buprenorphine maintenance treatment to Malaysia and compare the efficacy of drug counseling alone (DC) or DC combined with naltrexone maintenance (NTX+DC) or combined with buprenorphine maintenance (BUP+DC). STUDY DESIGN: Randomized, double blind 24 week clinical trial with recently detoxified opioid dependent subjects (N=126). Medications (active or placebo BUP or NTX) were dispensed three times per week under direct observation. Outcome measures included three times per week urine toxicology testing and weekly and monthly self-report of drug use and HIV risk behaviors. RESULTS: The subjects were comparable at baseline with regard to important demographic or drug use characteristics: (mean age 37 years; 69% Malay 29% Chinese ethnicity; 63% < 9 years education; 41% unemployed; 71% single; mean 15 years using opiates; 79% lifetime IDU; 41% current IDU). Retention (mean \pm SD days) was significantly higher ($p < .001$) with buprenorphine (132 ± 50) compared to naltrexone (100 ± 63) or placebo (83 ± 51). BUP+DC was associated with a significantly longer duration of documented abstinence (mean \pm SD days 52 ± 60 compared to 30 ± 52 for DC and 36 ± 57 for NTX+DC, $p < .05$ for both comparisons). IDU decreased significantly from baseline across treatment groups, but sexual risk behaviors did not decrease from baseline during treatment, and there were no significant differences associated with treatment condition regarding IDU or sexual risk behaviors. CONCLUSIONS: The superior efficacy of BUP+DC compared to either NTX+DC or DC only as well as the greater ease of induction and patient acceptance of buprenorphine strongly supports the implementation and dissemination of buprenorphine maintenance treatment. Supported by R01 DA14718, K24 DA000445

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- 701** **CONDITIONED TASTE AVERSION TO A VARIETY OF SUBSTANCES IS REDUCED IN ADOLESCENTS COMPARED TO ADULTS**
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The balance of reward and aversion during an individual's first experience with a drug contributes to his future drug taking behavior. Most drug use begins during adolescence and in this period the transition to abuse often occurs rapidly. We hypothesized that the balance between reward and aversion is shifted during this developmental window. We used conditioned taste aversion (CTA) to examine the aversive effects of a psychostimulant, cocaine, a cannabinoid, THC and an emetic, lithium chloride, in adolescent (28-day-old) and adult (65-day-old) rats. In CTA, rats learn to associate the sensations of an injected substance with the taste of a novel saccharin solution. Subsequent reduction in saccharin consumption indicates aversion to the injected substance. Adolescent rats exhibited reduced aversion to all three substances compared to adults. Results were most marked for cocaine, which generated less aversion at a range of doses (10-40 mg/kg). For THC and LiCl, age-specific differences existed at lower doses, while higher doses resulted in equivalent aversion in the two ages. These data suggest that adolescence may be a time of reduced susceptibility to aversive stimuli, or that adolescents are more impulsive or less likely to learn from aversive consequences. The latter explanation is consistent with the fact that we found similar results across drug classes. Another explanation may be that adolescents have less neophobia for the sweet taste of saccharin, and are therefore less likely to avoid it. Our data from saccharin consumption during association training suggests that either of these could be true. Adolescents consumed equal amounts of water and saccharin on the pre-association training days, but adults consumed less saccharin than water. The results suggest that one explanation for the increased prevalence of drug use during adolescence and the relative speed with which adolescents progress from use to dependence could be a lack of use-limiting effects of the drugs manifested here as a lack of taste aversion. Supported by NIDA DA09079.
- 702** **PRENATAL OPIATE EXPOSURE FOLLOWED BY POSTNATAL WITHDRAWAL ENHANCES THE CORTICOSTERONE RESPONSE TO COCAINE IN ADULT RATS**
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Activation of the hypothalamic-pituitary-adrenal (HPA) axis is associated with increased risk of drug abuse initiation, escalation, and relapse. Developmental insults that alter HPA axis responsivity thus have the potential affect addiction vulnerability. We previously found that postnatal withdrawal from chronic prenatal opiate exposure is a developmental stressor, activating the HPA axis. Presently we examine the corticosterone response to acute injection with saline or cocaine in adults that received prenatal exposure to the long-acting opiate 1- α -acetylmethadol (LAAM). Female Sprague-Dawley rats were administered 1.0 mg/kg/day LAAM or water via daily oral gavage for 28 days. Treatment continued throughout breeding and pregnancy. After birth pups from both groups were fostered to lactating, untreated dams. As adults the rats were implanted with jugular catheters (n=8-9 per group, half male and female). After recovery and adaptation to the blood draw procedure, the rats were injected with saline or cocaine (15 mg/kg, ip). One week later they received the alternate treatment, in a counterbalanced fashion. Blood was drawn at times 0, 15, 30, 45, 60, and 90 min post-injection. Sera corticosterone were measured by ELISA. ANOVA revealed no sex differences or interactions. Prenatal treatment did not affect basal corticosterone (80-93 ng/ml) or the response to saline. Both prenatal groups had elevated corticosterone to cocaine at 15, 30, and 45 min. However, the response to cocaine at 15 min was nearly two-fold greater in the prenatal LAAM compared to the prenatal water-treated group. This shifted time of peak response to cocaine to 15 min for prenatal LAAM vs. 30 min for prenatal water-treated rats. The magnitude of the corticosterone effect at 30 and 45 min was similar in both prenatal treatment groups. These data indicate that history of developmental exposure to opiates and opiate withdrawal affects the HPA axis response to acute cocaine challenge in adulthood. This may have implications for increasing abuse liability in affected populations.
- 703** **INCREASED ANXIETY-LIKE BEHAVIOR DURING NALOXONE-PRECIPIATED WITHDRAWAL FROM ACUTE OPIOID DEPENDENCE**
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Acute treatment with morphine enhances the potency of opioid antagonists to elicit withdrawal signs, demonstrating acute dependence on opioids. Naloxone-induced brain reward deficits as measured by brain stimulation reward thresholds are seen after a single pretreatment with a moderate dose of morphine (MOR; 5.6 mg/kg), and additional MOR treatments at daily intervals increase further these brain reward deficits (Liu & Schulteis 2004, *Pharmacol Biochem Behav*, 79:101). These brain reward deficits may serve as an animal model of the dysphoria that accompanies withdrawal in opioid addicts; the current study examined whether anxiety-like behavior seen in opioid withdrawal could also be measured following acute MOR pretreatment. ACUTE groups were injected once subcutaneously (SC) with vehicle, 5.6 or 10 mg/kg MOR 4 hr prior to SC naloxone (NAL; 0.33-3.3 mg/kg); 5 min after NAL, rats explored an elevated plus-maze for 5 min. REPEAT groups received vehicle, 5.6 or 10 mg/kg MOR daily for 4 days, with NAL treatment and p-maze testing occurring 4 hr after final pretreatment. NAL did not alter behavior in the absence of morphine pretreatment. ACUTE 10 mg/kg MOR resulted in a significant reduction in exploration of the open arms of the maze following NAL 3.3 mg/kg, but ACUTE 5.6 mg/kg MOR did not elicit a NAL-induced effect. REPEAT MOR at 10 mg/kg further shifted NAL potency to elicit reductions in open arm exploration (1.0-3.3 mg/kg NAL), and REPEAT 5.6 mg/kg MOR also elicited an effect (3.3 mg/kg NAL). Results indicate that increased anxiety-like behavior accompanies acute opioid dependence, but higher MOR doses appear necessary under ACUTE conditions to elicit effects in the plus-maze relative to doses that elicit brain reward deficits. REPEAT MOR experience with the lower dose begins to elicit NAL-precipitated reductions in open arm exploration, suggesting that anxiety-like behavior may be elicited more slowly as opioid dependence develops than brain reward deficits. Supported by DA010475 and VA MERIT Award to GS.
- 704** **CONTINGENCY MANAGED HOUSING AND BEHAVIORAL DAY TREATMENT IMPACTS DRUG ABSTINENCE AMONG HOMELESS: META-ANALYSIS OF FIVE BIRMINGHAM COCAINE STUDIES**
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A meta analysis was conducted from five clinical trials to assess the affects of contingency management (CM) and behavioral day treatment (BDT) on abstinence. Analyses were conducted for the two-month (11 treatment arms) and six-month (9 treatment arms) points after admission. Each treatment arm was classified as CM + BDT (5), CM only (1), BDT only (3), or neither of the three (2). For the two-month analysis, a model that included CM, BDT, and their interaction yielded a significant interaction (p=0.022), and the model-based abstinence prevalence estimates (pe) and standard errors (se) from lowest to highest were: neither treatment (pe=0.36, se=0.052), BDT only (pe=0.49, se=0.025), CM+BDT (pe=0.65, se=0.020), and CM only (pe=0.73, se=0.032). Pairwise hypothesis tests showed prevalence with neither treatment to be lower than that for all other treatment regimens (p<0.05), and CM only to have higher prevalence than either CM+BDT (p=0.0015) and BDT only (p=0.0006), but the difference between BDT only and CM+BDT was not significant (p=0.075). Because the interaction term for the six-months was not significant (p=0.06), estimates were generated using a main effect model. Model based mean estimates showed an effect for CM (prevalence of 0.58 for those with CM and 0.29 for those without, p<0.001), but not a significant difference for BDT (prevalence of 0.48 for those with BDT and 0.39 for those without, p=0.053). Results show that both CM and BDT are beneficial in producing abstinence, but the CM treatment appears to have a stronger effect than BDT.
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705 CUE-INDUCED BRAIN ACTIVITY CHANGES AND RELAPSE IN SMOKERS

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Background Imaging studies have identified the importance of the dorsolateral prefrontal cortex (DLPFC), the orbitofrontal cortex (OFC), the anterior cingulate cortex (ACC), and the amygdala in drug-related cue reactivity. Assuming a connection between cue reactivity and relapse, the aim of this study was to determine whether cue induced activity changes in these brain regions is able to predict outcome in a nicotine cessation treatment. Methods 18 smokers consuming more than 15 cig./day for more than 2 years participated in a fMRI study using a cue-reactivity paradigm. Smoking related and neutral videos clip: were presented in random order, each with a duration of 30 seconds. All subjects then participated in a 6 months nicotine cessation program. Of the 18 smokers, 9 (age: 38.9 +/- 6.9 yrs; 5 male, 4 female) relapsed during the treatment program, while 9 (age: 40.3 +/- 7.4 yrs; 3 male, 6 female) remained abstinent during this time period. The fMRI-examinations were performed on an Achieva 3.0T whole body MRI system (Philips, Best, Netherlands). Further technical details: Birdcage quadrature headcoil, GE-Single Shot EPI (TE/TR/Flip=35/3000/90°), 3.6x3.6x3.6mm³, 3 runs with each 245 dynamic scans. Pre-processing and statistical analyses were conducted with SPM2. Results The categorical comparison revealed enhanced activity in the "relapse group" in the DLPFC (bilateral), OFC (bilateral), ACC, supplemental motor area and parietal cortex ($p < 0.005$, uncorrected). Conclusion Consistent with our hypothesis, we were able to show that brain regions activation associated with smoking related cues were differentially more activated in smokers who relapsed during the six month cessation treatment compared to smokers that remained abstinent. These findings support the known role of frontal and cingulate regions in cue reactivity. Relapsing subjects with less activation in these regions resembled reported activation patterns of non-treatment seeking substance dependent subjects (Wilson et al., 2004).

706 DIFFERENCES IN CHARACTERISTICS BETWEEN IN- AND OUT-OF-TREATMENT HEROIN ADDICTS

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Half or more of heroin-addicted individuals in the U.S. are not enrolled in drug abuse treatment. Both duration and severity of drug use have been reported to be related to treatment entry, contributing to a belief that an addict must 'hit bottom' before feeling the need to enter treatment. To further clarify factors associated with treatment entry, selected ASI items as well as ASI composite scores of 82 heroin-dependent adults enrolling in six Opioid Treatment Programs and of 24 out-of-treatment heroin-dependent adults recruited from the community using targeted sampling were examined. The two samples were compared using chi-square goodness-of-fit tests for categorical variables and one-way ANOVA for continuous variables. No significant differences were found between the groups in terms of age, gender, education, lifetime arrests, years of heroin or cocaine use, or days paid for working. There were also no significant differences in the ASI Drug and Alcohol Use, Medical, Family/Social, or Psychiatric Status composite scores. However, the out-of-treatment group had significantly lower ASI Legal ($p < .009$) and Employment ($p < .02$) composite scores. Finally, the in-treatment group had significantly more prior treatment episodes ($p < .001$) than the out-of-treatment group. These results indicate that, in contrast to earlier reports, duration of drug use was not a factor in treatment entry, and that problem severity as might be suggested by drug use, family, medical, or psychiatric issues were likewise unrelated to treatment entry. While sample sizes dictate obvious caution in the interpretation of findings, the data suggest that the decision to enter drug treatment by a contemporary population of heroin addicts is not dictated by duration of drug use or by several of the factors that are often seen as related to problem severity. Rather, external factors, such as a higher degree of legal and employment problems and individual factors, such as prior treatment experience, may be primarily responsible for decisions to enter treatment.

707 GENDER DIFFERENCES IN THE PATTERN AND PREDICTORS OF THE CYCLE OF RELAPSE, TREATMENT RE-ENTRY AND RECOVERY

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This study explores gender difference in the pattern and predictors of transition between relapse, treatment re-entry, and remission over a 4 year period. Data are from 1,202 adults recruited between 1996 and 1998 from sequential admissions to a central intake unit and 12 treatment facilities in Chicago. Participants were predominantly African American (89%), female (60%) and used cocaine, alcohol, opioids, and marijuana. adults. Participants were interviewed annually 2 through 6-years post-intake (94+ % follow-up per wave). Participants were classified annually (1) in the community using, (2) incarcerated, (3) in treatment, or (4) abstinent. Most participants (79%) transitioned from one point in the cycle to another during the 4 years (31% two times, 19% three times, and 7% four times). The pattern of transitions and predictors of transition varied significantly by gender. The predictors varied by the type and direction of transition (e.g., using to abstinence vs. abstinence to using). Notably, among males more prior treatment (at the index intake) was related to remaining abstinent but among females it was related to relapsing. These finding indicate that the factor related to transitioning differ by gender and where the person is in the recovery cycle and suggest the importance of doing subgroup analysis. (Supported by NIDA DA15523.)

708 TEACHER REPORT OF AGGRESSIVE BEHAVIORS IN PRENATALLY COCAINE-EXPOSED AND NON-COCAINE-EXPOSED CHILDREN AT 9 YEARS OF AGE

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The purpose of the current study was to investigate aggressive behaviors in a sample of high-risk cocaine exposed children. The participants [$n=323$, 162 cocaine exposed (CE), 160 non-cocaine exposed (NCE)] were recruited at birth as part of a longitudinal study. At age 9, two teacher report measures, the Reactive/Proactive Aggression Questionnaire (Re/Pro) & Children's Aggression Scale Teacher version (CAST), were collected. It was predicted that CE children would have higher aggression scores as compared to NCE children. In particular, CE children were expected to have higher reactive aggression scores than NCE children. No mean differences were found on any of the aggression scores. In both CE and NCE children, mean scores on the CAST were similar to an independent sample of children diagnosed with Conduct Disorder. Regression analyses suggested that children's hyperactivity significantly predicted aggression at age 9. These results suggest that this high-risk sample display clinical ranges of verbal aggression and physical aggression. Further assessment of behavioral outcomes in this sample is warranted given the rates of aggressive behaviors seen at age 9.

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- 709** THE COMPLEX ISSUE OF TREATMENT READINESS IN AN OFFENDER POPULATION
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Motivational Enhancement Therapy (MET) is a treatment approach that utilizes motivational interviewing (MI) principles to enhance clients' internal motivation and commitment to change. This study examines the early effects of MET on drug court probationers' motivation for treatment. Drug court probationers were randomly assigned to either a two-session MET intervention (n=81) or a two-session drug education (DE) intervention (n=76) as they began treatment at one of three participating outpatient drug-free Baltimore treatment programs. The two groups did not differ at baseline in terms of motivation, drug abuse and criminal history, or demographic/background variables. At one month from baseline assessment the MET and DE groups did not differ in terms of motivation scores (Treatment Readiness - TR) or in change from baseline TR scores. Findings were next examined for the sample of all study participants (n=196) entering treatment, including 39 clients assigned to MET or DE who did not elect to attend their respective MET or DE sessions. Results indicated that one-month TR scores, unlike baseline TR scores, successfully predicted days retained in treatment. Similarly, positive change in TR scores from baseline to one month successfully predicted days retained in treatment. Finally, baseline evidence of depression and lifetime history of arrests were negatively related to days in treatment. Findings suggest that, for this population of criminal justice referrals, baseline measures of motivation provide an inaccurate estimate of clients' capacity to derive benefit from treatment, and that one month's experience with a treatment program appears critical to clarifying treatment readiness.
- 710** A STRUCTURED FIELD STUDY ASSESSING THE ABUSE POTENTIAL OF DIFFERENT OPIOID FORMULATIONS IN CANADA
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New opioid formulations should be evaluated for abuse potential. The objective of this study was to compare the abuse and tampering potential of a fentanyl matrix patch (FM) to other opioid formulations in Canada. It was hypothesized that a FM patch may have higher abuse potential compared to a fentanyl gel patch (FG). This field study used structured interviews with 42 tampering-experienced, recreational opioid users from 3 Canadian cities. Subjects were presented with 9 products (some hypothetical): 3 formulations (tablet [T], reservoir gel patch [G] and matrix patch [M]) for each of 3 opioids (fentanyl [F], oxycodone [O] and hydromorphone [H]). No products were actually administered. Abuse potential was assessed using two 7-point Likert scales (Value of Product, Likelihood to Tamper), rank order of desirability, a validated Opiate Attractiveness Scale (OAS), relative street value, and open narratives. Comparisons of each formulation to FM were made on rank data with nonparametric methods. The FT, FM and HT were the most valued and likely to be tampered with. The decreasing order of desirability was FT>HT>FM>FG>OT>HM>HG>OM>OG. OT was ranked highest on the OAS. FM was significantly (P<0.001) more attractive than all gel products (statistically similar in attractiveness to FT, HT, OT and OM). Overall, FM had the highest derived dollar value of the test products, followed by FT and FG; however, the differences were not statistically significant. Of 42 subjects, 60% preferred a matrix to a gel patch. Of subjects preferring a gel patch, 59% were from a region unfamiliar with the formulation. Fentanyl is attractive to opioid abusers regardless of formulation. In Canada, a fentanyl matrix patch may have a higher risk of diversion, tampering and abuse than other transdermal opioid formulations. This should be confirmed by prospective epidemiological studies. [Supported by Janssen-Ortho Inc.]
- 711** STREPTOZOTOCIN-INDUCED DECREASES IN DOPAMINE CLEARANCE AND LOCOMOTION ARE NOT RESTORED BY INSULIN REPLACEMENT
R. J. Sevak(1), W. A. Owens(2), L. C. Daws(2), A. Galli(3) and C. P. France(1), (1) Department of Pharmacology, and (2) Department of Physiology, University of Texas Health Science Center, San Antonio, TX and (3) Vanderbilt University, Nashville, TN
Changes in circulating insulin are correlated with changes in sensitivity to the behavioral effects of dopaminergic drugs and in vitro studies suggest that insulin pathways can regulate the expression and activity of the dopamine transporter (DAT); however, it is not clear whether insulin signaling, or some other mechanism, mediates these changes in dopaminergic function. The present study examined DAT activity (in vivo chronoamperometry) and locomotor activity in rats that received streptozotocin (STZ, 50 mg/kg, i.p.) and later a sustained-release insulin implant (Linplant). Seven days after STZ treatment, blood glucose concentration was markedly increased while body weight, spontaneous locomotion, and dopamine clearance were significantly decreased. Eight days after insertion of the Linplant (9 days after STZ), blood glucose concentration as well as body weight were normalized to pre-STZ values. However, for up to 23 days after insulin implantation, neither dopamine clearance nor locomotion recovered to pre-STZ values. To the extent that significant concentrations of insulin (from the s.c. Linplant) penetrated the brain, these results suggest that STZ might have actions, in addition to decreasing circulating levels of insulin, that contribute to its profound effects on brain neurochemistry and on behavior. Supported by DA 14684 (AG), DA 17198 (CPF) and DA18992 (LCD).
- 712** HEPATITIS C STATUS AMONG HEROIN AND COCAINE INJECTION DRUG USERS: THE ROLE OF INTELLECTUAL FUNCTION DEFICITS
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The present study sought to evaluate intellectual functioning as a possible risk factor of hepatitis C among injection drug users. This study is based on data from the International Neurobehavioral HIV Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of HIV, and Hepatitis A, B, and C in the U.S, South Africa, and Russia. The total U.S. sample consists of 632 injection and non-injection drug users between 15 and 50 years of age in the Baltimore region. The sample of the present study was limited to 183 injection drug using (44 African American and 139 White) subjects that were 65.0% male with 69.4% testing positive for hepatitis C at baseline. Intellectual functioning was measured by the Shipley with the sample partitioned into intellectual functioning quartiles according to their overall Shipley T-score. Multinomial logistic regression indicated that injection drug users in the lowest (OR = 5.07; 95% CI = 1.76; 14.56) quartile were significantly more likely than injection drug users in the fourth or highest quartile to test positive for hepatitis C while controlling for gender and ethnicity. Namely, 86.4% of injection drug users in the lowest quartile tested positive for hepatitis C, while 55.3% of injection drug users in the highest quartile tested positive for hepatitis C. The Shipley T-score controls for age and education so these variables were not entered in equations. Sample size limitations probably account for why the rate of hepatitis C infection among drug users in the second quartile approached but did not achieve significance when compared against the fourth quartile referent (OR = 2.37; 95% CI = 0.98; 5.71). The findings are the first in a line of investigation aimed at evaluating the degree to which variations in neuropsychological cognitive functions may serve as risk factors of HIV and hepatitis A, B, and C statuses among injection and non-injection drug users. The initial findings suggest that intellectual functioning deficits may be associated with hepatitis C status.

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- 713 DEVELOPING A TRAINING PROGRAM THAT HELPS COUNSELORS BECOME EFFECTIVE LEADERS OF SUBSTANCE ABUSE TREATMENT FACILITIES**
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(1) Danya International, Inc., and, (2) Danya Institute, Silver Spring, MD and (3) HHS/NIH/NIDA Intramural Research Program, Washington, DC
Effective treatment of substance abuse relies on many factors, and it is not surprising that our focus is usually on the addict. However effective treatment involves many components, and project IDEAL (Institute for the Development of Excellence in Administrative Leadership) has focused instead on improving treatment by increasing the skills of the treatment facility's new leader to meet the specific demands of substance abuse treatment. Client outcomes have been linked to effective leadership in recent research, however the skills and knowledge required are often different than what the newly promoted counselors used before. In too many situations, the transition from being an effective counselor to being an effective drug treatment leader is difficult and prolonged. There is often little help to guide the person through these new challenges. As a result, the treatment of the client can suffer along with the effectiveness and morale of the counseling staff. To meet Baltimore City's need to help counselors become effective leaders, the Danya Institute designed a multifaceted, innovative training program entitled Project IDEAL. It focuses on teaching new leaders via workshops, group meetings, online group interaction, and a mentorship with an experienced leader in the treatment community. The IDEAL project includes an evaluation component where the new leaders and their mentors are involved in the process of determining what new tools are needed and the best training methods to use. Our evaluation has helped design a program that increases both skills and the confidence to implement these skills. We have used feedback to develop training segments on; continuous quality improvement of substance abuse treatment, managing counselors, program vision and strategic planning, budgeting, fundraising in a profit and nonprofit environment, organizational development, leadership styles, conflict resolution, as well as using technology in treatment and management.
- 714 EFFECTS OF SMOKED MARIJUANA ON SLEEP DURING SIMULATED SHIFT WORK**
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Approximately 20% of workers in industrialized nations work nonstandard shift schedules, e.g., rotating and night shifts, and it has been well documented that several risks are associated with rotating-shift schedules, including sleep disruptions. It is possible that some workers who work irregular shifts smoke marijuana because they believe it will offset fatigue, improve performance, or sleep. The effects of marijuana on sleep of shift workers have not been studied. The purpose of this 23-day within-participant, residential laboratory study was to examine the effects of smoked marijuana on objective and subjective measures of sleep during simulated shift work. Participants (N = 10) smoked a single marijuana cigarette containing one of three THC concentrations (0, 1.9, and 3.56%) one hour after waking for three consecutive days under two shift conditions: day shift and night shift. Shifts alternated three times during the study, and shift conditions were separated by an "off" day. When participants received placebo, objective and subjective measures of sleep were significantly disrupted during the night shift work, relative to the day shift: total sleep time and participants' reported satisfaction with the previous evenings' sleep were decreased, while sleep onset latency was increased. Although the 3.56% THC cigarette increased sleep onset latency during night shift work, the drug produced few other effects on sleep measures. These data show that a single marijuana cigarette administered during the workday produce limited effects in individuals ongoing abrupt shift schedule changes. Supported by NIDA grant DA-03746.
- 715 SEXUAL RISK BEHAVIORS FOR HIV TRANSMISSION IN DRUG USER NETWORKS IN LOS ANGELES, CALIFORNIA**
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Research on risk behaviors that support transmission of HIV among drug users has largely focused on injection-drug users (IDUs). Comparatively little is known about drug-facilitated sexual behaviors that transmit HIV and other infectious diseases. The Los Angeles site for NIDA's Sexual Acquisition and Transmission of HIV Cooperative Agreement Program (SATH-CAP), is collecting data to evaluate behaviors (drug use and sexual) and network characteristics associated with HIV/STI infection within drug-using networks and from drug users to non-drug users. Participants were recruited using respondent-driven sampling (RDS) in which participants, themselves, recruited their drug-using peers and sexual partners into the study using recruitment vouchers. The first 211 participants in the SATH-CAP completed a self-administered, computerized questionnaire about their health, drug use, sexual practices, sexual partnerships, and social networks. Biological samples also were collected and tested for HIV, syphilis, rectal gonorrhea, and active drug use. Initial findings show participants range in age from 22-76, with an average of 42.8 (SD=8.1). 88.6% were male, with 86.4% reporting at least some same-sex sexual contact. 18.5% were Caucasian, 55.9% African-American, & 25.6% Latino. 90% averaged a high school education or less. 37% were IDUs, and 56% were currently homeless. Drug use was common with 31%, 29%, 9.5% and 3.8% reporting methamphetamine, crack, cocaine, and heroin use in the previous 30 days, respectively. 42.7% were HIV infected and 7.3% tested positive for syphilis. Findings suggest a high degree of infectious diseases that correspond to primary use of stimulants in this initial sample comprised mostly of men who have sex with men. High rates of HIV infection and syphilis in this sample underscore opportunities for modeling behavior and network elements that contribute to disease transmission. Acknowledgments: This study is supported by NIDA grant # DA017394
- 716 INTERPERSONAL DYNAMICS AND TREATMENT BARRIERS: AN ETHNOGRAPHIC STUDY OF DRUG-USING COUPLES**
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The drug treatment field, like the HIV prevention field, tends to place emphasis on the individual rather than the individual in social context. While there are a growing number of studies indicating that drug-using intimate partners are likely to play an important role in determining treatment options, little attention has been given to the experience and complex treatment needs of drug-using (heroin, cocaine, crack) couples. This study used in-depth interviews and ethnographic engagement to better understand the relationship between interpersonal dynamics and the treatment experience of ten relatively stable drug-using couples in Hartford, CT. Semi-structured and open-ended qualitative interviews were conducted with each couple and separately with each partner. Whenever possible, day-to-day realities and contexts of risk were observed via participant and non-participant observation of couples in the community. A grounded theory approach was used to inductively code and analyze nearly 40 1-1/2 hour transcripts and fieldnotes. Interpersonal dynamics, such as a dynamic of care and collusion, tended to keep couples out of the treatment system. When couples were interested in accessing treatment, structural barriers presented additional obstacles. A sole focus on the individual rather than the couple resulted in the denial of admittance of both partners to detoxification and treatment programs. Improvements to the treatment system in general will go a long way in improving treatment for couples, but couples-specific programming also needs to be developed.

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717 BASELINE DIFFERENCES IN COGNITION BETWEEN HIGH AND LOW USE OF METHAMPHETAMINE IN A MEDICATION TRIAL

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One hundred and fifty-three participants in a NIDA sponsored trial of Bupropion with methamphetamine abusers were given tests assessing memory, attention, processing speed, and working memory. Participants were divided into a lower use group (use of less than or equal to 18 days/month, $n = 71$) and a higher use group (use of greater than 18 days/month, $n = 82$). At baseline the groups differed significantly ($t_{148} = -2.6, p = .009$) on a memory measure comprised of recall and recognition for pictures and words (lower use group mean = 40.94, higher use group mean = 45.88). Further examination found that the effect was due to the recognition tests with words ($t_{148} = -2.7, p = .007$) and pictures ($t_{148} = -2.7, p = .024$) as the only significant components. Working memory as assessed by the Digit Symbol test also differed significantly between the two groups ($t_{151} = -2.6, p = .011$). Again the low use group (mean = 53) had lower scores than the higher use group (mean = 58). Scores on the measure of attention comprised of the Stroop and the d2 also were worse for the lower use group, but this did not reach significance. Processing speed did not differ between the two groups at baseline. When the cognitive battery was administered at the end of the study the lower use group was still significantly worse on the memory and working memory variables, and was close to being significantly worse on processing speed. Supported by NIDA Contract NOIDA-3-8824

719 ENHANCED SENSITIVITY TO STRESS AND DRUG CRAVING IN ABSTINENT COCAINE-DEPENDENT INDIVIDUALS COMPARED TO MATCHED CONTROL VOLUNTEERS

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Craving is a hedonic state involved in the transition from occasional to compulsive drug abuse. Moreover, stress may increase craving in cocaine abusers by contributing to allostatic load. This study aims to assess whether cocaine abusers demonstrate a disrupted stress response by reporting greater craving and negative mood alongside increased cardiovascular response, as compared with controls, when exposed to stress and drug-related cues. Forty recently abstinent treatment-seeking cocaine abusers and forty well-matched healthy controls were exposed to three, five-minute guided imagery scenarios comprising a personal stressful situation, a drug-cue related situation and a neutral relaxing situation, each presented on consecutive days, one imagery session per day. All were assessed for craving, subjective emotional state and cardiovascular response. Linear Mixed Effects (LME) models were performed in order to analyze the findings. The cocaine group showed significantly higher stress and drug-cue induced systolic blood pressure (SBP) compared with controls and significantly higher heart-rate across all conditions. In addition, they reported significantly higher stress and drug-cue induced craving (cocaine and alcohol), anxiety, anger, sadness and fear compared with controls. In all cases, the cocaine group also reported higher scores in either the stress or drug-cue conditions compared with the neutral condition. Current findings indicate enhanced stress and drug-cue induced sensitivity to cocaine/alcohol craving, negative emotions and cardiovascular responses in abstinent cocaine dependent individuals. Findings support the model that chronic cocaine abuse is associated with an allostatic state marked by an enhanced sensitivity to stress and drug craving. Such dysregulated stress responses in cocaine abusers represent an imbalance in stress-reward circuits that may contribute to increased relapse vulnerability when exposed to stressors and drug cues in the environment. (Supported by P50-DA16556 and K02-DA17232)

718 TEMPORAL LOBE VOLUMETRIC ASSESSMENTS IN PRENATALLY COCAINE-EXPOSED ADOLESCENTS: CORRELATION WITH PERFORMANCE ON THE REY-OSTERRIETH COMPLEX FIGURE

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As part of a multi-faceted exploratory neuroimaging project (MRS, MRSI, DTI) evaluating the effects of prenatal cocaine exposure, a subset of adolescents (age 12-14 yrs) from the longitudinal Miami Prenatal Cocaine Study underwent magnetic resonance imaging (MRI) using a 3T scanner equipped with an 8-channel phased-array receiver. T1-weighted images were acquired using MPRAGE: TR 2150 ms, TE 4.38 ms, TI 1100 ms, 160 1-mm slices with no gap, 1 mm³ spatial resolution, and ~5 min acquisition time. T1-weighted MRI data were segmented into gray matter, white matter and cerebrospinal fluid and volume and surface area measurements of specific cerebral regions were measured using FSL software (<http://www.fmrib.ox.ac.uk/fsl/>). Clinical interpretations of structural MRIs were normal. Brain volume comparisons were controlled for age, weight, height and head circumference. The Rey-Osterrieth Complex Figure (ROCF) was used, in part, to evaluate temporal lobe function by assessing perceptual organization, and visual memory. Preliminary data of this exploratory study suggest no group differences in mean volumes of the whole brain, frontal lobes, or posterior lobes. However, compared to those non-exposed ($n=8$), cocaine-exposed adolescents ($n=11$) had significantly smaller mean volumes of right and left lateral temporal gray matter and right lateral temporal white matter (p values < 0.05). On the ROCF, the prenatally cocaine-exposed group had significantly more "immediate recall" errors and a higher proportion of subjects scoring below normal on the number of "copy" and "immediate recall" errors (p values < 0.05). Both right and left lateral temporal gray matter volumes were inversely correlated with the error scores (p values < 0.05); left lateral temporal gray matter was also inversely correlated with "immediate recall" errors ($p < 0.05$), but not "copy" errors. R21 DA15906; T32 HD07473; R01 DA06556; M01 RR16587

720 KNOWLEDGE OF AND ATTITUDES TOWARD ADDICTIVE BEHAVIORS BY STUDENT PERSONNEL IN THE UPPER MIDWEST STATES

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The upper midwest region is one of the three regions of the country with the most serious problems with underage drinking and binge drinking by college students according to Wechler's survey (1994). The purpose of this study was to evaluate student personnel staff perceptions of problem substance use on college campuses. Universities, four year colleges and seminaries (religious-affiliated private colleges and universities) in IA, MN, NE, ND and SD were randomly selected to participate in the survey. Personnel working with students, including counselors, supervisors in residence halls, and prevention specialists, were solicited for participation in the study. Seminaries and religiously affiliated schools chose not to be involved in the study, because the issues were not seen as relevant to them. Preliminary data indicate that the majority of the student services professionals were concerned about freshmen males' and junior/senior women's alcohol consumption as well as use of tobacco products. The majority of respondents perceived that more than 20% of undergraduate students are binge drinkers. Of respondents who administered standardized surveys to students, half reported that approximately 75% of students drink. Therapy techniques used when counseling students who present with a drinking problem, none of the respondents reported using a 12-step approach, instead cognitive behavioral or motivational interviewing strategies were used. A number of respondents reported that they do not target problem gamblers in student health programs. This study demonstrated a need to enhance the training of college and university staff regarding prevention and treatment of underage and binge drinking among college students. Although a number of respondents indicated use of empirically supported treatments, the nature of the training they received to implement such treatments remains unclear. Lastly, data suggest that no individuals and institutions surveyed had a program or treatment in place for individuals with problem gambling.

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721 RELATIONSHIP BETWEEN MILITARY SERVICE AND SUBSTANCE ABUSE AMONG HOMELESS Dually DIAGNOSED VETERANS

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Background Little has been done to examine substance abuse and characteristics of the veterans' military service. We used preliminary data from a study of homeless, dually-diagnosed veterans entering the VA to examine relationships between substance use and military service experiences. Methods Data were collected on 119 veterans enrolled in the MISSION Program, a SAMHSA-funded demonstration project aimed at helping veterans transition from New Jersey VA Domiciliary care into the community. The present analysis examined associations between military service experiences and the initiation or increase of the use of alcohol and/or drugs. Results Eighty-eight percent of veterans reported that their use of alcohol or drugs either began or increased during military service, with 71% reporting initiation or increase of alcohol, 61% of illicit drugs and 43% of both alcohol and drugs. Among illicit drugs initiated or increased during military service, cocaine was the drug most frequently cited (42.1%), followed by heroin (28.9%) and marijuana (19.7%). By period of service, drug initiation or increase was more likely among post-Vietnam (66%) than Vietnam (41%) veterans. Veterans of the Army (67.5%) and Marines (64.3%) were somewhat more likely to report service-related drug use than veterans of the Navy (47.1%) or Air Force (25%) and veterans who had experienced combat were somewhat more likely to increase or initiate use than those with no combat experience (68% vs. 58%). Service-related drug use was more likely among African Americans (71.2%) than Whites (31.6%). Conclusions The findings suggest that military experiences have an impact on substance abuse and that the branch of service, period served and race are differentially associated with substance abuse. These findings have important prevention and treatment implications for homeless, dually diagnosed veterans, particularly given the large number of new veterans with war-time military service. Sources of Funding: CSAT T116576, NIDA R03 DA020434-01

722 ATTENUATING THE EFFECTS OF COCAINE WITH NOVEL SIGMA RECEPTOR ANTAGONISTS

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The physiological and psychological properties of cocaine are mediated by a number of different receptor types of which sigma plays a relevant role. Subtypes of the receptor system, sigma-1 and sigma-2, are both able to efficiently modulate cocaine actions in the body. This study was aimed at producing sigma selective antagonists that attenuate the toxicity and psychomotor effects of cocaine by interfering with cocaine's access to the receptor sites. One particular class of sigma receptor antagonists are the phenylethylene diamines. Aromatic methoxyl substituted analogs of BD1008 are known to be selective sigma receptor antagonists, and significantly reduce the effects of cocaine. Trifluoromethoxyl groups were introduced into the ortho, meta, and para positions of BD1008 analogs to increase their potency, lipophilicity, and stability towards metabolism. In vivo studies showed that of the 11 novel compounds synthesized, all three positions have a considerably high affinity for sigma receptors, with a slight preference for sigma-1 over sigma-2 (sigma-1 $K_i = 3 \pm 0.1$ nM, 1.13 ± 0.5 nM, 2 ± 0.2 nM, respectively; sigma-2 $K_i = 58 \pm 2$ nM, 11 ± 3 nM, 25 ± 2 nM, respectively, for the ortho, meta, and para positions in one series). The para-substituted analogs produced the greatest reduction in convulsions when the mice were pretreated with 5 mg/kg of each test drug then given 70 mg/kg of cocaine. These trifluoromethoxyl phenylethylene diamine analogs dramatically attenuated the effects of cocaine due to their high affinity for sigma receptors. The results of the study demonstrated their resourcefulness as a tool in the displacement of cocaine at receptor sites, and opens a window for further study of their regulatory effects on the physio- and psychological effects of cocaine.

723 METHAMPHETAMINE WITHDRAWAL SENSITIZES THE NMDA RECEPTOR RESULTING IN EXCITOTOXICITY IN THE HIPPOCAMPUS

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For the last 40 years, methamphetamine (METH) abuse has steadily increased in the US. Increases in METH abuse is alarming, since previous literature has established that use of METH can result in nerve terminal degeneration and neuronal cell death. Several brain regions appear susceptible to the neurotoxic effects of METH, especially the hippocampus, a region essential for learning and memory. Recent literature suggests that damage in the hippocampus may result from METH being able to block the NMDA receptor. During withdrawal, the NMDA receptor is no longer inhibited, resulting in overactivation of the receptor, potentially leading to excitotoxicity. However, few studies have examined this phenomenon. Therefore, the current study examined the neurotoxic effects of METH withdrawal on the rat hippocampus. METHODS: The current study exposed organotypic hippocampal slice cultures to .1-100 uM METH for 6 days. After treatment, slices underwent either 1 or 7 days of withdrawal. Following withdrawal, slices were treated with 5 uM NMDA and propidium iodide (PI), a fluorescent stain for damaged or dying cells. Subregions of the hippocampal complex (CA1, CA3, & DG) were quantified for PI uptake. RESULTS: The CA1 region displayed significant cellular damage at the 100 uM METH concentration after 1 day of withdrawal. Significant cellular damage was found at all concentrations of METH after 1 day of withdrawal in the DG. Following 7 days of withdrawal, all concentrations, except 10 uM of METH, resulted in significant cellular damage in the CA3. All concentrations of METH exposure resulted in significant cellular damage in the CA1 after 7 days of withdrawal. CONCLUSIONS: The results from the current studies suggest that METH withdrawal sensitizes the glutamatergic system to agonists, resulting in the observed neuronal damage. Furthermore, the duration of withdrawal, METH concentration, and hippocampal region appears to influence the severity of cellular damage that may occur.

724 ABSENCE OF RECOVERY OF THE CEREBRAL METABOLIC RESPONSE TO COCAINE IN MONKEY STRIATUM FOLLOWING PROLONGED ABSTINENCE FROM CHRONIC SELF-ADMINISTRATION

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Our previous studies have shown substantial and topographically extensive decreases in functional activity, as measured by local cerebral glucose utilization (LCGU), in both the pre- and post-commissural striatum of monkeys following 100 days of cocaine self-administration. However, the functional response of these brain regions following a period of abstinence and subsequent re-exposure to cocaine self-administration has not been described. We hypothesized that the changes observed following chronic cocaine exposure would be diminished following abstinence, indicating reversal of the neuroadaptations that had occurred during drug exposure. In the present study monkeys self-administered cocaine (0.3 mg/kg/injection under a fixed-interval schedule) for a period of 100 days followed by either 1 (n=4) or 3 (n=3) months of abstinence and were compared to controls whose responding had been maintained by food under identical schedules (n=4) and had undergone similar abstinence. Following abstinence animals were exposed to a single session of cocaine or food self-administration in which all monkeys acquired the full number of available reinforcers. Immediately following the final reinforcer, LCGU was assessed via the quantitative 2-[14C]deoxyglucose method. Contrary to our hypothesis, following both 1 and 3 months abstinence cocaine self-administration produced significant decreases in LCGU throughout both pre- and post-commissural striatum. This response was equivalent in magnitude and extent to the changes in LCGU after 100 days of exposure to self-administration with no abstinence periods. The absence of any change in the functional response to cocaine following a prolonged period of abstinence would suggest that the neuroadaptations associated with chronic cocaine exposure are robust and persistent, and may be resistant to a simple regime of abstinence. Further intervention may be necessary if reversal and recovery are to be achieved. Supported by grants DA09085 and DA06634

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725 RELATIVE RATE OF OPIOID ANALGESIC ABUSE IN COMMUNITIES IN THE U.S.

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Introduction: Anecdotal data suggest that the abuse of opioid analgesics is concentrated in discrete geographic areas within the U.S. The purpose of this analysis was to examine the relative rate of abuse of opioid analgesics by 3-digit ZIP code (3DZ) across the U.S. using data from a large toxic-surveillance system. Methods: The number of intentional exposure calls to Poison Control Centers (PCC) involving buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone extended release(ER) or other oxycodone was used as the numerator; the number of unique recipients of dispensed drugs (URDDs) by 3DZ per calendar quarter as the denominator. Data were obtained for the period 1/03-12/04 at the 3DZ level from up to 15 PCCs representing a regionally diverse sample of states. A mixed effects Poisson regression model was fit to the data, with drug and calendar quarter included as fixed effects and each 3DZ included as a random effect. The 3DZ random effect was obtained using an empirical Bayes method. A Z-statistic value of > 1.64 (1-sided p-value < 0.05) was used as the threshold for identifying potential outliers in abuse rates. Results: 347 3DZs (~35% of all 3DZs in the U.S.) were included in the analysis. Overall, 10 3DZs (2.9% of all participating 3DZs) in 4 distinct locations showed rates of intentional exposure to opioid analgesics that significantly exceeded the average rate per participating 3DZ. These included Sacramento, CA(3DZ 942), southeastern KY (3DZs 408, 409 & 413), Richmond, VA(3DZ 225) and southwestern WV (3DZs 247,248,256,258 & 259). Specific opioids involved also clustered by location: hydrocodone (3DZ 942), oxycodone ER (3DZ 225), methadone, morphine and oxycodone ER (SE KY), and methadone and oxycodone ER (SW WV). Conclusions: Findings indicate that cases involving intentional exposure to opioid analgesics are clustered in specific geographic areas in the U.S. These areas were predominantly located in rural, socio-economically depressed sections of Appalachia.

726 THE EFFECTS OF AEROBIC EXERCISE ON SENSITIVITY TO COCAINE

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Aerobic exercise markedly increases central dopamine concentrations and produces compensatory alterations in the density of postsynaptic dopamine receptors. Very few studies have examined whether these effects have functional consequences for sensitivity to psychomotor stimulants, particularly those with high abuse and dependence liability. The purpose of the present study was to examine the effects of aerobic exercise on sensitivity to cocaine on measures of conditioned reward and locomotor activity. Female, Long-Evans rats were obtained at weaning and randomly assigned to either sedentary or exercise conditions immediately upon arrival. Sedentary rats were housed individually in standard laboratory cages that permitted no exercise beside normal cage ambulation; exercising rats were housed individually in modified cages equipped with a running wheel permanently affixed to the interior of the cage. After 6 weeks under these conditions, the effects of various doses of cocaine were examined in the conditioned place preference procedure and in an open-field test of locomotor activity. In the conditioned place preference procedure, cocaine produced a dose-dependent place preference in both groups of rats. Exercising rats were significantly more sensitive than sedentary rats to the effects of cocaine in this procedure, and this effect was most pronounced at the highest dose of cocaine. In the locomotor activity test, cumulative doses of cocaine increased open-field activity in both groups of rats, but no significant differences were observed between the two groups. These data suggest that aerobic exercise increases sensitivity to the conditioned rewarding effects of cocaine, but does not alter sensitivity to its effects on locomotor activity (supported by Davidson College and US Public Service Grant DA 14255).

727 LIVE SUPERVISION VIA TELECONFERENCING IMPROVES ACQUISITION OF MI SKILLS AFTER WORKSHOP ATTENDANCE

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Substantial progress has been made in developing treatments for drug dependence, however new treatments have not been routinely adopted into community practice. Motivational interviewing (MI) is an efficacious treatment for substance abuse; however, it is a challenging technique to learn, and studies show that a didactic workshop is not adequate for acquisition of MI. This paper reports the results of a pilot project that developed a Teleconferencing Supervision method for training community-based substance abuse clinicians in MI. 13 clinicians (8 CASAC, 3 MD, 2 PhD) attended a 2-day MI workshop and completed 5 training counseling sessions at their place of employment via telephone over an 8 week period. During supervision sessions, clinicians were given live, real-time feedback through an ear-plug. Feedback was directed at training clinicians to use specific MI skills, encourage an MI-consistent counseling style, and avoid MI-inconsistent activity. Clinicians and supervisors then discussed each session in depth over the phone prior to the next training session; clinicians were provided with graphical feedback illustrating their performance against target criteria using the Motivational Interviewing Therapist Integrity instrument (MITI). Results indicated significant linear trends demonstrating improvement from the 1st through 5th supervisory sessions across targeted counseling behaviors: Open Questions ($r=.79$), Complex Reflections ($r=.59$), and Reflections to Questions Ratio ($r=.85$). Clinicians also demonstrated similar significant improvement in MI Spirit ($r=.99$) and Empathy ($r=.95$). These preliminary findings suggest Teleconferencing Supervision is a viable method for training community based clinicians in the proficient use of MI. An ongoing randomized trial comparing live supervision with delayed supervision of taped sessions and workshop only will further assess the benefits of live supervision in improving clinician acquisition of MI skills.

728 CHANGES IN REGIONAL BLOOD VOLUME DURING A 28-DAY PERIOD OF ABSTINENCE IN CHRONIC CANNABIS SMOKERS

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The quantitative measurement of cerebral perfusion is crucial for the study of both normal and impaired human brain function. Specifically, cerebral blood volume (CBV) and cerebral blood flow (CBF) studies have provided important insights into the acute and chronic effects of illicit substances such as cannabis. The objective of the present study was to examine changes in regional blood volume in focal regions of interest including the frontal lobe, temporal lobe, and the cerebellum during 28 days of supervised abstinence from cannabis. Dynamic susceptibility contrast MRI data were collected on 13 current, long-term cannabis users after 7 days and 28 days of abstinence (Days 7 and 28). Resting state CBV images were also acquired on 17 healthy comparison subjects. Data were acquired in the axial plane with a 1.5-Tesla GE Signa scanner following a bolus of gadolinium contrast agent. Previously we have shown that recently abstinent cannabis users (6-36 hours after last reported use) demonstrated significantly increased blood volumes relative to comparison subjects in the right frontal region, left temporal region and cerebellum. The present findings demonstrated that at Day 7, cannabis users continued to display increased blood volumes in the right frontal region ($p = 0.057$), left ($p = 0.004$) and right ($p = 0.028$) temporal regions, and the cerebellum ($p = 0.004$) relative to comparison subjects. However, after 28 days of abstinence, only the CBV values in the left temporal area ($p = 0.005$) and cerebellum ($p = 0.026$) remained significantly increased in cannabis users. These findings expand on previous reports of the acute effects of cannabis on CBF and suggest that regional differences in vascular response to chronic cannabis use can persist for at least several weeks. It would be of interest to extend the investigation beyond 28 days of abstinence from cannabis to determine whether CBV values eventually normalize.

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729 BUPRENORPHINE AND BUPROPION COMBINATION FOR OPIOID-DEPENDENT SMOKERS

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Although over 85 percent of the methadone-maintained opioid users smoke, few clinical trials targeted smoking cessation in this population. The goal of this study was to determine the safety and efficacy of bupropion treatment, in comparison to placebo, for cigarette smoking and drug use in opioid dependent smokers stabilized on buprenorphine. In this randomized, double-blind, placebo-controlled study 40 male and female opioid dependent smokers randomized to placebo (n=20) or bupropion (n=20) for 9 weeks. For the first week of the study, subjects were stabilized on buprenorphine (up to 24 mg) and the study medication bupropion (300 mg/day) or placebo. During the second week, subjects were encouraged to quit or decrease their smoking behavior. Smoking and drug use was monitored with thrice weekly CO levels and urine drug testing, respectively. Subjects received \$5 each time they provided clean urines and CO levels 0.05). Similarly cocaine negative urines were greater in the bupropion than placebo group (85 vs. 72 %, p>0.05). These results support the feasibility of combining buprenorphine with bupropion in opioid dependent smokers. The efficacy of this combination needs to be further examined in future clinical trials (Supported by NIH grant P-50 DA12762, P50-DA18197, K05-DA0454, K12 00167 and VA New England MIRECC).

730 PREVALENCE OF HEPATITIS C AMONG INJECTING DRUG USERS IN VINNITSA, UKRAINE

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Hepatitis C (HCV) is a major global public health problem. HCV is parenterally transmitted and one of the main causes of cirrhosis and HCV induced hepatocellular cancer. It's estimated that about 3% of the world's population have HCV. There are about 4 million carriers in Europe alone. In Ukraine, the number of people infected with HCV was 622,800 in 1999 which makes up of 1.2% of total population. The major risk factor for HCV infection in Ukraine it's needle sharing among injection drug users (IDUs). The aims of this study were to obtain a random sample of IDUs using the NIDA Community Based Outreach Model; to measure HCV prevalence among the IDUs in Vinnitsa city, Ukraine; to measure subjects' knowledge, attitudes and behavior about HCV infection. Individuals who had a high level of involvement in current drug user networks or had access to potential research subjects were recruited as peer outreach workers. During May-September 2005, 315 IDUs in Vinnitsa were recruited which represents an estimated 15% of active IDUs in the community. Prevalence of HCV among IDUs was 74.4% as measured by the rapid HCV tests (Acon One Step HCV Test Strip rapid test kits). Among study group 82.43% were males and 17.57% were females; median age was 28 years; 24.6% of the sample were married (no significant difference HCV-/HCV+ categories). Mean (SD) duration of opiate use was 7 (SD=6.72) years for HCV- and 9 (SD=6.0) years for HCV+ IDUs (p=0.01). Opiate use during last 30 days was greater in HCV+ compared to HCV- IDUs (19.4 days vs. 15.2, p=0.02). Percent of injecting partners was greater in HCV+ IDUs (6.2% of HCV+ vs. 3.8% of HCV-, p=0.07). This research demonstrates that HCV is quite prevalent among IDUs in Ukraine and is associated with risky drug use behaviors. HCV testing and treatment should be incorporated into HIV testing and opiate treatment efforts in developing countries with HIV and IDU epidemics.

731 COMMUNICATION ABOUT CONDOM USE AND REPORTED CONDOM USE AMONG PARTICIPANTS ENROLLED IN DRUG TREATMENT

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BACKGROUND: Enrollment in drug treatment has been associated with reduced HIV risk behaviors. This study examines the role of communication about condoms on condom use among patients in drug treatment. METHOD: Participants were men enrolled in NIDA CTN 0018, a gender-specific HIV prevention intervention trial. At study enrollment, participants were administered (via ACASI methodology) a structured self-report inventory focusing on sexual risk behaviors in the 90 days preceding enrollment into the study. The following results focus on the 213 methadone maintenance (MM) and 213 outpatient psychosocial (OPS) patients who reported heterosexual activity within the past 90 days. RESULTS: Participants in MM were more likely to possess condoms (58.4% vs. 43.5%, $\chi^2=11.6$, p<.001) and more likely to have taken condoms from the clinic (t=-5.58, p<.001) than those in OPS. Patients in MM reported higher proportion of condom use for anal sex ($\chi^2=4.3$, p<.05) and receiving oral sex ($\chi^2=6.1$, p<.05) than those in OPS with their main sexual partners. Participants in MM were more likely than those in OPS to have spoken with their main female partners about condom use (55.2% vs. 44.9%, $\chi^2=10.0$, p<.01). Furthermore, participants who spoke with their female partners about condom use were more likely to report condom use for vaginal sex ($\chi^2=41.3$, p<.0001), anal sex ($\chi^2=12.0$, p<.001) and receiving oral sex ($\chi^2=12.8$, p<.001). Participants reporting cocaine use were more likely to have taken condoms from the clinic (t=-3.49, p<.001) than those who didn't use cocaine. However, there were no differences in rates of condom use when participants were compared on cocaine use. CONCLUSION: Participants in MM programs reported better HIV prevention behaviors than those in OPS programs, including condom possession, communication about condom use & reported condom use.

732 PAXIL CR VERSUS PLACEBO IN THE TREATMENT OF OUTPATIENTS WITH COMORBID PTSD AND SUBSTANCE DEPENDENCE

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This pilot study was designed to assess the safety and efficacy of Paxil CR in the treatment of outpatients with comorbid posttraumatic stress disorder (PTSD) and substance dependence, in a 12-week, randomized, double blind, placebo (PBO) controlled trial. PTSD was diagnosed using the Clinician Administered PTSD Scale (CAPS-1); other diagnoses were assessed using the Structured Clinical Interview for DSM-IV (SCID). Substance use and PTSD symptoms were assessed throughout the trial using Time Line Follow-Back, urine drug screens, craving scales, Davidson Trauma Scale (DTS), Treatment Outcome PTSD scale (TOP-8) and the CAPS-2. Twenty-five subjects (Paxil CR=13, Placebo=12), mean age=35.5 (sd=11.1) were enrolled in the trial. 11 of 25 subjects (Paxil CR=4; PBO=7) completed the trial. Although there were no statistical differences in demographics between groups, there were significant baseline differences: PBO group had more severe baseline PTSD symptoms as evidenced by higher CAPS-2 (77.0 (13.8) vs. 65.0 (10.0); p<.05) and DTS (99.8 (16.1) vs. 69.2 (18.4); p<.001). There was no significant group difference in positive urine drug screens (PBO=33.3% vs. 66.7%; p=0.31), however mean days of substance use in the 30 days prior to study entry was 18.7 (9.8) for Paxil CR group vs. 11.0 (9.6), p=0.086. There was no difference in the mean terminal medication dose between groups (Paxil CR=42.3mg (9.6) vs. 38.5mg (16.4), p=0.50). Although PTSD symptoms improved in both groups over time (p<.05), there were no significant treatment differences in change scores for CAPS-2 (p=0.14), TOP-8 (p=0.68), DTS (p=0.10) or days of substance use in last 30 days (p=0.97). There was no difference in the incidence of side effects or laboratory parameters between groups. Unfortunately, power to detect statistical differences was low due to significant baseline differences and drop out. Although Paxil CR was well tolerated and appeared to be safe to use in this population, more data are needed to better understand the utility of Paxil CR in the treatment of substance abusers with PTSD.

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- 733 METHADONE MAINTENANCE PATIENTS IN THE THERAPEUTIC COMMUNITY: PRELIMINARY RESULTS**
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Background: Research has demonstrated that therapeutic communities (TCs) have beneficial effects in decreasing drug use, increasing employment, and decreasing criminal behaviors, with length of stay in the TC a consistent correlate of treatment success. In recent years TCs have modified to accommodate special populations (e.g. people with HIV/AIDS or co-occurring mental illness). The modifications are intended to allow these populations to stay longer and benefit more from treatment. Method: This study determined the effectiveness of treating methadone maintenance patients in a TC. It compared outcomes of 125 people receiving methadone maintenance who entered a TC, with 106 TC admissions admitted due to heroin use but not receiving methadone. The comparison group was balanced with the methadone group on three factors that independently predict retention in the TC: criminal justice history, co-existing mental illness, and expected length of stay. The study used equivalence testing to determine whether methadone patients benefited from treatment as much as the heroin-user comparison group. Results and Implications: Study retention exceeded 90% for followups at 6 and 12 months post admission. Both the percentages of opioid-negative urine screens (69% at 6- and 61% at 12-months) and those reporting no heroin use in the last 30 days (73% at 6- and 71% at 12-months) were statistically equivalent ($p < .05$). Adaptations to accommodate methadone patients included a methadone policy statement, regular staff training, a therapy group for methadone patients, and availability of alternative therapies. The project's limitations include its quasi-experimental design, yet it demonstrates how treatment of methadone maintenance patients is feasible in a TC. Support: R01DA014922, U10DA015815, P30DA009253
- 734 THE RISE OF METHAMPHETAMINE USE AMONG AMERICAN INDIANS IN LOS ANGELES COUNTY**
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Los Angeles County has the largest concentration of urban American Indians in the United States. With the rise of methamphetamine use nationally, and reports of increasing use among American Indians, a preliminary review of Los Angeles County treatment intake data was conducted. From 2001-2004, there was a significant increase in the number of American Indians using methamphetamine as their primary drug. By 2004, methamphetamine had supplanted alcohol as the most commonly reported primary drug by American Indians. American Indian females reported more methamphetamine use than males. In 2001, 39% of the females and 27% of the males entering treatment noted methamphetamine as their primary or secondary drug. In 2004, the numbers rose to 52% for females and 38% for males. An exploratory analysis of both American Indian and White primary methamphetamine users in 2004 showed little difference in the frequency of use among the two groups. Significant differences were found, however, with regards to the route of administration. While smoking was the most common route of administration for both groups, more American Indians used methamphetamine through inhalation and injected much less than Whites.
- 735 FUNCTIONAL ANALYTIC STRUCTURED SYSTEMIC TREATMENT: A TREATMENT FOR CO-OCCURRING MENTAL ILLNESS AND SUBSTANCE USE DISORDERS**
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Substance abuse and dependence is prevalent in minority patients with serious and persistent mental illness. The estimates of the proportion of mentally ill patients with substance use disorders ranges between 40% and 72%. Over the past three years, we developed and evaluated a structured behavioral treatment aimed at this clinical population. Integrated treatments for substance use and mental illness are rare and those that did exist required more than 5 days of treatment. The typical inpatient length of stay is less than 5 days. We developed an integrated treatment technology for inpatients and a manual for training therapists. The manualized treatment, Functional Analytic Systemic Treatment (FAST), was evaluated in a clinical trial. The evaluation design was a parallel group design. Patients meeting inclusion criteria were assigned randomly to the experimental treatment or treatment-as-usual groups. Inclusion criteria included a mental illness, a drug positive urinalysis at intake and consent. For the preliminary analyses the clinical outcome was attendance at the scheduled outpatient appointment. One hundred and twenty four patients have completed the study. Nearly 64% of patients receiving the experimental intervention attended the first scheduled post-hospitalization outpatient appointment. Nearly 36% of control patients attended the first scheduled appointment. These differences are significant (Fischer's Exact chi-square = 12.890; $p < 0.001$). We are now analyzing follow-up data. The Pennsylvania Department of Health supported this research.
- 736 PATHWAYS TO PRESCRIPTION OPIOID DEPENDENCE**
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The primary distinguishing feature of prescription opioids as drugs of abuse is their therapeutic purpose in society. For this reason, the pathways leading to dependence are more varied and complex than for other substances. For some individuals, first exposure to prescription opioids is entirely associated recreational use; either seeking pleasurable effects or ameliorating negative states (eg, heroin withdrawal). There is an increasing number of youth and adults reporting 'non-medical' use of these products, meaning intentional use without a physician's prescription for a legitimate medical condition. This broad definition not only encompasses use for recreational purposes, but also includes use for pain without a prescription (eg, obtained from peers/family). The nature of these behaviors is significantly different; impacting the dependence risk. For most individuals, exposure to prescription opioids is through legitimate medical use. Most attention to date in this area has focused on the risks associated with long-term exposure in the treatment of chronic non-cancer pain. The major risk factor for DSM-IV dependence identified in this population is a history of substance abuse. Very little is known about how the risks may vary for patients outside of the pain clinic setting (eg, different prescribing behaviors; different types of pain scenarios). Although generally accepted that short-term use for acute pain does not confer significant risk, an exception may be in those with a history of substance abuse in which this exposure may instigate a new substance problem or trigger relapse. A major risk factor requiring attention in this area is the influence of psychiatric comorbidity. For example, exposure to opioids therapeutically may relieve negative mood states prompting continued use non-medically. Research directed at understanding the phenomenology of the progression from prescription opioid use to dependence must broadly consider all of the many possible pathways. This will be the premise from which prevention and treatment approaches can emanate and from which the evaluation of interventions can occur.

- 737** Dually Diagnosed Patients Returning Home After Hospitalization: Exploring Treatment Continuity Using Data-Mining Techniques
G. Stahler(1), J. Mennis(1), S. Mazzella(1) and R. Spiga(2), (1) Temple University, and (2) Temple University School of Medicine, Philadelphia, PA
Relatively little research has focused on community and environmental factors that relate to continuity of treatment after discharge from inpatient interventions. This research study consists of a retrospective analysis of 271 dually diagnosed patients who were discharged from a hospital acute inpatient unit to various treatment programs in Philadelphia, and the main findings were reported in Stahler (2005). Overall, 44% of the sample attended their first postdischarge appointment within 30 days. The present research uses association rule mining, an exploratory data mining technique that extracts relationships among variables occurring over subsets of data, to examine meaningful subgroups of patients who either did or did not return home after discharge. Generally, the rate of treatment continuity is greater for those patients who did not return home following discharge. This effect is expressed most strongly within a number of patient subgroups, including patients with the following characteristics (rate of first postdischarge appointment attendance reported in parentheses): the absence of opioid use (65%), the absence of bizarre behavior (60%), African Americans (63%), and women (65%). Other subgroups, however, exhibited the opposite association with home return. For example, the rate of treatment continuity in white, non-opioid using patients was enhanced by returning home following discharge (68%). Further discussion will focus on the benefit of association rule mining for exploring meaningful subgroups in drug treatment populations, and the implications for discharge planning from inpatient treatment.
- 738** ENVIRONMENTAL ENRICHMENT INCREASES THE EXTINCTION RATES OF AMPHETAMINE SELF-ADMINISTRATION AND DECREASES THE REINSTATEMENT THRESHOLD FOR AMPHETAMINE-SEEKING BEHAVIOR
D. J. Stairs and M. T. Bardo, University of Kentucky, Lexington, KY
Rats raised in an enriched condition (EC) self-administer less amphetamine at low unit doses compared to rats raised in an impoverished condition (IC). Previous research from our laboratory has shown that EC rats show a faster rate of extinction of sucrose-maintained responding compared to IC rats and that EC rats reinstate responding following a sucrose prime, while IC rats do not. The current research investigated whether environmental enrichment differentially alters extinction rates of behavior maintained through amphetamine infusions, as well as whether EC and IC rats differ in the reinstatement of amphetamine-seeking following a drug prime. The extinction reinstatement model was used to test EC and IC rats self-administering intravenous amphetamine. Male Sprague Dawley rats were received at 21 days of age and then placed randomly into either an EC condition with novel objects and social cohorts or in an IC condition without objects or cohorts. At approximately 56 days of age, rats underwent catheterization surgery; following recovery, rats were trained to self-administer 0.1 mg/kg/infusion of amphetamine on an FR1 20-sec TO schedule of reinforcement for five days. After five days, the dose of amphetamine was decreased to 0.03 mg/kg/infusion for ten days. Following acquisition, rats underwent ten days of extinction where amphetamine was replaced with saline. Following the final day of extinction, rats received an acute injection of amphetamine (0, 0.25 or 1.0 mg/kg, SC) 15 min prior to the start of the session, with two days of extinction intervening between injections. Results showed that EC rats had a more rapid rate of extinction for amphetamine-maintained responding than IC rats. When primed with amphetamine, IC rats reinstated responding following 0.25 mg/kg of amphetamine, whereas EC rats only reinstated responding after 1.0 mg/kg of amphetamine. These results suggest that environmental enrichment may reduce drug abuse liability and relapse. Supported by: USPHS grants DA 16176 and R01 DA12964.
- 739** CONTINGENCY MANAGEMENT FOR ADOLESCENT MARIJUANA ABUSE
C. Stanger(1), A. J. Budney(1) and J. L. Kamon(2), (1) Center for Addiction Research, UAMS, Little Rock, AR and (2) UVM, Burlington, VT
A randomized trial tested the efficacy of a family based intervention for adolescent marijuana abuse, which included CBT plus 2 contingency management (CM) interventions: parent training (PT); and abstinence-based vouchers (V). A parallel group design compared CBT+PT+V (n=36) with CBT + a parent drug education curriculum (PE) (n=33). Youth receiving CBT+PT+V showed more weeks of continuous marijuana abstinence during treatment (CBT+PT+V: 7.6 vs. CBT+PE: 5.1, $t=-2.1$; $p=.04$). Those in the CBT+PT+V group were also more likely to achieve ≥ 8 weeks of continuous abstinence (53% vs. 30%, $X^2(1)=3.6$, $p=.06$) and ≥ 10 weeks of continuous abstinence (50% vs. 18%, $X^2(1)=7.7$, $p=.006$) during the program. We also tested whether changes in parenting and psychopathology accounted for substance use outcomes above and beyond treatment group in a structural model. The model had an excellent fit ($X^2 [18]=13.7$, $p=.75$, $TLI=1.09$, $RMSEA=.00$). Poor Parental Monitoring ($B=-.37$) and CBT+PT+V ($B=.23$) were both associated with ≥ 8 weeks of abstinence during treatment. Further, parental monitoring ($B=.36$) and during treatment abstinence ($B=-.52$) both predicted marijuana use in the follow-up period, accounting for a total of 54% of variance in use from discharge through 6 months. These findings support the hypotheses that CM would 1) engender longer periods of marijuana abstinence when added to CBT and 2) enhance maintenance of that effect following treatment. The Voucher procedure used an escalating schedule of reinforcement designed to get youth "invested" in achieving periods of continuous abstinence. PT instructed parents to use CM-based procedures following the formal treatment period. Which of these CM components (or both) contributed to these specific effects could not be tested in this initial study. Future studies will extend these findings by replicating this effect and testing the unique and synergistic effects of PT and V. These results further suggest that parental monitoring plays an extremely important role in adolescent substance use, both during and after treatment, and across both treatment conditions.
- 740** EARLY TREATMENT EVALUATION AS PREDICTOR OF PROXIMAL AND DISTAL POST-TREATMENT RECOVERY OUTCOMES
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ABSTRACT BODY: Background: Addiction treatment is associated with reduced substance use. Treatment gains are short-lived but are more likely to endure in the presence of recovery promoting cognitions and behaviors (e.g. motivation, participation in 12-step). Research has examined treatment processes associated with positive outcomes (e.g. therapeutic alliance). A potentially crucial, yet under-investigated domain in treatment and outcome research is clients' perceptions of satisfaction with the treatment program. Aim: This study used a repeated measures design to examine the relationship between clients' treatment evaluation and post-treatment outcomes. Methods: Consecutive admissions to publicly-funded inner-city outpatient drug treatment in NYC were interviewed within 2 weeks of admission (BL), at treatment end (DIS), and 6 months later (6MO, preliminary N=208). Predictor domain: Clients' treatment evaluation at BL (e.g., whether program meets expectations, working as a team with staff, treatment plan matching one's goals). Outcome domains: Treatment completion at DIS; 12-step affiliation, commitment to abstinence (motivation), and length of abstinence at DIS and 6MO. Hypotheses: BL scale scores on a 7-item Treatment Evaluation (TE) Scale ($\alpha=.74$) would predict outcomes at DIS and at 6MO, controlling for previous levels of the outcome domains. Findings: Results from regression analyses supported the study hypotheses for DIS outcomes but not for 6MO outcomes. Conclusions: Clients' early program evaluation may be critical to proximal treatment outcomes. Subsequently, other processes may intervene and determine whether treatment gains are maintained (e.g. self-help/aftercare activities, peers, stress). Additional research is needed to identify these intervening factors. Clinically, findings emphasize the importance of focusing on identifying clients' expectations and needs in the context of services available in treatment, and finding a fit between the two. Funded by National Institutes on Drug Abuse Grant R01DA015133-01A1.

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- 741 ELECTROPHYSIOLOGY OF THE MEDIAL PREFRONTAL CORTEX IN THE BEHAVING RAT: STUDIES OF ACUTE AND CHRONIC AMPHETAMINE TREATMENT**
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Repeated, intermittent administration of amphetamine (AMPH) leads to an augmentation of certain locomotor behaviors; this phenomenon of behavioral sensitization might reflect contributions to craving and relapse symptoms of addiction. Relatively few studies have looked at drug-induced plasticity in the medial prefrontal cortex (mPFC) in the induction or expression of behavioral sensitization. To first test the acute effects of AMPH (1 mg/kg, i.p.) on mPFC single-unit activity, male Sprague-Dawley rats were chronically implanted with bilateral electrodes and allowed to freely move in an open-field chamber. Single units were isolated and identified based on waveform parameters. Many of the recorded cells responded with a net increase in firing rate from baseline (non-movement) to post-AMPH (as much as 1100%), while other cells showed a 50% decrease from baseline to post-AMPH. Some cells also showed relatively no change from baseline conditions, even though there were increases in behavioral measures, such as locomotion and head movements. In a second, separate experiment that was designed to test the behavioral effects of repeated AMPH treatment, rats were allowed to habituate to an open-field environment and then tested on a ten-day sensitization regimen consisting of alternating injections of either saline or AMPH (1 mg/kg, i.p.). AMPH administration was paired with discriminative stimuli (flashing light and tone) in an attempt to produce robust sensitization. Following a seven day withdrawal period, rats were challenged with the same dose of saline or AMPH. Sensitization and conditioning effects were observed, although the effects were not robust. Together, these results suggest that acute AMPH treatment alters the function of mPFC neurons and that single-unit recordings from the mPFC would be beneficial in determining the functional role that this brain area has in the behavioral effects of chronic AMPH treatment.
- 742 FACTORS INVOLVED IN PREDICTING THE SUCCESS OF MODAFINIL FOR THE TREATMENT OF COCAINE-DEPENDENT SUBJECTS**
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Modafinil is a new drug that has been found to reduce cocaine use in cocaine dependant research subjects. It is believed that modafinil activates glutaminergic circuits while inhibiting GABA in the brain. Additionally, in vitro studies have found that it inhibits the re-uptake of dopamine. Our research group at the Treatment Research Center (TRC) published results of a double blind -placebo controlled study that found modafinil to significantly decrease cocaine use over an 8-week trial (Dackis, 2005). While the general results indicate that modafinil may be an excellent new option for the management of cocaine addiction, little has been reported on the subjects that were most responsive to treatment with the medication. The focus of this presentation will be on potential predictors of outcome for cocaine dependent patients treated with modafinil from our original published results. Preliminary analysis of this data indicates a number of interesting findings. First was that subjects treated with modafinil did not show a significant change in use prior to three weeks of being on the medication. After 3 weeks, while there was some variability in the amount of clean urines in both groups, the modafinil treated group maintained a significantly greater total number of clean urines than subjects receiving placebo. A second result that approached significance ($p=.06$) was that the modafinil treated subjects were better able to submit 3 consecutive cocaine negative (CLEAN) urine drug screens than placebo subjects. Third, the modafinil group provided more days of data than subjects receiving placebo, which suggests less compliance from the placebo groups. Additionally, we looked at predictive factors of outcome collected from data measures used during the trial, including ASI information, depression factors, and CSSA scores as potential predictors of outcome.
- 743 GENDER DIFFERENCES IN TREATMENT ENGAGEMENT AMONG A SAMPLE OF INCARCERATED SUBSTANCE ABUSERS**
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Gender differences have been noted in factors associated with substance abuse treatment entry, treatment retention, and treatment outcomes among substance abusers. However, limited research has focused on factors associated with treatment engagement among male and female substance abusers, and how those factors may differ across treatment programs. The purpose of this presentation is to examine gender differences in treatment engagement (TE), psychosocial functioning (PF), and criminal thinking (CT); 2) gender as a moderator of the relationship between TE and PF; and 3) gender as a moderator of the relationship between TE and CT. Participants were recruited as part of the NIDA funded Criminal Justice Drug Abuse Treatment Studies (CJ-DATS) Performance Indicators for Corrections protocol (Simpson, PI) from five collaborating research centers which included TCU, Univ. of KY, NDRI, Univ. of DE, and UCLA. Participants included 1,950 males from 15 programs and 824 females from 5 programs (N = 2,774 from 20 treatment programs). Participants completed a one-time survey which included TCU measures to focus on client indicators of treatment performance. Findings indicate that females reported more psychosocial dysfunction, less criminal thinking, and higher engagement than males. There was a stronger relationship between psychosocial variables and treatment engagement in female treatment programs when compared to male programs. Male programs had a significantly stronger relationship between cold heartedness (CT subscale) and low treatment engagement. Findings from this study suggest that it is important to examine factors that influence treatment engagement for male and female offenders. By assessing for factors that may influence treatment engagement early in treatment, programs may be able to target treatment interventions to address these problems in an effort enhance the retention rates, treatment experience, and treatment outcomes for substance using clients.
- 744 POSITIVE PSYCHOLOGY AND ADDICTION TREATMENT**
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Interventions and assessment tools from the field of positive psychology have the potential to improve addiction treatment outcomes. Patients seeking treatment for addiction often experience a "slump" early in treatment as they must face the consequences of their addiction and make difficult life change without the pleasurable escape provided by substance abuse. It is critical during this phase of recovery to help patients explore new ways of building pleasure, engagement, and meaning in their lives. Positive psychology interventions that boost happiness and reduce depression in normal individuals (Seligman, Steen, Park, & Peterson, 2005) may be modified to supplement standard CBT and MET based addiction treatment. Patients often associate happiness with euphoria or pleasure, and they can benefit in very practical ways from a broader conceptualization of the term (Duckworth, Steen, & Seligman, 2005; Seligman, Steen, et al., 2005). For example, by identifying and using their personal strengths in new ways, patients can learn to build happiness into their lives (Peterson & Seligman, 2004). Strengths inventories such as the Values in Action Inventory of Strengths (Values in Action Institute, 2002) provide concrete feedback about character strengths. Patients can consider how they might draw on strengths such as courage, perseverance, honesty, creativity, or curiosity to support their recovery. Building a sense of purpose and meaning in life by connecting to spiritual or religious faith and other people or institutions also helps to increase happiness and resilience (Haidt, 2005). In addition, patients can be encouraged to pursue activities that create engagement or flow-a sense of time stopping and complete absorption in the present moment-as a satisfying alternative to pleasure (Csikszentmihalyi, 1997; Csikszentmihalyi & Colleagues, 2005). Patients can use the Approaches to Happiness Questionnaire (Peterson, 2003) to track their evolving orientation toward pleasure and happiness.

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745 FACTORS ASSOCIATED WITH RECREATIONAL OPIOID USE IN HEROIN-DEPENDENT RESEARCH VOLUNTEERS

C. L. Steinmiller and M. K. Greenwald, Wayne State University, Detroit, MI

This retrospective study is examining factors associated with recreational opioid use in 210 (66F, 144M; 138 African-American, 70 Caucasian, and 2 other) heroin-dependent research volunteers. Drug and medical history data were obtained from questionnaires administered during screening. Analyses include demographic data (gender and race, excluding other), history of drug use (prescribed, recreational, and route of use), and potentially relevant medical conditions (e.g. chronic pain, dental pain). All volunteers (mean age=43 yr, mean education=12.4 yr) report chronic heroin use (mean duration= 21 yr), with 66% currently injecting heroin. Two multiple logistic regression analyses were used to identify factors related to lifetime and current recreational opioid use (predicted variables). Lifetime recreational opioid use was significantly associated with a history of using prescription opioids (chi-square=47.9, B=2.28, Wald=30.1, $p < 0.001$), and marginally associated with a history of dental pain ($p < 0.06$) and lifetime heroin injection ($p < 0.1$), whereas race, gender and chronic pain were unrelated. Past 30-day recreational opioid use was non-significantly greater among those with lifetime recreational opioid use (chi-square=2.52, $p < 0.1$), and was not significantly related to any other drug use or medical history factors. In summary, heroin users who have ever used a prescribed opioid are more likely to have ever used opioids recreationally; prescription opioid use appears to be a unique risk factor for recreational opioid use in this population, with a history of pain conditions tending to contribute modest risk. A limitation of this study is that age of onset data were not originally collected. Thus, the relative (predictive) order of pain conditions, prescription/medical use and non-medical use of opioids cannot be determined retrospectively. (Supported by NIH/NIDA R01 DA15462 and Joseph Young, Sr. Funds from the State of Michigan.)

746 FACTORS ASSOCIATED WITH HIV EDUCATION ATTENDANCE

R. Sterling(1), S. P. Weinstein(1), D. A. Calsyn(2), S. R. Doyle(2) and P. Crits-Cristoph(3), (1) Thomas Jefferson University, Philadelphia, PA, (2) University of Washington, Seattle, WA and (3) University of Pennsylvania, Philadelphia PA

Substance abusers are known to be at increased risk for HIV transmission. Recognizing this, NIDA, through its Clinical Trials Network recently undertook a study of the relative efficacy of a five-session gender specific intervention, REMAS, versus a single HIV/AIDS education (i.e., control) session, for current male patients enrolled in either methadone maintenance treatment (MMTP) or outpatient drug-free (ODF) care. The accumulating literature that indicates that HIV transmittal risk can be reduced through increased education led us to examine whether study entry factors that contribute to premature intervention termination could be identified. Subjects were 572 males evenly distributed across MMTP and ODF conditions; 293 were randomly assigned to the five session REMAS intervention. Overall, 52.7% of study participants completed the intervention to which they were assigned. No differences in attendance were observed across study condition as 51% of subjects assigned to REMAS and 57% assigned to the single session control group completed treatment, chi-square = 1.99, $p > .05$. A series of logistic regressions undertaken to examine the influence of study entry measures, including demographic factors such as age, race, years of education, and marital status as well as attitude toward condom use indicated that the only significant predictor of intervention attendance/completion was enrollment in methadone maintenance treatment.

747 RESULTS OF STATE POLICY CHANGE TO PLACE CLIENTS IN MORE APPROPRIATE TREATMENT SETTINGS

S. Stevens-Manser(1), M. Arocena(2), D. Wanser(2) and R. T. Spence(1), (1) Center for Social Work Research, University of Texas at Austin, and (2) Department of State Health Services, Austin, TX

Introduction In 2004, the Texas Dept of State Health Services used ASAM, CSAT TIP13, and studies by Hubbard (1994) and Simpson (1997, 1999) to develop Client Placement Guidelines (CPGs) to designate client low, medium or high severity based on clinical assessment. In a previous analysis, CPGs were retrospectively applied to 29,299 client assessments from 2003 This analysis found that 20% of clients were placed in higher level and 4% in lower level of care than recommended by the CPGs. Two major revisions were made in 2005 to improve the system: 1) independent assessment entities were procured regionally to ensure apt treatment placement and 2) provider contracts required use of CPGs to guide placement into treatment service levels. The present study examined one year of clinical data to determine if the recent changes resulted in more apt placement of clients and if treatment outcomes were affected. Sample and Methods A 2005 sample of 32,682 clients in treatment for the first time was used for analyses. These were compared to clients receiving services in 2004. Results In 2005, significantly more low severity clients were placed in outpatient (82% vs. 75%) and significantly more high severity clients were placed in residential (78% vs. 70%) services than in 2004. No between-group difference were found for medium severity clients. In 2005, significantly more high severity clients in residential continued to lower intensity level of care (33% vs. 23%) and significantly more low intensity clients in outpatient services completed treatment than in 2004 (53% vs. 47%). Discussion As funding does not meet actual treatment need, resources must be used more efficiently and effectively. The present study indicates that use of an independent assessment entity and CPGs result in greater fidelity to the placement model, and better outcomes in terms of completion and retention in treatment.

748 LOW-DOSE NALOXONE CHALLENGE FOR QUANTITATIVE OPIOID DEPENDENCE MEASUREMENT

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No studies have been reported in humans showing a quantitative, linear relationship between methadone (METH) dose and severity of naloxone (NLX)-precipitated withdrawal (WD). A technique with minimal discomfort to patients but allowing quantitative dependence assessment could be a useful predictor of outcome in clinical studies. We have previously reported (CPDD 2003) the results of our study in clinically stable METH patients testing the hypothesis that WD after low dose (0.1mg) NLX will be correlated with maintenance METH dose. In that study series, n=12, several withdrawal signs were changed significantly over time but no measures were correlated with METH dose except for heart rate, and several subjects showed little response to 0.1 mg. We are now testing a new series of subjects using 0.15 mg NLX (currently n=4 completed, n=12 planned). Active psychiatric disorders, medical disorders or taking other meds were exclusions. A dose of NLX (.15 mg) or saline placebo (PLA) i.m. was given on two days under double blind, counterbalanced conditions. Subjects were challenged at near trough METH levels at the same time every morning and were then given their daily METH. Subjective and observer-rated WD, craving, physiological measures, and salivary cortisol levels were determined. Repeated measures ANOVAs were performed for NLX vs. PLA effects over time. Correlation coefficients were calculated for peak difference scores (NLX-PLA) and METH dose. Maximal subjective and objective WD measures are on average doubled compared to those seen after the 0.1mg dose. Early results are statistically significant for subjective WD (ANOVA, drug x time, $F=4.04$, $p=.006$) and approaching statistical significance for objective withdrawal ($F=2.14$, $p=.084$). There is insufficient power to show significant correlation with METH dose but the higher levels of WD measured suggest that correlation may be seen with the completed sample. Results will be updated for all subjects (up to n=12) tested as of June 2006. (Support: NIH R29 DA1 1079, 5R01DA015832-02, Joe Young Funds, State of Michigan.)

749 ABSTINENCE INCENTIVE EFFECTS IN PSYCHOSOCIAL COUNSELING PATIENTS TESTING STIMULANT POSITIVE VS NEGATIVE AT TREATMENT ENTRY

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Previous research has documented the importance of drug use versus abstinence at treatment entry, as indicated by positive versus negative urinalysis test, as a predictor of treatment outcome. However, it is not known whether those with positive versus negative urine tests at treatment entry respond differentially to treatment interventions. The purpose of this secondary analysis is to determine whether participants testing stimulant positive versus negative at study entry benefited equally from exposure to abstinence incentives. Methods: Data were derived from a multisite study of abstinence incentive effects conducted in the Drug Abuse Treatment Clinical Trials Network at 8 psychosocial counseling treatment clinics nationwide. Primary outcome for this analysis was study retention. Results: Participants who tested stimulant positive (N = 108) versus negative (N = 306) at study entry were more likely to be <35 years of age, more likely to meet DSM criteria for stimulant dependence and for cannabis dependence and less likely to be entering treatment from a controlled environment. Cox Proportional Hazards analysis revealed a significant main effect of intake urinalysis result on study retention, with poorer outcomes (fewer retained for 12 weeks) for those testing positive versus negative at study entry - hazard ratio (95% CI) = 1.71 (1.26-2.31). Subgroup analyses revealed a significant effect of incentives on retention for the stimulant negative sample (55% incentive versus 32% control retained); HR = 1.86 (1.35-2.56). However, there was no significant effect for those testing positive (38% incentive versus 25% control retained); HR = 1.19 (0.73-1.93). Conclusions: These results replicate and extend previous observations about the poor treatment prognosis associated with a drug positive urine test at treatment entry. Further, the study demonstrates that the beneficial effects of abstinence incentives on retention in psychosocial counseling treatment are primarily to those who test drug negative at entry.

750 EFFECTS OF REPEATED COCAINE ON IMPULSIVITY IN RATS

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Previous studies have consistently demonstrated that cocaine-dependent subjects demonstrate greater impulsivity than non-drug using control subjects. However, it has not been determined whether impulsivity is a factor leading to or resulting from cocaine use. To clarify the relationship between cocaine use and impulsivity, we examined the effects of repeated cocaine injections in an animal model of impulsivity, the differential reinforcement of low-rate (DRL) procedure. Water restricted male rats were trained to respond under a DRL 20-sec schedule. Once stable responding was established, rats were exposed to either a "binge" regimen of cocaine (15 mg/kg 3 injections/day for 7 days; 3x/day), a "sensitization" regimen of cocaine (15 mg/kg 1 injection/day for 7 days; 1x/day), or the respective vehicle regimen. Injections began 1 hr after daily DRL sessions; in the 3x/day vehicle and cocaine groups injections were repeated at 1 hr intervals. Relative to vehicle-treated controls, rats treated with the 3x/day cocaine regimen earned significantly more reinforcers without a change in response rate, indicating decreased impulsivity. Rats treated with the 1x/day regimen did not perform differently from vehicle-treated rats. Seven days after termination of the repeated cocaine regimens, all rats were given a single 5 mg/kg challenge injection of cocaine before the DRL session. In the 3x/day cocaine-treated rats, the challenge injection did not increase response rate or decrease number of reinforcers obtained, indicating tolerance to the effects of cocaine on impulsivity; the vehicle-treated and 1x/day cocaine-treated rats did not display tolerance to the challenge injection. Thus, level of "impulsivity" and subsequent sensitivity to the effects of cocaine on impulsive is dependent on the frequency and extent of cocaine exposure. Understanding the relationship between repeated cocaine exposure and impulsivity will afford us a better appreciation for the long-term behavioral consequences of cocaine use, and better designed treatments for cocaine users. Supported by DA07287, DA06511.

751 THE ROLE OF NICOTINIC ALPHA7 RECEPTORS IN THE DOPAMINE-MEDIATED COMPONENT OF NICOTINE DISCRIMINATION

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The nicotine discriminative stimulus has been strongly linked to beta2* nicotinic receptors with little evidence of a role for alpha7 receptors, e.g. nicotine discrimination was blocked in beta2 knockout mice but was unaffected in alpha7 knockouts (Stolerman et al. 2004). However, alpha7 as well as beta2* receptors have been implicated in nicotine-stimulated dopamine overflow. This study focuses on the dopamine-mediated element in the nicotine stimulus by examining cross-generalisation between amphetamine and nicotine. Male alpha7 knockout and wild-type littermate controls descended from mice constructed by Orr-Urtreger et al. (1997) were bred in-house. Mice were trained to discriminate nicotine (0.8 mg/kg) or (+)-amphetamine (0.6 mg/kg) from saline in a two-lever operant conditioning procedure with a tandem VI30 FR10 schedule of food reinforcement. The knockout did not influence acquisition of discriminations that proceeded to final accuracies of about 90% (n=8-10). The knockout also did not affect dose-response curves for the training drugs, but it subtly influenced results of cross-generalisation tests. In mice trained to discriminate nicotine, there was partial generalisation to amphetamine (0.6-1.0 mg/kg) in wild-type mice and this effect was weaker in knockouts. Similarly, in wild-type mice trained to discriminate amphetamine, there was partial generalisation to nicotine, and at 0.8 mg/kg of nicotine only, this response was absent in the knockouts. The alpha7 antagonist methyllycaconitine attenuated the response to the training dose of amphetamine and the partial generalisation to nicotine in wild-type mice. Tests with a drug more selective than amphetamine are needed, but the findings to date support the concept of an alpha7-mediated dopaminergic element in nicotine discrimination. (Research supported by EU and MRC). Orr-Urtreger A, Goldner FM, Saeki M, Lorenzo I, Goldberg L, De Biasi M, Dani JA, Patrick JW, Beaudet AL (1997) *J Neurosci* 17: 9165-9171 Stolerman IP, Chamberlain S, Bizarro L, Fernandes C, Schalkwyk L (2004) *Neuropharmacology* 46: 363-371

752 BEHAVIORAL CONTINGENCIES CAN REDUCE THE COSTS OF COUNSELING SERVICES IN ADAPTIVE STEPPED-CARE TREATMENT APPROACHES

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Background: Increased counseling is often advocated in response to partial and poor response to routine drug abuse treatment. Adaptive stepped care models provide structured levels of service and a rational method of adjusting treatment intensity. However, poor attendance to enhanced services limits their effectiveness, decreases efficiency of clinic resources, and may increase the cost of services attended. Motivated Stepped Care (MSC) is an adaptive stepped care model that incorporates clinic-based behavioral contingencies to improve adherence to counseling schedules. Prior work has shown it to be associated with increased counseling attendance and reduced drug use in opioid-dependent patients receiving methadone. The present study evaluates the cost of this approach with versus without incentives to improve counseling attendance. Methods: Subjects (n=127) were opioid-dependent patients enrolled in a 2-group randomized evaluation of the efficacy of MSC to improve counseling attendance and reduce drug use: stepped care with incentives on attendance and drug use (MSC) versus standard stepped care without these contingencies (SSC). Additional data on treatment costs were obtained to determine the effects of counseling attendance rates on cost per service delivered. Results: Preliminary analyses show that increased attendance to individual counseling sessions in the MSC (94%) versus SSC (70%) condition was associated with a 26% reduction in cost per individual session attended, while the increased group counseling attendance rates in MSC (76%) versus SSC (28%) resulted in a 63% reduction in cost per group session attended. Additional analyses, including actual program (dollar) costs, will be presented. Conclusions: Improving patient adherence to prescribed counseling services can reduce the unit costs of increasing the intensity of treatment services for partial and poor responders to routine levels of care. Supported by NIH-NIDA grants P50 DA05273, K23 DA16250

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- 753 PARENTING PRACTICES AND ADOLESCENT MARIJUANA INVOLVEMENT: AN ASSESSMENT OF FIRST OPPORTUNITY AND FIRST USE OF MARIJUANA**
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The purpose of this research was to study the association between parenting styles and adolescent marijuana involvement by examining the age when youth experience their first opportunity to use marijuana and the age at first marijuana use. Participants were 799 predominantly African American youth who entered the first grade during the 1993-1994 academic year, and their parents. Survival analyses were performed on 535 of these youth who had, along with their parents, successfully completed at least one follow-up assessment by the 10th grade. Results indicated that children with authoritative parents (consistent discipline and good communication/warmth) experience their first opportunity to use marijuana at a later age than children of authoritarian (consistent discipline, but poor communication or warmth) or permissive (inconsistent discipline) parents. The same was true for marijuana use. The curves for permissive parenting and authoritarian parenting generally revealed earlier age of onset into both marijuana opportunities and use, followed by relatively parallel curves in the later years of the study. Among youth with permissive parents, the incidence of first opportunity to use marijuana was higher starting age 9, and the incidence of first marijuana use was higher starting age 11. These youth continued to have more opportunity and use throughout the study period. Compared to youth of authoritative parents, youth of authoritarian parents had a higher incidence of opportunity to use marijuana starting at age 12, and had a greater incidence of marijuana use by age 13. Results from this study suggest that parental discipline, communication, and warmth may be important targets for marijuana use prevention by not only targeting marijuana use, but also opportunities to use marijuana. Funding: NIDA F31DA016820; T32DA0725714; R01DA11796; NIMH R01MH57005.
- 754 A LOW DOSE OF ARIPIPRAZOLE ATTENUATES SOME OF THE ABUSE-RELATED EFFECTS OF D-AMPHETAMINE**
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Amphetamine misuse presents a significant public health concern. Despite increased reports of amphetamine abuse and dependence, a putative pharmacotherapy has yet to be identified. Previous research from our laboratory suggests that 20 mg aripiprazole, an atypical antipsychotic that has partial agonist activity at D2 receptors, attenuates many of the abuse-related effects of d-amphetamine. While 20 mg aripiprazole significantly attenuated the discriminative-stimulus and subject-rated effects of d-amphetamine, it also impaired performance on a computerized version of the DSST when administered alone, indicating that the attenuation observed may have been functional as opposed to receptor mediated. We hypothesized that a lower dose of aripiprazole (10 mg) would also attenuate the behavioral effects of d-amphetamine without impairing performance. To this end, 6 healthy volunteers learned to discriminate 15 mg d-amphetamine. After the discrimination was acquired, the effects of a range of doses of d-amphetamine administered alone and in combination with aripiprazole (10 mg) were tested. Subjective drug, performance, and physiological effects were also measured. Repeated measures analysis of variance was used to analyze the data. The results of the present experiment indicate that 10 mg aripiprazole attenuated some abuse-related behavioral effects of d-amphetamine. These findings suggest that 10 mg aripiprazole would be a reasonable starting dose for the treatment of stimulant abuse and dependence. Future research should examine the effects of chronic aripiprazole administration in combination with methamphetamine or cocaine.
- 755 WHO IS SMOKING AND WHO HAS QUIT: RESULTS FROM THE WMH SURVEYS**
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Recent international epidemiology efforts have seen improvements in study design and standardization of survey protocols that have made it possible to investigate population-level characteristics of tobacco smokers in countries spread throughout the world. This study report from multiple countries taking part in the World Health Organization (WHO) World Mental Health Initiative (WMH) presents basic comparative estimates on the epidemiology of smoking. We describe variations in tobacco smoking in relation to certain fixed personal characteristics (e.g., age & sex) as well as potentially modifiable characteristics such as employment and education for all smokers identified in each country, as well as by smoking status (active/current or former smoker). Weights and variance estimation take into account features of the complex survey design. In the U.S. and other more established market economies of the world, as many women smoke as men, but this is not the case in emerging market economies. The proportion of smokers never married was fairly consistent in every country, as was the proportion for those employed. However, the proportion of smokers working for pay was most consistent among established market economy countries. Under a quarter of male and female smokers in China and Lebanon indicated they had quit, while the proportions of smokers who had quit by sex were nearly comparable and approaching 50% in Columbia and several other countries, such as Netherlands, Belgium, and the US. Quitting was more common among younger adults in countries with an established economy as compared to similarly aged persons residing in countries with emerging market economies. In almost all countries, a large proportion of older smokers (55 years or older) were found to have quit. The WMH surveys provide epidemiologic data useful for national as well as global efforts to secure reductions in the risk and the prevalence of one of the most serious drug-related behaviors that influences health worldwide--namely, tobacco smoking. Acknowledgments: WHO World Mental Health Survey Consortium, DA016558, DA015799 & MH070884
- 756 THE CHANGING FACE OF THE SUBSTANCE ABUSE TREATMENT WORKFORCE: IS A CRISIS IMMINENT? IMPLICATIONS FOR RESEARCHERS, PROVIDERS, AND EDUCATORS**
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Daily in the United States approximately 1,092,546 individuals receive substance abuse treatment services in approximately 13, 623 treatment facilities (SAMHSA 2003). A majority (60%) of these treatment services are provided in private, non-profit settings (SAMHSA 2003). While there is excellent data regarding substance abuse treatment patients and facilities there is an absence of a national data set for the substance abuse treatment workforce. Using the results of two regional workforce studies by the Addiction Technology Transfer Center of New England and the Mountain West Addiction Technology Transfer Center several important trends can be identified. Overall, the majority of substance abuse treatment services in these two regions (eleven states or over 20% of the United States) are provided by white women with masters degrees, not in recovery, over the age of 40. This workforce is providing treatment services to a predominately non-white, male, client population between the ages of 25-40. In comparison, Mulligan, et al., (1989) seventeen years ago described the substance abuse treatment workforce as predominately composed of males, in recovery, with little formal education. The substance abuse treatment workforce has changed dramatically in the past two decades, specifically, in relationship to gender, race/ethnicity, age, and educational levels. This presentation will highlight recruitment and retention efforts needed to address current workforce needs. Specifically, recruitment efforts will speak to the fact that only 5% of the workforce is between the age of 21-30. Discussion around retention efforts will address sources of job dissatisfaction (e.g. low pay, paperwork, and relapsing clients). Finally, the shift from staff in recovery to staff not having a history of being in recovery will be discussed. This is a significant change for the substance abuse treatment workforce with important implications.

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757 CONTROLLED CLINICAL TRIAL OF FLUOXETINE AND VOUCHERS IN METHADONE-MAINTAINED PATIENTS WITH COCAINE DEPENDENCE

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Clinical studies testing the efficacy of fluoxetine (F) for cocaine dependence treatment have produced equivocal results. Some studies have not ensured adherence with F ingestion, and also have not had consistent levels of motivation for abstinence. This outpatient clinical trial tested the efficacy of F (60 mg per day) versus placebo (P) in cocaine dependence treatment, using a design that maximized daily supervised medication ingestion and that included voucher incentives (V) to improve motivation for cocaine abstinence. Participants (n=198) had active opioid and cocaine dependence, and were initially stabilized for the first 3 study weeks on up to 100 mg of daily methadone in a treatment/research clinic. Daily doses were ingested under supervision throughout the study to ensure adherence with medication ingestion. Following methadone stabilization, subjects were stratified and randomly assigned to one of four conditions (F, P, F+V, P+V). After stabilization on F (or P) during study weeks 4-7, patients assigned to V had a 12-week period during which cocaine negative urine samples were reinforced (study weeks 8-19, the primary period of study interest). At pretreatment baseline, groups differed only on legal status, with those in the F+V condition less likely to be legally free; therefore analyses used legal status as a covariate. Drug use outcomes were not confounded by differential retention, which was similar across groups (mean days retained: F+V=120.6; F=110.9; P+V=123.8; P=118.7; $p>0.05$). On the primary outcome index of cocaine positive urines there was a significant benefit of V ($p0.05$). These results demonstrate sensitivity of the study methods to detect significant benefits, but do not support use of F for treatment of cocaine dependence, and suggest it may actually undermine the effectiveness of voucher incentive treatment. Supported by R01 DA10754 and K02 DA00332.

758 TOXICOLOGICAL ANALYSIS IN RATS SUBJECTED TO HEROIN AND MORPHINE OVERDOSE

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In heroin overdose deaths the blood morphine concentrations vary substantially. To explore possible pharmacokinetic explanations for variable sensitivity to opiate toxicity we studied mortality and drug concentrations in male Sprague-Dawley rats. Groups of rats were injected intravenously (i.v.) with heroin, 21.5 mg/kg, or morphine, 223 mg/kg, causing a 60-80% mortality among drug-naïve rats. Additional groups of rats were pre-treated with morphine for 14 days, with or without one week of subsequent abstinence. Brain, lung and blood samples were analyzed for 6-monoacetylmorphine, morphine, morphine-3-glucuronide and morphine-6-glucuronide. Morphine pre-treatment significantly reduced mortality upon i.v. morphine injection, but the protective effect was less evident upon i.v. heroin challenge. The morphine pre-treatment still afforded some protection after one week of abstinence among rats receiving morphine i.v., whereas rats given heroin i.v. showed similar death rate as drug-naïve rats. Morphine i.v. administration to drug-naïve rats resulted in both rapid and delayed deaths, whereas heroin i.v. caused only rapid deaths. The morphine levels conformed to the predicted exponential elimination curve in all samples, ruling out brain accumulation of morphine as an explanation for delayed deaths. Very low levels of glucuronides exclude significant contribution of these metabolites to the toxicity. Spontaneous death of both heroin and morphine rats occurred at fairly uniform brain morphine levels.

759 CHANGES IN HCV KNOWLEDGE AND SELF-EFFICACY AMONG DRUG TREATMENT STAFF IN NYC: PRELIMINARY DATA ON THE EFFECTIVENESS OF AN INNOVATIVE STAFF TRAINING

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Drug users are disproportionately impacted by hepatitis C virus (HCV) infection, but many do not receive the support they need in the community. Drug treatment program staff are well situated to support and facilitate the provision of HCV services to their patients. Unfortunately, staff often have limited knowledge and self-efficacy to provide this support. Using data collected from staff (N=64) in two residential drug free and 2 methadone maintenance treatment programs in NYC, who were participating in the NIDA-funded study, "STOP HEP C," R01DA13409, we report their one month change in HCV knowledge and their self efficacy in helping their patients deal with the virus. Staff (N=30) in two of these programs (one of each modality) participated in a 6 hour HCV staff training intervention at baseline, while staff in the other two programs served as a control group and received the training after data collection was completed. Staff knowledge, as measured by a 20-item true-false scale, increased significantly among those that received the training, from an average of 12.3 correct to an average of 16.5 correct ($p<0.001$), while staff in the control programs did not show a significant improvement in HCV knowledge over time ($p=.59$). Staff self-efficacy, as measured by a 10-item, 11 point Likert scale with a range from 0 to 100, also increased significantly over the one month period for the staff that received the training (from an average of 59.9 to 75.9; $p<0.001$), while staff in the control programs did not improve significantly ($p=.50$). Results support the effectiveness of this staff training, a promising way to help vulnerable individuals with their HCV needs.

760 YOGA SESSIONS INCREASE BRAIN GABA LEVELS

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Introduction: Yoga has been reported to reduce symptoms in disorders that are associated with low GABA states (e.g. depression, anxiety, and epilepsy). Using magnetic resonance spectroscopy (MRS), brain GABA levels have been reported to be low in cocaine dependence, depression and anxiety. Design: The aim of this study was to compare changes in human brain GABA levels between yoga practitioners (YP) and comparison subjects (CS) after a 60-minute yoga or reading session, respectively. It was hypothesized that the performance of a yoga session would be associated with an increase in brain GABA levels, while the reading session would have no effect on GABA levels. GABA levels were measured in an axial slab using MRS in 8 YP and 11 CS. Results: There was a 27% increase in GABA levels in the YP group after the yoga session (0.20 mmol/kg) but no change in the CS group after the reading session (-0.001 mmol/kg) ($U = 17, Z = 2.23, p = 0.03$). Baseline GABA values were lower in females in the luteal stage, but changes in GABA values associated with the yoga session were unrelated to menstrual stage. Discussion: These findings demonstrate that in experienced yoga practitioners brain GABA levels increase following a session of yoga. This suggests that the practice of yoga should be explored as a treatment for disorders with low GABA levels, such as cocaine dependence. Future studies of brain GABA levels in females should establish menstrual stage at the time of scan acquisition as a potential covariate.

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761 GENDER DIFFERENCES IN RISK FOR FORCED SEXUAL CONTACT AMONG CLUB DRUG USERS

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Gender differences in reporting experiencing "date rape" were analyzed among an international sample of ecstasy users. Experiencing forced sex by a dating partner may be increased among females and males who report having sex while on Ketamine, Rohypnol, or GHB, drugs considered "date rape" drugs, or who report experiencing amnesia, a blackout, or being in a dangerous situation due to a date rape drug. In addition, we examined the possible effects of lack of parental monitoring at a vulnerable age. Club drug users from Miami, St. Louis, and Sydney, Australia were interviewed as part of the CD-SLAM study to evaluate the potential for ecstasy abuse and dependence using the Club Drug Risk Behavior Assessment and the Substance Abuse Module. Of the 624 respondents (mean age of 23.3, $sd=5.20$), 268 (43%) were women, and of these, significantly more (25%) had experienced date rape compared to the men (10%) ($\chi^2=26.90$, $p < .0001$). SAS logistic regression models by gender showed that date rape among men was significantly increased if they had had sex while on date rape drugs (OR 1.32, 95% CI 1.02, 1.71). Age, lack of parental monitoring and endorsing amnesia, black-outs or being in a dangerous situation due to a possible date rape drug were not significantly related to date rape. Among the women who had experienced date rape, risk climbed by age, with each year of life increasing the lifetime risk by 1.09 times, (95% CI 1.02, 1.16). Parental monitoring reduced their risk by .93 times (95% CI .88, .99). Date rape risk was not increased if the women endorsed having sex while taking date rape drugs or being endangered due to a date rape drug, yet further testing showed that women did not mix sex and date rape drugs less than the men. Although parental monitoring and not having sex while taking drugs affect the genders differently, both may help prevent forced sexual contact among populations of young adults, and may be important individual prevention strategies.

762 BASELINE DEPRESSION SYMPTOMS PREDICT POST-RESIDENTIAL SUBSTANCE USE DISORDERS ACROSS 1-YEAR FOLLOW-UP

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Objective: To determine if higher baseline depression symptoms among adolescents with SUD constitute an increased risk for post-residential treatment substance use across 1 year follow-up (f/u). Method: Adolescents (N = 153) admitted to residential SUD treatment were assessed using the Global Assessment of Individualized Need (GAIN), the Beck Depression Inventory (BDI), at intake, and at 3, 6, 9 and 12mo f/u. Ten demographic, psychiatric, substance and environmental factors were entered into general estimating equation (GEE) regression models. High depression symptoms were defined as BDI scores > 11. Results: Sample demographics were: Mean age 16.6 yrs (+ 1.4), 78% male, and 65% White; 28% African-American; 55% had baseline BDI scores > 11. The outcome of the number of days of any substance use in past 90 days (controlled for confinement) was independently associated with BDI > 11 (adjusted mean difference = 12.1 (CI 3.3, 20.9)); >2 year length of drug career (adjusted mean difference = 15.4 (CI 3.5, 8.6)); and presence of opioid use disorder (adjusted mean difference = 11.0 (CI 20.8, 1.3)). Variables not associated with higher risk were older age, male gender, and 5 GAIN problem severity scores (e.g. substance use related problems, externalizing behaviors, environmental risk factors). Conclusions: Higher baseline depression symptoms strongly predicted increased risk for post-residential substance use suggesting the need to develop treatments targeting this treatable psychiatric symptom factor indicating poor prognosis for outcomes.

763 LOW RESTING PERFUSION IN THE ANTERIOR CINGULATE PREDICTS INCREASED DEPRESSIVE SYMPTOMS IN COCAINE-DEPENDENT PATIENTS

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OBJECTIVE: Because cocaine patients often experience depressive symptoms, poor affect regulation may be an important dimension of their relapse vulnerability. A candidate brain region for affect dysregulation is the anterior cingulate (ACg), as clinically depressed individuals (vs. controls) exhibit significantly lower resting regional cerebral blood flow (rCBF) in this brain region. Previously, we found that cocaine patients also have lower resting rCBF in the ACg. Whether ACg hypoactivity correlates with depressive symptoms in cocaine patients is not yet known. In this study, we examined the link between resting rCBF in the ACg and current depressive symptoms in treatment-seeking cocaine patients. METHODS: Arterial spin labeled (ASL) perfusion fMRI was used to measure resting rCBF in detoxified male cocaine patients (n=15). Perfusion data were analyzed using SPM2. The relationship between Beck Depression Inventory (BDI) score and resting rCBF was then examined in a single regression analysis. RESULTS: The mean BDI score was 10.73 ($sd=5.7$). Thirty-three percent of the sample had mild to severe BDI scores. Regression analyses showed a clear inverse relationship ($t \leq -4.1$; $p < .001$) between relative rCBF in the left rostral and ventral ACg, and BDI scores. The anatomical area extended in a contiguous strip from subgenual ACg to supragenual and dorsal ACg on the left side. CONCLUSION: The results show that lower baseline rCBF in the left ACg predicts higher depressive symptoms in cocaine patients. This inverse relationship suggests that fronto-limbic dysregulation may be responsible for the high comorbidity of depression symptoms and cocaine dependence. It also suggests that affect dysregulation should be added to the growing list of vulnerabilities now linked to frontal deficiencies in cocaine patients. NIDA: T32, RO1-DA-10241, RO1-DA-15149, P60-DA-05186, P50-DA-12756, Research Div., VAMC, and VA VISN 4 MIRECC

764 A TRIAL OF INTEGRATED BUPRENORPHINE/NALOXONE AND HIV CLINICAL CARE

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Untreated opioid dependence adversely affects the care of patients with HIV. We conducted a pilot study to investigate the feasibility of integrating buprenorphine (BUP/NX) treatment into an HIV clinic and the efficacy of BUP/NX along with two levels of counseling for treating opioid dependence and improving HIV outcomes. Opioid dependent patients with HIV were enrolled in a 12-week study and randomized to BUP/NX with physician management (PM) (biweekly, 20-minutes), or PM plus nurse-administered Drug Counseling and Medication Adherence Management (PM+DC/AM) (weekly, 45-minutes). Outcomes included retention, illicit drug use via weekly urine toxicology, T-lymphocyte CD4 cell counts (CD4), and HIV-1 RNA log10 levels (HIV RNA). Of the 16 patients who received > one dose of BUP/NX: mean age 47, 94% men, 31% white, 81% > high school education, and 19% employed. Mean years of opioid dependence was 17, 81% primarily used heroin, 56% injected, mean years HIV diagnosis was 13, mean CD4 was 367, and mean HIV RNA was 3.85. 11/16 (69%) completed > 12 weeks of treatment, 2 are currently completing, and 3 discontinued. The proportion of opioid positive urines decreased from 100% at baseline to 33% (Month 1), 20% (Month 2), and 17% (Month 3) ($p=0.36$). The mean HIV-1 RNA declined from 3.66 at baseline to 3.3 (Month 1), 2.89 (Month 2), and 2.9 (Month 3) ($p=1$ year). We conclude that it is feasible to integrate BUP/NX and different levels of counseling into HIV care. Patients experienced good treatment retention and reductions in illicit opioid use. HIV biological markers remained stable or improved throughout treatment. Supported by NIDA grants: DA09803-04A2, DA00167, 2K12 DA00167-11, 2K24 DA000445.

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- 765** EFFECTS OF DEPOT NALTREXONE ON RESPONSE TO IV HEROIN IN HUMANS
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Naltrexone is an opioid antagonist currently approved as a treatment for opioid and alcohol dependence. Although it is highly effective in completely antagonizing the effects of opioids, medication noncompliance is a difficult obstacle to treatment. The present study was designed to evaluate the time course, safety, and effectiveness of a sustained-release formulation of naltrexone (Depotrex®). Methods: Five heroin-dependent individuals participated in an 8-week inpatient study. After a 1-week detoxification period, the effects of a range of heroin doses (0, 6.25, 12.5, 25 mg, i.v.) were examined. Participants then received 384 mg naltrexone base. The effects of heroin were again evaluated for the next six weeks. One dose of heroin was tested per day and the entire dose range was tested each week in non-systematic order. During a morning sample session, participants received a dose of heroin and \$20; subjective, performance, and physiological effects were measured both before and after drug administration. During an afternoon choice session, participants were given the opportunity to choose to self-administer the sampled heroin dose and/or money using a modified progressive ratio procedure. Results: Depot naltrexone antagonized the subjective effects of heroin for 4-5 weeks. Subjective ratings of withdrawal were reduced after Week 2 throughout the remainder of the study. There were no clinically significant cardiovascular effects. The effects of heroin on mean trough pupil diameter began to emerge by Week 5. Conclusions: The present results extend our previous findings by showing that the reinforcing effects of heroin were reduced for 4-5 weeks after administration of 384 mg depot naltrexone. This formulation of naltrexone produced a long-lasting antagonism of the effects of intravenous heroin, with minimal side effects. Given that the primary difficulty associated with naltrexone maintenance in opioid abusers is medication compliance, a formulation of naltrexone that requires only once-a-month administration has important and promising treatment implications.
- 766** NEW LEADS FOR THE TREATMENT OF NICOTINE ADDICTION: DISCOVERY OF NOVEL TRIS-QUATERNARY AMMONIUM ANTAGONISTS AT NEURONAL NICOTINIC RECEPTORS MEDIATING NICOTINE-EVOKED DOPAMINE RELEASE
S. P. Sumithran, G. Zheng, A. G. Deaciuc, P. A. Crooks and L. P. Dvoskin, University of Kentucky, Lexington, KY
bis-Quaternary ammonium salts such as decamethonium bromide are considered simplified analogs of d-tubocurarine, and together with hexamethonium, these two compounds have been utilized to differentiate between peripheral nicotinic receptor (nAChR) subtypes. We have previously shown that bis-azaaromatic quaternary ammonium compounds potently and selectively inhibit neuronal nAChRs mediating nicotine-evoked [3H]dopamine ([3H]DA) release from superfused rat striatal slices. In the current study, a sub-library of novel structurally-related N-1,3,5-tri-n-pent-1-nylphenyl and N-1,3,5-tri-n-pentylphenyl azaaromatic quaternary ammonium salts was constructed. The interaction of these compounds with nAChRs was determined at 100 nM using high-throughput screening assays. Hits included GZ550A, GZ552B, GZ554A, GZ555A, GZ557B and GZ558B, which showed 40-80% inhibition of nicotine-evoked [3H]DA release, and showed little inhibition (<15%) of [3H]nicotine binding (alpha4beta2* nAChRs) and [3H]methyllycaconitine binding (alpha7* nAChRs). In contrast, GZ551B and GZ558C, showed 59% and 35% inhibition of nicotine-evoked [3H]DA release, and 44% and 81% inhibition of alpha4beta2* nAChRs, respectively, and 4-8% inhibition of alpha7* nAChRs. An examination of the SAR within this novel series indicated that tris compounds in which the azaaromatic moiety was a 2-, 3- and/or 4-alkyl substituted pyridinium group exhibited the greatest inhibition at the 100 nM probe concentration in the nicotine-evoked [3H]DA release assay. Tris compounds containing a nicotinium head group showed the greatest inhibition at alpha4beta2* nAChRs. One of the hits, GZ558B, appears to be a selective antagonist at nAChRs mediating nicotine-evoked DA release. These tris-quaternary ammonium antagonists constitute novel leads in our search for subtype-selective nAChR antagonists as treatments for nicotine addiction. Supported by NIH Grants U19DA017548.
- 767** ESTRADIOL MODULATION OF NOCICEPTION, MORPHINE ANTINOCICEPTION, AND REPRODUCTIVE INDICES IN FEMALE RATS
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The present study tested the hypothesis that the dose and timing of estradiol (E2) exposure needed to alter nociceptive sensitivity and morphine antinociceptive potency is the same as that needed to induce maximal reproductive behavior and uterine weight. In a previous study, ovariectomized female rats implanted with a 1-mm E2 capsule for 28 days showed maximal reproductive behavior and uterine weight (similar to gonadally intact females in proestrus/estrus), and when tested on the hotplate, had longer response latencies and were significantly less sensitive to morphine than ovariectomized females receiving no hormone treatment (Stoffel et al., 2003). In the present study, female Sprague Dawley rats underwent a simulated estrous cycle regimen of E2 administration for 20 days in which E2 (0.25 - 25 ug) or vehicle injections were administered for two consecutive days of every four days. Rats were then tested for nociception and morphine antinociception on the 50 degree C hotplate and tail withdrawal tests, or for reproductive behavior, at 4, 24, 48, or 96 hr following the last E2 injection. E2 increased reproductive behavior and uterine weight in a manner that was dependent on dose and time of exposure (effects maximal at 2.5-25 ug, 24 hr after the last exposure). E2 also increased latency to respond on the hotplate test in a dose-dependent manner, and similar to E2's effects on reproductive indices, this effect was greatest at 24 hr after the last E2 injection. E2 also had dose- and time-dependent effects on morphine antinociceptive potency; for example, on the tail withdrawal test, 2.5 ug E2 significantly increased morphine potency compared to oil-treated controls, but only at 24 hr after the last E2 injection. These results suggest that the effects of E2 manipulations that are reproductively relevant on basal nociception and morphine antinociception depend on the dose of E2 exposure and the timing of the test relative to E2 exposure. The results support the hypothesis that E2 modulates nociceptive and reproductive systems in concert.
- 768** PROGESTERONE BLOCKS ACQUISITION AND EXPRESSION OF COCAINE REWARD THROUGH BLOCKING SPATIAL MEMORY FORMATION
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It has been recently demonstrated that sex differences in cocaine conditioned place preference (CPP) appear to be mediated in part by gonadal hormone dependent mechanisms. The present study aims to expand these results by determining the role of progesterone in the acquisition and/or expression of cocaine CPP in intact male and female rats and to further determine if the progesterone effects are mediated through learning and memory. For chronic progesterone treatment, rats received Silastic capsules with either progesterone (100%) or vehicle 1 week prior to conditioning. For acute progesterone treatment rats received s.c. injections of progesterone or vehicle before saline or cocaine (5 mg/kg in female and 20 mg/kg in males) on conditioning days (acquisition phase) or before testing (expression phase). Chronic progesterone replacement did not block cocaine-induced CPP. However, acute administration of progesterone during both the acquisition or expression phase of cocaine conditioning blocked cocaine-induced CPP in female but not male rats. Progesterone did not affect ambulatory or rearing behaviors. In an object recognition task, females showed better performance than male rats, and progesterone did not have any effect on either sex. However, in an object replacement task, a task mediated by spatial learning and memory, progesterone significantly impaired the retention in both male and female rats when compared to control groups. These results suggest that acute progesterone treatment interferes with cocaine-induced reward associations in intact female rats, possibly through spatial working memory consolidation, but not recognition memory. The observed sexual incongruities in progesterone effects on cocaine CPP may in part explain current sex disparities in overall cocaine use and rates of relapse. This work was supported in part by MIDARP, SCORE 506-GM60654 and SNRP NF 39534.

769 THE EFFECT OF MDMA ADMINISTRATION IN HUMAN BRAIN MEASURED BY ³¹P MRS

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Introduction: It has been established that 3, 4-methylenedioxymethamphetamine (MDMA) can be toxic to the human body, with hyperthermia as the most significant adverse effect. The theory of MDMA mediated hyperthermia entails activation of the sympathetic nervous system and hypothalamic-pituitary-thyroid/adrenal (HPA) axis. Subsequent norepinephrine release activates uncoupling proteins (UCP) and α 1- and β 3-adrenoreceptors, leading to heat accumulation through vasoconstriction. The identification of mitochondrial uncoupling in human brain as a putative impetus to hyperthermic alterations following MDMA dosing would provide great insight into its neurotoxic effects. **Methods:** We will conduct a pilot MDMA loading study in healthy adult male recreational users to identify changes in β -adenosine triphosphate (ATP) levels. The proposed 100 mg oral dose safely approximates self-administration in uncontrolled settings. Two visits will be included: a screening protocol with a structural scan at 1.5T and clinical evaluation, and an MDMA dosing protocol with 31P chemical shift imaging (CSI) scans at 4T. 31P CSI will be performed using a dual-tuned, quadrature birdcage-design 1H/31P whole-head coil from XLR Resonance Inc. (London, Ontario) operating at 68.9 MHz. For spectral analysis, a fitting routine using an iterative, non-linear, Marquardt-Levenberg algorithm will be employed. We will combine the 31P CSI data with structural image data to obtain gray and white matter metabolite values via tissue regression analysis. **Objectives:** Metabolic uncoupling can result in energy requirements exceeding ATP production because uncoupled mitochondria divert energy produced by cellular respiration from ATP synthesis to heat production. We hypothesize that a decrease in β -ATP, consistent with mitochondrial uncoupling, will occur following MDMA administration due to altered oxidative phosphorylation and activation of the sympathetic nervous system and HPA axis. **Acknowledgement:** This study is supported by a grant from NIDA INVEST Fellowship (Y.H.S.).

770 MECHANISMS UNDERLYING TRAMADOL- AND ITS ACTIVE METABOLITE M1-INDUCED PHARMACOLOGICAL EFFECTS IN MICE

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Tramadol belongs to a group of the centrally acting and clinically approved drugs used to treat pain disorders. It has been considered that tramadol forms the antinociceptive active metabolite o-demethyltramadol (M1), which shows high affinity for opioid receptors. The present study was then undertaken to investigate the mechanisms underlying tramadol- and M1-induced several pharmacological effects in mice. Chronic treatment with both tramadol (70 mg/kg, s.c.) and M1 (30 mg/kg, s.c.) produced a significant place preference for the drug-associated place in the conditioned place preference paradigm. Both tramadol (70 mg/kg, s.c.) and M1 (30 mg/kg, s.c.) produced a significant antinociception in mice. These effects were significantly suppressed by pre-treatment with either a μ -opioid receptor antagonist β -funaltrexamine (β -FNA, 40 mg/kg, s.c.) or a δ -opioid receptor antagonist naltrindole (NTI, 3 mg/kg, s.c.). Using membranes from the paraventricular gray (PAG) and thalamus of mice, we also found that M1 (10⁻⁷-10⁻⁵ M), but not tramadol (10⁻⁷-10⁻⁴ M), produced a concentration-dependent increase in [³⁵S]GTP γ S binding. Furthermore, both intracerebroventricular (i.c.v.) and intrathecal (i.t.) administration of M1 (30 nmol/mouse) produced a significant antinociception ($p < 0.001$ vs. saline), whereas neither i.c.v. nor i.t. administration of tramadol (10-100 nmol/mouse) produced antinociception. It should be noted that 3 days treatment with mouse cortical neuron/glia co-cultures of tramadol (10 μ M) increased the level of extracellular concentration of serotonin. The present study provides direct evidence that tramadol could display its pharmacological actions through metabolism to its active metabolite M1, which activates μ - and/or δ -opioid receptors. Furthermore, tramadol itself is not metabolized into M1 in the CNS, whereas it could mainly increase the released serotonin in the CNS.

771 IMPACT OF BEHAVIORAL INCENTIVES ON RESIDENTIAL TREATMENT ATTENDANCE IN DRUG-DEPENDENT WOMEN

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The purpose of this randomized clinical trial was to: 1) examine whether behavioral incentives improve attendance and retention in residential drug treatment; and 2) examine whether behavioral incentives affect patient motivation and self-perceived ability to remain abstinent from alcohol/drugs. Participants were 94 drug dependent women. They had a mean age of 37.1 years (range 25-49) and approximately three-fourths (74.6%) were African American. All participants provided written informed consent to study participation. Women randomized to the incentive group received vouchers for attending a once weekly group according to an escalating voucher schedule. Control group participants received no incentives for group participation. Both groups, however, were compensated for completion of follow-up assessment measures. Incentive group participants attended significantly more groups (mean 5.6) than control group participants (mean 3.2) ($p < .001$). Incentive group women also gave higher ratings than control group women to the statements "I am confident about my ability to stay drug free" (9.06 versus 8.45 ($p < .05$); "I am working hard to stay alcohol/drug free" (9.67 versus 9.14; $p < .04$); and "I feel confident and hopeful" (9.52 versus 8.80; $p < .01$). Study findings suggest that modest incentives improve patient group attendance. They are also associated with more positive ratings of self-efficacy and motivation to stay drug free. This research was supported by NIDA DA 11476.

772 PRE-ADOLESCENT PHENYLPROPANOLAMINE PRODUCES PERSISTENT PERTURBATIONS IN ACCUMBENS MONOAMINERGIC AND AMINO ACID TRANSMISSION: IMPLICATIONS FOR COCAINE ADDICTION

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In C57BL/6J mice, the repeated treatment with the sympathomimetic phenylpropanolamine (PPA; d,l-norephedrine) during postnatal days (PND) 21-31 enhances the expression of cocaine-conditioned reward, while reducing the expression of cocaine-induced locomotor sensitization when assessed in adulthood (10 weeks of age). To determine the neurochemical correlates of the behavioral effects of pre-adolescent PPA treatment, mice were treated with 40 mg/kg PPA during PND 21-31 and alterations in the ability of repeated cocaine (4 X 15 mg/kg) to alter accumbens levels of monoamines and amino acids were assessed at 10 weeks of age. Although, PPA pretreatment did not influence cocaine-induced increases in serotonin, PPA pretreatment completely abolished the cocaine-induced rise in both dopamine and norepinephrine. The effects of PPA pretreatment upon the amino acid response to cocaine were more complex than those for catecholamines and depended upon the number of cocaine injections. An acute cocaine injection did not alter the levels of GABA or glycine in saline pretreated controls. In contrast, PPA pretreated mice exhibited a cocaine-induced reduction in the levels of both amino acids and this effect showed tolerance with repeated cocaine treatment. While both pretreatment groups exhibited glutamate sensitization following cocaine administration, the magnitude of the glutamate rise was greater in PPA pretreated mice. Collectively, these data demonstrate that pre-adolescent exposure to PPA produces alterations in the monoaminergic and amino acid responsiveness to cocaine that persist into adulthood. If relevant to humans, these data suggest that childhood/early adolescent exposure to PPA, and/or other ephedrine derivatives found in over-the-counter cold and allergy medicines, can produce persistent perturbations in neurotransmission within limbic brain regions implicated in drug-induced psychomotor activation and addiction.

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- 773 PHARMACOLOGICAL AND TOXICOLOGICAL SCREENING OF A CHIMERIC HUMAN ANTI-COCAINE MONOCLONAL ANTIBODY**
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An immunotherapy utilizing an anti-cocaine monoclonal antibody (mAb) capable of inhibiting cocaine from entering the brain may prove effective for preventing relapse in cocaine addiction. We have used a novel transgenic mouse to develop a mAb (designated 2E2) with a high affinity and specificity for cocaine over its inactive metabolites. While most mAbs obtained through standard hybridoma technology are murine, 2E2 has approximately 87 % identity/homology to a human IgG1 immunoglobulin. This predominantly human sequence should enhance 2E2's safety and efficacy, which are key to the success of a therapeutic agent. Testing was carried out to determine whether 2E2 had any cross-reactivity for a wide range of commonly used medications and drugs potentially sufficient to decrease its efficacy. The mAbs affinity for a range of drug classes including nicotine, caffeine, opiates, amphetamines, phencyclidine and dopamine receptor agonists was measured using an ELISA. 2E2 had no or low affinity for these various compounds. However, 2E2 had an affinity for several investigational cocaine analogs sufficient to compromise their potential use as a co-therapy. A major concern is the potential for any in vivo toxicity that might result from 2E2 reacting against human tissues. This was evaluated by screening biotinylated 2E2 (that had unaltered affinity and specificity for cocaine) for any cross-reactivity with an extensive panel of human tissues in vitro. This screening was performed under GLP protocols by Charles River Laboratories (Frederick, MD) and the final immunopathology report concluded that at 2E2 concentrations of 2 - 200 ug/ml "no test article-reactivity or cross-reactivity was observed in the human tissue panel examined." This testing predicts a low potential for adverse reactions in humans and confirms mAb 2E2 as a lead candidate for advancement towards clinical trials.
- 774 HYPERTHERMIA INDUCED BY (±)3,4-METHYLENEDIOXYMETHAMPHETAMINE IN MONKEYS: IMPACT OF AMBIENT TEMPERATURE**
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Ambient temperature (TA) has a significant effect on the direction and magnitude of the body temperature response to (±)3,4-methylenedioxymethamphetamine (MDMA) exposure in rodents. The degree of hypo/hyperthermia observed also modulates the severity of lasting brain changes in "neurotoxicity" models. The effect of TA following MDMA may differ between species thereby affecting translation of preclinical results to the human situation. For example, humans exhibit elevations of temperature after MDMA under (low) TA conditions which result in hypothermia in rats. The thermoregulatory effects of MDMA have not been well described in nonhuman primates and it is unknown if, or to what degree, TA has the potential to affect lasting brain damage. This study was conducted to determine the effect of TA on body temperature alterations produced by MDMA in nonhuman primates. Body temperature and spontaneous home cage activity were monitored continuously in six male rhesus monkeys via radiotelemetric devices. The subjects were challenged intramuscularly with 0.56-2.4 mg/kg (±)MDMA under each of three TA conditions (18°C, 24°C, 30°C) in a randomized order. Temperature was significantly elevated following injection with all doses of MDMA under each ambient temperature condition. The magnitude of mean temperature change was ~1°C in most conditions suggesting a narrowly controlled thermoregulatory range in monkeys across a range of doses and ambient temperatures. No elevations of locomotor activity were observed in any condition. The finding of MDMA-induced hyperthermia in rhesus monkeys under the low TA condition is consistent with human studies, but is inconsistent with rodent studies. Therefore thermoregulatory responses to MDMA in the nonhuman primate may reflect the human condition more accurately than rodent models.
- 775 PROTEOMICS-BASED ANALYSIS OF COCAINE ADDICTION**
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The microarrays-based genomic and neurotransmitter-centric hypotheses of cocaine addiction have advanced our knowledge of long-term alteration in neuronal function in brain regions involved in sensitization, craving, withdrawal and relapse. To comprehend the intricate neuroadaptive machinery implicated in cocaine addiction we undertook a proteomics approach to monitor coordinate changes in the expression of multiple proteins. This non-candidate approach was used to compare cytosol-enriched proteins from nucleus accumbens (NAc) of control and cocaine overdose victims by two dimensional-differential gel electrophoresis (2D-DIGE), quantitative DeCyder™ image analysis followed by identification of target proteins by matrix assisted laser desorption ionization-time of flight-time of flight (MALDI-TOF)- mass spectrometry (MS and MS/MS). Quantification of 1400 proteins revealed that the vast majority of proteins apparently did not undergo major regulation. We identified 15 differentially regulated proteins ($p < 0.05$), some shown to be associated with cocaine overdose for the first time. To complement the previous study, we examined the functional (phospho) proteome of rhesus monkeys with chronic cocaine self-administration histories. The comparison of 125 phospho-proteins from the NAc by staining 2D-gels with Pro-Q® Diamond phospho-protein gel stain detected 15 proteins with differential status of their phosphorylated form ($p < 0.05$). The proteins were identified by MALDI-TOF-MS/MS providing the first proteomic scale phospho-proteomic analysis of primate brain tissue to demonstrate novel functional protein alterations as a function of cocaine self-administration. The powerful technique of expression- and functional-proteomics show the involvement of proteins regulating cytoskeleton, membrane, protein folding/binding, transporter activity, metabolism, neuro-protection and anti-oxidant functions, after cocaine self-administration in rhesus monkey and cocaine overdose victims.
- 776 COCAINE AND MARIJUANA USE: HIV INFECTION AND AIDS PROGRESSION**
D. P. Tashkin(1), C. Chao(2), G. C. Baldwin(1), M. D. Roth(1), R. Detels(2) and Z. F. Zhang(2), (1) David Geffen School of Medicine at UCLA, and (2) UCLA School of Public Health, Los Angeles, CA
Both cocaine and THC have been shown to have potent immunosuppressive effects, as well as the ability to enhance HIV replication and the loss of CD4 cells in the huPBL-SCID mouse. We therefore analyzed data from the Multi-Center AIDS Cohort Study (MACS) to determine the association between marijuana (MJ) and cocaine use and HIV seroconversion, as well as time to AIDS, P. carinii pneumonia (PCP) and Kaposi's sarcoma (KS). The study population is based on the pre-2001 cohort of homosexual and bisexual men in the MACS enrolled between 1984 and 1991, monitored at 6-month intervals. Cox proportional hazard survival analysis was used to study the association between MJ and cocaine use and 1) risk of HIV seroconversion in initially seronegative men who had more than one visit ($n=3236$), 2) time to AIDS or PCP in men who seroconverted after enrollment ($n=522$) and 3) time to KS in men who were seropositive at baseline or seroconverted before 1996 ($n=2579$). We restricted the follow-up time to the pre-HAART period (before 1996). Multivariate analyses were adjusted for age, race, education, tobacco smoking, alcohol, use of poppers, high-risk sexual behavior and anti-viral treatment. Analyses were not controlled for CD4 count due to the potential effects of these drugs on CD4 cells. Hazards ratios (95% C.I.) indicated a significant correlation between intravenous cocaine use and seroconversion and onset of AIDS, while hazard ratios with respect to seroconversion, AIDS, PCP and KS were: 1.2 (0.6-2.5), 2.8 (1.01-8.0), 0.54 (0.2-1.3), and 1.5 (0.9-2.4) for non-intravenous cocaine use; and, 1.05 (0.8-1.4), 1.06 (0.7-1.7), 1.03 (0.6-1.7), and 1.4 (0.99-1.9) for MJ use. These preliminary findings suggest that 1) regular use of cocaine intravenously is a significant risk factor for HIV infection and progression to AIDS, 2) regular use of cocaine by other routes may be a risk factor for progression to AIDS and 3) regular marijuana use may increase the risk of KS. Supported by NIDA grants DA03018 and DA08254.

- 777** WHAT ARE THE 3-YEAR OUTCOMES OF TREATMENT FOR HEROIN DEPENDENCE IN SYDNEY, AUSTRALIA? FINDINGS FROM THE AUSTRALIAN TREATMENT OUTCOME STUDY
M. Teesson(1), J. Ross(1), S. Darke(1), K. Mills(1), A. Williamson(1), A. Havard(1) and M. Lynskey(2), (1) National Drug and Alcohol Research Centre, University of New South Wales, Sydney, New South Wales, Australia and (2) Washington University, St Louis, MO
Aims: To systematically compare 3 year outcomes for entrants to three treatment modalities for opiate dependence, and a group of heroin users not currently in treatment, in terms of their drug use, criminal activity, physical and psychiatric health. Subjects: 535 entrants to treatment for heroin dependence in Sydney, Australia: methadone/ buprenorphine maintenance (n=201), detoxification (n=201), residential rehabilitation (n=133), and a comparison group of 80 heroin users not currently in treatment. Procedures: 19 treatment agencies were randomly selected, stratified by modality. All entrants to treatment were approached to complete a structured interview. Participants gave their consent to be followed up at 3, 12, 24 & 36 months. Results: 70% of the sample were successfully interviewed at 36 months. There were substantial reductions in heroin and other drug use across all three treatment samples. The majority of those who had entered treatment were abstinent from heroin at 36 months. While there was also an increase in one month abstinence in the non-treatment sample, this was considerably less. While current heroin use remained low among the treatment groups, the majority in all groups had used heroin within the last 36 months. Injection frequency, needle sharing and crime were dramatically reduced amongst the treatment groups, and were below levels in the non-treatment group. Levels of comorbidity were high in the sample, particularly PTSD and Borderline Personality Disorder. There was only limited improvement in psychological health at 36 months. Conclusions: The first natural history study of heroin users in Australia has follow-up rates of an international standard. Substantial reductions in drug use, risk taking and crime among the treatment groups was observed at 36 months, as were improvements in physical health. The role of psychopathology requires greater attention.
- 778** CURRENT DRUG SCHEDULING REVIEWS REPORTED BY THE DRUG ENFORCEMENT ADMINISTRATION
S. R. Tella, J. M. Tolliver, G. K. Feussner, B. A. Hayes, S. M. Carr and C. A. Sannerud, Drug Enforcement Administration, Washington, DC
As mandated by the Controlled Substances Act (CSA), DEA collects and reviews scientific, medical and other data for substances with abuse potential to determine their federal control status for placement into one of five schedules under the CSA. In December 2004, the Food and Drug Administration (FDA) approved (S)-zopiclone (or eszopiclone), the active isomer of zopiclone, a nonbarbiturate and nonbenzodiazepine sedative/hypnotic, for the treatment of insomnia and pregabalin [(S)-3-(aminomethyl)-5-methylhexanoic acid], an analgesic drug with calcium channel blocker properties, for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia. Based on its review, and the evaluation and recommendation of the Department of Health and Human Services (DHHS), DEA recently controlled zopiclone including its salts, isomers and salts of isomers in Schedule IV and pregabalin including its salts and all products containing pregabalin in Schedule V of the CSA. In May 2005, FDA approved a new animal drug application for veterinary use of a euthanasia drug product containing embutramide in combination with chloroquine phosphate and lidocaine. Based on its review and the evaluation and recommendation of DHHS, DEA recently published a notice of proposed rulemaking to control embutramide in Schedule III of the CSA. A hearing has been requested and the matter is currently pending in DEA. Scheduling recommendations from DHHS are currently pending on carisoprodol, a skeletal muscle relaxant, and on a petition requesting a change in the control status of hydrocodone combination products from Schedule III to Schedule II of the CSA. DEA has received four petitions to place tramadol under CSA control, and DEA is currently reviewing the available data. DEA has also collected information on butorphanol, dronabinol, GHB, ketamine, khat, tramadol, zopiclone and buprenorphine for use in possible international scheduling by the World Health Organization.
- 779** EFFECTS OF ACUTE D-AMPHETAMINE ON MEASURES OF MOOD, ATTENTION, RISK-TAKING AND BEHAVIORAL INHIBITION IN HEALTHY HUMAN VOLUNTEERS
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Controlled studies indicate that the mood-altering effects of d-amphetamine vary across individuals, and studies with both humans and non-humans indicate that the effects of d-amphetamine on measures of impulsivity are also variable. To date, there has been virtually no research assessing the relationship between individual differences in the subjective effects of d-amphetamine and impulsive behavior. Thus, the purpose of this study was to examine this relationship. Based on previous data, we hypothesize that subjects who show an increase in ratings of arousal will show a decrease in impulsive behavior after administration of d-amphetamine. This study examined subjective responses to the acute effects of oral d-amphetamine in healthy adult men and women. The effects of d-amphetamine on impulsive behavior were also studied using tasks assessing attention, risk-taking and behavioral inhibition. Volunteers (N=26) participated in a four-session double-blind randomized design study in which they received 5, 10 or 20 mg d-amphetamine or placebo. Participants completed mood questionnaires every half hour after ingesting the capsule for four hours. One and a half hours after capsule administration, participants completed the impulsivity tasks. D-amphetamine increased ratings of arousal. Preliminary evidence with the 26 of the planned 100 subjects suggests that d-amphetamine has modest effects on attention in these healthy volunteers, but no effects on risk-taking or behavioral inhibition. We will examine individual differences in these cognitive effects, in relation to the drug's subjective effects. Supported by DA02812
- 780** SELECTIVE IMPAIRMENTS OF EXECUTIVE FUNCTION IN YOUNG, FEMALE MDMA ("ECSTASY") USERS: EFFECTS THAT ARE NOT ATTRIBUTABLE TO CONCOMITANT CANNABIS USE
P. Terry and C. O'Brien, School of Psychology, University of Birmingham, Birmingham, UK
Several studies have suggested that long-term users of methylenedioxyamphetamine (MDMA or "ecstasy") exhibit various kinds of neuropsychological impairment, particularly in relation to memory function and impulsivity. However, the extent to which concomitant cannabis use might contribute to such impairments remains contentious. The present study tested whether specific aspects of executive functioning are affected by chronic MDMA use in a sample of young women who were moderate users of MDMA (N=13; mean frequency of use = 2.1 occasions/month, SD = 1.4 occasions/month). Most studies to date have included males who are heavy users. To control for concomitant cannabis use, comparisons were made with a group of women matched for cannabis use but who had not used MDMA (N=14), and also with a matched group of women who had not used either drug (N=14). The average age of the sample was 19.5 yrs (SD = 1.6 yrs); participants were matched for premorbid IQ. In accordance with current cognitive theory, we used a series of neuropsychological tests to measure specific submodalities of executive function, namely "shifting", "updating", and "inhibition"; we also tested memory function. MDMA users performed significantly worse than either control group on the "inhibition" task (Stroop colour-word reaction time). Impaired performance by the MDMA users on tests of "shifting" (alternating response patterns) and "updating" (monitoring and revising working memory representations) were task-dependent. The MDMA users also scored significantly lower than the other two groups on a test of verbal recall. The cannabis-only group did not differ from the non-drug user controls on any measure. The results are consistent with other studies that have tested similar functions in samples with male, heavier MDMA users. The impairments detected here cannot be attributed to concomitant cannabis use, nor to the use of other recreational drugs; they imply that even moderate use of MDMA can cause selective impairments of executive function in young women.

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- 781 RISK FACTORS ASSOCIATED WITH ABUSE OF PRESCRIPTION OPIOIDS: RESULTS OF A NATIONAL SURVEY**
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Abuse (i.e., non-medical use) of prescription opioids is a growing problem in the U.S. Well-documented gender differences exist regarding illicit substance and alcohol use disorders, but little is known about gender differences associated with the non-medical use of prescription opioids (NMUPO). The purpose of this study is to investigate risk factors associated with NMUPO in women compared to men. We performed an analysis of the 2003 National Survey on Drug Use and Health, an annual survey of members of U.S. households aged 12 or older. Gender was our main independent variable of interest. We conducted a logistic regression model, stratified by gender, of past year NMUPO. We utilized study-calculated weights and SUDAAN software to adjust for the complex sampling design and non-response. Among 55,230 respondents, 52% were female, 70% were white, and 4.9% reported non-medical use of prescription opioids in the prior year. Women were less likely than men to have past year NMUPO (4.5% vs. 5.2%, $p=0.009$). Women were more likely to be on state-sponsored medical assistance programs (11.2% vs. 7.0%, $p<0.0001$), not in the labor force (34.5% vs. 20.4%, $p<0.0001$), and to have serious mental illness (11.2% vs. 6.6%). In addition, women were less likely to have used alcohol (60.0% vs. 69.2%), cocaine (1.6% vs. 3.2%), marijuana (8.0% vs. 13.2%), or heroin (0.07% vs. 0.2%) in the past year ($p<0.0001$ for all comparisons). Using multivariable logistic regression stratified among women (only), we found serious mental illness (OR 1.63, 95% CI 1.25-2.13); cigarette smoking (OR 1.26, 95% CI 1.01-1.60); and first use of illicit substances after age 24 (OR 1.80, 95% CI 1.01-3.23) were risk factors for NMUPO in the prior year, whereas no association was found among men for the same risk factors. Clinicians should recognize that women with serious mental illness, women tobacco smokers, and women who first use illicit substances as adults are at increased risk for NMUPO compared to men. These differences should enable clinicians to better identify, prevent, and treat NMUPO in women.
- 782 COMPARISON OF FR1 AND VR5 REINFORCEMENT SCHEDULES DURING SELF-ADMINISTRATION TRAINING AND SUBSEQUENT CUE REINSTATEMENT TESTING OF COCAINE-SEEKING BEHAVIOR**
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An animal model commonly used to assess incentive motivational effects of cocaine-associated cues is the extinction/reinstatement model in which extinguished cocaine-seeking behavior is reinstated by response-contingent presentations of cues that were paired previously with cocaine infusions. While the majority of laboratories employ a fixed ratio (FR) 1 schedule of reinforcement during training and testing, our laboratory employs a variable ratio (VR) 5 schedule of reinforcement during self-administration training based on the rationale that, relative to a FR1 schedule, partial reinforcement schedules increase coupling between the cues and cocaine reinforcement and also increase resistance to extinction, which would likely yield higher rates of responding during reinstatement tests. However, we employ a FR1 schedule of cue reinforcement during reinstatement tests based on the rationale that the cues are less reinforcing than cocaine, and consequently, less likely to maintain responding on a VR5 schedule. Results from the present series of experiments demonstrate that: 1) training/testing on VR5/FR1 schedules, respectively, results in greater responding during reinstatement testing relative to FR1/FR1 schedules, 2) increased reinstatement responding is not simply due to a switch from a low density VR5 training schedule of cocaine/cue reinforcement to a high density FR1 testing schedule of cue reinforcement since reinstatement in a group down-shifted to a FR1 schedule for the last 12 days of training did not differ from a control group maintained on a VR5 schedule throughout training, and 3) animals trained on a VR5 schedule exhibit enhanced reinstatement when tested on a FR1 schedule of cue reinforcement relative to animals tested on a VR5 schedule. The findings suggest that our procedure offers an advantage of higher response rates during reinstatement tests relative to the procedure of training and testing on an FR1 schedule of reinforcement. Supported by DA11064
- 783 EFFECTIVE BUPRENORPHINE TAPERING: RESEARCH FINDINGS TO GUIDE PRACTICE**
C. M. Thomas(1,2), J. Annon(1), J. Fradis(1,2), A. Saxon(3), W. Ling(1) and *CTN Buprenorphine Study Group(4), (1) UCLA Integrated Substance Abuse Programs, and, (2) Friends Research Institute, Los Angeles, CA; (3) VA Puget Sound Health Care System, Seattle, WA and (4) NIDA CTN, Bethesda, MD
The safety and efficacy of buprenorphine has been established in research addressing pharmacological detoxification and treatment of opiate-dependent individuals. Investigations have illuminated best practices regarding specifics such as effective dose amount and frequency in both the buprenorphine only (Subutex) and buprenorphine and naloxone formulations (Suboxone), and guidelines for administering buprenorphine specify the need to taper both onto maintenance dose, as well as tapering off the drug. Recent studies have addressed effective tapering-on doses, however, little empirical evidence is available to guide rational selection of a buprenorphine tapering-off schedule. In this 11-site study, 516 adults seeking treatment for opiate dependence were randomized into one of two strategies to discontinue buprenorphine treatment after a 4-week stabilization period. Brief versus relatively lengthy tapering schedules (7 vs. 28 days) were compared for three buprenorphine maintenance dosages (8, 16, 24mg), with the outcome of interest the proportion of participants providing opiate-free urines at the end of the taper regimen. Based on previous research, it was hypothesized that the longer tapering schedule would result in a higher proportion of participants providing opiate-free urines at the end of taper regardless of the stabilization dose. Preliminary analyses indicate that a higher proportion of participants assigned to the 7-day taper group were present and clean at the end of taper than those assigned to the more gradual taper schedule (49.4 vs. 34.0, respectively). This pattern is mirrored in all maintenance dose groups at the end of taper. Other findings, including results for follow-up periods, as well as sample demographic characteristics and drug use patterns are also presented for both the complete sample as well as for sub-group comparisons. The important implications of these findings for clinical practice are also discussed.
- 784 ADOLESCENT AND PARENT AGREEMENT OF WITHDRAWAL SYMPTOMS OF YOUTH ENROLLED IN A BALTIMORE TOBACCO CESSATION RESEARCH PROGRAM**
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Numerous environmental, psycho-social, genetic, metabolic, and biologic contributors have been shown to impact adolescent tobacco cessation efforts. Experiencing withdrawal from nicotine has been identified as a barrier to adolescent tobacco cessation. Because of the importance of social support and collateral inquiry, we explored the agreement between self-report and parental report of withdrawal symptoms using Minnesota Withdrawal Scale. This analysis included 68 tobacco-dependent adolescent smokers enrolled in a randomized, double-blind, controlled clinical trial of nicotine replacement therapy ($n=68$) were 64.7% Caucasian, 63.2% female, age 15.3 ± 1.3 years. Withdrawal was assessed by rating the following eight symptoms on a scale of 0 to 3: craving for nicotine, irritable, anxious, difficulty concentrating, restless, impatient, increased appetite, and insomnia. Concordance was assessed using difference scores (adolescent score minus parent score for each symptom and for the total score), plus calculating the Kappa statistic (agreement beyond chance) for each symptom score. Parents tended to endorse greater withdrawal severity than their adolescents. The mean difference score (-2.07 ± 0.5) was significantly different from zero ($t=-4.03$, $p=0.0001$) suggesting little over-reporting by parents or under-reporting by teens. The mean difference score was negative for all individual symptoms except insomnia (for which it was zero), and statistically significant for five symptoms out of eight. Kappa statistics for each of the symptoms were in the marginal range (<0.40), and in the acceptable range only for increased appetite (0.43). Further examination of the lack of agreement between adolescents and parents in reporting adolescent tobacco withdrawal symptoms will elucidate its relevance to successful cessation. Supported by NIDA Intramural Funds

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- 785** FEASIBILITY OF IBUPROFEN FOR CANNABIS DEPENDENCE IN ADOLESCENTS
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Background – Few data exist to inform the pharmacotherapy of cannabis dependence (CD). Recently, ibuprofen has been shown to inhibit fatty acid amide hydrolase (FAAH), which metabolizes anandamide, an endogenous cannabinoid receptor agonist. This action occurs at physiologic doses and is crucial to ibuprofen's analgesic effect. For this reason, ibuprofen may be an indirect substitution therapy for CD. The current investigation studied the feasibility of conducting a clinical trial of ibuprofen for adolescent CD. Methods – 12 teens (12-19) with DSM-IV CD were enrolled in a 6-week open label trial of ibuprofen 200 mg twice daily. All received concurrent outpatient psychosocial drug and alcohol treatment. Measures included baseline and end-of-study past 30-day cannabis use as well as the Marijuana Craving Questionnaire (MCQ) and Side Effect Scale for Children and Adolescents (SEFCA) weekly. The MCQ is a 12-item questionnaire with 4 subscales. An intent-to-treat statistical analysis included calculating pre/post change in cannabis craving and past 30-day use. The frequency of side effects was also calculated. Results – 12 teens enrolled in and completed the study. The mean age was 15.3 years (SD=1.4). The mean percentage of ibuprofen doses taken was 82% (SD=16%). Mean past 30-day cannabis use decreased from 18.1 days to 6.2 days ($p<.005$). Mean MCQ scores decreased significantly from baseline for the emotionality (8.8 to 6.0; $p<.05$) and expectancy (10.4 to 7.8; $p<.05$), but not for the compulsivity and purposefulness subscales. All adverse events (AE's) were mild and transient. There were no serious adverse events (SAE's). Conclusions – These data support the feasibility and safety of conducting a controlled study of ibuprofen for teen cannabis dependence. Data from a historical control group are currently being collected. Funded by the Center for the Genetics of Antisocial Drug Dependence (DA 11015) and The NIDA K12 Physician Scientist Training Program in Substance Abuse (DA 5K12DA000357).
- 786** FIVE YEARS AFTER: LONG-TERM RECOVERY FROM HEROIN USE AMONG EX-OFFENDERS
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The DSM-IV-TR reports that only 20-30% of individuals meeting criteria for heroin dependence are able to successfully maintain long-term abstinence. These high relapse rates are particularly problematic because heroin use is inexorably linked to crime, and its intravenous use is associated with high rates of hepatitis, HIV and other infectious diseases. The process of sustained abstinence however, has not been sufficiently examined, particularly from a qualitative perspective. This presentation reports findings from a qualitative dissertation examining the process of sustaining long-term abstinence among former heroin-using ex-offenders by identifying impediments to, as well as effective coping strategies for, maintaining such recovery. The study population consisted of former heroin users who previously used the drug on an almost daily basis for at least a year, encountered some type of involvement with the criminal justice system (arrest or conviction) directly or indirectly related to their heroin use, and have remained abstinent from heroin use for a period of five years or longer. Face-to face semi-structured interviews were completed with 10 women and 15 men from the New York metropolitan area. The sample breakdown is comprised of approximately two-fifth Latino, one quarter White and two-fifth African-American respondents. Data analyses suggest that prior treatment experiences while helpful, may not be sufficient in addressing previous relapse triggers and maintaining prolonged abstinence. Key motivating factors in facilitating respondents' sustained long-term recovery efforts include a redefinition of self-identity and respect, religion/spirituality, familial interaction, a strong peer support network and their job/career. In addition, the study reveals the process of agency and ownership the participants demonstrate to facilitate their successes. The policy implications and future directions of the research are discussed.
- 787** EFFECTS OF CONTINGENT INCENTIVES AND BUPROPION ON SMOKING IN OUTPATIENTS WITH SCHIZOPHRENIA
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People with schizophrenia are three times as likely to initiate smoking and five times less likely to quit than smokers without mental illness (de Leon and Diaz, 2005). Bupropion reduces smoking in people with schizophrenia (Evins et al., 2001; George et al. 2002), and short, laboratory-based contingency management interventions reduce smoking in these patients (Tidey et al., 2002). We are conducting a 3-week RCT to test the separate and combined effects of these treatments. In week 1, participants are randomized to bupropion, 300 mg/day (BUP) or placebo (PLA). In week 2, participants are randomized to contingent (CM) or non-contingent reinforcement (NR). Participants then provide urine samples 3 times per week for 2 weeks, and samples are tested for cotinine levels using EMIT. In the CM condition, participants are reduced with gift cards for reducing their cotinine levels by at least 25% from the previous sample. In the NR condition, participants receive gift cards regardless of cotinine level. Eighteen patients have enrolled and 13 (70% male) have completed the study to date. At enrollment, these patients smoked on average 30.4 cigarettes per day and had been smoking daily for 28.9 years. Baseline urinary cotinine and breath CO levels were 1509 ± 161 ng/ml and 26.8 ± 2.7 ppm respectively, indicating high nicotine intakes. Fagerstrom nicotine dependence scores were 7.3, indicating high dependence. Results to date indicate that both BUP and CM reduce end-of-trial urinary cotinine levels by about 40% ($p's < .05$). Currently, the combination of these treatments does not reduce smoking more than each treatment alone; however, this may be due to the small sample size. Results to date thus support the feasibility and initial efficacy of bupropion and contingency management interventions for reducing smoking among people with schizophrenia. Supported by DA017566.
- 788** FROM CONDUCT DISORDER TO ANTISOCIAL PERSONALITY DISORDER: A 30-MONTH FOLLOW-UP
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Conduct Disorder (CD) has been a diagnosis well associated with adolescent drug abuse. Recent studies have noted a high prevalence of CD diagnoses in research utilizing young drug abusers. There is concern, however, regarding the the progression of antisocial personality aspects in samples of young drug abusers who mature. The purpose of this abstract is to examine the prevalence of the Antisocial Personality Disorder (ASPD). In a nutshell, do adolescent samples with large numbers of subjects who were diagnosed with CD have similar large numbers of persons who have the adult version of CD; that is, Antisocial Personality Disorder (ASPD). The study subjects were 390 drug abusers who had previously been enrolled in treatment some 30 months previously. The subjects' data collection was part of the "Persistent Effects of Treatment Study-Adolescent" (PETS-A) that was funded by the Center for Substance Abuse Treatment (CSAT). At the time of enrollment all subjects were under age 18 and at the time of the 30 month follow-up all were over age 18. Subjects were assessed with the Global Assessment of Individual Needs (GAIN) and the Personality Disorder Questionnaire-Revised (PDQ-R) and diagnoses made. Statistical analyses included descriptive statistics and Chi-square comparisons. Results were that the prevalence of ASPD at the 30 month follow-up was exactly the same (53%) as that of CD when the subjects were first enrolled. In addition, ASPD was strongly associated with legal problems, physical violence, poor decision making and acts of immorality. Antisocial aspects appear to be persistent characteristics of drug abusing populations and future treatment interventions will need to address antisocial behavior.

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789 SPIRITUALITY AND ITS RELATIONSHIP TO SUBSTANCE USE AND COMORBID CONDITIONS IN AN ETHNICALLY DIVERSE ADOLESCENT TREATMENT POPULATION

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Studies of spirituality/religion and substance use consistently show that adults and adolescents for whom spirituality is important are less likely to use alcohol and drugs. Differences by racial groups are also robust, with African Americans reporting higher levels of spirituality and lower rates of use. Similar results have been found in recovery samples of adolescents and adults. This study uses data from 3000 racially/ethnically diverse adolescents (46% White, 19% African-American, 12% Hispanic, 5% Native American, 1% Asian, 18% Multi-racial) entering substance abuse treatment in a variety of programs, including outpatient, residential, school-based, and in juvenile justice settings. The goal of the study was to examine spiritual orientation by ethnicity and gender and its relationship to a wide range of substance abuse and psychological domains. Data from the Global Appraisal of Individual Needs' (GAIN) 7-item Spiritual Social Support Index (SSSI, $\alpha = .84$ for this sample) and a variety of GAIN substance use and psychological scales were used for the analyses. Correlations between spiritual orientation, substance use severity, and comorbid conditions varied by race/ethnicity, sometimes dramatically. SSSI scores by racial/ethnic groups were significantly different ($F=15.27, p<.000$), with post hoc analyses showing Native American, Hispanic, African American, Asian, and Multi-racial adolescents significantly higher in their spiritual orientation than Whites. In addition, African American and Asian girls were significantly higher in spiritual orientation than boys of their race/ethnicity. Results lend support to incorporating spirituality/religion into adolescent treatment programming, especially for programs targeting racial/ethnic minorities. Future analyses will focus on the relationship between spirituality, post-treatment outcomes, and long term recovery by race/ethnicity and gender. (Supported by CSAT contract 270-2003-00006)

790 A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF NALTREXONE IN THE TREATMENT OF CONCURRENT ALCOHOL DEPENDENCE AND PATHOLOGICAL GAMBLING

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There is growing interest in developing pharmacotherapies for pathological gambling to complement the emergence of specific psychological interventions for gambling. Evidence from psychobiological studies and case reports has suggested that medications that target the opioidergic neurotransmitter system may be beneficial in reducing pathological gambling insofar as the reinforcement for such behavior may be partially mediated by release of endogenous opioids. Naltrexone, an opioid antagonist, has been shown to be efficacious in reducing alcohol consumption, another behavior thought to be partially reinforced by release of endogenous opioids. It is hypothesized that Naltrexone may be similarly efficacious in reducing excessive gambling behavior. A randomized, double-blind, Placebo-controlled trial was conducted to evaluate the effectiveness of Naltrexone as a treatment for concurrent alcohol abuse/dependence and pathological gambling. The sample consisted of 52 alcohol abusing/dependent pathological gamblers (screened according to DSM-IV diagnostic criteria) recruited from the community through newspaper advertisements. Participants were randomized at baseline to Placebo (25) and Naltrexone (27) conditions. Assessment and outcome measures included: Brief Symptom Inventory, Alcohol Dependence Scale, Time-line Follow Back measure of alcohol use and problem gambling, Gambling Urge Questionnaire, and Situational Confidence Questionnaire. Group outcome differences were evaluated in 2 (Group: Placebo, Naltrexone) X 5 (Time: Baseline, Post-treatment, 3-month, 6-month, and 12-month follow-up) repeated measures analysis of variance. Following a one-week Placebo run-in and 11 weeks of medication, during which participants also received 7 weeks of cognitive-behavioral counselling, and one year of follow-up, no significant group differences were found on any alcohol or gambling variable (i.e., frequency, quantity, expenditures). However, a strong time effect was found suggesting that treatment, in general, was effective.

791 GENETIC VARIABILITY AT BRAIN-DERIVED NEUROTROPHIC FACTOR IN OPIOID DEPENDENCE

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INTRODUCTION Brain derived neurotrophic factor (BDNF)-signaling pathway are relevant for opioid-induced plasticity. We conducted a case-control study with opioid-dependent patients and healthy controls to evaluate BDNF variability in opioid dependence and in relation to Methadone Maintenance Treatment (MMT) response. **METHODS** A total of 109 opioid-dependent patients on MMT and 46 healthy controls were included. Assessment included: socio-demographical data, MMT characteristics, personality traits (Cloninger's Temperament & Character Inventory, TCI) and psychiatric comorbidity (DSM-IV) by the Psychiatric Research Interview for Substance and Mental Disorders (PRISM). At least 6 months later to start in the MMT, patients were divided into responders and non-responders, based on illicit opiate use detected in urine controls or treatment drop-out. Genetic variability in BDNF was addressed by SNPlex with 44 SNPs along BDNF gene. **RESULTS** Most patients were male (75%) and responders to MMT (72%). Differences in most of scales of TCI were found between patients and controls. After adjusting for the observed differences in TCI scales and sex, five alleles showed significance ($p<0.05$): rs10767665, hcv1751795 rs2030324, rs7103873 and rs7934165. The best model for all five SNPs corresponded to a recessive model, being homozygotes for the rare allele more frequent in controls. When we analyzed MMT response, also differences were observed for four SNPs when recessive model of action was considered ($p<0.01$) being homozygotes for the rare allele more frequent in MMT responders than in non responders **CONCLUSION** Genetic variability at BDNF seems being associate with opioid dependence and response to MMT. **Acknowledgments** Marato TV3, FIS G03/005, G03/184

792 YOUTH LATINO IMMIGRANT POPULATION AND DRUG USE IN LEISURE AREAS

S. Tortajada(1), V. Agullo(1), M. Castellano(2), J. Valderrama(1), R. Aleixandre(1), J. Perez(3) and P. Needle(4), (1) Instituto de Historia de la Ciencia y Documentacion, (2) Generalitat Valenciana, Valencia, Spain, (3) Hospital Sant Pau, Barcelona, Spain and (4) Consultant to NIDA, Atlanta, GA

The purpose of this study is to describe drug consumption patterns among the Latin American immigrant population in the Autonomous Region of Valencia, Spain, and to establish a practical and theoretical basis for prevention of drug abuse in this population. Quantitative methodology was used to obtain sociodemographic data, drug consumption patterns, attitudes, and knowledge of preventive measures by means of a questionnaire. The sample included 15 year-old and older Latin American immigrants, from the Autonomous Region of Valencia. The most representative nationalities in Valencia are immigrants from Ecuador, Colombia, Argentina, Bolivia, Uruguay and Cuba. Six hundred questionnaires were administered to a representative sample of all the nationalities (310 women and 290 men), for a sampling error of $\pm 4\%$, and a confidence level of a 95,5%(1,96 σ). The questionnaire was administered in leisure areas. Data were analysed using SPSS 12.0 program. Latin American immigrants consider that the consumption of drugs in Spain is higher than in their countries of origin, although 63% of the sample considers that inhalants are more consumed in their countries. Two substances are considered to be very dangerous, heroin (83,7%), and cocaine (80,5%). There are significant differences ($\chi^2= 9,889, P\leq 0,042$) in the perception of danger of cocaine between male and female participants. Fifty-three percent think that it is easier to obtain drugs in Spain, and 48,5% do not know about any prevention programs. Immigrants from Argentina, Cuba and Uruguay have similar patterns of consumption and perceptions. Habits are associated with consumption and leisure areas frequented by immigrants depending on their country of origin. Research projects should take into account the differences between nationalities before proposing any preventive measures. Supported by Conselleria de Cultura, Educació i Sport, G.V.04B-093.CSISP.Direcció General de Salut Pública.Conselleria de Sanitat, G.V.

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793 COMPARISON OF DIFFERING COMPONENTS OF OPERATIONAL DEFINITIONS OF RELAPSE FOR SMOKING

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Relapse is a word frequently used by clinicians, researchers, program administrators, patients and people in the community to delineate the status of a return to substance use disorder behaviors following a period of abstinence. Communications regarding whether a patient has relapsed has tremendous implications within various systems. The success or failure of substance abuse treatments is often based on the prevalence of relapse of patients. In multi-site trial NIDA CTN-009, a study evaluating the efficacy of smoking cessation treatment that had participants with a broad range of other substance use disorders, we applied different operational definitions to relapse to investigate the difference in prevalence rates for nicotine use. Across 7 sites, 223 individuals participated in the trial with 153 assigned to the smoking cessation treatment (TX) and 72 assigned to treatment as usual (TAU). When considering a return to use after achieving abstinence, in week 1, 93% relapsed by self report of use in TX. At week 8 (end of treatment), 90% relapsed by self report of use after a period of abstinence. Additional analyses and results will be presented at poster presentation. Urine cotinine levels, co levels, and self-reported measures of use will be compared and presented. Issues related to operational relapse definitions for substance use disorders in clinical trials will be discussed.

794 BEHAVIORAL EFFECTS OF COCAINE IN RATS ARE ENHANCED BY STROMAL CELL DERIVED FACTOR 1 (SDF-1)

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Stromal-cell derived factor 1 (SDF-1) is a chemokine that has been shown to play an important role in various biological processes including neuronal development, inflammation, and tumor pathogenesis. SDF-1 functions through a single receptor, CXCR4, which belongs to the family of seven transmembrane G-protein coupled receptors. SDF-1 is detectable in both endothelial cells and neurons. Cocaine, a widely abused psychomotorstimulant, binds to transport proteins and prevents the reuptake of dopamine, serotonin, and norepinephrine into presynaptic neurons. The present study determined the effect of SDF-1 on cocaine-induced locomotor and stereotypic activity. Twenty-nine male Sprague-Dawley rats underwent surgery to implant a cannula within the right cerebral ventricle and were allowed to recuperate for 4 days. After habituating in the activity monitors for 30 minutes, each group was given an injection of SDF-1 (50 ng/dose) or saline ICV, followed 15 minutes later by an IP injection of cocaine (20 mg/kg) or saline. The animals were monitored electronically for 120 minutes to evaluate ambulatory and stereotypic activity. As expected, cocaine alone produced an increase in ambulatory and stereotypic activity. Locomotion and stereotypy following central administration of SDF-1 alone was not significantly different from that in saline-injected controls. Animals treated concomitantly with SDF-1 and cocaine showed a significant potentiation in both ambulatory and stereotypic activity as compared to those treated with cocaine or SDF-1 alone. This study demonstrates a functional interaction between SDF-1 and cocaine. [This work was supported by T2: DA07237 (EMU, JT), P30 DA13429 (MW Adler, EMU) and DA09580 (EMU).]

795 SLEEP HOMEOSTASIS IN METHADONE-MAINTAINED VERSUS CONTROL SUBJECTS

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Insomnia afflicts many individuals, but particularly affects those who are on chronic methadone treatment. A better understanding of slow-wave sleep (SWS) and its role in recovery from sleep loss could be invaluable in elucidating the homeostatic sleep mechanism and shedding light on how to treat disturbed sleep. Phosphorous magnetic resonance spectroscopy (MRS) is a technique that can be used to measure global and region-specific changes in the high energy phosphates: alpha-, beta-, and gamma-NTP (nucleoside triphosphate). In the present study, 6 short-term (1 year) methadone-maintained and 11 healthy control subjects underwent baseline (BL), supervised sleep deprivation (SD) and two nights of recovery sleep (RE). Sleep was recorded polysomnographically on BL and RE nights. MRI and MRS were performed on each following morning using a Varian/Unity INOVA 4 Tesla whole-body MR imaging system equipped with a dual-tuned proton/phosphorus, volumetric RF head-coil. All subjects experienced significant ($p < .05$) increase in SWS during RE night, but only control subjects experienced an increased sleep efficiency index (SEI) and total sleep time during recovery. Compared to short-term methadone subjects, long-term methadone subjects experienced significantly more ($p < .05$) disruptions in wake after sleep onset and a significant reduction in SEI during recovery. Control subjects experienced significant ($p < .05$) increases in beta NTP and PCr during recovery sleep, but there were no significant differences in any brain chemistry measures across treatment days in the methadone-treated subjects. These results suggest that changes in brain chemistry during recovery sleep in controls may reflect an intact homeostatic process while those of methadone-treated subjects may not be able to respond to insult or stress. Supported by NIDA grants DA016542, T32DA15036, KO2DA017324, K24DA15116, and KO5DA00343.

796 THE COMPULSION ZONE MODEL EXPLAINS THE DOSE-RESPONSE CURVE AND EFFECT OF SCHEDULES ON COCAINE SELF-ADMINISTRATION

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The Compulsion zone model of cocaine self-administration states that in trained animals cocaine induces responses (e.g., lever-pressing activity) when the cocaine level is in the range of the compulsion zone, i.e., above the priming threshold and below the satiety threshold. At concentrations above the satiety threshold, i.e., in the satiety zone, cocaine selectively inhibits the same responses. Therefore, the highest rate of cocaine self-administration is observed during the loading phase and in the beginning of the extinction phase of drug self-administration, when cocaine levels remain within the compulsion zone all the time. The rate of self-administration during the loading phase does not depend on the cocaine unit dose, but the number of injections does. During the maintenance phase of cocaine self-administration, cocaine levels remain in the satiety zone almost all the time. Intervals between injections represent the time required to eliminate the injected dose, and are proportional to the elimination half-life and to the logarithm of the unit dose. This explains the decrease in cocaine self-administration rate with an increase of the unit dose (the descending limb of the dose-response curve). The ascending limb is an artifact of an inappropriate statistical analysis. Any schedules, other than FR=1 with TO=0, simply limit the access to cocaine and therefore increase the time between injections, which constitutes periods of extinction. The higher the values for ratio or interval the lower cocaine levels are at the time when the requirements are met. The progressive ratio schedule measures how many times the animal can respond between injections while the cocaine levels remain within the compulsion zone. Therefore, the break-point depends on the dose, levels of both thresholds and the cocaine elimination half-life. The compulsion zone theory provides an explanation of the self-administration paradigm without producing the paradoxes inherent in the operant theory of acquired self-administration.

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797 REINFORCEMENT-BASED TREATMENT IS AN EFFECTIVE TREATMENT FOR DRUG DEPENDENCE DURING PREGNANCY

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Introduction: Methadone stabilization is recommended for many opiate dependent pregnant women. However, a large number of pregnant women either do not qualify for or do not want pharmacological therapy. Interventions are needed to improve abstinence rates and retention in treatment for non-methadone stabilized women. A clinical trial is being conducted at the Center for Addiction and Pregnancy (CAP) in Baltimore, MD, comparing a novel intervention, Reinforcement-based Treatment (RBT), to standard care practice in this population of women. Methods: Patients admitted to the program who did not want or did not qualify for methadone treatment were grouped as: 1) Standard Care (SC, n=24), those receiving standard drug abuse treatment at the program or 2) Enhanced Care (EC, n=31), those receiving RBT along with abstinent contingent housing for six months. The two groups were compared on demographic variables, days spent in treatment, and abstinence rates. The following results are based upon the data available to date. Results: The groups were similar on age, race, marital status, education and drug use history a treatment enrollment. Following consent to the study, approximately 50% of the SC group switched to methadone treatment (and therefore were disqualified from further study participation), versus only 16% of the EC group. The remaining participants (SC, n=12; EC, n=26) were compared on treatment outcome measures. Results indicate that the SC group spent significantly less time in treatment and had poorer abstinence rates compared to the EC group. The SC group was also significantly less likely to gain employment during treatment compared to the EC group. Conclusion: Preliminary results show that intensive treatment, along with contingent housing, contributes to improved outcomes for drug dependent women not receiving methadone treatment. Additional data comparisons will be presented at the 2006 CPDD annual conference, including abstinence rates of at 1 and 3 month follow-up. Funded by RO1 DA 14979

798 WEIGHT AND OTHER CARDIOVASCULAR RISK FACTORS INCREASE DURING METHADONE TREATMENT

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Opiate and cocaine users have increased risks for cardiovascular disease. We evaluated the weight at entry into methadone treatment and annually for three years. This was a retrospective chart review of 105 subjects who entered treatment in 2000-03 (mean age±SE: 41±0.7, AA 71%, M 57%) and who remained in treatment for 2 or more years. Weight, height, blood pressure, medical information and laboratory data were collected annually. Mean Body Mass Index [BMI] was calculated, and subjects were classified as underweight (BMI≤18.9), normal weight (19≤BMI≤24.9), overweight (25≤BMI≤29.9) or obese (BMI≥30). Mean methadone dose was 98±1.5 mg and was stable over time. Mean BMI was initially 25.6±0.6 and increased steadily to 31±0.7 after 3 years (p140/90) was diagnosed among 26% of subjects on admission, 40% at 1 yr, 39% at 2 ys, and 42% at 3 ys. Diabetes [DM] was present on admission in 2 subjects, 3 at 1 yr, 14 at 2 ys and 9 at 3 ys. BMI did not predict HTN on admission but did so subsequently (p<.001). BMI was not associated with DM. Sex, race, methadone dose, heroin or cocaine use did not affect the results. Medical staff provided dietary counseling to 14% of subjects on admission, 48% at 1yr, 63% at 2yr, 45% at 3yr. These data show increasing rates of cardiovascular risk factors during methadone treatment and suggest the value of incorporating broader medical and behavioral health care in substance abuse treatment.

799 ADHD SYMPTOM COUNT AND TOBACCO/OTHER SUBSTANCE USE AMONG COLLEGE STUDENTS

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Aim: There is emerging evidence that attention deficit disorder is a risk factor for tobacco and other substance use. This study aimed to examine substance use behaviors and their relationship to ADHD symptom count among a sample of college students. Methods: A convenience sample of 334 students from a state funded southeastern university was surveyed via the annual Core Alcohol and Drug Survey that surveys students' substance use patterns and attitudes. Current ADHD symptoms were assessed by the Current Symptom Scale (CSS). We also included items to assess conduct disorder and antisocial personality disorder. Results: All of the results below are statistically significant at p<.05. Among ever tobacco smokers, those respondents who smoked cigarettes twice a month or more reported more total ADHD symptoms, more inattentive symptoms, and more hyperactive symptoms than did occasional cigarette smokers (once a month or less). Recent (past 30 day) alcohol use was significantly related to total ADHD symptoms and hyperactive symptoms. Recent cigarette smoking was significantly related to the number of current hyperactive symptoms. Substance use was also related to the severity of ADHD symptoms. Age of first alcohol and marijuana use was significantly related to severity of both ADHD and hyperactive symptoms. In addition, age of first alcohol use was significantly related to severity of inattentive symptoms. Frequency of use in the past year was only significant between cigarette smoking and severity of hyperactive symptoms. Recent (past 30 day) alcohol use was significantly related to severity of total ADHD and hyperactive symptoms. Conclusion: ADHD was related to tobacco and substance use in almost a dose dependent manner. Implications for further epidemiological and treatment research is discussed. Corresponding author address: Himanshu P. Upadhyaya, 67 President Street, PO Box 250861, Charleston, SC 29425 Supported in part by NIDA grant R01 DA17460-01 awarded to Dr. Upadhyaya.

800 AN OPEN-LABEL STUDY OF THE SAFETY AND CLINICAL EFFECTIVENESS OF THE PROMETA™ TREATMENT PROTOCOL FOR METHAMPHETAMINE DEPENDENCE

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This study explored the safety and clinical effectiveness of the PROMETA™ protocol in the outpatient treatment of methamphetamine dependence. PROMETA™ was designed to address the underlying neuropathophysiology while also addressing the psychosocial and nutritional needs of stimulant dependent patients. Fifty adults diagnosed with DSM-IV TR methamphetamine dependence who expressed a desire to stop using were enrolled in the 13 week open-label study. Subjects received a regimen of oral hydroxyzine, gabapentin and multivitamins, and intravenous flumazenil in a 3-day initial treatment cycle, followed by booster treatments in a 2-day treatment cycle at day 21 of the study. Following cycle 1, subjects returned to the clinic for 12 weekly follow-up visits for data collection and psychosocial support using the BRENDA method, a standardized, brief psychosocial approach. Data were gathered on the frequency of methamphetamine use utilizing the Timeline Followback (TLFB). Urinalyses were employed to enhance the validity of self-reports. The 10-item Stimulant Craving Scale and the 4-item Methamphetamine Craving Scale were utilized to measure subjective perception of severity and intensity of cravings and likelihood of use when in the presence of certain environmental stimuli. The TLFB and questionnaires were administered anc urinalyses performed at baseline (pre-treatment) and at weekly clinic visits throughout the 13 week . Data will be presented on the number of days abstinent from methamphetamine use, change in self-reported cravings and urges to use methamphetamine, and change in percentage of subjects abstinent post-treatment. While data analysis is still continuing at present, anecdotal evidence from subject reports suggests PROMETA™ is effective in restoring normal sleep and functioning, reducing cravings and withdrawal symptoms, and initiating and maintaining abstinence from methamphetamine.

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801 THE MELATONIN / MELATONIN RECEPTOR SYSTEM IN REGULATING BOTH STRIATAL "CLOCK" GENE EXPRESSION AND THE DEVELOPMENT OF COCAINE-INDUCED BEHAVIORS

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Using mice mutant for various "clock" genes, the regulatory role of these transcription factors has been shown in the development of psychostimulant-induced behaviors. Moreover, elevated tyrosine hydroxylase levels observed in clock mutant mice have been correlated with their phenotype (i.e., increased reward to cocaine). However, there are few known regulators of clock genes in the dopaminergic system. The role of the neurohormone melatonin in regulating clock gene expression has been reported in hypothalamus. It has also been demonstrated that melatonin regulates the development of dopaminergic system-mediated addictive behaviors, such as cocaine-induced locomotor sensitization and reward. Since the major sites of action for melatonin (i.e., melatonin receptors) are present in the central dopaminergic system, we tested whether melatonin receptors mediate this regulatory effect of melatonin on both the development of cocaine-induced diurnal locomotor sensitization and clock gene expression. We used mice mutant for either MT1 or MT2 receptors and their matching wild type controls. To detect the development of locomotor sensitization, all groups received repeated injections of cocaine (20mg/kg) either during the day or at night for five consecutive days. We found that MT1 knockout mice developed sensitization to cocaine both during the day and at night whereas wild type mice and MT2 knockouts developed only daytime sensitization to cocaine. On the other hand, in the striatum at night, decrease PER1 and increased CLOCK protein levels that are crucial for the development of diurnal locomotor sensitization to cocaine are reversed in MT1 knockouts while these levels remained the same in MT2 knockouts. Our results strongly suggest that melatonin receptors and clock genes are novel targets for addiction treatment. Further research is needed to elucidate the functioning of clock proteins as transcription factors in the dopaminergic system and to study the regulatory role of melatonin receptor-mediated signaling pathways in this interaction.

803 ATTENTIONAL BIAS TOWARDS COCAINE-RELATED STIMULI: A COMPARISON OF COCAINE-DEPENDENT TREATMENT SEEKERS AND NON-TREATMENT SEEKERS

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Objective: The purpose of this study was to examine if an attentional bias towards cocaine-related verbal cues differed between cocaine-dependent individuals seeking treatment and those not seeking treatment. **Participants and Methods:** Eighteen male participants who were seeking treatment for cocaine dependence (9 Black and 11 Hispanic) and 20 male participants who were not seeking treatment for their cocaine dependence (19 Black and 1 Hispanic) completed a Stroop task modified to include drug-related words. Differences in reaction times between drug words and neutral words were the primary outcomes. **Results:** Treatment seekers exhibited slower reaction times in the presence of drug-related words, relative to neutral words (interference), whereas non-treatment seekers did not. Group differences were demonstrated only for cocaine-related words ($T(1, 36) = 2.37$, $p < .05$). **Conclusions:** The presence of verbal descriptors of cocaine-related stimuli and experiences altered performance on an automatic attentional task only in cocaine-dependent individuals who were seeking treatment. This suggests that verbal cocaine cues may have more salience to those who are seeking professional assistance to change their cocaine use than those who are not.

802 SEXUAL AND PHYSICAL ABUSE IN CHILDHOOD AND VICTIMIZATION IN ADULTHOOD AMONG SUBSTANCE-USING WOMEN

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We examined the association between childhood physical and sexual abuse, family dysfunction in childhood, early cocaine use and pathways to victimization in adulthood among (N=550) substance abusing women recruited for two community based HIV prevention studies. The women were predominantly African American (84%), with a mean age of 38 years (SD=7.2). The women were stratified into two groups, victimized in adulthood (VA) and non-victimized in adulthood (NVA). As children, VA's were more likely than NVA's to have been separated from their biological fathers (67% vs. 53%), forced to kiss or touch someone in a sexual way (39% vs. 14%), received unwanted kiss or touch (48% vs. 20%), forced to have sexual intercourse (33% vs. 15%), and beaten by a parent or a legal guardian severely (13% vs. 7%). Likewise, VA's were more likely than NVA's to report family disturbance in their childhood (70% vs. 58%). As adults, VA's were more likely than their NVA counterparts to have traded sex (69% vs. 48%), endorsed DSM-IV criteria for major depression (51% vs. 20%) and met DSM-IV criteria for cocaine dependence (81% vs. 61%). Preliminary path analysis confirmed a significant association between child sexual abuse and adult depression, cocaine dependence, sex trading and victimization in adulthood. Similarly, adult depression was found to be associated with both cocaine dependence and victimization in adulthood. The overall model showed reasonably good fit ($\chi^2 = 9402$, 17df, NFI=9801, CFI=1.0, and RMSEA=0.000). This analysis suggested that childhood sexual abuse is a strong predictor of adult victimization among substance using women. (DA11622 and AA12111, LB Cottler, PI).

804 KAPPA OPIOID AGONIST-INDUCED REINSTATEMENT OF COCAINE SEEKING IN SQUIRREL MONKEYS: A ROLE FOR STRESS?

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Kappa opioid agonists induce dysphoria and activate the neuroendocrine stress response in humans, mimic the effects of stress on cocaine conditioned place preference in mice, increase cocaine preference in rhesus monkeys and induce reinstatement of drug seeking in squirrel monkeys. The objective of the present study was to evaluate the potential role of stress in spiradoline-induced reinstatement of cocaine seeking by determining the degree to which the effects of spiradoline could be attenuated by the CRF1 receptor antagonist CP 154,526 and the alpha2 adrenoceptor agonist clonidine, both of which have been shown to attenuate stress-induced reinstatement of drug seeking. Squirrel monkeys were trained to self-administer intravenous cocaine under a second-order schedule in which drug seeking was maintained jointly by cocaine injections and a cocaine-paired visual stimulus. In subsequent extinction sessions, saline was substituted for cocaine and the cocaine-paired stimulus was omitted. During test sessions, only saline was available for self-administration but response-contingent presentations of the cocaine-paired stimulus were restored. Intravenous priming injections of the kappa opioid agonist spiradoline reinstated cocaine-seeking behavior in a dose-related manner, with maximum effects observed at doses of 0.1 mg/kg or higher. Pretreatment with CP 154,526 or clonidine prior to reinstatement sessions attenuated spiradoline-induced reinstatement by 50% or more compared to pretreatment with vehicle. The similar effects of clonidine and CP 154,526 in our study and in previous studies of stress-induced reinstatement of drug seeking suggest that spiradoline-induced reinstatement of cocaine seeking in monkeys could be mediated in part by noradrenergic and CRF mechanisms involved in the regulation of stress. (Supported by NIDA grant DA11054, and NCR grant RR00168.)

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- 805 CHARACTERISTICS OF MDMA USERS WHO ENDORSE TOLERANCE OR WITHDRAWAL**
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The NIDA funded Tri-City Study of Club Drug Use, Abuse and Dependence investigated the increased use of so called 'club-drugs' [MDMA (ecstasy), GHB, rohypnol, and ketamine] with the Substance Abuse Module (SAM) in St. Louis (n=297), Miami (n=186) and Sydney, Australia (n=155). Among the 638 respondents, 57% were male, 62% were Caucasian, and the median sample age was 22. Currently, the DSM-IV classifies MDMA as a hallucinogen and specifies that dependence can be diagnosed either with or without physiological dependence, which is characterized by the presence of tolerance, withdrawal, or both. Among MDMA users, 59% (n=377) met dependence criteria, with 98% of those reporting tolerance and/or withdrawal. Among those who used MDMA and alcohol (n=636), 16% endorsed tolerance and withdrawal for both drugs, 10% endorsed tolerance and withdrawal for ecstasy alone, and 4% endorsed tolerance and withdrawal for alcohol alone. A linear association was found between tolerance, withdrawal and MDMA pill use; users reporting both tolerance and withdrawal reported the highest usage followed by use among those with tolerance or withdrawal alone, and no tolerance or withdrawal use reported the least. MDMA tolerance and withdrawal will be compared with tolerance and withdrawal among other drug categories to learn more about how these subtypes are related to MDMA abuse and dependence. Additional discussion will offer greater detail about data collected from the aforementioned sites. Increased understanding of MDMA specific characteristics may improve DSM diagnostic classification for future revisions.
- 806 BRIEF COCAINE ABSTINENCE INDUCED BY VOUCHER AND CASH-BASED INCENTIVES**
R. Vandrey, M. L. Stitzer and G. E. Bigelow, BPRU, Johns Hopkins University, Baltimore, MD
Recent research suggests cash incentives are more potent reinforcers than vouchers. One concern in using cash incentives in contingency management treatments of drug dependence is that cash reinforcers could be used to purchase drugs and thus negatively impact quit attempts. The present study investigated the impact of incentive type (vouchers vs. cash) on inducing cocaine abstinence and cocaine use following payment. The 16-week study used a within-subject design to compare the effects of 8 intervention conditions (cash or vouchers worth \$0, \$25, \$50, \$100) on short-term abstinence from cocaine in cocaine-dependent methadone patients (N=12). A 9-day washout period separated each incentive condition. The two primary dependent variables were 1) % abstinent samples and 2) quantitative benzoylcegonine (BE) level. A PROC Mixed procedure in SAS was used with incentive type and value entered as factors with planned comparisons conducted via independent sample t-tests. Abstinence rates were greater during High (\$50/100) versus Low (\$0/25) incentive conditions (F=4.77, p<.05) independent of incentive type. Greater rates of abstinence were observed in the High incentive cash conditions compared with the High incentive voucher conditions (F=4.77, p<.05). A main effect of incentive value was also observed for BE level (F=13.08, p<.01). In both the voucher and cash conditions, BE level were significantly lower (indicating less cocaine use) during the High versus Low incentive conditions. There were no effects of incentive type on BE level. Neither incentive type or value affected cocaine use variables during the washout weeks. Consistent with prior studies, higher magnitude and cash incentives were associated with less cocaine use compared with low magnitude and voucher incentives, and there was no difference across conditions in rate of subsequent drug use. This is important from both a clinical and budgetary perspective because cash incentives are more cost effective than vouchers. Caution in interpreting these results is warranted due to use of a relatively small sample and short periods of abstinence.
- 807 EFFECTS OF ACUTE METHYLPHENIDATE AND ATOMOXETINE ADMINISTRATION ON SPONTANEOUS SMOKING IN HUMANS**
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The results of a previous study from our laboratory suggest that methylphenidate (Ritalin®), the most commonly prescribed medication for the treatment of Attention Deficit Hyperactivity Disorder (ADHD), dose-dependently increases cigarette smoking when administered acutely. Atomoxetine (Strattera®), an alternative ADHD medication with a different pharmacological profile to that of methylphenidate, is currently approved for the treatment of ADHD in both children and adults. To our knowledge, the effects of atomoxetine on smoking have not been examined. In this experiment the acute effects of a range of doses of atomoxetine (20, 40, and 80 mg), methylphenidate (10, 20, and 40 mg), and placebo were assessed in 8 cigarette smokers who were not attempting to quit, and were without ADHD or other Axis I psychiatric disorders. Each dose of methylphenidate and atomoxetine was tested once while placebo was tested twice. One hour after ingesting drug participants were allowed to smoke ad libitum for four hours. Measures of smoking included total cigarettes smoked, total puffs, latency to the first cigarette, and carbon monoxide levels. Snacks and decaffeinated drinks were available ad libitum, and caloric intake during the four-hour smoking session was calculated. Methylphenidate, but not atomoxetine, dose-dependently increased the total number cigarettes smoked, number of puffs, and carbon monoxide levels. Methylphenidate, and to a lesser extent atomoxetine, dose-dependently decreased the number of food items consumed and caloric intake. The results of this experiment extend previous findings showing that methylphenidate increases cigarette smoking and provide evidence that an alternative ADHD medication, atomoxetine, does not affect cigarette smoking. The current findings could have important clinical implications for the safer treatment of ADHD.
- 808 DO NATURAL REWARDS AND DRUGS OF ABUSE INTERACT WITH MIDBRAIN DOPAMINE?**
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Numerous studies have shown that dopamine release in the nucleus accumbens is increased by ingestion of food and water. Dopamine antagonists (e.g., haloperidol) act upon the motor system impeding the initiation of movements that are necessary for the emission of instrumental behaviors. Opioid antagonists (i.e., naltrexone) take away the hedonic value of natural rewards and drugs of abuse. These ideas were explored with rats in a choice situation with eight levers and differing travel requirements. By climbing barriers of 75 cm height, the rats traveled to four levers providing food pellets according to variable interval schedules of 300, 600, 1400 and 700 seconds. The same schedules of reinforcement were used in the other four levers providing saccharine pellets, but rats climbed barriers of 110 cm height when traveling to those levers. Rats developed a strong preference for saccharine pellets, but choice favored the levers requiring the shortest travel (less effort). Total response output in the levers was not affected by naltrexone, but it was reduced by haloperidol. The reinforcing value of food reinforcers was not eliminated by either naltrexone or haloperidol, questioning the generality of the anhedonic hypothesis.

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809 DECONSTRUCTING HIV PREVENTION INTERVENTIONS AMONG DRUG ABUSING FEMALE OFFENDERS: PRELIMINARY RESULTS OF LONG-TERM FOLLOW-UP EFFORTS

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Drug abusers and ex-offenders are considered difficult to recruit into studies despite data showing the opposite (Cottler et al., 1996). Our goal is to re-interview a subset of women recruited from the St. Louis Female Drug Court (N=114) between 2001 and 2004 who participated in a randomized, peer delivered HIV prevention trial, to better understand how future interventions can be tailored to this high-risk population. Since October, we have attempted to contact 62 of the 114 women: 1) 25 completed the mixed method interview; 2) 1 was coded ineligible as she could not recall enough information about the prior study; 3) 2 refused to enroll; and 4) 34 outstanding cases will soon be released for field tracking. Cases were opened for follow-up, on average, 38 months after the original baseline interview; on average it took 9 contact attempts to relocate the 28 cases (range 1-31). Respondents reported that the persistent, respectful efforts of our team to contact them were the reason they returned after this period of time. Respondents also reflected on the positive impact of the intervention on their sex and drug use practices, and indicated that the most important component of the intervention was being tested for HIV and STDs, even though it was also the scariest. They believed the testing and counseling helped them change their high-risk behaviors. Some reported that the knowledge exchanged during the group sessions helped them reflect and change their lifestyle; others reported that being part of the study brought a sense of purpose and meaning to their lives, making them feel important and not like "just a street girl". Women reported challenges to participating in the intervention, including: transportation, being re-incarcerated while in the study, fear of testing and obtaining the results, the length of the interview, and discomfort with the personal questions. Implications of these findings for tracking, as well as intervention development, will be discussed.

810 ASSESSMENT OF CLUB DRUG USE IN TREATMENT-SEEKING INDIVIDUALS WITH MARIJUANA DEPENDENCE

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Club drug use is becoming increasingly popular in the United States, has been associated with chronic psychiatric symptoms and neuropsychological abnormalities, and has recently been recognized as a significant component of polysubstance use. Patterns of club drug use and characteristics of club drug users are not homogeneous. Thus, treatment-seeking individuals with marijuana dependence may have a differential pattern of club drug use. We hypothesized that treatment-seeking marijuana dependent individuals would have significant club drug use, particularly significant ecstasy use. In this study, baseline assessments collected from 38 individuals participating in a pharmacological treatment study for marijuana dependence were examined. Individuals completed a 16-item self-report questionnaire assessing club drugs used, frequency and patterns of use, problems associated with use, and reasons for use. Descriptive statistics are presented. Subjects were primarily male (89.5%) and Caucasian (89.5%), with a mean age of 32.3 (+/- 9.3) years. As expected, a large number of individuals had used ecstasy (60.5%). However, methamphetamine and LSD use was also reported by many users (36.8% and 65.8% respectively), with many individuals reporting use of more than one club drug. The most common club drugs of choice were ecstasy (34.5%), methamphetamine (27.6%), and LSD (31.0%). Notably, 31.0% of individuals reported tolerance to club drugs. Common reasons for use were to forget problems, to dance all night, and feeling too high. These results emphasize the significant co-occurrence of club drug use in marijuana dependent individuals. To our knowledge, this is the first study to report on club drug use in treatment-seeking marijuana dependent individuals. Clinical implications and directions for future research are discussed. This work was supported by Grant K23DA015440 awarded to A.L. McRae.

811 MICE BECOME TOLERANT TO MORPHINE-INDUCED DEPRESSION OF NK CELL ACTIVITY: REINSTATEMENT OF SUPPRESSION FOLLOWING WITHDRAWAL

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The current studies addressed the question of whether chronic exposure to morphine and withdrawal from the drug altered NK cell activity and NK cell numbers. The data in the literature are sparse and conflicting. NK cell numbers in spleen were determined by flow cytometry and NK cell activity by release of ⁵¹Cr from labeled YAC-1 targets. To elevate basal NK numbers, mice were pretreated with alpha-galactosyl ceramide (a-GalCer), an immune stimulator. Mice were implanted with morphine slow-release pellets, and spleens harvested at 48 and 96 hr post implantation or at 15 or 24 hr after induction of withdrawal by removal of the pellets. Similarly treated controls received placebo pellets. It was found that subacute exposure to morphine (48 hr) depressed NK cell percentages and activity. By 96 hr both parameters returned to baseline. After withdrawal, these NK parameters were again markedly suppressed. These results show that mice become tolerant to the suppressive effects of morphine on NK percentage and activity, and that withdrawal of the drug leads to a second wave of immunosuppression. Supported by NIDA grants DA14223 and DA13429.

812 THE RELATIONSHIP BETWEEN MENTAL ILLNESS OR SUBSTANCE ABUSE TREATMENT AND CRIMINAL BEHAVIOR

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The relationship between co-occurring disorders and criminal behavior has not been well investigated, particularly among female offenders. This study of 586 female offenders compared criminal behavior in offenders with no history of substance abuse or mental health treatment (NO-COD) to offenders with a history of psychiatric treatment (MH), history of substance abuse treatment (SA), or history of both substance abuse and psychiatric (COD) treatment. The population was evenly split between Caucasians (45.7%) and African-Americans (44.9%). The average age was 34.4 years. The participants had the following as their primary charge: larceny/robbery (33.4%), homicide (17.2%), drug-related crime (16.2%), assault (13.3%), parole/probation violation (8.3%) or another crime (2.6%). On average, these participants were serving sentences of 9.9 years, with about 8% serving life sentences. 56.5% of women reported a history of SA treatment and 64.2% reported a history of MH treatment. Women who had a history of COD treatment (68.4%) or SA alone (72.8%) were significantly more likely to have a history of multiple incarcerations compared to women with MH (34.8%) or NO-COD (30.4%; p<.001). Similarly, participants who had a history of COD (48.3%) or SA (48.8%) were significantly more likely to have a history of parole/probation violations compared to offenders with MH (16.5%) or NO-COD (12.8%; p<.001). Finally, participants with COD (41.4%) were significantly more likely to have a history of juvenile justice involvement than participants with MH (28.5%) or SA (27.5%) or NO-COD (23.6%; p=.003). Results indicate that a history of SA appeared to have the strongest association with recidivism and parole violations compared to a history of MH. Having a history of COD appeared to be related to juvenile crime and may indicate that mental illness increases the risk of juvenile justice involvement. Alternatively, a history of juvenile justice involvement may increase the likelihood that women will receive mental health services.

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813 PARTICIPATION IN SELF-HELP GROUPS FOR DUALY DIAGNOSED PERSONS IS ASSOCIATED WITH INCREASED CONFIDENCE TO COPE WITH MENTAL ILLNESS

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Background: Self-help processes (e.g., helping others, mutual learning) facilitate recovery among persons dually diagnosed with substance use and psychiatric disorders who participate in dual-focus 12-step groups based on the Double Trouble in Recovery (DTR) model. Objective: Examine mental health coping confidence and consumer satisfaction among dually diagnosed persons attending DTR in an outpatient mental health treatment setting. Methods: A cross-sectional survey was administered to DTR group participants (n=19). Measures included: 3 self-help process scales; Helper-Therapy (HT), Reciprocal-Learning (RL), Emotional-Support (ES) (Magura et al., 2003); an adapted version of the Mental Health Confidence Scale (Carpinello et al., 2000); and a scale measuring overall DTR satisfaction. Spearman-rho (r) correlations were computed among the measures. Results: Subjects attended DTR for an average of 3.9 months (range 1 to 8). Satisfaction with the DTR group was moderately high (mean=6.4 on 11-pt. scale with 0 as lowest and 10 as highest). DTR satisfaction was significantly associated ($p<.05$) with increased confidence to cope with mental illness ($r=.81$) and greater involvement in self-help processes (HT, $r=.52$; RL, $r=.56$; ES, $r=.55$). Longer participation in DTR also was associated with increased confidence to cope with mental illness ($r=.47$). Conclusion: The comparatively high level of satisfaction with DTR, the association between DTR satisfaction and self-help processes, and the positive relationship between length of DTR attendance and confidence to cope with mental illness suggests that dual focus groups will be well-received and benefit comorbid patients in psychiatric treatment programs. [NIDA grant R01 DA015912]

814 DEMONSTRATION OF THE FEASIBILITY OF REAL-TIME, PRODUCT-SPECIFIC, PRESCRIPTION OPIOID ABUSE SURVEILLANCE: THE NAVIPPRO SYSTEM

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Currently available systems for surveillance of prescription opioid abuse are neither "reliable comprehensive, or timely".¹ The National Addictions Vigilance Intervention and Prevention Program (NAVIPPRO) is a surveillance system for prescription drug abuse that will allow immediate access to data by pharmaceutical companies, regulatory authorities, etc., on the abuse/misuse of medications. Real-time product-specific data on opioid medication use are captured by NAVIPPRO, based on the Internet version of the Addiction Severity Index–Multimedia Version (ASI–MVonline). The ASI–MVonline is completed by substance abusers entering treatment, who indicate which of 46 specific opioid products (including generics) were used in the past 30 days. Client responses are immediately captured by a central server for analysis. Analyses of the first 132 clients' data, collected from November 2005 through early January 2006, revealed that 47% reported using at least one of the 46 products in the past 30 days. Of those, 62% reported having a chronic pain problem. Of those reporting use of analgesics, 61% used these drugs in a manner not prescribed. The top three products used are Lortab (28%), Percocet (20%), and Vicodin (18%). Comparing those who use and those who do not use prescription opioids, there were no significant differences for gender. Younger clients were more likely to use any opioid ($\chi^2=6.2$, $p=.013$) and to use these inappropriately ($\chi^2=4.5$, $p=.034$). White substance abuse clients were more likely to have used prescription opioids in the past 30 days ($\chi^2=7.9$, $p=.005$), but not more likely to have used them inappropriately. The results suggest that it is feasible to collect and analyze real-time, product-specific prescription opioid abuse data, which has the potential to generate timely product-specific abuse rates. IGAO (2003). Prescription drugs: OxyContin abuse and diversion and efforts to address the problem. (GAO-04-110).

815 THE ASSOCIATION BETWEEN POSITIVE AND NEGATIVE ECSTASY-RELATED INFORMATION AND COLLEGE STUDENTS' FUTURE LIKELIHOOD TO USE ECSTASY

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This study presents initial findings from the College Life Study (CLS) regarding the association between students' exposure to ecstasy information and their likelihood to use ecstasy if offered the opportunity in the future. Face-to-face interviews were conducted with 1,253 first-time first-year college students attending a large public university. The interview covered a variety of topics, including alcohol and other drug use, and several suspected risk and protective factors for drug use involvement. A subsample of 816 were administered supplemental questions about exposure to ecstasy information. Respondents indicated if they had previously heard any or all of six negative (e.g., "ecstasy puts holes in your brain") and four positive statements about ecstasy (e.g., "ecstasy makes you feel wonderful"). The number of positive and negative statements heard was separately calculated to form two summary scores. The mean number of negative and positive statements heard by students was 3.7 and 2.4, respectively. Thirty students (3.7%) had used ecstasy and 69 (8.6%) responded that they would maybe or definitely use it if offered in the future. Logistic regression tested the association between the positive and negative summary score and the likelihood of future ecstasy use, holding constant age, race, mother's education, the number of other illicit drugs used and prior ecstasy use. The number of positive statements heard was significantly positively associated with a greater likelihood to use ecstasy in the future ($p=.008$). Although many students had heard negative statements about ecstasy (e.g., 89% had heard "ecstasy can kill you"), exposure to negative statements was not associated with future likelihood to use ecstasy. Although many college students have heard a considerable amount of ecstasy-related information, both positive and negative, innovative prevention approaches are needed that do not solely focus on negative consequences of ecstasy use.

816 EVALUATION OF THE REINFORCING AND SUBJECTIVE EFFECTS OF HEROIN IN COMBINATION WITH DEXTROMETHORPHAN/QUINIDINE

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Both pre-clinical and clinical studies have suggested that NMDA antagonists may be useful in the treatment of opioid dependence. This double-blind, inpatient study evaluated the effects of 0, 30, and 60 mg dextromethorphan/quinidine (DMQ) on the reinforcing and subjective effects of heroin in non-dependent heroin abusers. Nine participants were admitted and subsequently detoxified from heroin over the course of several days. They were then stabilized on 0, 30, or 60 mg of DMQ in the morning, 2.5 hours before heroin administration. Participants were maintained on each dose of DMQ for 3 weeks. The effects of heroin (0, 12.5, and 50 mg) were studied under each maintenance dose condition. DMQ and heroin doses were administered in non-systematic order both within and between participants. Planned comparisons revealed statistically significant increases in progressive ratio breakpoint values and positive subjective ratings as a function of heroin dose. However, there were no consistent changes in any of the responses as a function of DMQ maintenance dose. Although it is not possible to determine conclusively that the dose selections of dextromethorphan in combination with quinidine were active at NMDA receptors, the dose selections were based on a convergence of data from the literature suggesting that they should have activity at these receptors. In sum, results from the present study suggest that maintenance on dextromethorphan in combination with quinidine may have a limited role in the treatment of opioid dependence.

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817 SELECTIVELY WILLING: ATTRACTIONS AND BARRIERS TO HIV VACCINE RESEARCH PARTICIPATION AMONG CRACK-COCAINE-USING WOMEN IN PHILADELPHIA

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Distrust is a challenge which confronts HIV prevention research conducted among populations experiencing high HIV incidence. Such individuals often experience social marginalization due to drug and/or sexual behaviors, poverty, racism, sexism, and homophobia, and are often leery of involvement with the medical establishment. In this study, semi-structured qualitative interviews were conducted among women crack cocaine users regarding HIV prevention research, including a Phase II trial of an HIV vaccine. The social contexts of drug use, HIV, and research were explored, including reasons for or against involvement in HIV vaccine research. Respondents expressed varying degrees of desire to participate, which was influenced by the type of research, procedures involved, perceived risks and benefits, and the significance of the study in their lives. Preliminary analysis suggests that major attractions included: the opportunity to get information and to potentially help others, as well as compensation for time and travel. Several respondents also mentioned positive impressions of research staff, and some perceive that they experience benefits from their interactions with them. Major barriers included: aversions to injections, distrust, and perceived potential consequences of participation such as: unknown potential side effects of the vaccine, the potential to test false-positive on future HIV tests, and negative meanings ascribed to participant's roles (i.e. "guinea pig", "lab rat", "test dummy"). In addition, women discussed how logistical issues and personal commitments could also impede research participation. Findings highlight the importance of understanding community perceptions of vaccine research and using such knowledge to tailor education, recruitment, and other study procedures to respond to social and structural contexts in which research is carried out.

819 DISCRIMINATIVE-STIMULUS EFFECTS OF D-AMPHETAMINE IN WOMEN AND MEN

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Men and women may respond differently to drugs of abuse. The results of some recent studies suggest that women are more sensitive to the effects of stimulants such as amphetamine and cocaine than men. In order to assess potential sex-differences in sensitivity to the effects of d-amphetamine, we conducted a retrospective-analysis of six studies that employed identical d-amphetamine discrimination procedures and subject-rated drug-effect measures. Thirteen women and fourteen men were included in the analysis. In all studies, participants learned to discriminate 15 mg oral d-amphetamine. After acquiring the discrimination (i.e., $\geq 80\%$ correct responding on 4 consecutive sessions), the effects of a range of doses of d-amphetamine (0, 2.5, 5, 10 and 15 mg) were assessed. As expected, d-amphetamine functioned as a discriminative-stimulus and produced prototypical subject-ratings and cardiovascular effects. Men and women were not found to differ in their ability to discriminate d-amphetamine, nor did they differ in terms of the subject-rated effects of d-amphetamine. The results of this study suggest that men and women are not differentially sensitive to the effects of d-amphetamine. Future research should be conducted to determine if menstrual cycle phase might affect the discriminative-stimulus effects of d-amphetamine in women.

818 A DATA ANALYSIS PROCEDURE TO IDENTIFY EFFICACIOUS COMPONENTS IN A MULTI-COMPONENT INTERVENTION FOR HOMELESS COCAINE-DEPENDENT CLIENTS

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In this trial, 196 cocaine-dependent participants received a multi-component day treatment and either no housing, abstinence-contingent housing, or non-abstinence-contingent housing. Drug use was monitored with urine toxicology. Primary data analyses showed a therapeutic effect for housing, but did not test for the effects of individual components of the multi-component treatment. The secondary data analyses to be reported focused on the effects of Therapeutic Goal Management (TGM), because TGM is a key theory-based behavioral component of the treatment. Duration of participation in each component was recorded. We divided all components into 3 categories: TGM, Typical Outpatient (TO) (e.g., Process Group), and Other (e.g., Stress Management Group). We then correlated duration of exposure to the different component categories with each other (mean $r = .81$) and with abstinence. The bivariate correlations between abstinence and TGM, TO, and Other were .57, .52, and .31, respectively. Two multivariate models were fit to examine the effects of TGM on abstinence in relation to the effects of the other components. When we included housing group and TO, TGM exposure was positively related to abstinence ($p = 0.0001$) but TO exposure was not ($p = 0.98$). When we included housing group and Other, TGM exposure was positively related to abstinence ($p < 0.0001$) but Other exposure was negatively related to abstinence ($p = 0.019$). These results indicate that the effects of TGM on abstinence are strong after controlling for housing group, TO, and Other, while the effects of TO and Other are minimized after controlling for housing and TGM. Conclusive causal inferences cannot be made in the absence of experimental data, but these results strongly suggest that TGM provides a powerful and robust effect on abstinence that is independent of the abstinent contingent housing manipulation and of the other treatment components.

820 DRUG USE AND ETHNIC IDENTITY AMONG RECENT IMMIGRANTS TO THE US OF HISPANIC ORIGIN

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Objectives: (1) To assess the scope of drug use among recent immigrants of Hispanic origin who reside in Baltimore, Maryland; (2) To test feasibility and psychometric characteristics of an instrument to assess ethnic identity; and, (3) To explore the association between ethnic identity and drug involvement among recent Hispanic immigrants. Methods: A survey with 158 Hispanics 18-35 years old was carried out using the Street Intercept method. Drug involvement was measured using questions on exposure opportunities and actual drug use from nationally representative surveys and prior studies. Ethnic identity was measured using an adapted version of Phinney's Multigroup Ethnic Identity Measure (1992). Results. An estimated 70% of all survey participants used alcohol in the past year, and 49%, in the past month. Also, 27%, 11% and 6% have used marijuana in their lifetime, past year, and past month, respectively. Surprisingly, 13% reported to have ever used cocaine in their lifetime, and about 8% used in the past month. With respect to the ethnic identity measure, Cronbach's alpha was 0.67 for the whole scale. Factor analyses revealed important differences compared to prior research with different minority groups. Conclusions. Drug involvement in this sample of Hispanics is higher than in other studies. Acknowledgment. Study is supported by subcontract from Johns Hopkins University with funds from grant U48DP000040 from the CDC, and grants from U24DA012390, and RO3DA17796 from NIDA, and grant P60MD000217 from the NCMHHD. We also thank the Hispanic Apostolate/Legal Immigration Services for their support.

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821 DAILY STRESSOR SENSITIVITY, ABUSE EFFECTS, AND COCAINE USE IN COCAINE DEPENDENCE: GENDER DIFFERENCES

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This study highlights respondent sensitivity to daily hassles as it relates to situational cocaine use and perceived long-term effects of abuse exposure. Data were drawn from a larger study on stress reactivity in cocaine dependence. Participants (n=65) were cocaine dependent men and women without comorbid posttraumatic stress disorder (PTSD). They completed the Early Trauma Inventory, the Daily Hassles Scale (DHS), the Inventory of Drug-Taking Situations (IDTS), and the Time-Line Follow-Back (for prior 90 days). There were no gender differences on severity of cocaine use. Among men and women, greater reactivity to daily hassles was associated with greater likelihood of cocaine use in negative situations, but not positive or temptation situations. Gender differences emerged in the relationship of everyday stress reactivity (DHS scores) to perceived long-term effects of general trauma and abuse exposure. Cocaine dependent men with higher daily hassle scores were more likely to report current relationship and emotional effects from general trauma exposure, childhood emotional abuse, and childhood physical abuse. Among cocaine dependent women, higher daily hassle scores were associated only with a greater likelihood of current emotional effects from childhood emotional abuse. Abuse exposure rates were significant, and appear to be associated with long-term sensitivity to daily stressors. These results are interesting in light of the PTSD exclusion criteria employed in the study. It is also interesting to note that cocaine dependent men and women appear to use more frequently in negative situations when they are reporting more distress from day-to-day stressors. This may provide information on targets for treatment through identification of triggers for use. The gender difference in associations between abuse exposure and sensitivity to daily hassles may also inform relapse prevention efforts. Data collection is ongoing and additional analyses are planned to examine reactivity to laboratory stressors as it relates to sensitivity to daily hassles.

823 TOWARD A FUNCTIONAL UNDERSTANDING OF ADOLESCENT DOPAMINE FUNCTION: IMPLICATIONS FOR ADDICTION

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Age-related maturation in forebrain dopamine (DA) systems may contribute to the more rapid progression to addiction that drug-using adolescents can experience. We have been developing a model to describe important developmental differences in the function of DA systems that could lead to this vulnerability to drug abuse. We previously showed using cyclic voltammetry that electrically-evoked DA release is lower in periadolescent than adult rats. We presently report results of synaptosomal DA uptake and DA and metabolite content. Developmental increases in striatal DA content (by HPLC) mirror the developmental path of DA release. Striatal DA content was lowest in the youngest rats we studied (PN28), increased at PN42, and was greatest in PN65 and PN90 rats. Synaptosomal uptake studies found that DA clearance rates are similar in adolescent and adult striatum. Because uptake matures before release rates, our observations suggest that extracellular DA levels should be lower in adolescent striatum, agreeing with published observations using dialysis. The ratio of HVA/DA is an index of turnover or the activity state of DA terminals. DA turnover was highest in PN28 rats and fell developmentally to be lowest in the adults. The increased turnover at the youngest age may reflect functional compensation for the immature DA content and the lower release/uptake ratio. We postulate that this neural compensation contributes to a pattern of greater behavioral effects in PN28 induced by DA uptake inhibitors (methylphenidate, nomifensine, GBR12909, and cocaine) and greater cocaine-stimulated increases in DA efflux in PN28 rats. Our model of adolescent DA function consists of lower DA content, release rate, release/uptake ratio and possibly extracellular levels, all of which may be compensated for by increased turnover. This functional state would then be quite susceptible to disruption by DAT inhibition, resulting in greater drug-induced increases in DA and motor stimulation. Supported by DA019114.

822 A HUMAN LABORATORY MODEL OF VOLATILE SOLVENT ABUSE: PRELIMINARY RESULTS

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The effects of abused inhalants are difficult to study in humans because of safety and ethical issues. One way to study inhalant abuse is by assessing abuse liability-related effects (e.g., drug liking, euphoria) of volatile anesthetics, which can be safely and ethically administered to humans. Volatile anesthetics are abused, and they are behaviorally and chemically similar to commonly abused volatile solvents, like the ones found in glue and paint thinner. The present two ongoing studies are concerned with two questions: 1) Does subjective response to a volatile anesthetic predict subsequent self-administration (choice)? and 2) Does subjective response to a volatile anesthetic predict subjective response to morphine? In both experiments subjects inhale 0.4% sevoflurane and 100% oxygen (O₂) in Phase 1, and subjective effects are assessed. In Experiment 1, Phase 2 consists of three sessions in which subjects can choose to inhale a dose of sevoflurane (0.27, 0.4, 0.53%) or placebo or "neither." In Experiment 2, Phase 2 consists of two sessions in which subjects receive cumulative intravenous doses of either morphine (0, 2.5, 5, 10 mg/kg) or placebo. Preliminary data suggest that subjects who report abuse liability-related subjective effects of sevoflurane are more likely to choose sevoflurane (Experiment 1) and to report abuse liability-related effects of morphine (Experiment 2) than subjects who report neutral effects or effects associated with a lack of abuse (e.g., drug disliking, dysphoria). The first experiment assesses the relationship between subjective and reinforcing effects, and the second provides data relevant to the possibility that inhalant abuse may increase the likelihood of subsequent opiate abuse. This research was funded by the National Institute on Drug Abuse, Grant DA-15934.

824 THE US BORDER IN CONTEXT: HOW DOES DRUG USE COMPARE?

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The prevalence of drug and alcohol use and misuse among residents of the Texas/Mexico border, observed through an in-person survey of 1200 adults, is compared with that of adults living in the interior of the state, as estimated by the NSDUH, with Hispanics nationwide, also from the NSDUH, and with data from the Mexican side of the border, in order to put the border findings into a larger context. Findings from the border survey are also compared with substata estimates from the NSDUH that include the border region. When compared to estimates for Texas as a whole, border adults were less likely than adults statewide to drink alcohol, binge drink or use illicit drugs, but were more likely to report substance dependence. When compared with Hispanics nationwide, again border Hispanics were less likely to drink, binge drink, or use illicit drugs, but slightly more likely to report heavy alcohol use and substance abuse or dependence. Mexican survey data indicate that 8% of Mexicans aged 12-65 living in urban areas of the northern (border) region of Mexico had ever used an illicit drug (compared with 33% of Texas border residents from the present border survey); and 11% of northern Mexicans were heavy drinkers as compared to 7% in the border survey. Some 5% of adults aged 18-65 in the northern region of Mexico had a past-year substance-related disorder, substantially lower than the rate of 13% substance abuse or dependence in the Texas border survey. These comparisons are imperfect, due to differences in survey methodologies and samples and high standard errors for some estimates; however, the pattern of lowest drug use in Mexico and highest in the interior of the US appears to be consistent with other research, and belies the perception that drug use levels on the border might be inflated by the high levels of trafficking there. However, border residents may experience more adverse consequences (abuse/dependence) from substance use. From a methodological standpoint, it is also interesting to note that the substata estimates recently published by NSDUH are within the confidence limits of the use levels observed through the direct border survey.

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825 DEPENDENT VS. NON-DEPENDENT COCAINE USERS: COCAINE PHARMACODYNAMICS, SELF-ADMINISTRATION AND TRAIT CHARACTERISTICS

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This double-blind, between-group, 4.5-wk inpatient study compared individuals with DSM-IV COC dependence (n=8) to users without dependence (n=8) matched for sex, race and COC exposure years (mean=14.2 yr). After careful medical screening, a battery of tasks was completed on trait measures. Subjects participated in a COC test session (0, 12.5, 25 & 50 mg, iv, 1 hr apart). COC self-administration was then evaluated with a Relapse Choice and progressive ratio (PR) procedure; each had 7 trials, a 15-min ITI, and was preceded by a sample session 24 hr before (6 total 2-day trials). Subjects chose between decreasing amounts of money or COC (0, 12.5 or 25 mg, i.v.) during choice sessions and could complete an escalating work requirement during PR sessions. DEP users self-administered more COC (p=.039) and chose their 1st injection sooner (p=.047) in the choice test; there was a similar trend with the PR (p=.056). Pharmacodynamic data from the dose-response sessions also revealed group differences. The DEP users reported greater desire (p=0.029) and craving for COC (p=.028). While the groups reported comparable ratings for magnitude of drug effect, high and liking after COC, the observers rated the NON-D group higher on drug effect, difficulty concentrating, fidgety, edgy/irritable, and moody (p<.05); while the NON-D subjects rated themselves higher only on "suspicious" (p=.014). No group differences were seen on the NEO, Barrett or Zuckerman scales, but there were trends for the DEP users to have higher scores on Impulsiveness (p=.059) and Adventurousomeness (p=.069; Eysenck). These data suggest that DEP users' higher rates of COC use in and out of the lab are coupled with greater craving. NON-D users exhibited greater responses to COC, particularly negative effects, which were observable but not always self-rated. Trait measures suggest that those with DEP may have greater impulsivity, but further analyses are needed. Supported by NIDA R01 DA14653 (SLW).

827 RELATIONSHIP BETWEEN INTIMATE PARTNER VIOLENCE AND HEALTH STATUS AMONG DRUG-DEPENDENT WOMEN IN DRUG TREATMENT

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Adverse health outcomes are consistently associated with intimate partner violence (IPV) however; findings regarding effects of IPV type and recency are less well established, particularly for women with drug dependence. The study question was: Is IPV type (physical, sexual or emotional) and recency (i.e., current: within past year or past) associated with poorer perceived health upon entry into drug treatment? A non-random sample of 100 women, primarily dependent on heroin or cocaine, was consented to one-time face-to-face interviews within 2 weeks of entry into out-patient drug treatment. Instruments included: Abuse Assessment Screen (AAS), Medical Outcomes Survey Short Form (SF36), Brief Symptom Inventory, and the Severity of Violence Against Women Scale. Preliminary findings for this report are limited to abuse as defined by the AAS and perceived health status as measured by the SF36. Women reporting the specific IPV category were compared to women who did not report that category. SF36 raw component scores (i.e., physical function, role-physical, role-emotional, energy/fatigue, emotional, social function, pain, & general health) and composite (physical & mental) scores were standardized. Higher scores are associated with better health. T-tests were conducted with SPSS 14 for Windows. The most frequent IPV category reported was current emotional (72.7%), current sexual the least frequent (28.4%), 25% reported being afraid of their partner, and 9.8% reported no history of interpersonal violence. Significant associations were found for current sexual IPV and emotional (p=.04), social function (p=.05), and general health (p=.04). Fear of partner also had significant associations with physical function (p=.01), role-physical (p=.01), social function (p=.02), general health (p=.00) and the physical composite score (p=.01). IPV appears to be related to perceived health however, the association varies with IPV type and recency. When evaluating any type of IPV women should be specifically asked about fear in their intimate relationships.

826 ONE STOP SHOP: A MODEL OF INTEGRATED ANTIVIRAL AND SUBSTANCE DEPENDENCE TREATMENT FOR INJECTING DRUG USERS

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Successful treatment of hepatitis C and HIV in injecting drug-using populations is enhanced by concomitant treatment of substance use. Unfortunately there is little integration between blood borne virus treatment services and substance use treatment. Here we describe a 'one stop shop' model of on site substance use and hepatitis C treatment in Melbourne, Australia. Turning Point Alcohol and Drug Centre is a specialist substance-use treatment centre providing methadone and buprenorphine maintenance pharmacotherapy for opiate dependence. Clinicians are also accredited hepatitis C antiviral prescribers. During treatment for opiate dependence, BBV screening identifies potential candidates for BBV treatment. Interested clients can then receive counseling, immunization, therapy or disease progression monitoring. BBV therapy is initiated on site after substance use stability is achieved, and although treatment is conducted within funding criteria, emphasis is made on managing co-morbidities effectively to facilitate therapy rather than excluding potential candidates. Hepatitis C therapy is directly observed at an onsite pharmacy. Ongoing management of HCV treatment occurs in consultation with specialist infectious disease clinicians and gastroenterologists from nearby hospitals. Preliminary data will be presented. Although in its early days, we have found the concept of combined on-site availability of therapy for opiate dependence using pharmacotherapy, HCV antiviral therapy and a dispensing pharmacy to be popular among clients. The mainstay of treatment remains opiate pharmacotherapy. This model of care facilitates a coordinated management of IDU's treatment goals in a sympathetic environment.

828 MORPHINE UP-REGULATES FUNCTIONAL EXPRESSION OF NEUROKININ-1 RECEPTOR IN NEURONS

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Neurokinin-1 receptor (NK-1R), the neuropeptide substance P (SP) preferring receptor, is highly expressed in areas of the central nervous system that are implicated in behavior, especially in the management of depression, anxiety and stress. Repeated exposure to opioids may sensitize neuronal systems involved in stress response. In the present study, the effects of morphine, the principal metabolite of heroin, on the functional expression of NK-1R were assessed in primary rat cortical neurons. We demonstrated that mu-opioid receptor and NK-1R are co-expressed in rat cortical neurons. Morphine enhanced NK-1R expression in primary rat cortical neurons at both the mRNA and protein levels. The up-regulated NK-1R by morphine was functional, since morphine-treated cortical neurons had greater SP-induced calcium mobilization than untreated cells. Blocking opioid receptors on the cortical neurons by naltrexone or CTAP (a mu-opioid receptor antagonist) abolished morphine's action. Investigation of the mechanism(s) responsible for morphine-mediated NK-1R up-regulation showed that morphine had the ability to activate NK-1R promoter. In addition, morphine induced the phosphorylation of p38 MAPK protein in rat cortical neurons. These data suggest a plausible cellular mechanism involved in opioid-mediated neurological disorders.

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- 829 RESTORATION OF MDMA-INDUCED SEROTONIN DEPLETION BY ADMINISTRATION OF L-5-HYDROXYTRYPTOPHAN**
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Background. Repeated administration of 3,4-methylenedioxyamphetamine (MDMA) to rats produces a persistent decrease in brain 5-HT content, a decrease in 5-HT transporter (SERT) binding, but no decrease in SERT protein expression as measured by Western blots (Wang et al. JPET 314:1002-12, 2005). Our data suggests that MDMA administration depletes brain 5-HT, but leaves the 5-HT nerve terminals intact. Hypothesis. Administration of the 5-HT precursor, L-5-hydroxytryptophan (5-HTP) to MDMA-treated rats will restore depleted tissue stores of 5-HT. Methods. We utilized an immunoradiography method to detect brain 5-HT using fixed tissue, a primary rabbit anti-5-HT antibody, a secondary [35S]-anti-rabbit antibody, and visualization with a Packard Cyclone Phosphoimager. Rats were perfused with 4% paraformaldehyde under pentobarbital anesthesia and 40 μ M brain sections prepared for immunoradiography using standard procedures. Control experiments demonstrated that administration of reserpine, at a dose that depletes brain 5-HT by 90%, eliminated the 5-HT signal. Rats (n=6 per group) received MDMA or saline (7.5 mg/kg ip, q 2 hr x 3 doses). Previous studies showed that this dosing regimen decreases brain 5-HT content by 50-60% without reducing DA or NE. Two weeks later, rats received either saline or 5-HTP/benserazide, each at 50 mg/kg ip, sacrificed 120 min later. Benserazide was administered 30 min before the 5-HTP. Brain sections were prepared for 5-HT immunoradiography at the level of the caudate and hippocampus. Results. 5-HTP administration to saline-treated rats did not increase the 5-HT signal in caudate or hippocampus. MDMA-treatment reduced the 5-HT signal in the caudate (33 % of control) and hippocampus (35 % of control). 5-HTP administration to MDMA-pretreated rats significantly increased the 5-HT signal in caudate (74 % of control) and hippocampus (54 % of control). Conclusion. These data support the hypothesis that MDMA-treatment reduces the 5-HT content of otherwise intact nerve terminals
- 830 ESTIMATING THE REINFORCING EFFICACY OF 3,4-METHYLENEDIOXYMETHAMPHETAMINE AND ITS ISOMERS IN RHESUS MONKEYS**
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(\pm)3,4-methylenedioxyamphetamine (MDMA) is a ring-substituted analog of methamphetamine (MA) and a drug of abuse. Like MA, MDMA releases monoamine neurotransmitters, particularly dopamine (DA) and serotonin (5-HT). Self-administration of MDMA by laboratory animals has been reported, but the reinforcing efficacy of the isomers of MDMA is unknown. The purpose of this study was to compare (+)-MA, MDMA, (+)-MDMA and (-)-MDMA using a progressive-ratio (PR) schedule of reinforcement in rhesus monkeys. Under a PR schedule, response requirement increases until self-administration stops. The maximum number of injections self-administered serves as a measure of reinforcing efficacy. Rhesus monkeys (n=6, MA and MDMA; n=5, (+)-MDMA and (-)-MDMA) were prepared with chronic i.v. catheters and allowed to self-administer cocaine or saline in daily baseline sessions. When responding was stable, MA (0.006-0.1mg/kg/inj), MDMA (0.025-1.6mg/kg/inj), (+)-MDMA (0.025-0.4 mg/kg/inj) or (-)-MDMA (0.1-0.8mg/kg/inj) was made available in test sessions. MA, MDMA and (+)-MDMA functioned as positive reinforcers in all monkeys with ED50s of 0.03 \pm 0.005, 0.2 \pm 0.013 and 0.11 \pm 0.015mg/kg/inj, respectively (p others, p<0.05). Two of five monkeys took (-)-MDMA above saline levels at 0.4 and 0.8mg/kg/inj. Thus, MDMA and (+)-MDMA were consistent reinforcers, but weaker than MA, whereas (-)-MDMA was, at best, a weak reinforcer in some monkeys. The reinforcing efficacy of MDMA appears to derive primarily from (+)-MDMA. Potency relationships paralleled their relative potencies as DA releasers in vitro, arguing that DA release contributed to reinforcing effects. The reduced reinforcing efficacy of MDMA and its isomers relative to MA corresponded to their higher 5-HT releasing potency. These data support the hypothesis that increasing 5-HT releasing potency relative to DA is associated with weaker reinforcing effects. (Supported by Grants DA-10352 and DA-15343, W.L.W.)
- 831 GENDER DIFFERENCES IN THE EFFICACY OF INTERVENTION TRIALS ON PREVENTING TOBACCO SMOKING AMONG CHILDREN AND ADOLESCENTS**
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Introduction: Several childhood and early adolescent interventions have shown to be effective in preventing the onset of tobacco use. However, gender variation in the intervention efficacy is often ignored. In this study, we estimate the impact of two primary school interventions on preventing the initiation of tobacco smoking in youths stratified by gender. Methods: Upon entry into primary school in 1993, a total of 678 urban, primarily African American public school students were randomly assigned to a control group or one of two one-year interventions that sought to improve early primary school performance and behaviors: a classroom-centered intervention and a family-school partnership intervention. Youths were followed annually from grade 6 to 12 and completed ACASI interviews which assessed the onset of tobacco smoking. Discrete-time survival analyses assessed time to first tobacco smoking as a function of intervention status after adjusting for parent's socioeconomic status, parenting characteristics, household tobacco use, teacher's rating of authority acceptance and shy behaviors, children's own self-report depressed mood at first grade. Results: Boys in the intervention groups were less likely to initiate tobacco use compared to the boys in control group (estimated 56% in either intervention group as compared to 64% in the control group; adjusted Hazard Ratio=0.7, 95% CI: 0.5, 0.95). In contrast, there was no significant difference regarding onset of tobacco smoking between girls in the intervention groups (55%) and control group (53%). Comments: The findings suggest that the intervention trials targeting risk behaviors in early childhood is effective in preventing or delaying the onset of tobacco smoking among boys, but not girls. Strategies to prevent adolescent risk behaviors may need to be specifically designed for different genders. Acknowledgements: NIMH R01MH57005, NIDA R01DA11796 and NIDA 12390.
- 832 GENE EXPRESSION PROFILES IN CORTICAL NEURONS TREATED WITH NICOTINE, ETHANOL, OR BOTH USING A PATHWAY-FOCUSED CDNA MICROARRAY**
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Epidemiological studies reveal that smoking and drinking are highly correlated behaviors, however very little is known about the molecular mechanisms underlying these two behaviors in the brain. In this study, a pathway-focused cDNA microarray was used to identify genes/pathways that are differentially expressed in cortical neurons of the C57BL/6 mouse when treated for five consecutive days with (a) 75 mM ethanol, (b) 0.1 mM nicotine, or (c) 75 mM ethanol plus 0.1 mM nicotine. Using a balanced microarray design containing both technical and biological replicates within each group, we identified 61 differentially expressed genes in the ethanol-treated cortical neurons compared with untreated neurons. Among these, 38 were up-regulated and 23 were down-regulated. Similarly, we identified 118 differentially expressed genes in nicotine-treated cortical neurons relative to controls, of which 58 were up-regulated and 60 were down-regulated. However, when the neurons were co-treated with nicotine and ethanol under the same conditions, 80 genes were found to be differentially regulated, of which 43 were up-regulated and 37 were down-regulated, thereby abrogating the effects of the drugs when administered independently. Among these genes, 6 were found to be modulated in all three treatments; these were chosen along with four representative genes involved in the platelet derived growth factor (PDGF) signal pathway for verification using real-time RT-PCR. A comparison of gene expression profiles from the three treatments suggests that the expression patterns altered by nicotine and ethanol are highly related for several gene families and pathways, such as cell proliferation, protein modification and degradation, and signal transduction. In summary, this study provides clues to the regulatory mechanisms of cortical neurons in response to ethanol and nicotine treatment.

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833 TRAUMA, PTSD, OPIATE USE, ABUSE AND DEPENDENCE: IDENTIFYING COMMON PATHWAYS

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Background: Comorbidity of PTSD and opiate use is well documented. Multiple pathways are involved in the longitudinal course of trauma, PTSD, opiate use, abuse and dependence. Objective: To identify different patterns of pathways from trauma exposure to PTSD, opiate use to abuse and dependence by taking into account timing of each "milestone." Methods: The sample (n=634) for this study was drawn from the third wave Vietnam veterans study (VES-III) conducted in 1996-7 as a part of follow-ups over 30 years. The sample originated in 1972 included a general-sample of Vietnam veteran returnees with an oversample of those returnees who had been tested positive for illicit drug use excluding marijuana. Only veterans available in both 1972 and 1996 surveys were included. Measures include timing of opiate use, abuse and dependence from the 1972, 1974 and 1996-97 with lifetime retrospective timing of trauma and PTSD symptoms and diagnoses obtained in 1996-7. Results: In this sample, the unweighted lifetime prevalence of trauma, PTSD, opiate use, abuse and dependence were 90.2%, 26.8%, 70.2%, 14.7% and 12.5%, respectively; and 22.9% for comorbid PTSD/opiate dependent cases. The average time of opiate use was 5.6 years and dependence was 10.6 years. For veterans with a lifetime diagnosis of PTSD, the average duration of PTSD diagnosis was 22.1 years. Of 28 potential pathways, 17 likely pathways were analyzed. The most common patterns were: trauma→no PTSD→no opiate use for the trauma-first group (21.6%); opiate use→trauma→no PTSD→opiate dependence for the opiate-first group (12.6%); and for the group with opiate and trauma occurring simultaneously, opiate+trauma→no PTSD→opiate dependence (4.7%). Conclusion: The high prevalence of lifetime clinical comorbidity reflects high levels of combat and opiate exposures while deployed in Vietnam. Opiate exposure before or with simultaneous trauma exposure is likely to have a common outcome of opiate dependence; while trauma exposure without PTSD development is more likely to result in no opiate use (supported by DA09281, MH17104).

834 OPTIMIZING ANALYSES OF ARTERIAL SPIN LABELING PERFUSION FMRI FOR DRUG ABUSE STUDIES

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Here we compared standard processing procedures for ASL perfusion fMRI with an empirical, optimal data processing method in a recent nicotine cue reactivity dataset (Franklin et al., SFN 2005). Data acquisition comprised of two sessions separated by 30-60 minutes. Each session contained a resting condition (5 min) and a (non-smoking or smoking) video condition (10 min) with a counterbalanced order across subjects. 600 images were obtained from each of the 13 subjects using a CASL sequence (TR=3 sec, matrix=64x64x14, FOV=220x220x140 mm³). CBF images were calculated using both a standard and optimal approach from the motion-corrected and smoothed tagged-untagged pairs. The standard approach used simple pairwise subtraction, while the optimal approach used sinc-subtraction of the pairs. General linear model (GLM) based statistics analysis was performed on the spatially normalized CBF images. A nuisance covariate from the global CBF values was used to correct global fluctuations. In the optimal approach extreme outliers were omitted to calculate global CBF, and an extra nuisance covariate was also used to remove the effects of spiky CBF images by generating a spike indicator vector based on the head motion and the global CBF variance. Both the standard fMRI processing way and the proposed optimal way yielded significant activation patterns in amygdala and insula gyrus (P20) for the primary contrast (smoking video minus non-drug video). However, the optimal way resulted in higher peak t-value and cluster extensions in both target regions: peak t=7.72 vs. 5.7 and cluster number=141 vs. 40 in amygdala, peak t=7.19 vs. 5.62 and cluster number=161 vs. 64 in insula. Optimizing the analytic strategy may greatly enhance the yield from paradigms employing ASL perfusion fMRI. Supported by: NIDA RO1DA-10241, DA-15149, NIDA P60-DA-05186, Research Division, Dept of VA Med Center, and VA VISN 4 MIRECC and Alexander Foundation.

835 THE CB1 RECEPTOR ANTAGONIST SR141716 SELECTIVELY ALTERS EXTINCTION OF AN APPETITIVELY CONDITIONED BEHAVIOR

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Little is known about the neurobiological processes underlying extinction of aversive versus appetitive conditioning. For example, evidence suggests that blockade of cannabinoid CB1 receptors impairs extinction in fear conditioning paradigms; however, less is known about the role of CB1 receptors in extinction of appetitively-conditioned behaviors. Therefore, the present study examined the effects of the CB1 receptor antagonist SR141716 on extinction of appetitive conditioning in C57Bl/6 mice. Mice were trained to nose poke for the liquid nutritional drink Ensure under an FR1 schedule of reinforcement, and delivery of Ensure was paired with both a light and tone. After responding was well established, an extinction paradigm was introduced during which mice were pretreated with either 3.0 mg/kg SR141716 or vehicle. Subsequently, responding was reinstated in both groups by reintroducing the light and tone cues. Responding during extinction was initially increased (i.e., the extinction burst) and then decreased in vehicle-treated mice. In SR141716-treated mice, the extinction burst was significantly decreased relative to vehicle-treated mice. Responding during the cue-induced reinstatement session did not differ between the two groups. Therefore, whereas CB1 receptor blockade impairs extinction of conditioning with aversive stimuli, the CB1 antagonist SR141716 did not impair extinction in an appetitive task and attenuated the extinction burst. These data suggest that different neural mechanisms may underlie the extinction of appetitive versus aversive conditioning with the CB1 receptor playing a disparate role in extinction of these two behaviors. Supported by grants F32 DA019312, DA 002749, and P20 MD00175.

836 PRELIMINARY EVIDENCE OF HPA AXIS ACTIVATION AND PROLACTIN RELEASE BY ALCOHOL AND OPIOID ANTAGONISM IN HUMANS

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Recently animal models suggested substantial changes in hpa axis induced by alcohol administration. In addition NMDA and opioid receptor antagonism studies indicated modification of withdrawal and deprivation effects. Therefore we hypothesized similar increases in hormone level in alcohol consuming human subjects, possibly blocked by antagonism of glutamatergic or opioidergic neurotransmission. Ten healthy male and female human participants were challenged in four sessions by receiving either naltrexone orally, memantine IV, both agents or placebo. In a final step alcohol was administered orally (totally 0.6 g alcohol/kg). Blood samples were taken after naltrexone, memantine and alcohol application. Endocrinologic activity was monitored by measuring Prolactin, Cortisol and ACTH. Significant differences were seen in Cortisol and ACTH level after opioid blockade (p<0.05), while alcohol had no impact on these hormones. In contrast hyperprolactinemia was purely induced by alcohol itself (p<0.05). Neither naltrexone nor memantine led to any significant change. In conclusion alcohol induced hyperprolactinemia has substantial implication for sexual dysfunction in alcohol affected patients.

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837 COMBINED SUBSTANCE USE AND HIV PREVENTION FOR INCARCERATED ADOLESCENTS

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The purpose of this study is to test the feasibility of a substance use and HIV prevention school-based indicated prevention program that is adapted for use with 80 incarcerated male and female, Hispanic and African American adolescents. This population is extremely vulnerable to the combination of HIV/AIDS risk behaviors and substance use. Participants for the project are adolescents detained at 24-hour secure juvenile correctional facilities who attend on-site alternative high schools while incarcerated in Los Angeles County Probation Camps. The intervention combines two evidence-based interventions that target substance use and HIV risk behavior, respectively. The project consists of two phases. Phase one includes pilot study results of qualitative adolescent feedback on the intervention along with focus group feedback of school personnel and health educators who are implementing the intervention. The student evaluation provided students' perspectives on gender/cultural appropriateness, and whether the program helped them abstain from drug use and HIV risk behaviors. Themes that emerged during the focus group interviews of school personnel and health educators include program content, logistics and other implementation concerns. A description of how the phase two trial implementation is informed by phase one results is also presented. This project is supported by NIDA R21 DA018578.

838 PREDICTORS OF SUBSTANCE USE DISORDERS IN ADOLESCENT PSYCHIATRIC INPATIENTS

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Psychiatric and substance use disorders (SUD) may occur independently during adolescence; however, a significant degree of co-morbidity of these two types of disorders is seen, particularly with illness severe enough to warrant hospitalization. Multiple factors may contribute to this high rate of co-morbidity. Although SUD are common in adolescents, the prevalence of SUD in youth with a wide variety of psychiatric diagnoses requiring hospitalization is unclear. The purpose of this study was to examine rates of SUD in psychiatric inpatients (aged 12-18) at two major public psychiatric treatment centers for adolescents in Virginia. The goals were to characterize these populations and to determine unique and shared predictors of SUD. This was a retrospective chart review of inpatients admitted between July 2003 and June 2004 (n=636). Exclusion criteria were: age 18 years at time of admission, or meeting diagnostic criteria for moderate to profound (or unspecified) mental retardation, autistic disorder, or other major developmental disorder of childhood. Chi-square or ANOVA procedures were used to compare and contrast the populations on key variables among the 250 discrete variables included on the data extraction form. Logistic regression models were run with data from each of the sites separately and with data from all adolescents combined. Populations from the two facilities were similar in gender, racial composition, and average age at the time of admission. The rate of SUD in the combined populations was 28%. Older age, legal involvement, being sexually active, being diagnosed with a childhood disruptive disorder, and using tobacco (tobacco use quadrupled the risk) were all significant independent predictors of receiving a SUD at discharge. Screening for these predictors may facilitate detection of substance use in psychiatrically ill youth and may lead to development of better treatment strategies for co-morbidity in adolescent psychiatric patients.

839 DIFFERENCES BETWEEN IMPAIRED DRIVERS CONVICTED IN WET, MOIST AND DRY COUNTIES

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Background: A primary purpose for restricting the sale of alcohol is to reduce the secondary problems associated with alcohol consumption, such as DUI which is strongly correlated to the accessibility of alcohol (Cohen et al., 2001). Although restricting alcohol sales can be effective in reducing the number of DUI arrests, impaired driving continues to occur under this policy. Given the variability in access to alcohol, the purpose of this study was to examine whether those convicted of DUI in areas which partially or completely restrict alcohol sales differ from DUI offenders who are convicted in areas without these restrictions. Method: A total of 23,065 DUI assessment records from persons convicted of DUI in Kentucky were examined. The records were split into three groups based on the level of alcohol sales restriction of the county in which they were convicted: no alcohol sales restriction (wet county), partial alcohol sales restriction (moist county) and complete alcohol sales restriction (dry county). Data were analyzed using ANOVA and chi-square analysis. Results: DUI offenders convicted in wet counties scored higher on the alcohol screening instrument (AUDIT) than the other groups, whereas those convicted in dry counties scored higher on the drug screening instrument (DAST). Rates of substance dependence were significantly higher among those convicted in dry counties as compared to those convicted in wet counties (17.1% vs. 11.4%). In addition, those convicted in dry counties were slightly more likely to be male (83.1% vs. 79.6%), be a repeat offender (25.1% vs. 21.7%), and fail to complete their education or treatment program (28.4% vs. 20.6%) than those in wet counties. Implications: The study suggests that, on average, DUI offenders convicted in dry counties may be more drug-involved and have more severe substance related issues. Practitioners in these areas may face greater challenges in treating DUI offenders.

840 THE CONTEXT OF DRUG AND ALCOHOL USE AMONG SEX WORKERS IN PRETORIA, SOUTH AFRICA

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High unemployment and low education in South Africa have forced many women to engage in sex work to support themselves and their family. Anecdotal reports suggest that sex workers use alcohol and drugs to reduce the discomfort and anxiety in having to conduct sex work. However, substance use has been known to impair behavior and may increase the risk for other negative consequences, such as victimization. Thus it is important to examine the context of substance use in this population. We use data from an NIAAA-sponsored randomized trial of a woman-focused, culturally sensitive HIV prevention intervention for Black and Coloured sex workers in Pretoria, South Africa to examine frequency of use and dependence on alcohol and drugs, and to examine whether substance use is associated with conducting sex work and victimization by clients and main sexual partners. Two hundred eighty five female sex workers who reported alcohol use on at least 13 of the past 90 days were recruited from street outreach between April 2004 and December 2005. Data from the baseline interview show that in the previous month, 92% reported getting drunk at least once, 48% used marijuana, and 13% used crack. Twenty-seven percent reported daily marijuana use and 5% daily crack use. Women reported drinking 4 or more drinks an average of 10 days in the past month, with an average of 11 drinks per day on days they drank. Sixty-five percent were characterized as alcohol dependent and 41% as drug dependent. Alcohol and marijuana use were both associated with sexual victimization by clients, alcohol use was associated with sexual victimization by main sexual partners, and marijuana use was associated with physical victimization by main sexual partners. Women were no more likely to drink alcohol or use drugs on days they had clients. Findings indicate that substance use among sex workers increases their risk of victimization by both clients and boyfriends. Reducing substance use may reduce negative health consequences in this population.

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841 EFFECT OF ARIPIPRAZOLE ON ESCALATED METHAMPHETAMINE SELF-ADMINISTRATION IN RATS WITH AN EXTENDED ACCESS

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Previous research showed that self-administration of cocaine or heroin by rats gradually increased with extended access whereas it remained stable with short access. In the present experiment, self-administration of methamphetamine by rats with extended access was examined. Additionally, changes in the dopaminergic system in rats with extended access were probed with administration of aripiprazole, a partial D2 dopamine receptor agonist. Wistar rats were trained to self-administer methamphetamine (0.05 mg/kg/injection) in a one-hour session. After the acquisition of self-administration, the rats were divided into two groups. In one group (LgA rats), a session length was extended to six hours whereas it was kept to one hour in the other group (ShA rats). After 15 sessions of an escalation phase, the dose-response function of methamphetamine and the effect of aripiprazole (1, 3, 10 mg/kg, s.c.) on the dose-response function were examined under a progressive-ratio (PR) schedule. With six-hour access, LgA rats exhibited an escalating pattern of methamphetamine self-administration with significant increase achieved from session 5 compared with session 1. LgA rats maintained higher responding than ShA rats at all doses of methamphetamine tested under a PR schedule. The pretreatment with aripiprazole shifted the dose-response function of methamphetamine to the right in both LgA and ShA rats. However, the effect of aripiprazole was greater in LgA rats compared with ShA rats. Thus, the data suggest that decreased dopaminergic function in LgA rats is related to escalation in self-administration of methamphetamine under a prolonged access condition (Supported by NIDA grants DA-10072 to G.F.K.)

842 CHRONIC COCAINE EXACERBATES AIDS-RELATED DECLINE IN FINE MOTOR CONTROL IN THE SIV/MACAQUE MODEL OF AIDS

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Pig-tailed macaques were treated daily with saline (N=6), cocaine 1.7 mg/kg i.m. (N=6) or cocaine 3.2 mg/kg i.m. (N=5) for at least two months prior to infection with Simian Immunodeficiency Virus (SIV delta B670). The monkeys were trained on a behavioral battery including measures of psychomotor speed, gross locomotor activity and fine motor control. Cocaine was administered after daily behavioral testing was complete. Chronic cocaine administration exacerbated the known decline in fine motor control following SIV infection. The coordination of both hands necessary for performance of the bimanual motor skills (BMS) task was impaired following SIV infection, cocaine 1.7 mg/kg/day and cocaine 3.2 mg/kg/day, and there was a significant interaction between SIV and cocaine. Further, cocaine's effects were dose-dependent in that animals receiving 1.7 mg/kg/day and 3.2 mg/kg/day were more impaired following SIV infection than SIV-infected animals receiving saline, and monkeys receiving 3.2 mg/kg/day were significantly more impaired than monkeys receiving 1.7 mg/kg/day. Performance of the other measures of motor and psychomotor performance, including simple reaction time, choice reaction time, stop-signal reaction time, and gross motor activity, were not different between the groups. The BMS task is among the most sensitive measures of impairment in function used in the SIV/macaque model. Performance of the BMS task is likely impaired by dysfunction in a variety of brain regions and not related to specific brain areas. Performance of tasks such as simple reaction time and stop-signal reaction time are heavily dependent on intact frontal cortical and striatal brain regions. Cocaine did not change the expected decline in function in these tests. Together these results suggest that cocaine and SIV interacted to exacerbate the expected decline in CNS function.

843 GENDER DIFFERENCES IN SMOKING EXPECTANCIES AND THE RELATIONSHIP OF EXPECTANCIES TO AMOUNT OF SMOKING

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Beliefs about the effects of smoking are correlated with level of smoking and may play a role in relapse after smoking cessation. Participants (n=59) in the current study were 27 male and 32 female smokers recruited into a placebo-controlled clinical trial to examine selegiline hydrochloride as a pharmacological aid for smoking cessation. Smoking expectancies were assessed at baseline using the Smoking Consequences Questionnaire – Adult version (SCQ-A). No gender differences were found for demographic variables (e.g., age) nor for most smoking variables including level of smoking, plasma cotinine level, or level of nicotine dependence. Female smokers reported a longer duration of smoking (M=32.54, SD=10.34) than male smokers (M=25.67, SD=11.60; p<.05). Male and female smokers differed significantly only on expectancies related to negative affect reduction with female smokers reporting stronger endorsement (p<.05); however, this difference became nonsignificant after co-varying for duration of smoking (p=.14). Expectancies related to stimulation, weight control, craving, and negative social impression were significantly associated with amount of smoking for both genders (ps<.05) while negative affect reduction and negative physical feelings beliefs were also associated with smoking for women. Linear regression analyses demonstrated that for men, negative social impressions and addiction beliefs accounted for a significant amount of variance (total R²=0.88, p<.001) while for women addiction and stimulation beliefs accounted for a significant amount of variance (total R²=0.69, p<.001) in current smoking. Based on these results, information about the ways that expectancies relate to smoking for men and women may be used to develop, enhance, or tailor intervention efforts with the goal of increasing success at cessation and preventing relapse. Supported in part by NIDA grants R01-DA-15757 and K02-DA-16611 (to TPG), and pilot funds from the Yale Transdisciplinary Tobacco Use Research Center (to AHW).

844 BRAIN IMAGING STUDY OF ORIENTATION AND MOTOR COORDINATION IN REGULAR USERS OF MARIJUANA

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Heavy use of marijuana is claimed to damage critical skills related to attention, memory and learning. There is evidence of damage to short term memory, visual scanning and attentional shifting in regular smokers of marijuana. Chronic use of marijuana is also linked to impaired motor skills and may affect driving safety. We have used a virtual reality maze task requiring orientation and motor coordination with 12 regular users of marijuana. Participants smoked low nicotine cigarettes (0.1 mg) with either 13 mg Delta9-Tetrahydrocannabinol (THC), 17mg THC or without THC. They were scanned in 2 Positron Emission Tomography (PET) scans using [18F] Fluorodeoxyglucose (FDG). They performed the virtual reality maze task, in one session after smoking a cigarette with 17 mg of THC and on the second session after smoking a cigarette without THC. Results showed that smoking cigarettes with 17mg THC increased heart rate and blood pressure and it was rated as pleasurable and satisfying. Regular marijuana smokers under 17 mg THC hit the walls more often on the virtual reality maze task than under cigarettes without THC or cigarettes with 13mg THC. Analysis of the brain imaging results using Statistical Parametric Maps (SPM2) showed that performance on the task under 17mg THC activated areas that are responsible for motor coordination and attention, the middle and medial frontal cortices and anterior cingulate, and deactivated areas responsible for visual integration of motion in the Occipital lobe. These findings imply that marijuana affects cognitive-motor skills and brain mechanisms that modulate coordinated movement and driving.

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- 845** MEASURING SUBSTANCE USE OUTCOME IN DUALY DIAGNOSED PATIENTS: A COMPARISON OF THREE METHODS
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Objectives: Patients who enter drug abuse treatment studies frequently abuse more than one drug. Measuring substance use outcomes in these individuals can represent a challenge. Two of the most common methods used are measuring 1) days of any substance use and 2) days of use of the individual's "drug of choice." Method: As part of a randomized controlled trial comparing Integrated Group Therapy (IGT) to Group Drug Counseling (GDC) in patients with bipolar disorder and substance dependence, we compared different measures of substance use treatment outcomes. Our first method (for our primary outcome analysis) used "days of any substance use." We compared this approach to the results obtained by using "preferred drug" (according to a self-report questionnaire in which patients were asked to name their preferred drug) and "the substance that caused the most problems" (according to the Addiction Severity Index (ASI) interview). Results: All three methods showed that patients in IGT used fewer days than patients in GDC, both during the 5-month treatment period and the 3-month follow-up. We found the strongest between-treatment group differences during treatment for the use of any substance, followed by the ASI "problem" substance, then the "preferred" substance. During follow-up, days of any substance use again showed the strongest treatment between-group difference, but this was followed by preferred substance, then problem substance. Further, substance use decreased over time only when using days of any substance use. Interestingly, IGT patients used the preferred substance on more days than the problem substance, whereas GDC patients used their problem substance on more days than their preferred substance. Conclusions: All three measures of substance use showed that IGT patients had better outcomes than GDC patients in this treatment outcome study for patients with bipolar disorder and substance dependence. However, since many patients use more than one substance, results may vary depending on the substance use outcome measure used.
- 846** THE ANTINOCICEPTIVE EFFECT OF DELTA-9-Tetrahydrocannabinol IN THE ARTHRITIC RAT INVOLVES THE CB2 CANNABINOID RECEPTOR
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CB2 receptor activation results in antinociception in animal models of acute, neuropathic, and inflammatory pain. We evaluated the role of the CB2 receptor in mechanonociception in non-arthritic and arthritic rats. The antinociceptive effect of THC was determined in rats following administration of the CB1 receptor-selective antagonist, SR141716A, and the CB2 receptor-selective antagonist, SR144528. Male Sprague-Dawley rats were rendered arthritic using Complete Freund's Adjuvant (CFA) and tested for mechanical hyperalgesia using the paw-pressure test. Arthritic rats had a baseline paw-pressure of $83 \pm 3.6g$ versus a paw-pressure of $177 \pm 6.42g$ in normal rats. Rats were injected with SR144528 or SR141716A (5 mg/kg; i.p.) in 1:1:18 (ethanol:emulphor:saline) vehicle and tested 1 hr later for mechanical nociception. THC (4 mg/kg, i.p., a non-cataleptogenic dose) in 1:1:18 vehicle was administered 30-min prior to testing. %MPE was determined where $\%MPE = \frac{[test(g) - baseline(g)]}{500g - baseline(g)} \times 100$. All results were expressed by mean \pm SEM and analyzed using ANOVA with comparisons using Dunnett's test. SR144528 significantly attenuated the antinociceptive effect of THC in the arthritic rats (% MPE reduced from $89 \pm 6\%$ to $27 \pm 14\%$), but not in the non-arthritic rats (% MPE $90 \pm 5\%$ versus $83 \pm 6\%$, respectively). SR141716A partially, but significantly attenuated THC-induced antinociception in both the non-arthritic and arthritic rat. Administration of SR141716A or SR144528 alone did not result in a hyperalgesic effect as compared to vehicle. Our results are consistent with findings that the CB2 receptor plays a role in cannabinoid-mediated antinociception, particularly in models of chronic inflammatory pain. This work was supported by National Institute on Drug Abuse Grants # DA-05274, DA-07027, and 5P01DA-09789.
- 847** TECHNOLOGY TRANSFER TO COMMUNITY-BASED TREATMENT: COMPARISON OF FEASIBILITY AND ACCEPTABILITY OF CONTEXT-TAILORED TRAINING VS. STANDARD WORKSHOP
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Little is known about effective transfer of research-based interventions to addiction treatment providers. Standard continuing education workshops lack support for practice, implementation, and maintenance of skills. This paper compares feasibility and acceptability of an alternative training model, Context Tailored Training (CTT) with the traditional workshop model as part of a Motivational Interviewing training outcome study. In CTT, 5 training sessions are spaced at biweekly intervals and conducted in a community program. Timing and manner of training core elements and modules is guided by trainee goals. Between training sessions, a "simulated patient" meets with each trainee and records a clinical interview upon which trainees receive written feedback. Trainers and trainees identify an individual to serve as "champion" for the intervention in the agency. Feasibility issues specific to CTT are: hiring, training and retention of actors as simulated patients; costs and perceived utility of providing feedback on practice interviews; and replicability of a tailored model across sites. We will also address issues of comparative feasibility between CTT and workshop, including: recruitment and retention of trainees, costs of and barriers to implementation; and trainee satisfaction. Data will be presented based on CTT at 4, and workshop at 2, agencies. Recruitment for both methods is high, but retention is better in workshop training. CTT introduces additional costs, i.e., travel and personnel. The methods have some shared and some non-shared advantages and disadvantages. Workshop and CTT participants do not differ in their satisfaction with training. *Supported by NIDA Grant #DA016360(Baer - PI)
- 848** MALINGERING DETECTION IN PSYCHIATRIC INPATIENTS: AN EXPLORATORY STUDY
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Malingering research in psychiatric inpatients is limited, demonstrates inconsistent base rates, 5-50% (Bagby, 1994), and the reasons why patients malingering have never been determined. This study established a malingering base rate of 53% using psychiatric inpatients (N=60) from a large metropolitan hospital. Nearly 78% of this population was diagnosed with a substance use disorder. The Structured Interview of Reported Symptoms (SIRS) and The Structured Clinical Assessment of Malingering (SCAM), a face valid malingering interview, were administered on day of discharge. Most frequent malingered symptoms were suicidal ideation, voices and depression. Reasons for malingering included wanting detoxification, the sentiment that doctors don't believe them, and homelessness. The modal malingering was 35 to 45 years of age and reported a recent family fight. Malingering is common within the inpatient population and patients are far more willing to reveal malingering than expected than is psychometrically detected by the SIRS. This research was supported by the Pennsylvania Department of Health.

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- 849** AN 8-[N-(4'-PHENYL)-PHENETHYL CARBOXAMIDO] ANALOGUE OF CYCLAZOCINE
M. Wentland(1), M. VanAlstine(1), R. Kucejko(1), R. Lou(1), D. J. Cohen(2), A. L. Parkhill(2) and J. M. Bidlack(2), (1) Rensselaer Polytechnic Institute, Troy, NY and (2) University of Rochester, Rochester, NY
A novel analogue of cyclazocine has been made where its phenolic hydroxyl group was replaced by an [N-(4'-phenyl)-phenethyl]-carboxamido appendage. This compound was designed to test our hypothesis that opioid receptors contain a putative hydrophobic pocket complementary to the 8-substituent of certain 2,6-methano-3-benzazocines. Target compounds were made where the distance between the N of an 8-carboxamido group and an aryl group varied as well as the nature of the aryl group itself. The target having a 4-biphenyl appendage, known to be a privileged functional group for recognition to G protein-coupled receptors, and a two methylene spacer displayed very high affinity for the mu ($K_i = 0.30$ nM), delta ($K_i = 0.74$ nM), and kappa ($K_i = 1.8$ nM) opioid receptors. As determined in [³⁵S]GTPgammaS assays, this new analogue of cyclazocine was shown to be a pure antagonist at the mu receptor and agonists at the delta and kappa receptors (Supported by NIDA DA12180 and KO5-DA00360).
- 850** CHRONIC MARIJUANA USERS SHOW DECREASED INTEGRITY IN NEURAL PATHWAYS ASSOCIATED WITH EXECUTIVE FUNCTION AND MEMORY
M. J. Wesley(1), C. A. Hanlon(1), L. B. Livengood(1), R. Kraft(2), J. Zhu(3), C. Wyatt(4) and L. J. Porrino(1), (1) Dept. of Physiology and Pharmacology, (2) Dept. of Biomedical Engineering, (3) Dept. of Radiology and Radiation Oncology, Wake Forest U. School of Medicine, NC and (4) Virginia Tech, VA
The inability of marijuana smokers to perform accurately on tests of frontal executive processing is well-known. Recent data from our laboratory has demonstrated that chronic marijuana users are significantly impaired on the Iowa Gambling Task, a paradigm which examines decision making and response inhibition. The behavioral abnormalities in chronic marijuana smokers were shown by Functional MRI to be associated with significant increases in right dorsolateral and ventrolateral prefrontal cortex (PFC) activity. To examine the possibility that compromised myelinated neuron fiber pathways might account for the observed discrepancy between increased brain activity and poor performance, we collected diffusion tensor imaging (DTI) data on a subset of this same cohort of subjects (13=users; 6=controls). Overall, there were significant decreases in fractional anisotropy (FA), a measure of fiber orientation coherence in white matter, throughout the brains of marijuana users compared to controls ($p < 0.05$). These marijuana-related changes in FA were present in distributed neural regions including the genu and splenium of the corpus callosum, the internal capsule, and the occipital and prefrontal radiata bilaterally. A prominent cluster of FA reduction in marijuana users was in the lateral prefrontal radiations, carrying efferent and afferent information to the dorsolateral and ventrolateral PFC ($p < 0.01$). While these changes in FA were bilateral, the spatial extent of FA reduction was greater on the right prefrontal radiations, consistent with our functional data and suggestive of some laterality differences in these populations. Supported by DA07246 (MJW), DA10230 and DA06634 (LJP).
- 851** SOCIAL MARKERS OF MATURATION AND THE TRANSITION TO YOUNG ADULTHOOD IN A CLINICAL SAMPLE OF ADOLESCENTS TREATED FOR SUBSTANCE USE DISORDERS
M. K. White, Chestnut Health Systems, Bloomington, IL
The experience of making the transition from adolescence to young adulthood brings with it some of the most significant events of a lifetime over a period of just a few years. In particular, most adolescents experience some combination of socially significant achievements, also called social maturation markers (SMM), including achievements in education, employment and economics, and family. Achieving these SMM is associated with substantial life change, which can be stressful and lead to negative outcomes, especially for adolescents who have been treated for substance use disorders and are at high risk for relapse. This study (1) developed a Theory of Adolescent Developmental Pathways (ADP) and (2) compared the usefulness of seven alternative models based on three theories for predicting the impacts of SMM on adolescents' substance use and illegal activity outcomes to see which models improved what could be explained with background characteristics only. Data are from the Cannabis Youth Treatment (CYT) project, a multisite randomized experiment that studied 600 adolescents from four outpatient adolescent substance abuse treatment clinics and collected data through 30-months after treatment intake. Three of the seven models offered significant improvement over the model with background characteristics only for predicting outcomes. Change in social environment was the leading predictive indicator of both substance use and illegal activity outcomes. This suggests targeting indicators of healthy developmental pathways and using continuing care models to improve long-term outcomes.
- 852** LIFE MEANING AS POTENTIAL MEDIATOR OF 12-STEP PARTICIPATION BENEFITS ON STABLE RECOVERY FROM POLYSUBSTANCE USE
W. White(1) and A. Laudet(2), (1) Chestnut Health Systems, Bloomington, IL and (2) National Development and Research Institutes, New York, NY
Twelve-step participation is useful in sustaining recovery. Several domains including social support, motivation and coping have been examined as mediating this relationship. Spirituality, a key aspect of 12-step recovery, remains under-investigated in addiction recovery research. In particular, life meaning/purpose has not been systematically examined, nor has the association among 12-step participation, meaning and recovery. Using a repeated measures design, we investigated these associations and tested the hypothesis that meaning mediates the effects of 12-step participation on recovery. Former polysubstance users in recovery from one month to 10+ years recruited from the community in NYC (preliminary N = 207), mostly inner-city residents with long and severe history of crack use, were interviewed 3 times at yearly intervals (BL, F1 and F2). In bivariate analyses controlling for baseline level of the outcome, greater 12-step meeting attendance and involvement in 12-step recovery (e.g., having a sponsor, working the steps) in the first year of the study predicted greater F1 meaning, and greater F1 meaning in turn increased the likelihood of sustained recovery at F2 (abstinence for the year between F1 and F2). Multiple regression results from the stricter Baron and Kenny mediation test were in the predicted direction but did not reach significance in this preliminary dataset. Life meaning appears to be an important recovery-promoting factor and may play a part in bringing about the benefits of 12-step participation on recovery. Additional research is indicated to elucidate this process and to examine the possible role of life meaning as a common factor across recovery paths - spiritual, religious and secular. Funded by National Institutes on Drug Abuse Grant R01 DA14409 and by the Peter McManus Charitable Trust.

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853 RESPIRATORY DEPRESSION DURING METHADONE INDUCTION

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In comparison to street heroin use, participation in methadone maintenance is associated with decreased mortality. However, there is an elevated mortality risk during the first 2 weeks of methadone treatment. We have previously shown significant respiratory depression amongst a small sample of participants commencing methadone treatment. The present study was designed to describe the changes in plasma R-methadone concentration during the first 2 weeks of induction and how these relate to changes in respiration, pupil diameter and withdrawal severity. On each of the first 14 days of methadone treatment, both immediately prior to dosing and 3 hours later (the time of peak concentration), blood samples were collected for analysis by LC/MS/MS and measures made of opioid effect and opioid withdrawal. The sample comprised 10 heroin users commencing methadone treatment; dose changes were determined by treating physicians according to usual clinical practice. There was a correlation between dose and both peak ($r=0.72$) and trough ($r=0.88$) plasma R-methadone concentrations. However, consistent with the long half-life of R-methadone, plasma concentrations continued to rise for a number of days after each dose change. There was evidence of some degree of respiratory depression in all patients and a clinically significant degree (respiratory rate less than 8 breaths per minute or oxygen saturation less than 96%) in 2 out of 10 patients. In one, this occurred following dose increases, while in the second the dose was very low and had not increased for several days previously. For the group as a whole, the standard pre-dosing clinical measures of withdrawal severity, sedation and pupil diameter were not predictive of respiratory depression at time of peak concentration. The results show that respiratory depression is not necessarily uncommon in patients commencing methadone treatment and any reduction in mortality rates would come at the cost of markedly increased patient monitoring or increased dosing frequency.

855 WITHDRAWN

854 EFFECTS OF CHRONIC METHAMPHETAMINE USE IN THE PREGNANT RAT AND HER LITTER

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These studies were designed to establish (+)-methamphetamine (METH) effects in pregnant rats and their fetuses as an aid to our understanding of human health effects. METH abuse by human mothers can lead to intrauterine growth restriction, premature delivery, and learning disabilities. To add to the problem, it is a popular drug among women of child-bearing age. For the studies, timed-pregnant Sprague-Dawley rats were implanted on gestational day 7 (GD 7 - prior to organogenesis) with sc osmotic minipumps that were prepared to deliver saline or METH (3.2, 5.6, 10, and 17.8 mg/kg/day). Ranges of mild to lethal (at 17.8 mg/kg/day) effects were found. METH-induced locomotor analysis was performed on the dams from GD 7 - GD 21. Maternal weight changes were also assessed. At GD 21, the dams and pups were sacrificed and the brains and sera were collected for determination of METH and (+)-amphetamine (AMP) concentrations. Complex dose-response relationships were observed for dam's weight during the study, as well as for METH and AMP concentrations in the brains and sera of both the dams and fetuses on GD 21. No differences were found in the litter weight on GD 21. In conclusion, the results of these studies provide the data needed for establishing an experimental pregnancy model in rats for studying monoclonal antibody medications for use in preventing adverse health problems in pregnant females and their fetuses. This research is supported by NIDA DA07610.

856 IN VIVO EFFECTS OF INSULIN ON DOPAMINERGIC FUNCTION AND AMPHETAMINE PHARMACOLOGY

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Recent studies suggest that the clearance of dopamine (DA)-mediated by the high-affinity, presynaptic DA transporter (DAT)-is regulated by insulin. Receptors for insulin are co-localized with DAT on midbrain DA neurons and have been shown to maintain DAT cell surface expression in vitro. Hypoinsulinemic animals manifest a reduced clearance of DA and a resistance to the behavioral effects of amphetamine (AMPH)-like stimulants. To verify the novel ability of insulin to modify DAT function, blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging (fMRI) was used to measure the response of insulin-depleted rats to AMPH. One week after depletion of insulin with a single injection of streptozotocin (STZ), male Sprague-Dawley rats underwent multi-slice gradient echo fMRI throughout the forebrain at 9.4 Tesla. AMPH (3 mg/kg, ip) stimulated a robust BOLD signal increase within the caudate putamen of untreated control subjects, and this effect was markedly attenuated in STZ-treated, hypoinsulinemic rats. The diminished BOLD response to AMPH was not apparent in the frontal cortex. Parallel studies using high-speed chronoamperometry demonstrated a potent reduction in AMPH-stimulated DA efflux in the striatum of STZ-treated rats. Collectively, these data are consistent with those from previous studies that suggest insulin can regulate DAT and are among the first to support this concept in vivo. Ongoing studies are examining how the regulation of DA systems by insulin is modified after repeated exposure to AMPH. Investigation of this unique mechanism for altering DA clearance capacity by insulin will provide a better understanding of the neural underpinnings of AMPH action. Targeting insulin signaling pathways to modulate DA homeostasis may also provide promising pharmacotherapeutic strategies for psychostimulant dependence. Supported by EB002326 and RR17799 (JCG), DA018992 (LCD) and DA14684 (AG). Equal author contributions by LCD, MJA and AG.

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857 FIRST-YEAR RESULTS OF THE WHOLE DAY FIRST-GRADE PROGRAM

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We present results from a randomized trial of a classroom-based universal prevention program, the Whole Day First Grade Program (WD), targeting early aggressive, disruptive behavior and poor academic achievement, two antecedents of substance use and mental disorders. WD integrates classroom behavior management, family/classroom partnerships, and teachers' instructional practices around reading. The trial is carried out in 24 1st grade classrooms in 12 schools with 3 consecutive cohorts of 1st graders. Teachers and students were randomized to an intervention or standard control classroom (SC). We hypothesize that improving teachers' practices will improve classroom environment which will positively impact student behavior and achievement, and that mastery in these areas will reduce substance use and mental health disorders later. We report results for the 1st cohort from independent observations of off-task behavior (n=490). Data were collected at baseline (fall of 1st grade) and in spring of 1st grade. The outcome was the child's average off-task score in a time sampling framework; during each minute the observer coded child behavior. Each child's average score was predicted based on child characteristics, classroom characteristics, and time (morning vs. afternoon). We used multilevel modeling with school as a blocking factor including covariates and random effects at the child and classroom levels with their interactions, correctly adjusting significance levels for the classroom randomization. At baseline there were no significant differences between WD and SC classes on off-task behavior, indicating successful randomization. By end of year we found boys' off-task behavior was reduced by more than half from 21% to 9% for each 10-second time interval in the afternoons, a less structured setting than mornings (mixed model F-test is $F(1,8,8.27)=4.60$, $p=.06$). These early results demonstrate effectiveness in reducing early aggressive/disruptive behavior, a proximal outcome directly associated with substance use disorders.

859 THE IMPACT OF NEIGHBORHOOD DISORGANIZATION AND SOCIAL CAPITAL ON ADOLESCENT DRUG USE, DRUG DEPENDENCE AND ACCESS TO DRUG TREATMENT

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The purpose of this research is to test whether community-level risk factors, specifically neighborhood disorganization and social capital, are associated with adolescent drug use, dependence and access to treatment. There is limited research on community-level risk factors for drug use and dependence, few of which used adolescent samples. Communities have been primarily understood in terms of drug exposure opportunities, which tells us more about drug use than drug addiction. Previous research has not determined whether community-level factors, beyond geographic availability of services, influence access to substance abuse treatment. This is a secondary analysis of data from the 1999 and 2000 National Survey on Drug Use and Health (NSDUH) using only youth between the ages of 12 to 17 years of age. Neighborhood disorganization was self-reported by youth in response to eight items and ten items measured social capital. Substance dependence is based on a series of questions regarding symptoms and impairment that are consistent with the criteria specified in the DSM-IV. A little more than half of the youth reported never using drugs (54.28%), 41.10% reported lifetime drug use and 4.62% (n=1,762) were drug dependent in the past year. After controlling for individual and family level characteristics, medium and high levels of social capital were negatively associated with drug use and drug dependence. Social capital was unrelated to access to drug treatment. Neighborhood disorganization was positively associated with drug use, drug dependence and access to treatment. Community-level characteristics are associated with adolescent drug use, dependence and access to drug treatment; even after controlling for individual- and family- level characteristics. Identifying community-level risk factors may enhance the development of effective adolescent intervention programs; as well as inform strategies to address the unmet need for adolescent drug abuse treatment.

858 THE INFLUENCE OF CIGARETTE SMOKING IN OPIOID-MAINTAINED PREGNANT WOMEN

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Prenatal tobacco exposure is associated with several medical and developmental consequences, including increased mortality and low birth weight. At present little is known about the consequences of tobacco smoking in opioid maintained pregnant women and the impact on neonatal outcome measures. This study examined prospectively the effects of cigarette smoking in 128 synthetic opioid maintained pregnant women and their neonates in a prospective way. Tobacco exposure was measured by the Fagerström Test for Nicotine Dependence pre and post partum. In addition we investigated the actual cigarette consumption based on maternal self-report. The mean age of the study participants was 25.66 years (range 16-37) with a mean duration of opioid dependence of 5 years. Fifty percent of the women received oral slow release morphine, 37.5% methadone and 12.5% buprenorphine. The first contact to the addiction clinic took place during second trimester (mean=17.5 week of pregnancy, $SD=9.54$). At that time 98.4% of the women were smokers with a mean consumption of 21.22 cigarettes per day (two participants non-smokers). Based on our results a significant reduction of cigarette consumption was determined at post partum ($p<0.001$), with a mean consumption of 13.74 cigarettes per day. In addition we found a lower degree of nicotine dependence to be associated with significant higher neonatal birth weight when compared to heavy nicotine dependence ($p=0.045$). But our results did not show neonatal head circumference or APGAR-scores to be related to the amount of cigarettes. Moreover, we did not find significant effects of cigarette consumption and severity of nicotine dependence in regard to the severity of neonatal abstinence syndroms (NAS) or duration of neonatal treatment. These findings have to be carefully interpreted, as tobacco exposure is based on self-report data. More accurate measurements will be necessary in order to investigate the specific role of nicotine in opioid-exposed infants.

860 CHILDHOOD ADHD AND LATE ADOLESCENT PSYCHOSOCIAL FUNCTIONING

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Although some exceptions exist, there is a converging body of studies suggesting that ADHD during childhood confers an elevated risk for later drug use and substance use disorders in adolescence. However, it is less clear the extent to which childhood ADHD affects adolescent functioning across a range of psychosocial domains other than drug abuse. We present findings from our late adolescent (mean age 19.7) follow-up (wave 4) assessment from the University of Minnesota ADHD Prospective Study. ADHD-only (N=29), ADHD-externalizers (CD or ODD) (n=90), and control (n=93) children recruited from the community have been regularly assessed during an 8-year span. Our findings focus on parent and youth measures of psychosocial functioning as a function of group status. After controlling for several possible confounds (gender, SES, single-parent status, and substance use disorder history), the findings indicate a consistent pattern of poorer functioning across all domains (aggression, conduct, interpersonal, school success, physical health, mental health, and legal) among youth in the ADHD-externalizing group when compared to controls. No group differences were found for the ADHD-only vs. control comparisons. Also, psychosocial outcomes were not moderated in the ADHD groups by exposure to psychostimulant medication during childhood. Implications of the findings in light of the community-based ADHD sample will be discussed.

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861 DOES PERSONALITY PREDICT PERFORMANCE ON BEHAVIORAL TASKS OF INHIBITORY CONTROL IN COCAINE ABUSERS?

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Personality accounts for a meaningful portion of the variance in motivation for substance use and sensitivity to the effects of drugs. The current study examines differences in personality between cocaine and control subjects and the association between personality and behavioral deficits in inhibitory control as a function of group. Forty-two cocaine abusers and 111 control subjects were administered the Multidimensional Personality Questionnaire (MPQ); a subgroup completed two performance-based measures of inhibitory control - the Attention Network Task (ANT; $n = 19$ cocaine, 95 controls) and the color-word STROOP ($n = 41$ cocaine, 108 controls). Results from MANOVA: indicated that cocaine abuse is inversely associated with the superfactor positive emotionality (explained by lower scores on well-being, achievement, and social closeness) and the control subscale (of the constraint superfactor), $d_s = -.61$ to $-.81$; and positively related to the stress reaction and alienation subscales (of the negative emotionality superfactor), $d_s = .92$ and $.86$. Cocaine abuse was also associated with significantly greater conflict on the ANT. Results from regression models indicated that, for cocaine abusers only, higher MPQ constraint predicted greater conflict on the ANT ($\beta = .41$, $p < .05$), and higher MPQ positive emotionality predicted poorer inhibitory control on the STROOP ($\beta = -.44$, $p < .01$). The MPQ results in the current study are consistent with previous studies demonstrating relationships between drug abuse disorders, disinhibition, and negative affect. The MPQ-inhibitory control correlations further suggest that self-reported self-control and positive emotionality in cocaine addicted subjects is related to less control (resolution of cognitive conflict) on performance-based measures, possibly implicating impaired insight to deficits in drug addicted individuals. This interpretation is consistent with documented prefrontal cortical structural and functional deficits in drug addiction.

863 IMAGING DOPAMINE RELEASE IN ALCOHOL AND COCAINE ABUSE

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Background: Imaging has demonstrated abnormalities in the dopamine (DA) system in cocaine, amphetamine abuse and stress induced abnormalities in alcoholism. We used PET to examine D2 binding potential (BP) and extracellular DA release (DArel), as well as stress-induced hormone response, among individuals with and at risk for alcohol dependence, and with cocaine dependence. Methods: Ten alcoholic and 8 healthy adults (mean age 45) underwent two [¹¹C]raclopride PET scans: one preceded at -5min. by IV saline, and the second one preceded at -5min. by 0.3mg/kg IV amphetamine (AMP). BP and DArel in the ventral striatum (VS), putamen, and caudate nucleus was assessed for both scans. Subjects also underwent the Trier Social Stress Test (TSST), with simultaneous measurements of plasma cortisol, prolactin, beta-endorphin, and adrenocorticotropin. In a second study, 30 healthy adults (age 18-27), with and without family histories of alcoholism, were studied as above. In a 3rd study, 17 chronic cocaine users (mean age 42) were compared to 12 healthy controls (mean age 36). Results: Alcoholics had lower baseline BP, as well as post-AMP BP, in putamen, caudate, and VS ($p < 100\%$) in the anterior and posterior putamen ($p < 100\%$ in cocaine and less (20-70%) in alcohol abuse. Measurements of the DA system in alcoholic and at-risk populations are indicated to elucidate the pathophysiology of alcohol use disorders.

862 RELATIONSHIPS BETWEEN EMERGENCY ROOM UTILIZATION AND MEASURES OF ALCOHOL USE BASED ON AN INTENSIVE SCHEDULE OF RANDOM BREATH SAMPLE COLLECTIONS AND SELF-REPORTS IN C. J. Wong, K. Broadwater, P. Nuzzo, M. Needham, M. Fingerhood, G. Bigelow, D. Svikis and K. Silverman, Johns Hopkins University, Baltimore, MD

This study examined the relationships between emergency room utilization and measures of alcohol use based on an intensive schedule of random breath collections and self-report assessments in homeless alcohol dependent adults. Homeless and unemployed alcohol dependent adults ($N = 124$) were enrolled in a randomized three-group study that evaluated an employment-based treatment for alcohol dependence. Participants were enrolled in a model workplace in which they received job skills training every weekday for 6 months. Participants in two of the groups received voucher pay for attendance and work in the workplace. Breath sample collections and assessments of past 24-hour self-reported alcohol use were scheduled an average of 2 per week per participant at random times between 9 am and 5 pm throughout each week. Participants received \$35 for each breath sample collected. Self-reports of hospital and emergency room utilization were assessed throughout the study. Thirty-one (31%) percent of the participants reported attending an emergency room and reported an average of 2.2 emergency room visits during the study. Sixty-one (61%) percent of scheduled breath samples were collected, and 31.3% of breath samples were positive ($BAL \geq .003$ g/100mL) for alcohol. Bivariate correlations showed significant relationships between the number of emergency room visits and alcohol positive breath samples ($r = .36$; $p < .001$), percentage of breath samples with a BAL greater than .05 ($r = .37$; $p < .001$), mean BAL ($r = .36$; $p < .001$), self report of drinking alcohol prior to breath sample collection ($r = .32$; $p < .001$), and self-reported heavy drinking (≥ 5 drinks per day; $r = .36$; $p < .001$). This study provided a rare and intensive assessment of alcohol use and emergency room utilization in homeless alcohol dependent adults over an extended (6 mo) period. Emergency room use was high and was significantly related to indices of alcohol use.

864 EMERGENCY DEPARTMENT VISITS INVOLVING BUPRENORPHINE ABUSE: 2003-2005

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Introduction: Buprenorphine is a Schedule III partial mu-opioid agonist that has long been used as an analgesic and, since 2003, as a treatment for opioid dependence in the U.S. Currently, a more restrictive scheduling is being considered based primarily on reported abuse in France and India. Relatively little is known, however, about the incidence of buprenorphine abuse in the U.S. The purpose of this analysis was to review a national adverse drug event related surveillance system for data on buprenorphine abuse. Methods: Data were obtained from the Drug Abuse Warning Network's Internet-based query system which provides authorized users access to unweighted data on drug-related Emergency Department (ED) visits reported by nationally representative sample of hospitals with 24 hour emergency departments. We analyzed cases reported for all opioids and for those involving buprenorphine only between 6/03 and 10/05. For cases involving probable drug abuse (categorized as "Other" per the revised DAWN case type hierarchy) we assessed the chief complaint, patient demographics, route of administration, and patient disposition. Results: Of the 321 buprenorphine cases reported to DAWN between 6/03-10/05, 159 (49.5%) involved probable drug abuse. These cases represented 0.43% of all probable drug cases involving opioid analgesics reported to DAWN during this period. Patients were predominantly Caucasian (70%), male (57.2%), and between 25-44 years of age (47%). The most commonly reported chief complaints were: withdrawal (86 complaints out of 286 or 30%), digestive problems (19.2%), respiratory conditions (17.1%) and psychiatric conditions (9.8%). Of the 48 cases for which a route of administration was reported, 90% indicated oral, and 10% injection. Analyses of case disposition data indicated that the majority (64%) were released to home. Conclusions: Buprenorphine abuse-related ED visits represented an extremely small percentage of all opioid analgesic abuse-related ED visits from 6/03 to 10/05, and primarily involved Caucasian males in young to mid-adulthood.

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865 TEMPORAL DISCOUNTING OF COCAINE AS A REINFORCER BY RHESUS MONKEYS

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A delay between a behavior and its reinforcer typically weakens behavior. This phenomenon, temporal discounting, has made substantial recent contributions to our understanding of drug abuse. However, temporal discounting of actual drugs as reinforcers has not been studied. The purpose of this study was to begin to examine temporal discounting in monkeys whose lever pressing was maintained by cocaine. Subjects were prepared with double-lumen i.v. catheters and allowed to choose between two doses of cocaine injected as a consequence of pressing two levers under a fixed-ratio 1 schedule. After sampling each injection, 16 choices were available daily in trials spaced by 10 minutes. One dose, the delayed dose, was always 0.2 mg/kg/injection and was delivered with an unsignaled delay (0-300 secs) between lever press and injection. The other dose, the immediate dose, varied between 0.012 and 0.4 mg/kg/inj and was injected immediately after the lever press. Dose and delay conditions were in effect for at least four consecutive sessions and until choice was stable for three consecutive sessions. Next, lever/reinforcer pairings were reversed until the same criteria were met. For each delay, the ED50 of the immediate dose was calculated as a measure of the value of the delayed dose. Temporal discounting functions were established using the hyperbolic discounting function $V=A/(1+kD)$ where V represents value (ED50), A is the fixed dose (0.2), D is the delay to the fixed dose and k is a parameter that indicates rate of discounting. Generally, dose-response functions for the immediate dose shifted to the left as delay increased. R2 values for the discounting function ranged from 0.5 to 0.9. The value of k was generally < 0.01 , low compared to studies with food as the reinforcer. This is the first experimental determination of the generality of the hyperbolic discounting function to drug reinforcers. This approach may allow the application of an animal model to the study discounting the value of drugs as a function of the delay to their presentation. (Supported by grants DA-08731 and DA-15343).

866 EFFECT OF METHYLPHENIDATE PRETREATMENT ON INTRAVENOUS NICOTINE SELF-ADMINISTRATION IN RATS

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Acute administration of amphetamine or bupropion increases the rate of cigarette smoking in humans, as well as the rate of intravenous nicotine self-administration in rats. Conversely, chronic administration of bupropion is known to decrease cigarette smoking in humans, and it was recently shown to preferentially alter nicotine- vs. food-maintained responding in rats in our laboratory. In the present experiments, we sought to extend these findings by determining the effect of methylphenidate, a stimulant medication widely prescribed for treatment of attention deficit hyperactivity disorder (ADHD), on nicotine self-administration in rats. Male Sprague-Dawley rats were initially pretrained to lever press for sucrose reinforcement (45 g Noyes pellet). Following this, one group of rats ($n=7$) underwent intravenous catheterization surgery and then responded for nicotine (0.03 mg/kg/infusion) under a fixed ratio 5 (FR 5) 20-sec time out (TO) schedule of reinforcement during daily 60-min sessions. Food was restricted to 20 g per day, given at the end of each self-administration session. A separate group of rats ($n=8$) responded for sucrose under similar experimental conditions. Once responding stabilized, each group was administered methylphenidate (1.25-10 mg/kg, sc) 10 min prior to experimental sessions using a counterbalanced, within-subject dose-order design. An analysis of variance of the nicotine self-administration data revealed a significant main effect of dose, with post-hoc tests indicating that 2.5 and 5 mg/kg methylphenidate significantly ($p<.05$) increased the number of nicotine infusions earned relative to saline. In contrast, an analysis of variance of the food-maintained responding data revealed that methylphenidate significantly decreased the number of sucrose pellets earned across the same dose range. In conclusion, acute methylphenidate specifically increased nicotine self-administration in rats, analogous to recent clinical results showing that acute methylphenidate increases cigarette smoking. Supported by USPHS grants P50 DA 05312 and U19 DA17548.

867 SYSTEMATIC ASSESSMENT OF ABUSE OR DIVERSION IN A CLINICAL TRIAL OF ANALGESICS

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Objective: To systematically evaluate risk assessment of medication handling events in an opioid analgesic clinical trial of subjects with osteoarthritis pain of the hip or knee. Methods: This multicenter, randomized, double-blind, parallel group study was conducted from 26-Jun-2003 to 21-Jul-2004. During the 7-day run-in period 274 subjects were converted to Vicodin® from their previous analgesic regimens. Supplemental analgesics were allowed. Two hundred three subjects were then randomized and switched from Vicodin® to 7-day buprenorphine transdermal system (BTDS), 10 or 20 µg/h, for the 14-day double-blind phase. The Investigator identified cases of possible abuse or diversion for each subject by completing the Abuse and Diversion Case Report Form (CRF) and answering a follow-up questionnaire, as needed. CRFs were reviewed in detail by the study assessment staff and narratives were created for each event. Results: Thirty-two medication handling investigations were conducted during this study: no cases involved clinical study drug supply issues; 7 cases involved drug-handling practices at sites; and 25 cases involved possible events of abuse or diversion by 25 subjects (9.2% of 274 run-in subjects). After review of the 25 subject cases of possible abuse or diversion, the results indicated 10 instances of study noncompliance, 9 cases of loss or theft not due to abuse or diversion by subject, and 6 cases of possible abuse (2.2% of 274). All 6 cases of possible abuse by subjects involved Vicodin® during the run-in phase. There were no cases of possible abuse or diversion by subjects involving BTDS during the 14-day double-blind phase where BTDS was the only study drug. Conclusions: Systematic assessment of specific events in clinical trials can better inform risk management programs that are deployed following drug approval.

868 HEALTH STATUS AND SYMPTOMS AMONG YOUNG FEMALE ECSTASY AND OTHER DRUG USERS

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A significant number of young, low-income women experiment with ecstasy outside of club or rave settings. No study has reported overall health status among this group of women. A cross-sectional survey was conducted among 696 women aged 18 to 31 who sought gynecological care in southeast Texas between December 1, 2001, and May 30, 2003. Survey information included participants' demographics, obstetric & gynecological history, other physical health conditions and symptoms and mental health symptoms. Our study showed that 14% of participants (106/696) reported ever using ecstasy. Among Ecstasy users ($n=106$), 47% reported using it within the last 12 months, 64% reported ever using marijuana and 45% ever using any other major drugs including cocaine, heroin, LSD, PCP, etc. Our bivariate analyses showed that Ecstasy users were less likely to have obstetric and gynecological history than other illicit drug users, while were as likely as exclusive Marijuana users. Ecstasy users reported the highest number of chronic health conditions such as diabetes, heart disease, and depressive symptoms measured by SALSA. Further, Ecstasy users were as likely as other illicit drug users to report other physical symptoms such as aches, pains, nausea, vomiting, or heart pounding. After controlling for demographic characteristics, compared to none users, Ecstasy users were more likely to have more physical conditions and symptoms, and depressive symptoms. Compared to exclusive marijuana users, Ecstasy users were more likely to have more physical conditions and depressive symptoms. Compared to the users who used other illicit drugs except ecstasy, there is no significant difference. In conclusion, our findings demonstrated that ecstasy users, similar to other major illicit drug users, appear to have more physical and mental health problems than exclusive marijuana users and those who have never used any illicit drugs. Thus drug education and treatment need to target not only substance abuse problems but also deteriorated physical health conditions of young polydrug users including ecstasy users.

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- 869** BLOCKADE OF CB1 RECEPTOR BY AM 251 INHIBITS COCAINE'S REWARDING EFFECTS AND COCAINE-PRIMED RELAPSE BY A DA-INDEPENDENT MECHANISM
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Previous studies demonstrate that blockade of CB1 receptors by SR141716A significantly inhibits THC, heroin, ethanol, nicotine, but not cocaine self-administration or cocaine-conditioned place preference. In the present study, we examined whether the novel highly potent and selective CB1 receptor antagonist AM251 inhibits cocaine self-administration, cocaine-induced enhancement of brain stimulation reward and cocaine-induced reinstatement (relapse) of drug-seeking behavior. Systemic administration of AM251 (1, 3, 10 mg/kg i.p., 30 min prior to testing) dose-dependently lowered (37, 43, 60%, respectively) the break-point for cocaine self-administration under a progressive ratio reinforcement schedule, and dose-dependently inhibited (maximally 60%) cocaine-triggered reinstatement of drug-seeking behavior. Similarly, AM 251 (0.3, 1, 3 mg/kg) also dose-dependently attenuated (74, 65, 96%, respectively) 2 mg/kg cocaine-induced enhancement of brain stimulation reward. In contrast to AM251, SR141716A maximally lowered the break-point for cocaine self-administration by ~30% and cocaine-enhanced brain stimulation reward by ~40%. In vivo microdialysis demonstrated that cocaine priming significantly elevated extracellular DA (+400% over baseline) and glutamate (+180%), but without change in GABA levels in the nucleus accumbens, while AM251 (1, 3, 10 mg/kg) selectively attenuated cocaine-induced increases in glutamate, but not in DA levels in the nucleus accumbens. AM251 alone dose-dependently elevated extracellular glutamate, but not DA or GABA levels. Taken together, these data suggest that blockade of CB1 receptors significantly inhibits cocaine's rewarding effects and cocaine-primed relapse, a mechanism correlated with AM251-induced increases in extracellular glutamate, but not with a reduction in cocaine-induced increases in DA in the NAc.
- 870** COMPARISON OF THE PHARMACOLOGICAL ACTIVITIES OF DAMGO AND HERKINORIN ON THE MU RECEPTOR AND G PROTEINS IN CHO CELLS EXPRESSING THE CLONED HUMAN MU OPIOID RECEPTOR
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Background. Previous studies established that DAMGO and herkinorin (HERK), a nonnitrogenous neoclerodane diterpene, are fully efficacious mu agonists. However, HERK, unlike DAMGO, does not promote mu receptor internalization. Hypothesis. Chronic HERK and DAMGO treatment will differentially change the expression and function of G proteins. Methods. We used CHO cells expressing the cloned human mu opioid receptor (hMOR-CHO) in various assays. Results. DAMGO and HERK were full agonists in the [³⁵S]GTP-γ-S (GTP-S) binding (EC50 values DAMGO = 12.8 nM and HERK=92.5 nM) and the inhibition of forskolin-stimulated cAMP assays (EC50 values DAMGO = 3.23 nM and HERK=48.7 nM). Chronic exposure to HERK, but not DAMGO, increased basal GTP-S binding. Chronic exposure to both drugs produced moderate tolerance to both drugs (~3-4 fold) in the GTP-S binding assay. Chronic HERK, but not DAMGO, increased the basal Bmax of the high-affinity GTP-S binding site. Both drugs diminished the ability of DAMGO to increase the Bmax of the high-affinity GTP-S binding site. Chronic DAMGO produced moderate tolerance to both drugs (~3-4 fold) in the cAMP assay. In contrast, chronic HERK eliminated the ability of either drug to inhibit forskolin-stimulated cAMP. In the presence of forskolin, naloxone further increased cAMP after chronic HERK, but not after chronic DAMGO. Western blot analysis showed that chronic exposure to drugs (morphine, DAMGO and HERK) produce differential effects on Gal2 protein expression. Conclusion. The current data indicated differential agonist regulation of mu opioid receptor and G proteins in hMOR-CHO cells. Since morphine and HERK do not trigger receptor internalization, we hypothesize that agonist-specific regulation of MOR/ β-arrestin interactions may explain these phenomena. Acknowledgement. This research was supported in part by the Intramural Research Program of the NIH, NIDA and NIDA grant 1R01DA018151-01A2.
- 871** FLUTAMIDE REDUCES BENZOYLECGONINE LEVELS FOLLOWING COCAINE INFUSION IN MEN
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A number of reports have shown that male cocaine users experience more adverse brain and vascular effects than their female counterparts. This could be due to testosterone, which may potentiate cocaine's vasoconstrictive effects. We examined whether the antiandrogen, flutamide (FL), alters cocaine's effects in men with histories of occasional cocaine use. Subjects (N=10) were studied twice in a within-subject, repeated-measures design. They were administered FL (250 mg) or placebo in a blind and randomized order on alternate days followed 2 hours later by intravenous cocaine (0.4 mg/kg). Vital signs, subjective ratings (Addiction Research Center Inventory), and blood samples were obtained at baseline and periodically for 1 hour after cocaine administration. Cocaine, benzoylecgonine (BE), and ecgonine methyl ester (EME) were measured by gas chromatography/mass spectrometry. There were no differences between FL and placebo on physiologic or subjective responses. Similarly, FL did not alter plasma cocaine or EME levels. By contrast, FL significantly reduced BE levels (F_{1,9} = 5.3, p < 0.05), which were 19% lower 1 hour after cocaine infusion. These findings suggest that antiandrogen pretreatment either inhibits BE production or enhances its elimination following cocaine infusion. As BE promotes central and peripheral vasoconstriction, testosterone's effects on BE levels may contribute to increased vasoconstriction in male cocaine users and could lead to sex differences in cocaine's vascular effects that develop in chronic cocaine abusers. Supported by NIDA grants DA14674, DA09448, DA03994, DA17324, DA15032, and DA00343.
- 872** EFFECTS OF CLOCINNAMOX AND NOR-BINALTORPHIMINE ON THE CONDITIONED PLACE PREFERENCE AND LOCOMOTOR ACTIVITY PRODUCED BY MORPHINE AND BUTORPHANOL
D. J. Yamamoto, C. V. Everett, K. R. Blauth, N. J. Schaefer and R. M. Allen, University of Colorado at Denver and Health Sciences Center, Denver, CO
Butorphanol is a mixed-action opioid agonist that functions as a low-efficacy agonist at both mu- and kappa-opioid receptors. In this study, we used standard three-compartment conditioning apparatuses to 1) compare the place preference and locomotor effects produced by morphine and butorphanol in Sprague-Dawley rats and 2) test the receptor mechanisms that mediate these effects. A preference ratio (PR) was calculated dividing post conditioning time in the drug-paired compartment by post conditioning time in the drug + vehicle-paired compartments. Four conditioning trials with morphine (0.032 – 10 mg/kg, i.v.) produced dose-dependent increase in PR up to a dose that produced some toxicity (10 mg/kg). The effects of butorphanol (0.001 – 10 mg/kg, i.v.) were biphasic, with maximal PR at 0.1 mg/kg, then decreasing (but greater than control) up to a dose that produced some toxicity (10 mg/kg). In contrast, the dose-response curves for both morphine- and butorphanol-elicited locomotor activity (LMA) were biphasic, with the increases in LMA elicited by lower doses attenuated when higher doses were administered. Neither the rewarding nor locomotor effects of 10 mg/kg butorphanol were altered significantly following 24 h pretreatment with the irreversible kappa opioid receptor antagonist, nor-binaltorphimine (1 mg/kg, i.v.). The irreversible mu-opioid receptor antagonist, clocinnamox (1 mg/kg, i.v.), slightly attenuated the preference produced by 10 mg/kg morphine but not the preference produced by 10 mg/kg butorphanol. In light of these negative findings, we plan to test the effectiveness of intravenous antagonist doses against other behavioral measures and test higher antagonist doses against the place preferences produced in this procedure. Supported by a UCD Faculty Development Award (RMA), UCD Undergraduate Research Opportunity Program awards (DJY, NJS, KRB, CVE) and a UCD Psychology Faculty Fund for Undergraduate Research award (CVE).

873 MEDICATION OF L-TETRAHYDROPALMATINE SIGNIFICANTLY INCREASED THE ABSTINENCE RATE IN HEROIN ADDICTS

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Objective: To evaluate the clinical efficacy of L-tetrahydropalmatine (L-THP), a dopamine D1, D2, and D3 receptor-binding compound extracted and purified from Chinese herbal medicine, on craving and abstinence in heroin addicts. **Methods:** A double-blind clinical trial was approved by the IRB with a total of 119 heroin-only dependents, who met the DSM-IV criteria and were in good health. They were admitted into a clinical setting for two months and were recruited for this study with signed consent forms from each subject. These in-patients were randomly divided into two treatment groups: L-THP (60 mg twice a day) and placebo (twice a day), respectively. The medication was started 7-10 days after admission and lasted for one month. Scores for protracted withdrawal syndrome and craving were assessed every week after admission. **Results:** The scores for pain, palpitation, tension and sleep disorder for the L-THP group were significantly lower than those of the placebo group ($P < 0.05$) one week after treatment. L-THP treatment significantly reduced symptoms of drug craving ($P < 0.05$) compared with placebo two weeks after treatment and the scores of craving reduction were maintained thereafter. Three months after patients were discharged, the follow-up study showed that the abstinence rate for the L-THP-treated group was 46.2% and for the placebo group was 14.8%. The difference was statistically significant ($P < 0.01$). **Conclusion:** Our clinical observations showed that one-month long L-THP treatment showed a significant efficacy on craving reduction. The abstinence rate of the L-THP group was significantly improved, in comparison with the placebo group. Further mechanistic studies will be conducted to elucidate the mechanisms responsible for the treatment efficacy on heroin-dependent subjects.

874 PROBABILITY DISCOUNTING AMONG CIGARETTE SMOKERS AND NON-SMOKERS: MOLECULAR ANALYSIS DISCERNs GROUP DIFFERENCES

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Despite numerous studies documenting differences in temporal discounting among cigarette smokers and non-smokers, studies of probability discounting have had mixed results. The present abstract seeks to clarify these results with a molecular analysis of data obtained from a study of probability discounting. Thirty cigarette smokers and 28 non-smokers were compared using a probability discounting procedure. Indifference points were obtained at 7 probabilities (95% - 1%) for 3 hypothetical reward magnitudes. As expected, indifference points decreased as probability decreased. These data were fit to a hyperbolic model of discounting after converting probabilities to odds-against. Examination of discounting parameter h indicated the expected Reverse-Magnitude Effect, with large-magnitude rewards discounted more than small magnitude rewards. The group difference between smokers and non-smokers, though in the predicted direction, was not statistically significant. However, a molecular analysis of indifference points indicated that differences were obscured by a floor effect. Specifically, indifference points obtained from high probabilities ($\geq .50$) were lower for cigarette smokers relative to non-smokers, while not observed with indifference points obtained from low probabilities ($< .50$). Examination of other studies confirms this analysis. Thus, this molecular analysis suggests that the prior inconsistent results are due to floor effects resulting from the inclusion of low probabilities.

875 DELAY DISCOUNTING PREDICTS POSTPARTUM RELAPSE TO CIGARETTE SMOKING AMONG PREGNANT WOMEN

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Women who quit smoking on their own shortly after learning that they are pregnant are referred to in the literature as "spontaneous quitters" (see Solomon & Quinn 2004 for a review). Spontaneous quitters exhibit greater success in initially quitting smoking than the general population of smokers, but higher-than expected relapse rates postpartum. Although a variety of socio-demographic and pre-pregnancy smoking characteristics have been examined, much remains to be learned about the variables that affect relapse in spontaneous quitters. One such variable that may be important and is the focus of the present study is delay discounting (i.e., the rate at which people discount the value of delayed rewards). Indeed, an emerging area of research demonstrates that drug abusers discount delayed rewards significantly more than non-drug abusers, suggesting that this characteristic may increase vulnerability to drug abuse (see Bickel & Marsch 2001 for a review). For example, smokers discount the value of delayed monetary rewards significantly more than nonsmokers. In the present study, delay discounting for money was assessed in 40 spontaneous quitters enrolled in a relapse prevention study. At baseline, discounting was negatively correlated with age ($r = -0.40$, $p = 0.01$) and years of education ($r = -0.31$, $p = 0.05$) and positively correlated with a history of depression ($r = 0.47$, $p < 0.01$). In univariate analyses, baseline delay discounting ($t = -3.05$, $p < 0.01$) and having a history of depression ($\chi^2 = 4.22$, $p = 0.04$) predicted smoking status at 6 mos postpartum, but only delay discounting remained a significant predictor in multivariate analyses. The results provide initial evidence that an increased propensity to discount delayed rewards may contribute to postpartum relapse in spontaneous quitters.

876 ABNORMAL ACTIVATION AND REDUCED NEURONAL INTEGRITY OF BRAIN CIRCUITS INVOLVED IN COGNITIVE CONTROL IN OPIATE USERS

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Long-term opiate use has been associated with attenuated activity in the dorsal anterior cingulate cortex (dACC) during performance of executive control tasks. However, these studies have been conducted in small samples and it is unclear how this relates to the neuronal viability and functional integrity of the region. We used fMRI to scan 30 opiate dependent subjects on substitution therapy and 30 matched healthy controls while performing a novel cognitive interference task that produces reliable dACC activation. Proton MRS using short TE spectra was also obtained from the left and right dACC in the same scanning session using a 3T scanner. Reaction-time (RT) data revealed a significant main effect of task for both errors and RT-interference ($p < 0.001$; 329msec for controls and 336msec for opiate users), but no group differences. Functional analysis revealed significant activations ($p < 0.05$ cluster-wise corrected) of networked regions including the dACC, superior parietal (sPTL), as well as inferior and superior frontal gyri. A direct comparison of the groups revealed relatively greater activity in the sPTL, dorsolateral-prefrontal and extra-striate cortices of opiate users. Additionally, in controls, RT-interference was significantly correlated with functional activity of both the dACC ($r = .46$; $p < 0.01$) and sPTL ($r = .43$; $p < 0.01$), while errors were correlated with activity of the dACC only ($r = .72$; $p < 0.001$). These 'normal' brain activity-behaviour associations were not apparent in opiate users. Finally, opiate users showed a specific reduction of N-acetylaspartate (NAA) concentration in the dACC ($p < 0.01$). Overall, the additional activation of posterior brain regions; the dissociation of the 'normal' brain activation-behaviour associations; and reduced dACC NAA concentration, suggests disruptions in the neuronal and functional integrity of the dACC and prefrontal-parietal networks in opiate addiction.

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- 877** GENDER DIFFERENCES IN ASSOCIATION OF THE hPER2 GENE POLYMORPHISMS WITH COCAINE DEPENDENCE
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Previously, we demonstrated a differential regulation of the clock genes Per1 and Per2 expression after acute and chronic cocaine administration in the rat striatum. Other studies showed that the Per2 gene was involved in regulation of glutamate reuptake in the mouse brain and cocaine- and alcohol-induced behaviors. In humans, variations of the PER2 gene were found to be associated with regulation of alcohol consumption. In this study, we tested single nucleotide polymorphisms (SNPs) in the human PER1 and PER2 genes for association with cocaine dependence in an American Caucasian population. We genotyped 96 cocaine-dependent and 71 control subjects for nine SNPs in PER1 and five SNPs in PER2 genes. No statistically significant differences were found in genotype or allele frequencies of the SNPs studied in both genes between cocaine dependent subjects as a total group and control subjects. However, when the data were stratified according to gender, two alleles in PER2 gene, 1071G in intron 3 ($p=0.025$) and 1965G in exon 17 ($p=0.012$), were significantly overrepresented in female cocaine dependent subjects compared to female controls. The association of those SNPs were even stronger in the subgroup of cocaine dependent subjects with alcohol dependence ($p=0.005$, and $p=0.003$, respectively). These point-wise significant results are not significant experiment-wise after correction for multiple testing. However, these findings are still suggestive that the genetic variations of PER2 gene may contribute to a variety of neurochemical alterations which may be involved in drug addictive behaviors. (Supported by NIH-NIDA KO5-DA00049, DA05130, MH44292).
- 878** STARTSMART: EVALUATION OF A MIDDLE SCHOOL TOBACCO PREVENTION PROGRAM
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Students Making Advertisements to Reduce Smoking (StartSMART) is an innovative school based tobacco prevention curriculum funded by the National Institute on Drug Abuse. The program was developed in response to overwhelming evidence that youth as young as 12 years old are experimenting with tobacco. Although the nation's schools are providing tobacco education, there is still a need to improve their current tobacco awareness and prevention programs. With the assistance of agencies such as the CDC, specific recommendations have been established to assist school systems in delivering tobacco prevention messages to both children and adolescents. Despite these recommendations, few schools are implementing programs that meet each of CDC's criteria. Throughout the eight-session curriculum, StartSMART follows the guidelines, utilizing a social marketing approach to deliver tobacco prevention education and inform youth of the tobacco industry's tactics to target them to smoke. Using a strong theoretical framework to guide skill development, StartSMART enables students to observe, learn, and participate in delivering positive tobacco prevention messages. The program culminates with the production of student developed anti-tobacco advertisements through the use of a video camera with in-camera editing. This presentation includes preliminary results of an outcome evaluation as well as completed activities from students participating in the study such as final scripts and storyboard developed for the anti-tobacco advertisements. Other components developed for this program including the parent support guide, administrator's guide, and sample content from the support website will also be presented.
- 879** SUBJECTIVE AND MIOTIC EFFECTS OF PRESCRIBED DOSES OF OXYCODONE AND HYDROCODONE IN VOLUNTEERS
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Oral oxycodone and hydrocodone are opioids that are commonly prescribed in combination with acetaminophen for relief of moderate to moderately severe pain. A recent study conducted in an emergency department demonstrated that these drugs at a commonly prescribed dose (5 mg of the opioid) were equianalgesic for the first hour after their administration (Marco et al. 2005; Acad Emerg Med 12:282-8). In the present study we tested the subjective and miotic effects of two commonly prescribed doses of hydrocodone and oxycodone combination products to determine if they were equipotent on measures other than analgesia. Sixteen volunteers participated in a placebo-controlled crossover design in which doses of 5 and 10 mg of oxycodone and hydrocodone were tested. These doses were given in combination with 325 and 650 mg of acetaminophen respectively. A 650 mg acetaminophen control condition ensured that this drug had no effects by itself. Results demonstrated that 5 mg of oxycodone produced a few subjective effects, but hydrocodone at the same dose did not. Oxycodone at 10 mg produced a number of subjective effects, including decreased VAS ratings of "in control of body" and "in control of thoughts," increased ratings of "dizzy" and "difficulty concentrating," and side effects including itching and sweating. Hydrocodone at the equivalent dose produced a few subjective effects but none of those listed above. Drug liking and "wanting to take again" ratings were elevated with the 10 mg doses of both drugs. Miosis was produced by all doses of both opioids, but oxycodone induced a greater degree of miosis than did hydrocodone. Acetaminophen alone had no measurable effects. We conclude that although an analgesic study suggests equipotent effects, our results demonstrate that on other endpoints oxycodone is more potent than hydrocodone. Further, when prescribing 10 mg of oxycodone for acute pain, physicians might want to inform patients that there is a high likelihood that certain effects will be felt that would contraindicate certain activities (e.g., working and driving). Funded by NIDA grant DA-08573.
- 880** CIRCUMSTANCES ASSOCIATED WITH RISK OF ABUSE OF OPIOIDS IN CLINICAL TRIALS
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Introduction: Systematic assessment of situations involving possible abuse of opioid analgesics during the pre-marketing clinical trial stage provides insight into circumstances associated with increased risk. Methods: Anomalous medication handling events (AMHE) occurring in subjects enrolled in 8 outpatient chronic non-malignant pain trials were identified and evaluated for possible abuse. Circumstances of increased risk were evaluated. Results: Increased risk was associated with certain subject factors, clinical trial design features, and types of medications used. Subject risk factors include undisclosed substance abuse, even though current or past abuse was a study exclusion criterion. Strict documentation of the subject's medical history is needed, especially for subjects from outside a doctor's practice. Trial design issues include the phase when medications are introduced, if the type of medication is disclosed (open-label) or blinded, and the presence of placebo arms. One trial had a 2.2% case rate (6 of 274 subjects) that solely involved run-in, open-label hydrocodone. Another trial showed a 1.1% (5/464) case rate associated with the use of open-label rescue (immediate-release hydromorphone) in subjects given placebo or with documented inadequate pain control. Risk associated with a trial design using open-label opioid rescue is also shown in 2 ongoing trials which have a similar maintenance of analgesia design with buprenorphine transdermal system (BTDS). One trial has a placebo arm and uses immediate-release oxycodone as rescue and the second has a low dose BTDS (5 mg or 5 micrograms/hour) arm with acetaminophen or ibuprofen rescue. The trial with the placebo arm and oxycodone rescue had a 2.4% (4/138) case rate for oxycodone, while the other trial had a 0.5% (1/198) case rate for BTDS. Correlation with pain outcomes provides insight into drug-seeking behavior for pain control compared with that for abuse. Conclusion: Assessment of AMHE during clinical trials provides understanding of circumstances associated with possible abuse. This effort can inform risk management actions for risk minimization.

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- 881** CO-EXPRESSION OF GLUTAMATE AMPA RECEPTOR SUBUNITS AND FOS PROTEIN EXPRESSION ELICITED BY COCAINE CUES IN RATS
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Environmental cues associated with cocaine can elicit craving in humans and cocaine-seeking behavior in rats. We have reported an increase in neuronal activation, measured by Fos protein expression, in the prelimbic (PrL) cortex, cingulate cortex (CgC), basolateral amygdala (BIA), nucleus accumbens shell (NAS) and core (NAC) following exposure to cocaine-associated environmental cues. This experiment examined whether neurons exhibiting an increase in Fos also co-express glutamate AMPA receptor subunits. Rats were trained to press a lever that resulted in cocaine infusions that were paired with light/tone cues. Rats then underwent 22 days of abstinence from cocaine, during which they were exposed daily to either the self-administration environment with presentations of the cues previously paired with cocaine infusions (Extinction group) or an alternate environment (No Extinction group). Extinction was used to devalue the motivational significance of the cocaine self-administration environment and cues. Cocaine-seeking behavior (i.e., lever presses in the absence of cocaine reinforcement) in response to cue presentation was then assessed in both groups. Rats were euthanized 90 min later. Brain sections were co-labeled for Fos and glutamate receptor 1 (GluR 1) or 2/3 (GluR 2/3) subunits. We replicated our findings that rats in the No Extinction group exhibited greater cocaine-seeking behavior and an increase in Fos immunoreactive cells in the PrL, CgC, BIA, NAS, and NAC relative to rats in the Extinction group. We also found an increase in cells co-expressing Fos and GluR 1 or GluR 2/3 in the No Extinction group relative to the Extinction group; however, the increase in the proportion of cells exhibiting co-expression across groups was only evident in the CgC and NaS of cells co-labeled with Fos and GluR 1. The results suggest that glutamate is likely involved in Fos expression induced by exposure to cocaine cues and that GluR 1 subunits in the CgC and NAS may be particularly critical. Supported by DA13649
- 882** PROJECT YOUTH CONNECT OF NORTHERN COLORADO-EXPANDED: A RURAL ADOLESCENT DRUG PREVENTION, MENTORING PROGRAM
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Project Youth Connect of Northern Colorado - Expanded was a three-year, federally-funded, U.S.D.H.H.S. Center for Substance Abuse Prevention grant with a randomized design of 227 high-risk, low income, students (64% Hispanic, 14% Native American) in Grade 5. There were 108 control and 119 treatment students across three cohorts (years). The treatment program consisted of 2 hours of one-on-one mentoring by trained adult mentor/advocates from the communities, with 2-4 hours of weekly, after school life skills (Botvin's Life Skills and the Second Step Violence Prevention curricula), cultural activities, recreation, and academic tutoring for a year. The theoretical framework was based on research related to the Risk Reduction/Resiliency Model of Prevention, and Bandura's Social Learning and Self-Efficacy theories. Results indicated that there were no significant differences between the treatment and control groups with regard to drug use, school bonding, school attendance, academic performance and discipline referrals at baseline, exit and follow-up. However, results of teacher interviews and questionnaires indicated that the treatment group in Cohort I had statistically significantly more positive changes in academic skills, social skills, life skills, and leadership than the control group, chi-square (1, N = 84) = 9.57, $p < 0.002$. Further examination of the Cohort I data I revealed that twice as many youth improved socially in the treatment group as in the control group, chi-square (1, N = 84) = 6.04, $p < 0.014$. Interestingly, at one site in Cohort II, youth made significant improvements in academic skills, social skills, life skills, and leadership, indicating that characteristics and skills of the Mentor are important to success. Qualitative data from parent focus groups indicated positive changes in the treatment group, such as helping with chores, doing their homework and spending time with their family. Although these results are mixed, valuable insights regarding school-based interventions will be provided.
- 883** WITHIN-SESSION OPERANT RESPONDING IS NOT DETERMINED BY TITRATION OF NUCLEUS ACCUMBENS DOPAMINE OR REMIFENTANIL, WHOLE BRAIN REMIFENTANIL, OR BLOOD REMIFENTANIL
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An individual's drug abuse pattern is determined by a multitude of factors. Among these, simple pharmacokinetic determinants of within-binge drug consumption are sorely under-investigated. We therefore investigated if within-session operant responding for the ultra-short acting mu opioid agonist remifentanil (RMF) was determined by blood or brain RMF levels or changes thereof by quantifying nucleus accumbens (NAC) RMF and dopamine (DA) levels by in vivo microdialysis and LC/MS/MS in an operant runway procedure, and by quantifying RMF pharmacokinetics in whole brain and blood. The comparison of temporal changes in RMF levels with rat RMF self-administration behavior (Panlilio and Schindler 2000 *Psychopharmacology* 150: 61-66; Panlilio et al. 2003 *Psychopharmacology* 167: 9-19), suggested that titration of blood RMF, whole brain RMF, or intra-accumbens RMF or DA levels did not determine a rat's decision to re-emit a response during a multiple-injection drug self-administration session (Crespo et al. 2005 *Psychopharmacology* 183: 201-209). Even a detailed peri-event analysis failed to detect any RMF "threshold", "ceiling", or "rate of change" that determined operant responding for RMF (Crespo et al. 2006 *Ann. N.Y. Acad. Sci.*, in press). Our findings strongly suggest that titration of blood or brain RMF levels does not determine a rat's intra-session operant responding. This work was supported by the Austrian Science Fund Grant P16394-B05 and by the Verein für Experimentelle Psychiatrie, Psychotherapie und Pharmakologie (VEPPP).
- 884** SYNERGISTIC DESIGN OF POLAR BIS-PYRIDINIUM ANALOGS CONTAINING A 1,4-DI-(1-BUTYNYL)PHENYLENEDIYL LINKER: INTERACTION WITH BOTH NICOTINIC RECEPTORS AND THE BLOOD-BRAIN CHOLINE
Z. Zhang(1), A. G. Deaciuc(1), P. R. Lockman(2), D. D. Allen(2), L. P. Dwoskin(1) and P. A. Crooks(1), (1) College of Pharmacy, University of Kentucky, Lexington, KY, and (2) School of Pharmacy, Texas Tech University, Amarillo, TX
bis-[Dodecane-1,12-diyl]-3-picolinium dibromide (bPiDDB) decreases nicotine self-administration in rats (Neugebauer et al., 2006) and appears to gain CNS access via the BBBCT (Crooks et al., 2004). The purpose of the present study was to design bis-azaaromatic quaternary ammonium analogs with high affinity at nicotinic receptors (nAChRs) and high affinity for the BBBCT. Hemicholinium-3, the classical BBBCT ligand, is dicationic and contains a rigid linker moiety which affords a fully extended separation of the quaternary ammonium head groups. We have synthesized bis-pyridinium analogs structurally related to both the more conformationally flexible bPiDDB molecule and hemicholinium-3, which incorporate a rigid 1,4-di-(1-butynyl) phenylenediyl linker. When compared to both bPiDDB and hemicholinium-3, which have K_i values of 36 and 54 μM , respectively, at the BBBCT, these novel analogs showed higher affinity ($K_i = 0.5\text{-}8.4 \mu\text{M}$) for the BBBCT. One analog, ZZ1109, exhibited the highest affinity for the BBBCT ever reported. Thus, these analogs are expected to have good brain bioavailability. We have been able to identify specific molecules in this class of high affinity BBBCT analogs which also have high affinity at nAChRs. ZZ1115 had a K_i of 870 nM at [3H]methyllycaconitine binding sites ($\alpha 7^*$ nAChRs) and low affinity ($K_i = 8.4 \mu\text{M}$) at [3H]nicotine binding sites ($\alpha 4\beta 2^*$). The results suggest that polar bis-pyridinium analogs containing a conformationally restricted 1,4-di-(1-butynyl)phenylenediyl linker can be designed that possess two synergistic activities, i.e., facilitation of transport into the CNS via the BBBCT and high affinity for specific neuronal nAChRs. Supported by U19DA017548.

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885 BIVALENT LIGANDS AS PROBES FOR CANNABINOID RECEPTOR OLIGOMERIZATION

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Research suggests that G-Protein coupled receptors (GPCRs) exist as homo- and hetero-oligomers. In some cases, this receptor oligomerization is essential for receptor function (e.g., the GABAB receptor). Bivalent ligands for opioid receptors, defined as two pharmacophores linked by spacers, have been shown to be able to selectively target homo or heterodimers and display unique pharmacological properties as compared to their monomeric subunits (Waldhoer et al., 2005). Indeed, Daniel et al. (2005) have proposed that the μ - δ heterodimer is the fundamental signaling unit that mediates tolerance and dependence through specific signal transducer(s) that recognize and couple to the heterodimer but not μ receptor monomers/homomers. Our efforts have focused on the synthesis and testing of bivalent ligands for the cannabinoid receptors (CB1 and CB2), which belong to the class A subdivision of GPCRs as do the opioid receptors. Bivalent ligands of SR141716A (rimonabant), a potent CB1 receptor antagonist, containing amine linkers of varying lengths have been synthesized and evaluated (Table 1). The binding affinity of each compound was measured in competition assays with [3 H]CP55,940 and [3 H]SR141716A. Several of the compounds tested demonstrated comparable binding affinity to SR141716A. In particular, a linker between 10 and 18 methylene units seemed optimal for binding affinity in both the N-H and the N-methyl series. Included in these studies is the preparation of monovalent ligands with capped amine spacer as controls as well as expression vectors for cannabinoid receptors incorporating fluorescent tags (CFP and YFP) to use as FRET probes for dimerization. The results of the continued studies with these bivalent ligands will be presented.

886 SILENCING THE PTEN GENE REDUCES STRIATAL NEUROTOXICITY INDUCED BY HIV-1 TAT AND OPIATES

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Exposure to opiate drugs of abuse reportedly enhances progression of human immunodeficiency virus-1 (HIV-1) encephalitis in a mu-opiate receptor dependent manner. We previously reported that striatal neurons are targets of the HIV-1 viral proteins transactivator of transcription (Tat) and glycoprotein 120 (gp120), and that Tat-induced neurotoxicity in vitro is exacerbated by morphine in a naloxone reversible manner. Striatal neurons exposed to Tat show increased [Ca^{++}] $_i$, and subsequent activation of both caspase-3 dependent and caspase-independent (endonuclease-G) apoptotic pathways (J NeuroVirol. 10:141, 2004). Since Tat-induced neurotoxicity involves activation of multiple cell death pathways and is not attenuated by caspase inhibitors we explored a novel therapeutic approach that targets signaling pathways upstream of mitochondrial apoptotic events. TransSignal Protein/DNA Arrays identified transcription factors likely involved in Tat-morphine synergy (ex: AP-1/NFAT, forkhead factors, GATA, Rel/NFkB). Many of these alter phosphorylation of Akt/PKB by PI3-kinase, with subsequent effects on targets of pAkt that enhance proliferation or cell survival. Embryonic striatal neurons were transfected with siRNAs targeting PTEN (phosphatase and tensin homology on chromosome 10) (PTENsi), the major negative regulator of Akt/PKB phosphorylation, using Amara nucleofection technology, which prolongs transgene expression for up to 2 weeks. Real time RT-PCR showed significant reduction of PTEN mRNA in neurons transfected with the PTENsi construct. Neurons were exposed to 100mM Tat(1-86) 8 days post-transfection and digitally imaged at 0-72 hrs to assess survival of individual cells. Tat significantly increased the death of neurons transfected with control construct by 72 hrs from 15.1% to 32.0% (N=4). However, PTEN silenced neurons were protected, surviving at a level identical with controls (12.4% vs. 12.8%). Our findings identify PI3-kinase/Akt as a major point of convergence and possible therapy for neurotoxic effects of Tat and morphine. Support: P01 DA19398 & DA15097.

887 THE EFFECT OF OPIATES ON THE ACTIVITY OF HUMAN PLACENTAL AROMATASE

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Methadone and buprenorphine(BUP)are used for treatment of the pregnant opiate addicts. The major placental enzyme metabolizing these two opiates and L-acetylmethadol (LAAM) is aromatase/cytochrome P450 19 which is a key enzyme in the biosynthesis of estrogens by human placenta. In addition, methadone, BUP, LAAM and their metabolites are competitive inhibitors of placental aromatase. Therefore, the aim of this investigation is to determine the effect of 16 opiates, most could be administered to pregnant patients for therapeutic indications, on the activity of placental aromatase in the conversion of testosterone to estradiol (E2) and 16 α -hydroxytestosterone (16-OHT) to estriol (E3). These opiates were from the following classes: phenanthrenes, phenylheptylamines, phenylpiperidines, benzomorphans and morphinans. Data obtained indicated that, whether the opiates were structurally related or not, they either inhibited, had no effect or caused a slight activation of aromatase activity. Moreover, their effect on E3 formation was more pronounced than that on E2 and could be explained by the lower affinity of 16-OHT than testosterone to aromatase. The opiates that inhibited the activity of aromatase and their respective IC50 values for E3 formation were: oxycodone, 141 \pm 45 μ M; codeine, 613 \pm 55 μ M; fentanyl, 35 \pm 6 μ M; sufentanil, 12 \pm 7 μ M; (+)-pentazocine, 785 \pm 49 μ M. Oxycodone and codeine did not inhibit E2 formation and the IC50 values for fentanyl, sufentanil and (+)-pentazocine were >1000 μ M. The agonists, morphine, heroin, hydromorphone, oxymorphone, hydrocodone, propoxyphene, meperidine, (-)-pentazocine, levorphanol and dexrophan and the antagonists naloxone and naltrexone, caused a slight increase in E3 formation but had no effect on E2. Therefore, the IC50 values for fentanyl and sufentanil suggest that their circulating concentrations in vivo could affect placental E3 formation. However, it is unlikely that the acute administration of either opiate would affect maternal and or neonatal outcome. Supported by a grant from NIDA to M.S.A.

888 NEW LEADS FOR THE TREATMENT OF NICOTINE ADDICTION: DISCOVERY OF NOVEL BIS-QUATERNARY AMMONIUM ANTAGONISTS AT NEURONAL NICOTINIC RECEPTORS MEDIATING NICOTINE-EVOKED DOPAMINE RELEASE

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Bis-3-picolinium-1,1'-dodecanediyl dibromide (bPiDDB) and its analogs have been previously shown to potently and selectively inhibit neuronal nicotinic receptors (nAChRs) mediating nicotine-evoked [3 H]dopamine ([3 H]DA) release from superfused rat striatal slices. In the current study, 8 novel bPiDDB analogs, in which the dodecyl linker moiety is connected to the two pyridinium head groups in a C2,C2', C3,C3', C4,C4' or C3,N' orientation, rather than the N,N' orientation in bPiDDB, were synthesized. The interaction of these compounds with nAChRs was determined at 100 nM utilizing high-throughput screening assays. Results show that none of these compounds had affinity for the $\alpha 7^*$ nAChR in the [3 H]methyllycaconitine binding assay. GZ528B, GZ529A and GZ529B exhibited no affinity for $\alpha 4\beta 2^*$ nAChRs in the [3 H] nicotine binding assay; the remaining compounds showed only μ M affinity at the latter site. Leads in this series included GZ527B [N,N'-dimethyl-4,4'-(1,12-dodecanediyl)bispyridinium diiodide], GZ528A [N,N'-dimethyl-2,2'-(1,12-dodecanediyl)bispyridinium diiodide], GZ529A [N-methyl-3-(12-(3-picolinium))-pyridinium bromide/iodide] and GZ530A [N-methyl-3-(12-S-nicotinium)-pyridinium bromide/iodide], and showed 43-67% inhibition of nicotine-evoked [3 H]DA release. The full concentration response was determined for the most attractive lead compound, GZ527B, which afforded an IC50 value of 50 nM and I $_{max}$ of 100%. Thus, these structurally diverse compounds are at least 100-fold selective as antagonists at nAChRs mediating nicotine-evoked DA release and represent new leads in our search for subtype-selective nAChR antagonists as treatments for nicotine addiction. Supported by NIH Grants U19DA017548.

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889 OPPOSITE EFFECT ON RAT LATERAL HYPOTHALAMIC OREXIN mRNA LEVELS BY MORPHINE WITHDRAWAL AND BY CHRONIC "BINGE" COCAINE OR WITHDRAWAL FROM COCAINE CPP

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It is established that hypothalamic neuropeptide orexin (OX) is involved in the regulation of sleep, arousal, feeding and stress. Recent studies have shown a novel role for OX activation in: a) morphine-induced dopamine (DA) release in nucleus accumbens; b) morphine, cocaine or food-induced seeking behavior; and c) morphine withdrawal and dependence. The present studies were designed to examine OX mRNA levels in rat lateral or medial hypothalamus (LH or MH) after: 1) chronic intermittent escalating-dose morphine exposure and acute spontaneous withdrawal; 2) chronic "binge" pattern cocaine; 3) cocaine-induced conditioned place preference (CPP); and 4) acute "binge" pattern cocaine with pretreatment of NMDA, DA or opioid receptor (MOR) antagonists. Both single-dose (10 mg/kg) and chronic escalating-dose of morphine (up to 120 mg/kg/d on d 10) had no effect on LH OX mRNA levels. However, OX mRNA level increased (55%) after 12-h acute morphine withdrawal. Although acute "binge" cocaine (3x15 mg/kg for 3 h) had no effect, OX mRNA level decreased (15%) after chronic steady-dose "binge" cocaine (45 mg/kg/d for 14 d) and decreased (25%) after chronic escalating-dose "binge" cocaine (up to 90 mg/kg/d on d 14). In cocaine CPP study (5 injections of 10 mg/kg for 10 d), rats displayed CPP 4 d after last conditioning session, and a decreased OX mRNA level was found in LH (20%), but not in MH. NMDA antagonist MK-801 (0.5 mg/kg) decreased LH OX mRNA level (30%), and the decrease was not altered by acute "binge" cocaine. Neither DA antagonists (SCH23390, 0.5-1 mg/kg or sulpiride, 25-50 mg/kg) nor MOR antagonist (naloxone or naltrexone, 1 mg/kg) altered OX mRNA level. Our results suggest that a) acute morphine withdrawal increased OX gene expression; b) in contrast, either chronic "binge" cocaine or withdrawal from cocaine administered during conditioning decreased OX gene expression; and c) NMDA receptors exerted tonic stimulatory effects on OX gene expression.

891 TWO PATTERNS OF CRAVING INDUCED BY HEROIN REWARD AND WITHDRAWAL LEAD TO THE RELAPSE TO HEROIN USE IN RATS

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Relapse to heroin use is the major clinical problem in the treatment of heroin addiction. In humans, conditioned effects of opioid withdrawal may contribute, at least in part, to drug craving. However, the opiate withdrawal that enhances the drug seeking is still unclear. In the present experiments, rats were initially trained to self-administer heroin (50 µg/kg /infusion; delivered over 5 s; maximal injection limits 25 injections) in 4 hours daily sessions. The sessions were completed for 1, 5, 10, and 14 days, respectively. To observe the drug seeking behavior induced by associated reward learning and withdrawal, we determined the drug seeking 1 day or 14 days of forced abstinence after the termination of heroin self-administration. Linear regression showed that the drug seeking elicited by conditioned cues at 1 day or 14 days was positive related to the training number of heroin self-administration. After 14 days of forced abstinence, the all groups showed more vigorous drug-seeking behavior than the those after 1 day of withdrawal. The drug seeking induced by conditioned cues were increased following the pretreatment with naltrexone at 1 day of termination of drug, but not changed at 14 days of withdrawal. The present studies demonstrate the two forms of craving induced by primary reward learning and withdrawal cause the drug seeking behavior(supported by the NBRP of China 2003CB515404, NNSF of China 30470544).

890 REPEATED GHB ADMINISTRATION IN RATS DOES NOT AFFECT STIMULATED DOPAMINE EFFLUX OR ALTER AUTORECEPTOR FUNCTION

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Illicit use of the club drug GHB (gamma-Hydroxybutyrate) is rapidly increasing in the United States due to its putative euphoric, anabolic and sedative properties. Recent reports of overdose, death and criminal use in sexual assaults suggest that GHB use represents a significant public health problem. The present studies in rats examined the effects of repeated GHB administration on forebrain dopamine systems that contribute to drug-mediated reinforcement. We initiated these experiments because prior studies of GHB effects on dopamine and of its reinforcing properties are few and conflicting. Adult male Sprague Dawley rats were administered GHB either i.p. or p.o. twice daily in an escalating dose paradigm over 14 days. The GHB dose increased gradually from 0.5 to 2.5 g/kg. GHB i.p. induced peritoneal tenderness and/or pathology in all rats while the p.o. route was well tolerated. Body weights of all GHB treated rats were significantly less than controls. The day following the final injection, rats were anesthetized and mounted in a stereotaxic apparatus for fast scan cyclic voltammetry using carbon-fiber microelectrodes. Dopamine release was evoked by electrical stimulation of the ascending axon tract at multiple stimulation frequencies (10 - 60 Hz). Dopamine efflux across the frequency range was similar in GHB and vehicle treated rats. To investigate possible GHB induced changes in autoreceptor function, 0.5 mg/kg haloperidol (D2 antagonist) was administered to all rats. Similar to previous reports, haloperidol induced a robust, frequency-dependent increase (5-fold at 20 Hz) in stimulated dopamine efflux. Repeated GHB administration did not alter the haloperidol effects. In summary, two weeks of GHB administration (by either route) neither altered baseline dopamine release and uptake nor affected autoreceptor-mediated effects of a D2 antagonist despite inducing a significant weight loss in all rats. Subchronic GHB did not induce adaptations in the regulation of extracellular dopamine that can occur with chronic treatment with addictive drugs. Supported by DA14608.

892 RACIAL/ETHNIC DIFFERENCES IN PARENTAL CONCERN ON DRUG USE IN A NATIONALLY REPRESENTATIVE SAMPLE

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Introduction: Parental concern and negative attitudes toward drug use may decrease the risk drug involvement of their children. Yet, few studies have examined differences in parental concern on drug use by race, and they are subject to selection bias (e.g., treatment samples), or incomplete model specification (i.e., unaccounted confounding of socioeconomic differences across race/ethnicity groups). We explore racial/ethnic differences in parental concern regarding their children's drug use in a nationally representative sample. Methods: The data are from the 2003 National Survey of Children's Health, a random-digit-dial household survey of children under 18 years of age (n=102,353, response rate=55.3%). One child was randomly selected from each household. The respondent was the parent or guardian who knew most about the child's health. In this study, parents of children aged 6 to 17 were asked about their concern about drug use (n=65,913). The responses were recoded as "concern a lot" and "concern a little or not at all". Logistic regression models controlled for gender, age, family structure and poverty level, tobacco use in the household, accommodating the survey design. Results: An estimated 20% of the parents had a lot of concern on their children's drug use. Differences by race were evident: 32% among African American (AA), 19% among White (W), and 24% among other races. Controlling for confounders, AA parents were estimated to be have higher odds of being concerned on their children's drug use (OR= 1.9, 95% CI: 1.7, 2.1) compared to W parents. Also, independently, parents of children without a mother were estimated to have higher odds of concern on the children's drug use (OR= 1.9, 95% CI= 1.6, 2.3). The odds of concern were higher with an increase of each child's age year (OR= 1.2; 95% CI= 1.2, 1.2). Comments: This study suggests that parental concern on adolescence drug use varies significantly by race. AA parents worry more on their children's drug use. Acknowledgments: NIDA grant 12390 and CMHHD grant MD002217.

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893 PHARMACOKINETIC FACTORS ASSOCIATED WITH MDMA-INDUCED 5-HT DEPLETION IN RATS

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Background. \pm -3,4-Methylenedioxymethamphetamine (MDMA or Ecstasy) administration causes depletion of brain 5-HT that is believed to reflect neurotoxicity. The acute pharmacokinetic parameters associated with MDMA-induced 5-HT depletions have not been well studied. **Hypothesis.** We predicted that sustained high levels of circulating MDMA would be required to cause long-term depletion of brain 5-HT. **Methods.** Male rats fitted with jugular catheters were treated with i.p. injections of MDMA (2, 4 or 8 mg/kg) or saline. One group received single injections, whereas another group received 3 injections, one every 2 h. Serial blood samples were withdrawn and body temperatures were measured post-injection. Plasma levels of MDMA and its metabolite, \pm -3,4-methylenedioxyamphetamine (MDA), were determined by GC/MS. Two weeks after MDMA treatments, rats were decapitated and post-mortem brain tissue was assayed for monoamines using HPLC-ECD. **Results.** In the single dose study, MDMA levels in plasma increased in parallel with the dose administered. The MDMA Cmax after a 2 mg/kg dose was 300 ng/ml, similar to the Cmax observed in humans given a recreational dose. No single injection of MDMA caused long-term depletion of 5-HT. In the repeated dose study, MDMA levels in plasma rose in a non-linear fashion. Specifically, MDMA Cmax values were greater than expected after the 2nd and 3rd doses, in agreement with studies in humans. Only repeated injections of 8 mg/kg caused significant depletion of brain 5-HT in rats (~40% depletion). **Conclusions.** Our results suggest that behaviorally-active doses of MDMA engender similar pharmacokinetics in rats and humans. Repeated high doses of MDMA cause drug accumulation in the bloodstream, and sustained drug levels above 1000 ng/ml are associated with long-term depletions of 5-HT in rat brain. **Acknowledgement.** This research was generously supported by the NIDA IRP.

894 RACIAL DIFFERENCES IN SYRINGE PURCHASING AND CARRYING

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We examined racial differences in pharmacy access to syringes and in attitudes toward carrying syringes among 420 out-of-treatment injecting drug users (IDUs) in North Carolina. Participants were recruited between 2003 and 2005 by street outreach workers using a targeted sampling approach. The present analyses are limited to African-American and non-Hispanic white participants. The sample was 76% male, 74% African-American, with a mean age of 41 years. Sixty-eight percent had a high school diploma or GED, and 20% were married. Thirty percent were homeless, and 68% were unemployed. HIV prevalence was significantly higher among African-Americans compared to among non-Hispanic whites (10% vs. 1%, $p = 0.001$). African-Americans had been to prison significantly more times than non-Hispanic whites (mean 2.1 vs. mean 1.5, $p = 0.035$) for non-Hispanic whites. African-Americans were significantly less likely to obtain syringes from pharmacies than from other sources (e.g. drug dealers, friends, etc.) (52% vs. 77%, $p < 0.001$). Furthermore, African-Americans were significantly more likely than non-Hispanic whites to report that they were afraid to carry a syringe (57% vs. 44%, $p = 0.025$). In logistic regression models that adjusted for confounders, African-Americans were significantly less likely than non-Hispanic whites to obtain syringes from pharmacies (OR = 0.33, 95% CI=0.20, 0.55) and significantly more likely to report being afraid to carry syringes (OR=1.7, 95% CI=1.03, 2.69). The limited pharmacy access to syringes and increased fear carrying them among African-Americans are particularly disturbing given the concentration of HIV among them. Additional implications of these findings will be discussed.

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