National Institute on Drug Abuse

Director's Report

to the

National Advisory Council on Drug Abuse

February, 1999

Index

[Home Page] [Office of Director] [First Report Section]

National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Research Findings

Basic Research

Normally Silent Synapses in Spinal Cord Become Active to Produce Chronic Pain

Silent glutamatergic synapses have been reported in various portions of the central nervous system (CNS) and are believed to underlie some nervous system plasticity. Using patch-clamp techniques in a slice preparation, NIDA grantee Min Zhou (University of Washington in St. Louis, St. Louis, Missouri) has found silent glutamatergic synapses in the spinal pain pathways of rats. This research suggests it is likely that the recruitment of these synapses contributes to chronic pain both by increasing the intensity of noxious sensory input (hyperalgesia) and by allowing normally non-noxious stimuli to activate pain pathways (allodynia). This research may help in the development of technologies to diminish chronic pain. Li, P., Zhuo M. Nature, 393, pp. 695-698, 1998.

Controlling for the Effect of Hair Color in Drug Tests

The ratio of eumelanin (brown-black pigment) to pheomelanin (reddish-yellow pigment) was recently shown to provide a good control for variations in PCP concentration found by hair color. PCP was found in the hair of multiple strains of rats and mice to whom PCP had been administered and who differed in the pigment composition of their hair. If these results were replicated in humans, this ratio could help eliminate the effect of hair color on drug test results for at least some drugs of abuse. Slawson, M.H., Wilkins, D.G., Rollins, D.E. J. Anal. Tox., 22, pp. 406-413, 1998.

Endothelial Cells and Abused Drugs

Dr. George Stefano and his colleagues have demonstrated recently that both morphine and anandamide stimulated endothelial cNOS and inhibit LPS- and IFN-stimulated iNOS. Inhibition of the adenylate cyclase cascade was also noted due to simultaneous generation of NO. These findings provide information regarding the relationship between cNOS and iNOS as well as the functional significance of cAMP cascade in the regulation of NOS activity that may contribute to a better understanding of endothelial regulatory activities. Stefano, G.B., Salzet, M., Magazine, H.I., et al., J. Cardiovascular Pharmacology, 31, pp. 813-820, 1998.

Neurotoxic Doses of Methamphetamine Induced Reactive Gliosis

Reactive microglia have been shown to play an active role in some models of cell damage. Dr. Teresa Hastings of the

University of Pittsburgh and her research team have investigated whether reactive glial changes occur in the striatum following neurotoxic administration of methamphetamine (METH) in rats. They demonstrated a temporally organized reactive gliosis throughout the striatum in these rats. Hyperplastic responses by reactive glia were maximal at two days post-METH and resolved to near control levels by six days. Furthermore, the magnitude of this response was greatest in the ventrolateral striatum, a subregion previously shown to undergo the greatest pathology. Inspection of other brain regions of the neuraxis revealed focal hyperplastic changes of microglia in piriform cortex, parietal cortex, periaqueductal gray and red nucleus that were of greater magnitude than those observed in the striatum. Collectively, these data demonstrate a robust activation of glial cells in regions known to exhibit METH-induced pathology and identify other brain regions at risk among METH abusers. LaVoie, M.J., Hastings, T.G., Card, J.P. Soc. Neuroscience Abstract, 24, p. 1243, 1998.

Associations to Rewarding Events are Not Dopaminergic

A major problem in the development of medications to prevent relapse to drug abuse is that our understanding of the reinforcing properties of drugs of abuse is based on the brain reward model. The brain reward model suggests that the dopaminergic nucleus accumbens plays a major role in mediating the reinforcing effects of drugs. However, clinical trials based on this model have been disappointing because dopaminergic antagonists do not seem to prevent relapse. For this reason, the Institute is encouraging studies to examine mechanisms beyond the nucleus accumbens to determine if there are non-dopaminergic mechanisms playing a major role in relapse. Recently, Dr. Ettenberg reported that dopamine receptor antagonism did not reduce subjects' motivation to seek food. Rats were trained to discriminate between two olfactory cues predicting either the presence or absence of food reinforcement in a goal box of a straight-arm runway. Rats learned to run the alley rapidly in the presence of the cue associated with food. A dopamine antagonist (halperdol) pretreatment did not alter this pattern of behavior. Thus the same dopamine antagonist treatments that disrupt food reinforcement do not prevent the food-seeking behavior produced by food-predictive cues. These findings are most likely applicable to the failure of dopamine antagonists to prevent drug relapse since relapse is generally accepted to result from environmental cues related to the drug experience. McFarland, K. Ettenberg, A. Behavioral Neuroscience 112(3), pp. 630-635, 1998.

Chronic Running Activity Decreases Sensitivity to Morphine-Induced Analgesia

The effects of exercise on morphine-induced analgesia were examined in male and female rats. Male rats housed in activity wheels (active group) for 20 days were more sensitive to pain than rats housed in standard laboratory cages (inactive group). Additionally, both active male and female rats displayed decreased morphine-induced analgesia relative to inactive controls. Moreover, females that had been inactive and then were permitted to run showed less morphine-induced analgesia relative to inactive rats, and to their own nociceptive responses when sedentary. In contrast, morphine-induced analgesia in initially active females who were housed in standard cages for 17 days prior to a second nociceptive test was enhanced relative to their first nociceptive test and to presently active rats. These observations showed that the attenuation of morphine analgesia induced by running is reversible and not permanent. Short term exposure to exercise (24 h running) had no significant effect on morphine-induced analgesia. These results indicate that chronic activity can decrease morphine's analgesic properties. These effects may be due to cross tolerance between endogenous opioid peptides released during exercise and exogenous opioids. Kararek, R.B., Gerstein, A.V., Wildman, R.P., Mathes, W.F., D'Anci, K.E. Pharm. Biochem. and Behav., 61(1), pp. 19-27, 1998.

Homer Regulates Metabotropic Glutamate Receptors-induced Intracellular Calcium Release

Homer (or Homer 1a) is a neuronal immediate early gene that is enriched at excitatory synapses and binds group 1 metabotropic glutamate receptors. Homer modulates the activity and assembly of the metabotropic receptor. NIDA grantee Dr. Paul Worley and his coworkers at the Johns Hopkins University School of Medicine recently characterized a family of Homer-related synaptic proteins derived from 3 distinct genes (Homer 1b/c, 2a/b, and 3). Like Homer immediate early gene (Homer 1a), all new members bind group 1 metabotropic glutamate receptors. In contrast to Homer 1a, new members are constitutively expressed and encode a C-terminal coiled-coil domain that mediates self-multimerization. Coiled-coil-Homers form natural complexes that cross-link metabotropic glutamate receptors and are enriched at the post synaptic density. Homer 1a does not multimerize, and blocks the association of metabotropic glutamate receptors with Coiled-coil-Homer complexes. Group 1 metabotropic glutamate receptors activate phosphatidylinositol turnover and trigger intracellular calcium release. Dr. Worley and his coworkers discovered that Homer-related synaptic proteins (Homer 1b/c, 2a/b, or 3) form a physical tether linking metabotropic glutamate receptors with inositol trisphosphate receptors. A novel proline rich "Homer ligand" (PPXXFr) is identified in group 1

metabotropic glutamate receptors and inositol trisphosphate receptors and these receptors co-immunoprecipitate as a complex with Homer-related synaptic proteins from brain. Expression of Homer 1a, which lacks the ability to cross-link, modulates metabotropic glutamate receptors-induced intracellular calcium release. These studies identify a novel mechanism in calcium signaling and provide evidence that an immediate early gene, whose expression is driven by synaptic activity, can directly modify a specific synaptic function. Xiao, B., Tu, J.C., Petralia, R.S., Yuan, J.P., Doan, A., Breder, C.D., Ruggiero, A., Lanahan, A.A., Wenthold, R.J., Worley, P.F. Neuron 21, pp. 707-716, 1998; Tu, J.C., Xiao, B., Yuan, J.P., Lanahan, A.A., Leoffert, K., Li, M., Linden, D.J., Worley, P.F. Neuron, 21, pp. 717-726, 1998.

Alpha7 Subunit and Subtypes of Receptors in Embryonic Sympathetic Neurons

Previous work has shown the presence of the a7 subunit of the nicotinic acetylcholine receptor to be present in the brain. Yu and Role recorded from sympathetic neurons in order to determine the physiological role of a7 nicotinic receptors in the brain. They report evidence that the a7 subunit contributes to three distinct heteromeric nicotinic acetylcholine receptors in chick embryonic sympathetic neurons. The currents evoked by nicotinic agonists in embryonic sympathetic neurons are different than the currents evoked by nicotinic agonists in the hippocampus in the brain where the nicotinic receptors appear to be composed only of homomeric a7 subunits and are highly permeable to calcium. The three different currents evoked by nicotinic agonists differ with respect to their sensitivities to a-bungarotoxin and methyllycaconitine, single channel conductances, and open times. This work suggests that alternative processing and trafficking of the a7 nicotinic acetlylcholine receptors subunit in neurons profoundly affects the functioning and pharmacology of nicotinic receptors. Yu, C.R., Role, L.W. Physiology (Lond), 509, pp. 651-65, 1998.

Stress and Adolescent Development

In a recent paper, Dr. Carol Kellogg and her associates report that restraint, as a form of stress, induced Fos in a broader spectrum of neurons in young adult than in juvenile male rats. The Fos protein, a product of an immediate early gene, is transiently expressed in neurons after stimulation. The lack of Fos-positive cells in specific areas of juveniles may relate to maturation of specific brain nuclei as age-related differences were observed in Fos production. These findings provide insight into the temporal regulation of the nuclei activated by the stressors as well as into the adolescent development of brain regions involved in mediating various stress responses. Kellogg, C.K., Awatramani, G.B., Piekut, D.T. Neuroscience, 83(3), pp. 681-689, 1998.

[Home Page][Office of the Director][Report Index][Next Report Section]

Archive Home | Accessibility | Privacy | FOIA (NIH) | Current NIDA Home Page

National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse
February, 1999

Research Findings

Behavioral Research

The Economics of Polydrug Abuse

Researchers at the University of Vermont are examining polydrug abuse in heroin abusers. In a simulation, where drugs were not actually given, heroin abusers were asked to purchase various drugs in a simulated market place. The researchers discovered that as the price of heroin increased, purchases decreased. Interestingly however, as the price of heroin increased, purchases of Valium and cocaine increased indicating that for heroin addicts these drugs substituted for heroin. Other results indicated that when income rose in the simulation, the demand for heroin and cocaine increased proportionally more than the rise in income. However, purchases of marijuana, alcohol and Valium did not change as income increased. Drug choices in the simulation were related to actual real-world drug use to the extent that volunteers who said they would purchase large quantities of valium, alcohol and cocaine in the simulation were found to actually use these drugs in real life. These results show that simulations are useful for understanding the relationship between the price of a drug and consumption, and polydrug abuse in the natural setting. Petry, N.M., Bickel, W.K. NBER Working Paper Series, Paper 6415, February 1998.

Does Nicotine Improve Memory?

Kenneth Perkins and his colleagues at the University of Pittsburgh studied how environmental context can mediate the effects of nicotine on working memory by introducing a distractor during the memory task. Smokers and non-smokers were administered nicotine (aerosol spray) or placebo. In comparison to non-smokers, or to conditions with no distractions, nicotine in the presence of the distracting stimuli improved smokers' short-term memory. These results suggest that environmental conditions, such as the presence of a distracting stimulus, may play an important role in mediating the effects of nicotine. Grobe, J.E. Perkins, K. et al. Experimental & Clinical Psychopharmacology 6, pp. 209-216, 1998.

Do Cigarette Cravings Reduce Language Ability?

Rolf Zwaan at Florida State University asked whether cigarette smoking urges interfere with language comprehension, perhaps by taking up working memory resources. Smokers (but not non-smokers) who heard a smoking urge script showed less accuracy during a sentence comprehension task. Also, smokers read the sentences significantly faster than nonsmokers. These results indicate again that smoking urges and cravings interfere with cognitive processing. Zwaan, R., Truitt, T. Experimental & Clinical Psychopharmacology, 6, pp. 325-330, 1998.

Do Addicts Have Altered Perceptions of Future Events?

Warren Bickel and his colleagues at the University of Vermont studied whether heroin addicts show shortened time horizons and decreased sensitivity to future consequences of their behavior compared with nondrug users. Heroin addicts enrolled in a buprenorphine treatment clinic were tested on the Stanford Time Perception Inventory (STPI) personality questionnaire, the Future Time Perspective (FTP) task, and the Bechara card task (which measures preferences for decks of cards that vary delayed and immediate rewards and punishers). Heroin addicts in comparison to controls: 1) scored lower on the STPI indicating less future orientation; 2) were less likely to predict events far into the future and less likely to systematically organize events in the future on the FTP scale; and 3) in the card task, were less likely to win money than controls because they more often played from a deck that contained greater immediate gains, but that resulted in large, delayed punishers and overall net losses. Petry, N., Bickel, W., Arnett, M. Addiction, 93, pp. 729-738, 1998.

Acute Effects of Alprazolam in Women with Premenstrual Dysphoric Disorder (PMS)

Research by Dr. Suzette Evans and colleagues at New York State Psychiatric Institute suggests that acute administration of alprazolam is not a useful treatment for PMS. Double-blind testing of mood and performance changes under varying doses of alprazolam and placebo during the luteal and follicular phases of subjects with confirmed PMS indicated substantial changes in mood as a function of the cycle phase. Alprazolam, however, failed to improve negative mood, but instead increased negative mood in the follicular phase and it impaired task performance in both phases. Subjective measures indicative of abuse liability did not increase following alprazolam administration. Alprazolam's failure to improve negative mood premenstrually, its increase in negative mood in the follicular phase, and its impairment of task performance in both phases argue against its clinical usefulness when administered acutely. Evans, S.M, Haney, M., Levin, F.R., Foltin, R.W., Fischman, M.W. Neuropsycho-pharmacology, 19, pp. 499-516, 1998.

Contingency-Management for Treating Drug Abuse in Individuals with Schizophrenia

Dr. John Roll and his colleagues at the University of Vermont examined the feasibility of using contingency-management interventions for the treatment of drug abuse in individuals with schizophrenia using cigarette smoking as an example of drug use. The first and third weeks of the three-week study served as the baseline for 11 individuals with schizophrenia. In the second week, during which patients could earn money by abstaining from cigarette smoking, abstinence was significantly greater than during the two baseline weeks. These results illustrate the potential sensitivity of drug use to reinforcement contingencies in this population, suggesting that contingency-management interventions are a feasible option for treating drug abuse of individuals with schizophrenia. Roll, J.M., Higgins, S.T., Steingard, S., McGinley Experimental and Clinical Psychopharmacology, 6, pp. 157-161, 1998.

Alcohol Enhances Oral Methadone Self-Administration

Alcoholism has been implicated in relapse to opiate dependence in methadone-maintenance patients. Few animal studies, however, have examined the effects of methadone-alcohol interactions. Dr. Richard Meisch at the University of Texas Health Science Center found that rhesus monkeys who did not readily self-administer methadone did consume significant amounts of a methadone-alcohol drug combination (in comparison to a choice of water). In this combination condition, methadone was consumed on the order of 4.8 to 6.8 mg/kg, well above the range of maintenance doses used in an opiate dependent population. Previous studies with methadone maintenance patients have found that supplemental methadone beyond the normal maintenance dose can serve as a reinforcer. Since the availability of oral ethanol has been demonstrated to enhance drug intake with other classes of abused drugs in animal self-administration studies, these results suggest that alcohol may enhance the reinforcing properties of methadone. Shelton, K.L., Macenski, M.J., Meisch, R.A. Pharm., Biochem. & Behav., 61, pp. 367-374, 1998.

Methylphenidate's Subjective Effects and Similarity to D-Amphetamine

Methylphenidate (Ritalin) is self-administered by non-human primates and may have significant abuse potential in man. Few studies have directly compared the subjective effects of methylphenidate with the potent addictive compound, d-amphetamine despite their structural and neuropharmacological similarities and the overlap in their behavioral effects. Dr. Craig Rush from the University of Mississippi Medical Center in Jackson, Mississippi has compared these two psychostimulant drugs. Research volunteers were tested for their ability to distinguish between

the intero-ceptive effects of 20 mg of d-amphetamine and various doses of oral methylphenidate. The study found that subjects reported a similarity of subjective effects between the two drugs. Moreover, the two drugs produced similar dose-response functions on self-report rating of effects such as "alert/energetic", "elated" and "like drug". Rush, C.R., Kollins, S.H. Pazzaglia, P.J. Exp. Clin. Psychopharm., 6, pp. 32-44, 1998.

Effect of Clonidine on Stress- and Drug-induced Relapse to Heroin and Cocaine Seeking

This presentation demonstrated evidence that in rats both clonidine and lofexidine (alpha-2 nor-adrenergic agonists) block footshock stress-induced cocaine and inhibit heroin reinstatement. Implications are that clonidine and lofexidine may be useful in decreasing the relapse to cocaine or heroin associated with stress that may occur in the longterm outpatient post detoxification period where the incidence of relapse to abused drugs is so high. Lofexidine may offer greater clinical utility than clonidine as a medication for relapse, as recent published double-blind controlled trials of lofexidine v. clonidine in opiate withdrawal suggest significantly less hypotensive effects of lofexidine at equieffective doses for withdrawal. Erb, S., Mueller, D., Shaham, Y., Leung, S. and Stewart, J. Effect of Clonidine on Stress- and Drug-induced Relapse to Heroin and Cocaine Seeking. Soc. for Neurosci., 24, p. 498, 1998.

Generalization Between Cocaine's Effects and a Stress "Cue"

Dr. Nick Goeders at Louisiana State University Medical Center in Shreveport, LA has been studying similarities between internal states due to stress and the internal states associated with cocaine. Experimenter-induced stress has been observed to induce a relapse to drug self-administration in an animal model, but the mechanism for this effect is unknown. Rats responded to restraint stress as if they had received cocaine, suggesting that the stress produced an internal state resembling the interoceptive stimulus properties of cocaine. The investigators speculate that this stress-induced internal state may mimic the anxiogenic properties of cocaine shown in other behavioral paradigms, or may resemble the drug's positive subjective effects if the internal state reflects "freedom from restraint". Mantsch, J.R., Goeders, N.E. Psychopharmacology, 135, pp. 423-426, 1998.

Cognition and Nicotine Metabolism

Cotinine is the major and persistent metabolite resulting from cigarette smoking, and its possible effects on memory and attention during or following smoking have not been fully explored. A report by Dr. Neal Benowitz and associates has indicated that cotinine administered orally to non-smokers resulted in decreased reaction time and a decline in recall memory. It was suggested that cotinine may play a role in the withdrawal symptoms seen during smoking abstinence. Herzig, K.E., Callaway, E., Halliday, R., Naylor, H., Benowitz, N.L. Psychopharmacology, 135, pp. 127-132, 1998.

Effects of THC and Anandamide Administration

Recent research by Dr. William Martin and associates has focused on the effects of D9-THC and on physical dependence and withdrawal. In one study, the acute administration of these compounds produced behavioral effects that were substantially reversed by pretreatment with a cannabinoid antagonist (SR141716A). The behavioral effects of anandamide were distinguishable from those of D9-THC, with anandamide inducing less ataxia. Following ten days of D9-THC, a challenge with SR141716A produced evidence of physical withdrawal. In contrast to the D9-THC effects, the authors reported only limited behavioral effects from withdrawal of anandamide, its precursor arachidonic acid, or a fluorinated methylanandamide chosen for its metabolic stability. Lichtman, A.H., Wiley, J.L., LaVecchia, K.L., Neviaser, S.T., Arthur, D.B., Wilson, D.M. and Martin, B.R. Eur. J.Pharm., 357, pp. 39-48, 1998; Aceto, M.D., Scates, S.M., Razdan, R.K., and Martin, B.R. J. Pharm.& Exp. Ther., 287, pp. 598-605, 1998.

[Home Page][Office of the Director][Report Index][Previous Report Section] [Next Report Section]

Archive Home | Accessibility | Privacy | FOIA (NIH) | Current NIDA Home Page

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National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Research Findings

Clinical and Services Research

Open Trial of Bupropion to Treat ADHD in Adolescents with Substance Use Disorders and Conduct Disorder.

Dr. Riggs and colleagues at the University of Colorado School of Medicine assessed the efficacy of bupropion to treat attention deficit hyperactivity disorder (ADHD) in adolescent males diagnosed with comorbid conduct and substance use disorders. The primary aim was to treat the ADHD and thereby indirectly reduce drug use and other behavior problems. Preliminary data indicate a reduction in ADHD symptomatology, antisocial behavior and level of drug abuse. Riggs, P.D., Leon, S.L., Mikulich, S.K. and Pottle, L.C. J. Am. Acad. Child Adolesc. Psychiatry, 37(12), pp. 1271-1278, 1998.

Fluoxetine Treatment of Depressive Disorders in Methadone Maintained Opioid Addicts

Drs. Petrakis, Carroll, Kosten, and Rounsaville at Yale University in Connecticut evaluated the efficacy of fluoxetine as a treatment for depression in a population of methadone maintained opioid addicts. Forty-four methadone maintained opioid addicts with depression received either fluoxetine or placebo in addition to their methadone, in a double-blind randomized trial, for 12 weeks. Depressive symptoms decreased significantly overall with no significant differences between the groups treated with fluoxetine versus placebo. In addition, drug use outcomes, including cocaine and heroin self-reported use and urine toxicology were measured. There was a significant decrease in heroin use in treatment, but no medication effect. Cocaine use was unchanged from pre-treatment to endpoint. Data analyses were conducted on a subsample of subjects with the most severe depression but there was no medication effect on either the depressive symptoms or on cocaine use. The findings suggest that fluoxetine is not effective in treating depression or cocaine use in this population. Drug and Alcohol Dependence, 50(3), pp. 221-226, 1998.

Superior Efficacy of Cognitive-Behavioral Therapy for Urban Crack Cocaine Users When Compared to 12 Step Facilitation: Main and Matching Effects

Drs. Maude-Griffin, Hohenstein, Humfleet, Reilly, Tusel, and Hall at the University of California and the San Francisco Veterans Affairs Medical Center evaluated the efficacy of manualized cognitive-behavioral therapy (CBT) and 12-step facilitation (12SF) in treating cocaine abuse by randomly assigning 128 subjects (126 males and 2 females; 80% African American; 84% unemployed; 75% homeless; 82% had a comorbid psychiatric disorder) to one of the two treatment conditions. In each treatment condition, subjects attended 3 group therapy sessions and one individual counseling session each week for 12 weeks. Patient-treatment matching effects such as depression history, abstract

reasoning ability, religious beliefs, drug use severity, and disease model beliefs, were evaluated. The study showed that the CBT participants were more likely to achieve 4 consecutive weeks of abstinence from cocaine than participants in the 12SF group (44% vs. 32%) verified through urine toxicology. Patients with depression and those with high abstract reasoning scores were more likely to benefit from the CBT than the 12SF. Drug use severity and belief in a disease model did not interact significantly with treatment condition to predict continuous abstinence. In this study African Americans with strong religious beliefs appeared to benefit more from 12SF than the CBT in achieving cocaine abstinence. This study is the first to demonstrate the superior efficacy of CBT for cocaine abuse when compared to another active psychotherapy. In addition, this study provides support for patient-treatment matching since the results suggest that both CBT and 12SF may be differentially effective for different subgroups of cocaine abusing patients. J. of Counseling and Clinical Psychology, 66(5), pp. 832-837, 1998.

Group Cognitive-Behavior Therapy For Dual-Diagnosis Women

Dr. Lisa Najavits developed a manualized treatment specifically adapted to the clinical needs of women with comorbid post-traumatic stress disorder (PTSD) and substance use disorder. No effective treatment has been identified for this substantial subpopulation of female drug abusers who also experience PTSD (33-59%). Outcome results on 17 women who completed the protocol treatment showed significant improvements in substance use, trauma-related symptoms, suicide risk, suicidal thoughts, social adjustment, family functioning, problem solving, depression, cognitions about substance use, and didactic knowledge related to the treatment. Results were based on assessments at pre-treatment, during treatment, post-treatment, and 3-month follow-up. The data suggest that women substance abusers with PTSD are highly responsive and able to show marked improvements when provided with a treatment that is adapted to their needs. Najavits, L.M., Weiss, R.D., Shaw, S.R., and Muenz, L.R. "Seeking Safety": Outcome of a New Cognitive-Behavioral Psychotherapy for Women with Posttraumatic Stress Disorder and Substance Dependence. Journal of Traumatic Stress, 11, pp. 437-56, 1998.

Cotinine: Effects with and Without Nicotine

The purpose of this study was to examine the effects of the metabolite of nicotine, cotinine, in comparison to the effects of the nicotine patch, and a combination thereof during cigarette abstinence. More specifically, this study examined the effects of cotinine on physiological measures, subjective measures assessing craving, withdrawal symptoms and mood, and performance measures. A between-subject, 2 x 2 factorial design was used, with the daily administration of a 15-mg nicotine patch (Nicotrol) versus placebo patch as one factor and 80 mg of oral cotinine fumarate versus placebo drug as the other factor. Baseline measures were obtained while the subjects smoked cigarettes on an ad lib basis for 1 week. Subjects (n=106) were then randomly assigned to one of four treatment conditions and for the next 14 days were required to be abstinent from cigarettes and take the study drugs. Cotinine administration, with or without nicotine patch, produced serum cotinine concentrations 3-4 times higher than during ad lib smoking. Results showed a reduction of self-reported tobacco withdrawal symptoms using the nicotine patch alone. Cotinine alone had no effect on withdrawal symptoms. However, when nicotine patch was combined with cotinine, the beneficial effect of the nicotine patch on withdrawal symptoms was absent. Therefore, cotinine appears to antagonize the effects of nicotine in the alleviation of withdrawal symptoms at concentrations higher than that attained from normal smoking. This effect does not appear to be mediated by changes in nicotine disposition. (author abstract) Hatsukami, D., Pentel, P.R., Jensen, J., Nelson, D., Allen, S.S., Goldman, A. and Raphael, D. Cotinine: Effects with and Without Nicotine. Psychopharmacology, 135, pp. 141-150, 1998.

Methylphenidate Treatment for Cocaine Abusers with Adult Attention-Deficit/ Hyperactivity Disorder: A Pilot Study

Attention-deficit/hyperactivity disorder (ADHD) is common among cocaine abusers seeking treatment. This open trial was carried out to assess the efficacy of sustained-release methylphenidate for the treatment of cocaine abuse among individuals with ADHD. Twelve patients who met DSM-IV diagnostic criteria for adult ADHD and cocaine dependence were entered into a 12-week trial of divided daily doses of sustained-release methylphenidate ranging from 40 to 80 mg. In addition to the pharmaco-therapy, patients also received individual weekly relapse prevention therapy. Individuals were assessed weekly for ADHD symptoms; vital signs and urine toxicologies were obtained 3 times a week. Of the 12 patients entered, 10 completed at least 8 weeks of the study and 8 completed the entire study. Using both a semistructured clinical interview and a self-report assessment, patients reported reductions in attention difficulties, hyperactivity, and impulsivity. Self-reported cocaine use and craving decreased significantly. More importantly, cocaine use, confirmed by urine toxicologies, also decreased significantly. These preliminary data

suggest that under close supervision, the combined intervention of sustained-release methylphenidate and relapse prevention therapy may be effective in treating individuals with both adult ADHD and cocaine dependence. (author abstract) Levin, F.R., Evans, S.M., McDowell, D.M., and Kleber, H.D. Methylphenidate Treatment for Cocaine Abusers with Adult Attention-Deficit/Hyperactivity Disorder: A Pilot Study. Journal of Clinical Psychiatry, 59, pp. 300-305, 1998.

Chronic Disulfiram Treatment Effects on Intranasal Cocaine Administration: Initial Results

Simultaneous abuse of cocaine and alcohol is common. Alcohol decreases negative stimulant effects and potentiates "high." Disulfiram (Antabuse) is being studied in outpatient trials as a cocaine pharmacotherapy with the rationale that inability to modulate cocaine effects with alcohol may decrease cocaine use. Authors examined the interaction of disulfiram and cocaine in a randomized, double-blind, placebo-controlled study where subjects were chronically treated with disulfiram and then participated in intranasal cocaine administration studies. Disulfiram 250 mg/day treatment significantly increased plasma cocaine concentrations ($p = .013$), heart rate (cocaine 1 mg/kg, $p = .046$), and systolic (cocaine 2 mg/kg $p = .003$) and diastolic (cocaine 2 mg/kg, $p = .022$) blood pressure. "High" and "nervous" ratings were nonsignificantly increased. The combination of "high" with increased anxiety in the context of inability to lessen negative effects with alcohol may be an effective treatment in selected patients. The significant pharmacokinetic interaction must be considered in the decision regarding use of disulfiram. (author abstract) McCance-Katz, E.F., Kosten, T.R., Jatlow, P. Chronic Disulfiram Treatment Effects on Intranasal Cocaine Administration: Initial Results. Biological Psychiatry, 43, pp. 540-543, 1998.

Amantadine Hydrochloride is Effective Treatment for Cocaine Dependence

Amantadine hydrochloride, a dopamine agonist, seems conceptually suitable as a candidate for cocaine dependence treatment. Authors report on a 16-week double-blind, randomized, placebo-controlled rapid evaluation of amantadine (100 mg bid) trial with 69 cocaine dependent subjects (34 amantadine, 35 placebo) in a community-based clinic in LA. Matrix Model counseling served as the psychosocial base for the trial. Subjects attended clinic 3 times per week (M,W,F) to provide data (urine samples, questionnaires) and to receive counseling (90 minute groups). Dependent variables were urine toxicology results as compiled by the Treatment Effectiveness Score (i.e., the number of "clean" urines for each subject) and Joint Probability at 8 and 16 weeks (i.e., number of subjects providing "clean" urines divided by number of subjects in that condition at that point). Though TES analyses fall just short of significance for amantadine (MA=16.0 "cleans"; MP=10.9 "cleans"; $P<.08$), significantly fewer amantadine subjects used cocaine at weeks 8 (A=13/34 subjects (0.38); P=5/35 subjects (0.14); $z=2.27$, $p=.01$) and 16 (A=9/34 subjects (0.27); P=3/35 subjects (0.09); $z=2.27$, $p=0.01$). Authors conclude that amantadine is sufficiently promising in efficacy to warrant further evaluation with large scale clinical trials. (author abstract) Shoptaw, S., Ling, W., Kintaudi, K., Rawson, R.A. Amantadine Hydrochloride is Effective Treatment for Cocaine Dependence. College on Problems of Drug Dependence, 60th Annual Scientific Meeting, Scottsdale, AZ , p. 132, 1998.

Several 'Endophenotypes' Have Been Described as Possible Markers for Drug Abuse Vulnerability

William G. Iacono and colleagues at the University of Minnesota have reported psychophysiological measures associated with increased risk for drug abuse. One example is based on "preception" -- ability to take advantage of the predictability of an aversive event to diminish its psychological impact; the second, on "antisaccades" -- the ability to generate a saccade in the direction opposite to an abrupt movement of tracking target. In the preception experiment, subjects watched the sweep hand of a clock and were told that a loud, unpleasant noise would be heard at infrequent times. Sometimes these blasts would be predictable by appearance of a warning stimulus; other times there would be no warning. Skin Conductance Responses (SCRs) and Heart Rates (HRs) were measures of how well the subjects made use of the warning information. Results showed that poor modulators -- individuals whose SCRs were higher for the predictable loud noises and whose HRs did not differentiate predictable from non-predictable -- had significantly more symptoms of alcohol and nicotine dependence. These results were interpreted as biologically based support for the theory that individuals at risk for substance dependence have poor inhibitory control related to a dysfunctional Behavioral Inhibition System (BIS). Taylor, J., Carlson, S.R., Iacono, W.G., Lykken, D.T., and McGue, M. Individual Differences in Electrodermal Responsivity to Predictable Aversive Stimuli and Substance Dependence. Psychophysiology, 36, pp. 1-6, 1998. In the antisaccade experiment, subjects are required to make an eye movement in the direction opposite to a moving target which is contrary to natural tendency. Those who are less successful are said to have a more faulty control on inhibitory mechanisms. The results showed a higher error rate in this task among "high risk" 17 year-old boys compared to "low risk" boys. (High and low risk are defined as to

whether fathers did or did not have a diagnosis of illicit drug abuse or dependence with co-morbid antisocial personality disorder). Additionally MZ twins discordant for drug abuse/dependence were nevertheless concordant for high error rates, suggesting a genetically based susceptibility for this deficit independent of diagnosis. Iacono, W. G. Identifying Psychophysiolgical Risk for Psychopathology: Examples from Substance Abuse and Schizophrenia Research. Psychophysiology, 35, pp.1-17, 1998.

Lowered P300 Electrical Evoked Responses were Associated with Drug Abuse Vulnerability

Iacono and colleagues demonstrated that the commonly reported electrical evoked response potentials (ERP) --P300-- to rare stimuli had a major genetic component because the amplitude was correlated by as much as .87 between one hemisphere of a monozygotic twin to the other hemisphere of the co-twin. Several studies in Iacono's lab showed that a reduced amplitude of this ERP was found in individuals with substance abuse problems or those at risk. In one study, there were significantly more cases of alcohol, illicit drug, and nicotine dependence among individuals with small P300 amplitudes than among the group with large amplitudes. Secondly, lower P300 amplitudes were reported in men who had alcohol abuse either alone or co-morbid with antisocial personality disorder, drug dependence, or both (smallest amplitude). Lower amplitudes were also reported in 17 year-old boys whose fathers had these diagnoses. Finally, there were lower P300 amplitudes in 17 year-old boys who subsequently (3 years later) developed an illicit drug abuse/dependence or nicotine dependence. Iacono, W.G. Identifying Psychophysiolgical Risk for Psychopathology: Examples from Substance Abuse and Schizophrenia Research. Psychophysiology, 35, pp.1-17, 1998.

Group Counseling Versus Individualized Relapse Prevention Aftercare Following Intensive Outpatient Treatment for Cocaine Dependence: Initial Results

Ninety-eight male cocaine-dependent patients who completed an intensive outpatient program were randomly assigned to either standard group counseling (STND) or individualized relapse prevention (RP) aftercare. Heavier cocaine and alcohol use and low self-efficacy predicted more cocaine use during the intensive outpatient treatment phase of the study, whereas lifetime diagnoses of alcohol dependence, major depression, and anxiety disorder predicted less cocaine use. Rates of complete abstinence during the 6-month study period were higher in STND than RP, whereas RP was more effective in limiting the extent of cocaine use in those who used during Months 1-3. Matching analyses indicated patients who failed to achieve remission from cocaine use during intensive outpatient treatment and those with a strong commitment to abstinence did better in RP than in STND, whereas patients less committed to abstinence did better in STND than RP. McKay, J.R., Alterman, A.I., Cacciola, J.S., Rutherford, M.J., O_Brien, C.P., and Koppenhaver, J. Journal of Counseling and Clinical Psychology, 66(5), pp. 778-788, 1997.

Predictors of Participation in Aftercare Sessions and Self-Help Groups Following Completion of Intensive Outpatient Treatment for Substance Abuse

The goals of this study were to identify predictors of greater participation in aftercare treatment sessions and self-help groups during the first 3 months following completion of a 4-week intensive outpatient rehabilitation (IOP) program. The subjects were 138 male veterans who a) met DSM-III-R criteria for lifetime diagnoses of both alcohol and cocaine dependence (n=67), alcohol dependence only (n=48) or cocaine dependence only (n=23); b) completed an IOP program; and c) expressed a desire to enter a formal aftercare program. Analyses examined relationships between predictor variables from five different domains and number of aftercare sessions and self-help groups attended in the last week of each month of the follow-up period. Of the predictor variables that were examined, only remission from cocaine and alcohol dependence during IOP and higher AIDS risk behavior scores in the prior 6 months contributed independently to the prediction of greater participation in aftercare. Further analyses identified several variables that were differential predictors of participation in individualized relapse prevention aftercare versus standard 12-step focused group aftercare. More years of cocaine use, greater current legal problems, and a lack of current alcohol dependence predicted greater self-help participation at the level of a trend. Remission from substance use dependence during IOP may be an important criterion for moving to the next level of care. However, the results of this study also look at factors present during the course of aftercare. McKay, J.R., McLellan, A.T., Alterman, A.I., Cacciola, J.S., Rutherford, M.J., and O_Brien, C.P. J. Stud. Alcohol, 59, pp.152-162, 1998.

Using State Information Systems for Drug Abuse Services Research

Political and social demands for effective and cost-effective drug and alcohol treatments challenge public policy makers and services researchers to assess provider performance, monitor patient outcomes, and document effectiveness and cost-effectiveness of care. The information systems built and maintained by public health authorities are an under used source of data on provider performance, patient characteristics, treatment completion, readmission rates, treatment outcomes, and costs of care. The Maine, Massachusetts, and Ohio substance abuse information systems were used to demonstrate the benefits and pitfalls of state substance abuse databases to study the organization, costs, and cost-effectiveness of publicly funded treatment services. McCarty, D., McGuire, T.G., Harwood, H.J. and Field, T. American Behavioral Scientist, 41(8), pp. 1090-1106, 1998.

Service-level Costing of Drug Abuse Treatment

A methodology is developed for estimating the cost of delivering specific substance abuse treatment services. Based on data from 13 programs, it was estimated that the average cost of residential treatment is $2,773 per patient per month and outpatient treatment costs an average of $636 per patient per month. Data are presented on the cost per patient per month for individual treatment and nontreatment services, average number of services, costs per unit of service, and intensity of services. In addition to their applications to insurance benefit cost estimation and as an aid in the design of cost-effective treatment, these data illustrate the costing of best practice adolescent treatment consistent with a Center for Substance Abuse Treatment (CSAT) Treatment Improvement Protocol. Anderson, D.W., Bowland, B.J., Cartwright, W.S. and Bassin, G. Journal of Substance Abuse Treatment, 15(3), pp. 201-211, 1998.

Mapping-Enhanced Drug Abuse Counseling Urinalysis Results in the First Year of Methadone Treatment

Urinalysis (UA) tests for opiates and cocaine were obtained over a 12-month period for a total of 155 long-term patients who participated in treatment in one of three urban methadone centers. At admission, patients were randomly assigned to "node-link mapping" (n=82) or "standard" (n=73) counseling treatment. Node-link mapping is a strategy for visually representing interrelationships between patients' ideas, feelings, and experiences. These multirelational maps are developed (usually by counselors) during individual and group counseling sessions to clarify patients' issues and problems. The results revealed that (a) mapping patients had significantly fewer opiate-positive UAs during months 2-6 of treatment and (b) session attendance was a significant predictor of cocaine-positive UAs over months 2-12 for mapping patients. The findings suggest that mapping-enhanced counseling is an effective method for improving outcomes during the first six months of treatment. Dees, S.M., Dansereau, D.F., and Simpson, D.D. Journal of Substance Abuse Treatment, 14(1), pp. 45-54, 1997.

Current Approaches to Drug Treatment for Women Offenders

Treatment approaches at eight corrections- and community-based programs in New York City and Portland, Oregon are reviewed. Data were obtained from life history interviews conducted with 60 women and from observation of treatment. Drug abuse treatment programs for women offenders employ a range of therapeutic interventions to address drug use and criminality. Recently, programs have begun to address victimization experiences as an integral if not central feature of women's drug use and participation in illegal activities. Programs have tailored treatment approaches for women offenders by offering incest and domestic violence survivor groups, assigning therapeutic rather than punitive sanctions, and training corrections staff to support treatment goals. Welle, D., Falkin, G.P., Jainchill, N. Journal of Substance Abuse Treatment, 15(2), pp. 151-163, 1998.

Predicting Drug Treatment Entry Among Treatment-Seeking Individuals

This study examines factors contributing to treatment entry in a sample of 276 drug abusers who actively sought referral to drug treatment. At 6 months after referral to a treatment program, about 62% had entered treatment. Treatment-entry and non-entry subjects did not differ in socio-demographics (age, gender, race/ethnicity, education), type of drug use, or years of use. Legal coercion was found to be an effective factor promoting treatment entry. Those having prior successful treatment experience were also more likely to re-enter treatment. However, those with more severe problems (drug related and other) seemed less likely to enter treatment, suggesting that psychological distress and family problems may undermine motivation to follow through on treatment referral. The findings also indicate that attention is needed to improve treatment access and to address related issues such as eligibility criteria,

waiting list alternatives, and transportation. Hser, Y.I., Maglione, M., Polinsky, M.L., and Anglin, M.D. Journal of Substance Abuse Treatment, 15(3), pp. 213-220, 1998.

Management of Adults Recovering From Alcohol or Other Drug Problems

This study offers a practical approach to relapse prevention in the primary care setting for physicians who encounter relapse to drug or alcohol use in patients recovering from drug disorders. Working within a supportive patient-physician relationship, the primary care physician can help recovering patients decrease their susceptibility to relapse by employing strategies based on effective drug abuse treatment. Drawing on the therapeutic relationship and skills they already possess, primary care physicians can have an important, productive, and satisfying role in the long-term management of patients in recovery from alcohol or other drug problems. Friedmann, P.D., Saitz, R., and Samet, J.H. JAMA, 279, pp. 1227-1231, 1998.

Organizational Correlates of Access to Primary Care and Mental Health Services in Drug Abuse Treatment Units

Organizational factors were found to be associated with access to primary care and mental health services in drug abuse treatment. Findings were based on a national probability survey of 618 outpatient drug abuse treatment programs in 1995. It was found that publicly-funded programs, programs with more human resources, and methadone programs delivered more primary care services. Greater access to mental health services was found in publicly-funded programs, Joint Commission on Accreditation of Health Care Organizations-accredited programs, nonmethadone programs, and programs with more staff psychiatrists or psychologists delivered more mental health services. Friedmann, P.D., Alexander, J.A. and D'Aunno, T.A. Elsevier Science Inc., 1998.

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National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Research Findings

AIDS Research

Increased Transmission of Vertical Hepatitis C Virus (HCV) Infection to Human Immunodeficiency Virus (HIV) Infected Infants of HIV and HCV Co-infected Women

The transmission of perinatal HCV infection was studied retrospectively in infants born to HCV and HIV co-infected women enrolled in a prospective natural history study of HIV transmission. Infant HCV infection was assessed by RNA PCR. The overall rate of vertical HCV transmission was 16.4% (9/62). The rate of HCV infection was higher among HIV-infected infants than among HIV-uninfected infants (40% vs.5%; OR, 8.2; p=.009). This difference in transmission was not related to maternal HCV viral load by branched DNA assay, or mode of delivery. The rate of HCV transmission in HIV-uninfected infants of HIV and HCV co-infected mothers was similar to that reported for infants born to HIV-uninfected mothers. Papaevangelou, V., Pollack, H., Rochford, G., Kokka, R., Hou, Z., Chernoff, D., Hanna, Krazinski, K., Borkowsky, W. J Infect Dis., 178, pp.1047-52, 1998.

Sex Differences in HIV-1 Viral Load and Progression to AIDS

A study of HIV-1 viral load differences in men and women was performed in an ongoing cohort study of injection drug users. Women were found to have significantly lower viral load measurements than men. HIV-1 was measured by branched chain DNA at baseline, and by reverse-transcriptase PCR and quantitative microculture on follow-up three years later. Median viral load measurements were significantly lower in women than men by all three methods. Viral load measurements in women were 38- 65% of those in men. The association of lower viral load in women remained even after adjusting for CD4 cell count, race, and drug use. While men and women had statistically similar time to AIDS, women with the same viral load as men had a 1.6-fold higher risk of AIDS, or, equivalently, women with half the viral load of men had a similar time to AIDS. These results suggest that, while men and women have similar time to AIDS, there is a different relationship between viral load and AIDS in women compared to men. While a biological mechanism remains to be elucidated, these findings have implications for timing of initiation of therapy relative to viral load thresholds in women. Farzadegan, H., Hoover, D., Astemborski, J., Lyles, C.M., Margolick, J.B., Markham, R.B., Quinn, T.C. Lancet, 352, pp.1510-1514, 1998.

Gp120 May Facilitate the Entrance of HIV into Body Compartments

Gp120, an envelope protein found in HIV, may facilitate the entrance of HIV-infected monocytes into body compartments by enhancing immunocyte-endothelium interactions that favor transmembrane migration. Long-term or continuous exposure of the endothelia to morphine and anandamide resulted in a significant enhancement of

monocyte adherence and this appeared to be due to desensitization of endothelium to further NO release. Whereas gp120 did not stimulate the release of constitutive endothelial NO, morphine and anandamide elicited the release of NO. Collectively, these findings suggest that the continued presence of abused substances may result in more rapid progression to AIDS probably due to a higher viral load in individuals that abuse these substances and have HIV. Stefano, G.B., Salzet, M., Bilfinger, T.V. Journal of Cardiovascular Pharmacology, 31, pp. 862-868, 1998.

Comprehensive Treatment for HIV Positive Cocaine and Opioid Dependent Patients: Preliminary Findings

Drs. Avants, Margolin, DePhilippis, and Kosten from Yale University in Connecticut have recently reported on a preliminary study in which 6 HIV positive opioid and cocaine dependent patients were provided a 12 week comprehensive pharmacological and psychosocial treatment program designed to address the treatment needs of HIV positive drug users. This program included buprenorphine (12mg/day), buproprion (150 mg/day), and twice weekly manual-guided group therapy. Preliminary findings showed decreases in IV cocaine use, cocaine craving, and depressive symptoms compared to outcomes of the patients receiving the standard methadone maintenance treatment. Journal of Substance Abuse Treatment, 18(3), pp. 257-258, 1998.

Assessment of HIV Risk

Dr. Chawarski and colleagues at Yale University propose a number of solutions aimed at improving validity and efficiency of assessment of HIV risk in drug abusing populations. Five domains of assessment are discussed; intravenous drug use, high-risk sexual behaviors, knowledge of HIV transmission and methods of prevention, psychological aspects of behavioral change, and epidemiological factors of HIV transmission. The paper also discusses format, scope and context, as well as scoring procedures that may improve discriminability and sensitivity to detect change over the Risk for AIDS Behavior (RAB), one of the most commonly used instruments to assess risk behavior. Finally the AIDS Risk Inventory (ARI), a risk assessment instrument which incorporates methodological improvements discussed in the paper, is described. Chawarski, M.C., Pakes, J., Schottenfeld, R.S. Journal of Addict Dis., 17, pp. 49-59, 1998.

Perinatal Transmission of Hepatitis C Virus from HIV-1 Infected Mothers

Antepartum plasma hepatitis C virus (HCV) RNA was quantified in 155 mothers enrolled in the Women & Infants Transmission Study (WITS) who were co-infected with HCV and HIV, and HCV RNA was serially assessed in their infants. Of 155 infants born to HCV-antibody positive mothers, 13 (8.4%) were HCV infected. The risk of HCV infection was 3.2-fold greater in HIV-infected infants compared with HIV-uninfected infants (17% vs. 5.4%, $p=0.04$). The median concentration of plasma HCV RNA was higher among the 13 mothers with HCV-infected infants (2.0 x 10(6) copies/mL) vs. 142 mothers with HCV-negative infants (3.5x 10(5) copies/mL; $p<0.001$). There were no instances of HCV transmission from 40 mothers with HCV RNA concentrations of <10(5) copies/mL. The results indicated that HIV-infected infants have a higher risk of HCV infection than HIV-uninfected infants, but that women dually infected with HIV-1 and HCV with little or no detectable HCV RNA have a low risk of transmitting HCV to their infants. Thomas, D.L., Villano, S.A., Riester, K.A., Hershow, R., Mofenson, L., Landesman, S.H., Hollinger, F.B., Davenny, K., Riley, L., Diaz, C., Tang, H.B., and Quinn, T. J. Infect Dis.,177, pp. 1480-1488, 1998.

Declining HIV Seroprevalence in New York City Suggests A New Phase of the Epidemic

Researchers assessed recent trends in HIV seroprevalence among IDUs in New York City by analyzing temporal trends from 1991 to 1996 in 5 studies of IDUs recruited from a detoxification program, a methadone maintenance program, and research storefronts in the Lower East Side and Harlem areas, and a citywide network of STD clinics. A total of 11,334 serum samples were tested. From 1991 through 1996, HIV seroprevalence declined substantially among subjects in all 5 studies: from 53% to 36% in the detoxification program, from 45% to 29% in the methadone program, from 44% to 22% at the Lower East Side storefront, from 48% to 21% at the Harlem storefront, and from 30% to 21% in the STD clinics (all $p<.002$ by chi square tests for trends). The duration of the epidemic, the available death rate data, and the declining seroprevalence among long-term injectors all indicate loss of HIV-seropositive persons as a contributing factor to the decline in HIV seroprevalence among IDUs in New York City. In addition, continuing risk reduction, recent HIV incidence studies, and declines in HIV among new injectors indicate risk reduction or low HIV incidence as another contributing factor. These reductions in HIV seroprevalence among IDUs in

New York City indicate a positive, new phase in the very large epidemic. HIV prevention efforts should be continued to maintain these favorable trends. Des Jarlais, D.C., Perlis, T., Friedman, S.R., Deren, S., et al. Declining Seroprevalence in a Very Large HIV Epidemic: Injecting Drug Users in New York City, 1991 to 1996. Am. J. Public Health, 88(12), pp.1801-1806, 1998.

HIV Risks are Associated with Multiperson Use of Injection Equipment in IDU Networks

This paper examines serial use of drug injection equipment and paraphernalia, using concepts and methods from ethnographic research in combination with social network theory to help understand the behavioral transactions that link IDUs in the drug acquisition, preparation, and injection process. Seven of the sites in the NIDA Cooperative Agreement (CA) for AIDS Community-Based Outreach and Intervention Research program conducted an ethnographic substudy of injection episodes among out-of-treatment IDUs to examine drug acquisition and multiperson use of paraphernalia, drugs, and needles/syringes. Ethnographers observed 54 injection episodes in which IDUs were linked by HIV risk behaviors, and developed a typology of higher-risk, lower-risk, and nonsharing-risk networks. Multiperson use of injection paraphernalia or drug solution occurred in most injection events (94%). Serial use of syringes/needles occurred infrequently (14%) relative to "backloading" (37%) and reuse of paraphernalia (cookers 84%, cottons 77%, water 77%). Higher risk injection networks were characterized by larger size and pooling of resources for drugs. Study findings suggest several public health recommendations. Specifically, in addition to emphasizing use of sterile syringes/needles, HIV prevention efforts should focus attention to the more subtle and elusive behaviors involved in multiperson use of drug preparation and injection paraphernalia that are used to transfer drug solutions among injectors. At a minimum, this information should be a standard part of all prevention messages for IDUs, combined and incorporated into existing prevention strategies, including outreach, drug user treatment, HIV antibody testing and counseling, and syringe exchange programs. Needle, R.H., Coyle, S., Cesari, H., Trotter, R., et al. HIV Risk Behaviors Associated with the Injection Process: Multiperson Use of Drug Injection Equipment and Paraphernalia in Injection Drug User Networks. Substance Use and Misuse, 33(12), pp. 2403-2423, 1998.

Noninjecting Drug Users More Likely to Change Drug Use than Sexual Risk Behaviors

Researchers analyzed data from five of the study sites in the NIDA Cooperative Agreement (CA) for AIDS Community-Based Outreach and Intervention Research program to determine how the outcomes of noninjecting drug users differed after receiving either the standard or the enhanced intervention. In this analysis, change in behavior was stratified into two categories based on a matrix of levels of risk: improved or worsened conditions. Three key variables were analyzed: change in crack/cocaine use, change in the number of sexual partners, and change in the frequency of condom use. There were 1,434 noninjecting crack/cocaine users in the sample, classified according to their self-reports of never having injected drugs or of at least not injecting in the 12 months before the interview. Of these, 82% improved crack/ cocaine use at the follow up. The enhanced intervention group showed more improvement in crack/cocaine use than the standard intervention group. Overall, 76% reported reducing sexual partners, maintaining a one-partner relationship, or abstaining from sex at both time periods. Women in the enhanced intervention group improved more than women in the standard intervention (81% vs 75%). In terms of condom use, more respondents worsened than improved (55% vs 45%). This study confirms that HIV/AIDS interventions can reduce crack/cocaine use; however, high-risk sexual behaviors are more difficult to change. Reasons for this lack of improvement and suggestions for future interventions are discussed. Cottler, L.B., Leukefeld, C., Hoffman, J., Desmond, D., Wechsberg, W., et al. Effectiveness of HIV Risk Reduction Initiatives among Out-of-Treatment Noninjection Drug Users. J. Psychoactive Drugs, 30(3), pp. 279-290, 1998.

Psychosocial Risk and Protective Factors for Condom Use Among Female Injection Drug Users

This study was designed to examine the influences of domains of psychosocial risk and protective factors on male-partner condom use in a cohort of 209 female HIV-positive (HIV+) and HIV-negative (HIV-) injection drug users (IDUs) by use of a cross-sectional, retrospective design. Information was collected from a structured questionnaire and included data on psychosocial risk and protective factors in the personality, family, and peer domains; HIV status; and condom use. Among HIV+ IDUs, personality risk factors (e.g., unconvention-ality), family (e.g., low maternal identification), and peer factors were related to less male-partner condom use. Resources and condom availability were associated with greater male condom use with both HIV+ and HIV- IDUs. These findings suggest the need to use specific psychosocial interventions to prevent risky sexual behavior among HIV+ and HIV- female IDUs. Brook, D.W., Brook, J.S., Whiteman, M., Gordon-Maloul, C., Win, P.T., Masci, J.R., Roberto, J., de Catalogne, J., and

Amundsen, F. Psychosocial Risk and Protective Factors for Condom Use among Female Injection Drug Users. American Journal on Addictions, 7, pp. 115-127, 1998.

HIV Risk among Latinas

This study examined the psychosocial risk factors for HIV infection in a community sample of Latinas. National data indicate that women of various Latin and South-American nationalities (including Latinas of Mexican decent) are nearly three times more likely to acquire AIDS than other women in the United States. Structural equation models were used to test relationships among predictors, mediators (including components of the Health Belief Model), and sex-related outcomes and behavior in a random, cross-sectional community sample of 227 sexually-active Latinas (M-age = 32). Acculturation was significantly associated with higher HIV- related risks in their primary relationships. Older Latinas were less likely to make behavior changes or use barrier methods of contraception to prevent HIV and had higher rates of unintended pregnancies compared to younger Latinas. Marriage was related to greater risk in relationship and less behavior change. Theoretical models accounting for ethnicity, race, and culture are needed to understand better unwanted sexual outcomes for Latinas, including HIV risks. The need for strategies that specifically address these issues for HIV prevention and counseling programs for Latinas is discussed. Newcomb, M.D., Wyatt, G.E., Romero, G.J., Tucker, M.B., Wayment, H.A., Vargas, J. H., Solis, B., & Mitchell-Kernan, C. Acculturation, Sexual Risk Taking, and HIV Health Promotion Among Latinas. Journal of Counseling Psychology, 45, pp. 454-467, 1998.

HIV Risk among African-American Youth

Ramirez-Valles and colleagues examined the community and personal risk factors for HIV infection among a predominantly African-American sample of teenagers at risk for drug abuse. Sexual activity among high-school-aged youths has steadily increased since the 1970s, emerging as a significant public health concern. Yet, patterns of youth sexual risk behavior are shaped by social class, race, and gender. Based on sociological theories of financial deprivation and collective socialization, the authors developed and tested a model of the relationships among neighborhood poverty; family structure and social class position; parental involvement; prosocial activities; race; and gender as they predict youth sexual risk behavior. Structural equation modeling was used to test this model on a cross-sectional sample of 370 sexually active high-school students from a midwestern city; 57 percent (n = 209) are males and 86 percent are African American. Family structure was found to indirectly predict sexual risk behavior through neighborhood poverty, parental involvement, and prosocial activities. In addition, family class position indirectly predicts sexual risk behavior through neighborhood poverty and prosocial activities. Ramirez-Valles, J., Zimmerman, M.A., and Newcomb, M.D. Sexual Risk Behavior among Youth: Modeling the Influence of Prosocial Activities and Socioeconomic Factors. Journal of Health & Social Behavior, 3, pp. 237-253, 1998.

Factors Identified in HIV Sex Risk Behavior Change among Puerto Rican Drug Users

Researchers studied change in sex risk behaviors and factors related to change among 911 IDUs and 359 crack smokers recruited from the San Juan metropolitan area. A total of 1,004 (79.1%) of the drug users at baseline were assessed at follow-up. Abstinence from sex behavior increased from 54.6% to 61.1%, use of condoms during vaginal sex also increased from 26.4% to 36.9%. In multivariate analysis, significant predictors of abstinence were gender, injection drug use, HIV seropositivity, and not having a steady partner. Predictors of using condoms during vaginal sex were HIV seropositivity, STD diagnosis and participation in an HIV prevention program. These findings indicate that additional HIV prevention efforts are needed to reduce sex risk behaviors among drug users who have a steady sex partner as well as among drug users who are HIV negative. Robles, R.R., Marrero, C.A., Matos, T.D., Colon, H.M., et al. Factors Associated with Changes in Sex Behavior among Drug Users in Puerto Rico. AIDS Care, 10(3), pp. 329-338, 1998.

Racial Comparisons of HIV Risk Found to Have Little Utility in Rio de Janeiro, Brazil

Racial identities in Brazil are dynamic concepts which can only be understood if situated and explored within appropriate cultural contexts. The fluidity of racial identification in Brazil became empirically evident in this study, conducted in the context of a prevention initiative targeting segments of the Rio de Janeiro population at high risk for HIV/AIDS. Comparisons of client data at baseline and follow-up assessments form the analytic core of the research program, since its main objective is to slow the spread of AIDS through an intervention designed to promote behavioral change. Using quality control procedures to link client information collected at different points in time,

researchers found that 106 clients (i.e., 12.5% of the 849 clients in the follow-up sample) had changed their racial identification. Specifically, 5.7% changed from black to white, 30.2% from black to brown, 20.8% from white to brown, 3.8% from white to black, 23.6% from brown to black, and 15.1% from brown to white. Analyses of the shifts in racial self-identification suggest that interviewer characteristics were an important influence on a client's self-reported race. One of the strongest predictors of a change in racial identity was having a different interviewer at baseline and follow-up. Those assigned a black interviewer at follow-up were less likely to change their race than those interviewed by a white, but clients interviewed by different white interviewers at baseline and follow-up were most likely to change race. Interestingly, members of all racial categories were equally likely to shift their identification at the second contact, so that racial identity at baseline was not predictive of race changing at follow-up. In the U.S., race continues to be one of the most significant and consistent predictors of HIV risk and serostatus. By contrast, in Brazil, race was found to have very little utility for predicting HIV risk, sexual activity, drug use, and behavioral changes. Surratt, H.L. and Inciardi, J.A. Unraveling the Concept of Race in Brazil: Issues for the Rio de Janeiro Cooperative Agreement Site. J. Psychoactive Drugs, 30(3), pp. 255-260, 1998.

Geographic Information Systems Used to Assess Spatial Patterns of Drug Use

Researchers in Baltimore explored the use of Geographic Information Systems (GIS) to study whether frequency and type of drug use are geographically located within the city of Baltimore independent of neighborhood characteristics. They also sought to assess geographic factors associated with sample selection attrition. GIS is typically used to capture, store, manipulate, display, and analyze geographically referenced data, so that the spatial relations among variables can be assessed, such as those among census tracts, transportation routes, block-level crime, and household residences. For this study, 597 out-of-treatment IDUs, who were part of an ongoing project, AIDS Linked to Intravenous Experiences (ALIVE), made up the study sample, in addition to those with whom they shared drugs. The participants had been recruited into an HIV intervention program called Stop AIDS for Everyone (SAFE), the clinic for which was located three blocks from the ALIVE clinic. Drug users who resided further from the clinic reported more sharing of syringes, and in the western section of the city, a greater proportion of IDUs reported daily cocaine use and any use of crack cocaine. Even after adjusting for individual level and census tract data on demographic characteristics, geographic residential location continued to be associated with drug use. The results of this study suggest that type and frequency of drug use is associated with specific geographic areas, independent of neighborhood characteristics. These results have implications for the location of drug use interventions, needle exchange, and other HIV prevention activities. Latkin, C., Glass, G.E., and Duncan, T. Using Geographic Information Systems to Assess Spatial Patterns of Drug Use, Selection Bias and Attrition among a Sample of Injection Drug Users. Drug and Alcohol Dependence, 50, pp. 167-175, 1998.

Study Finds that Shooting Gallery Managers are at Great Risk of Communicable Diseases

Researchers in Puerto Rico assessed HIV risk behaviors, HIV seroprevalence, and tuberculosis infection in 464 IDUs, 12.5% of whom managed shooting galleries. The median frequency of drug injection was higher in shooting gallery managers than in nonmanagers. A trend was observed for purified protein derivative reactivity to increase according to the length of time spent as a gallery manager, but it was not statistically significant. However, anergy rates increased significantly with increases in the number of months spent as shooting gallery manager. Multivariate analyses showed that IDUs reporting shooting gallery management experience of >25 months were more likely to be infected with HIV. Prevention programs need to emphasize strategies to protect the health of shooting gallery clients and, in particular, shooting gallery managers. Additional studies are required to determine effective strategies for reducing the risk of HIV and TB infection in shooting galleries. Robles, R.R., Marrero, C. A., Reyes, J.C., Colon, H.M., et al. Risk Behaviors, HIV Seropositivity, and Tuberculosis Infection in Injecting Drug Users Who Operate Shooting Galleries in Puerto Rico. JAIDS, 17(5), pp. 477-483, 1998.

HIV Prevention Protocols Adapt to Evolving Changes in Substance Abuse Environments

Applied research in HIV prevention with out-of-treatment drug users occurs in an environment that is constantly changing. As a consequence, it is necessary for researchers to identify changes in drug use and sexual risk patterns, develop and evaluate appropriate interventions to respond to those changes, and find ways to make effective use of new technologies as they are developed. An example of this is the collaborative revision of NIDA's Standard Intervention for HIV prevention by the six final study sites in the NIDA Cooperative Agreement (CA) for AIDS Community-Based Outreach and Intervention Research program. In this paper, researchers from these six sites review the history of the National AIDS Demonstration Research (NADR) and CA programs and recent changes made

to the Standard Intervention protocol. The review illustrates the processes and rationale involved when responding to changes in the substance abuse environment and adapting HIV prevention protocols to those changes. Wechsberg, W.M., Desmond, D., Inciardi, J.A., Leukefeld, C.G., et al. HIV Prevention Protocols: Adaptation to Evolving Trends in Drug Use. J. Psychoactive Drugs, 30(3), pp. 291-298, 1998.

Multisite Study Finds Acceptability of the Female Condom by High Risk Women

In 1996, six study sites participating in the NIDA Cooperative Agreement (CA) for AIDS Community-Based Outreach and Intervention Research program initiated a collaborative project to examine the acceptability of the female condom among women at high risk for HIV infection. Specifically, they sought to introduce the female condom to a large sample of women drug users, to explore its acceptability as a risk-reduction device among these women, and to examine correlates of its use. In this paper, individual site data are presented from three of the participating sites, San Antonio (115 women), St. Louis (106 women), and Rio de Janeiro (97 women). The women represented a diversity of background characteristics at each of the three sites, with a median age of 28 in Rio de Janeiro, and one of 36 in St. Louis. More women were single in both Rio and St. Louis, but more were married or cohabiting in San Antonio. Most of the women in the study in St. Louis were African American, and most were Latina in San Antonio and multiracial in Rio. The findings from this study are presented as preliminary and representative of women in just three of the six sites. Nonetheless, they signify one of the largest cohorts of high-risk, drug-involved women studied to date in terms of their experiences with the female condom. While use rates varied widely by site, use was related most closely to frequency of sex, the number of sex partners, trading sex for drugs, and male condom use. In San Antonio, women who engaged in high-risk sex for drug exchanges were almost 3 times more likely to try the female condom than were nontraders. In Rio, female condom use was much more likely among users of the male condom, suggesting that substitution of female condom use for male condom use may have occurred among those who were dissatisfied or had partners who were unhappy with some aspect of the male condom. Finally, women at 2 of the 3 sites favored the female condom over the male condom and rated it higher on the basis of overall satisfaction. The authors conclude that, as an innovative device that was unfamiliar to almost all the women in the study, the female condom was favorably received. The fact that large proportions of the women at each site used the female condom on more than one occasion also suggests that those who had a positive first-use experience were willing to continue using it as a method of risk reduction. Surratt, H.L., Wechsberg, W.M., Cottler, L.B., Leukefeld, C.G., et al. Acceptability of the Female Condom Among Women at Risk for HIV Infection. American Behavioral Scientist, 41(8), pp. 1157-1170, 1998.

Stages of Adaptation and Negotiating Behavioral Change in HIV+ Adolescent Girls

A demonstrative case of an HIV-positive girl is presented in order to illustrate the stages of adaptation that HIV positive youth undergo (i.e., acceptance, resumption of life, coping with reminders of serostatus). Also discussed is the process by which this individual changes her behavior (e.g., reduction in transmission behaviors, adherence to medical programs, improving quality of life) and the integral role and contributions the service provider can make in the behavioral-change process for HIV-positive youth. Finally, this case illustrates some of the unique issues encountered by HIV-positive women and how those issues can be incorporated into a comprehensive, coordinated, and continuous system of care through an intervention such as Teen Linked through Care (TLC). Lightfoot, M. and Rotheram-Borus, M.J. Negotiating Behavior Change with HIV-Positive Adolescent Girls. AIDS Patient Care, 12(5), pp. 395-401, 1998.

Prevention of Substance and Sexual Risk-Taking in Hispanic Women

The concepts of risk and resilience, which are at the heart of health promotion and risk prevention are discussed, and used to demonstrate the acceptability of these concepts in the development and pilot testing of a primary prevention intervention to reduce substance abuse and risky sexual behaviors among low-income, predominantly Mexican-American women. Six important findings emerged from this pilot study: 1) Motivation and readiness are key to recruitment and consistent participation; 2) The quality of the content and materials and the use of participatory learning principles and teaching methods are key to effective teaching and learning; 3) The importance of a trusting and caring environment is essential; 4) The intervention must be tailored to life's realities and must address felt needs; 5) Risky behavioral decisions are often not taken rationally or consciously; 6) Cultural and family norms play a significant role in decision-making. Lindenberg, C.S., et al., Resilience and Risk: Preventing Substance Abuse and Sexual Risky Behaviors Among Low-Income Minority Young Women. Maternal Child Nursing, 23(2), pp. 99-104, 1998.

[Home Page][Office of the Director][Report Index][Previous Report Section] [Next Report Section]

Archive Home | Accessibility | Privacy | FOIA (NIH) | Current NIDA Home Page

National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Research Findings

Epidemiology, Etiology and Prevention Research

Drug Use in Sons of Fathers with Substance Use Disorders

In a study using the CEDAR cohort at the University of Pittsburgh to determine the relevance of preadolescent psycho-pathology and substance use for predicting early adolescent alcohol and cannabis involvement, sons of substance dependent fathers (High Risk or HR, n=102) and sons of fathers without lifetime substance use disorder diagnoses (Low Average Risk or LAR, n=164) were assessed at age 10-12 and again at ages 12-14 using similar semistructured interviews that obtained measures of psychopathology and substance use behavior. Preadolescent tobacco experimentation and early adolescent regular alcohol use were more prevalent in HR than in LAR subjects. Logistic regression analyses were conducted to evaluate the effects of preadolescent psychopathology and substance use behavior on early adolescent substance use behavior. Preadolescent conduct disorder and tobacco use were found to be highly predictive of early adolescent marijuana use. Preadolescent conduct disorder alone predicted adolescent alcohol use. Adolescent tobacco use was predicted by the presence of preadolescent oppositional defiant disorder. Preadolescent anxiety disorders appeared to protect against adolescent tobacco use. The association between early cigarette smoking in preadolescence and later adolescent smoking of marijuana found in this study suggests that reduction of childhood tobacco use may be a valuable goal for prevention programs that seek to forestall the developmental trajectory toward cannabis and other drug use behavior. Clark, D.B., Kirisci, L., Moss, H.B. Addictive Behaviors, 23, pp. 561-566, 1998.

Familial and Nonfamilial Factors in the Prediction of Disruptive Behaviors in Boys at Risk of Substance Abuse

Researchers using the CEDAR cohort sought to identify (1) a core disruptive behavior disorder (DBD) postulated to presage a substance use disorder, and (2) the relative importance of parental DBD phenotypes, and familial and nonfamilial environmental factors in the determination of DBD in male children (aged 10-12 yrs). DBD symptom counts and measures of familial and nonfamilial environmental variables were collected from intact families ascertained through the presence (SA+) or absence (SA-) of substance dependence in fathers. DBD symptom counts for sons were based on symptoms of Conduct Disorder (CD), Oppositional Defiant Disorder (ODD), and Attention Deficit Hyperactivity Disorder (ADHD); counts for parents reflected historical CD and ODD and current Antisocial Personality Disorder (ASPD). Sons' psychiatric assessments were based on K-SADS-E interviews with sons supplemented by mothers' reports on their sons. Familial environmental factors reflected the shared environment including social and physical aspects of the neighborhood and the home, and nonfamilial environmental variables referred to similar factors impacting only individual family members. Multivariate analyses revealed that both behavioral symptoms and environmental measures were significant discriminators of the families. In SA+ families, the child's DBD score was best predicted by magnitudes of parental dyssocial behaviors and by familial environmental

factors. However, in SA- families, only familial environmental factors were significant predictors of the child's DBD. These findings suggest that in addition to independent contributions of familial and nonfamilial factors, strong genotype-environment interactions may determine DBD in children and that may contribute to the liability for a substance use disorder. Majumder, P.P., Moss, H.B. Murrelle, L. Journal of Child Psychology & Psychiatry & Allied Disciplines. Vol. 39(2), pp. 203-213, 1998.

Secondary Prevention Effects Among High Risk Adolescents

Recent reviews of the prevention literature raise the question of whether primary prevention programs deter use among youth at highest risk for drug abuse. This study examines the secondary prevention effects of the Midwestern Prevention Project (MPP) in Indianapolis (I-STAR). Prevalence rate comparisons and logistic regression were conducted on four waves of follow-up data from sixth and seventh grade baseline users of cigarettes, alcohol, and marijuana who received a social influences-based curriculum in Indianapolis, Indiana. Across four follow-ups, baseline substance users in the program group consistently demonstrated higher rates of reduced use for all three types of substances relative to the control group, except the 3.5 year follow-up for baseline marijuana users. The logistic regression models evaluated at each follow-up demonstrated statistically significant secondary prevention effects on cigarettes at the initial follow-up (6 month), and on alcohol for the first two follow-ups (up to 1.5 years). Models considering repeated measures structure showed significant secondary prevention effects on all three substances (adjusted odds ratios are 1.53, 1.54, and 3.96 for cigarettes, alcohol, and marijuana, respectively). Social influences, school-based, primary prevention programs are able to successfully reach and influence high risk adolescents in a non-stigmatizing manner. Chou, C.P., Montgomery, S., Pentz, M.A., Rohrbach, L.A., Johnson, C.A., Flay, B.R., MacKinnon, D.P. Effects of A Community-Based Prevention Program on Decreasing Drug Use in High Risk Adolescents. American Journal of Public Health, 88, pp. 944-948, 1998.

Family Values and Adolescent Problem Behaviors

This 18-year study explored the influence of early family values on adolescent problem behaviors in 199 conventional and nonconventional families. Many of the nonconventional parents in this study identified with and were involved in the countercultural movements of the 1960's. Children raised in such families were more likely to be exposed to multiple risks associated with counterculture lifestyles such as drug use. The longitudinal nature of this study offers a unique opportunity to investigate intergenerational values transmission in families who have been followed since their children were born. In addition, children with more serious problem behaviors, such as heavy drug users and dropouts who often are excluded from other studies, have been retained in this sample. Factor analyses of the values of the mothers at the first trimester of their pregnancy were replicated among the adolescents 18 years later and revealed two value dimensions: Traditional/achievement and humanistic/egalitarian. Mothers also reported the extent of their identification with and commitment to the 1960's counterculture. Adolescent problem behavior was indicated by drug use, delinquency, high school dropout, and sexual behavior. The longitudinal predictive path model was tested with latent variable structural equation models. Early maternal values predicted similar adolescent values. The positive and significant correlations between the values of mothers and their teenage children suggest intergenerational transmission of values rather than evidence of a generation "gap" in values. Teens, at an age when rebelling and questioning authority is common, did not develop substantially different values than their mothers. Traditional values of the mother and the adolescent protected the adolescents against problem behaviors. Adolescents higher in both traditional/achievement and humanistic/egalitarian values reported less delinquent behavior. Humanistic/egalitarian values increased drug use risk. However, maternal countercultural identity protected adolescents against hard drugs. Generally, a stronger commitment to values reduced the risk that adolescents would become involved in severe problem behaviors. An important finding of this study is that the greatest risk factor for problem behaviors was the lack of commitment to any set of meaningful values. Garnier, H.E., and Stein, J.A. Values and the Family: Risk and Protective Factors for Adolescent Problem Behaviors. Youth & Society, 30, pp. 89-120, 1998.

Genetic and Environmental Risk Factors in Cannabis Use, Abuse, and Dependence: A Study of Female Twins

This study examined the role of genetic and environmental risk factors in the development of cannabis use, abuse and dependence. Analyses of interviews with 485 monozygotic and 335 dizygotic female twin pairs demonstrated that both genetic and familial-environmental factors explained liability to cannabis use, while heavy use, abuse, and dependence symptoms were solely related to genetic factors, with heritabilities ranging from 62%-79%. Thus, while

family and social factors play a key role influencing the risk to initiate cannabis use, heredity appears to determine the progression to abuse and dependence. These findings in women are consistent with other studies of genetic factors in drug abuse liability in men. Kendler, K.S., Prescott, C.A. Amer. J. of Psychiatry, 155(8), pp. 1016-1022, 1998.

Genetic and Environmental Risk Factors in Cocaine Use, Abuse, and Dependence: A Study of Female Twins

A study of cocaine use in monozygotic and dizygotic female twin pairs found that both genetic and environmental factors accounted for twin resemblance in liability to cocaine use, while resemblance for cocaine abuse and dependence symptoms was due solely to genetic factors. Heritability for cocaine abuse was estimated at 0.79. These findings are consistent with those of other studies of male veterans, adoptees, animals, and other drugs, and highlight substantial individual variation in liability to cocaine abuse and dependence. Family and social factors, toward which interventions might be targeted, are most salient to issues of drug initiation. Kendler, K.S. and Prescott, C.A. British Journal of Psychiatry, 173, pp. 345-350, 1998.

Social Context Effects in Development of Adolescent Substance Use

This article demonstrates a latent growth curve methodology for analyzing longitudinal data of adolescent substance use. Hypotheses concerning the form of growth in alcohol, cigarette, and marijuana use, and covariates influencing the form of growth, were tested. Participants were male and female adolescents (N=664) assessed at three time points. A common trajectory existed across the developmental period with significant increases in all three substances. Second-order multivariate extensions of the basic latent growth modeling framework suggested that associations among the individual differences parameters, representing growth or change in various substance use behaviors, could be adequately modeled by a higher-order substance use construct. Inept parental monitoring, parent-child conflict, peer deviance, academic failure, gender, and age, were significant predictors of initial levels and the trajectory of substance use. Duncan, S.C., Duncan, T.E., Biglan, A., and Ary, D.V. Contributions of the Social Context to the Development of Adolescent Substance Use: A Multivariate Latent Growth Modeling Approach. Drug and Alcohol Dependence, 50, pp. 57-71, 1998.

Disruptive, Delinquent and Aggressive Behavior in Female Adolescents with a Psychoactive Substance Use Disorder: Relation to Executive Cognitive Functioning

Researchers at CEDAR reported a study with four objectives: (1) to determine whether female adolescents with a psychoactive substance use disorder are more impaired than controls on a battery of neuropsychological tests of Executive Cognitive Functioning (ECF); (2) to determine whether these individuals exhibit higher levels of disruptive, delinquent and aggressive behavior compared with controls; (3) to determine whether ECF is related to disruptive, delinquent and aggressive behavior in this population; and (4) to determine whether these relations are moderated by drug use. Multiple indicators of ECF, and disruptive, delinquent and aggressive behavior, as well as drug use, were used to test these relations in 188 female adolescents who qualified for a Mental Disorders-III-Revised (DSM-III-R) diagnosis of a psychoactive substance use disorder and 95 normal controls (aged 14-18 yrs). ECF was related to disruptive, delinquent and aggressive behavior even when chronological age, SES and drug use were accounted for. The final regression models suggested that drug use was more strongly related to disruptive and delinquent behavior, whereas ECF was more strongly related to aggression. Giancola, P.R., Mezzich, A.C., Tarter, R.E. Disruptive, Delinquent and Aggressive Behavior in Female Adolescents with a Psychoactive Substance Use Disorder: Relation to Executive Cognitive Functioning. Journal of Studies on Alcohol. Vol. 59(5), pp. 560-567, 1998.

Progressions of Alcohol, Cigarette, and Marijuana Use in Adolescence

A study at the Oregon Research Institute examined the progression of alcohol, cigarette and marijuana use among adolescents based on level of use as well as dichotomous use or nonuse. The investigators applied latent growth curve analysis to study the relative impact of level of use of prior substances on use of target substances in the following year and development of use over a 4-year period. Subjects were 374 males and 389 females with a mean age of 13.23 yrs. at first assessment. They and their parents completed a series of self-report questionnaires. The study examined three models to determine (1) the effect of prior cigarette use on alcohol use and development and

the relationship between change in cigarette use and the development of alcohol use (N=115), (2) the effect of prior alcohol use on cigarette use and development and the relationship between change in alcohol use and the development of cigarette use (N=199); and (3) the effect of prior alcohol and cigarette use on marijuana use and development, and the relationship between change in alcohol use and cigarette use and the development of marijuana use (N=287). Results showed that level of cigarette use predicted subsequent levels of alcohol use 1 year later among previous nonusers of alcohol and that, over the 4-year period, those who increased their cigarette use developed faster in their use of alcohol. Marijuana use was predicted better by cigarette use than alcohol use, and higher users of cigarettes at T1 were not only more likely to be higher users of marijuana at T2 but also to increase more rapidly in their use of marijuana over the next 4 years. Duncan, S.C., Duncan, T.E., & Hops, H. Journal of Behavioral Medicine, 21, pp. 375-388, 1998.

Wide Variations in Types of Drug Trafficking Enterprises

An exploratory study sought to chart the variations in a large sample of drug trafficking organizations prosecuted in New York City between 1984 and 1997. Researchers developed a 2-dimensional typology of 39 drug trafficking organizations based on tasks and structure. Each of the 39 cases was involved in retail sales (street level dealing) as well as earlier stages of drug distribution (manufacture, importing, wholesale, and regional distribution). Four categories were identified under the task dimension: manufacturer/preparer, importer/smuggler, wholesale distributor/transporter, and regional distributor/dealer. Four categories were also identified for organizational structure: freelance (no formal hierarchy or division of labor), family (cohesive family businesses), communal (bound by common identities, such as ethnicity, religion, residency), and corporation (well-defined, formal hierarchy and division of labor). The drug trafficking organizations represented by these cases ranged widely, from small, loosely structured "freelance" groups to large, hierarchical "corporate" organizations. There was also a high degree of specialization in the tasks performed by the organizations, and a weak relationship between organizational type and these tasks. The small freelance groups were more likely to be involved in tasks higher in the distribution chain (wholesale), whereas the larger organizations were more involved at the lower (retail) levels. Regardless of their structure or task, all the organizations relied to a greater or lesser extent on ethnic ties, particularly the communal businesses. The wide variety of drug trafficking organizations found in this study has implications for tailoring interventions to target specific criminal enterprises. Natarajan, M. and Belanger, M. Varieties of Drug Trafficking Organizations: A Typology of Cases Prosecuted in New York City. J. Drug Issues, 28(4), pp. 1005-1026, 1998.

Effect of Father Involvement on Adolescent Substance Use

This study examined the effects of family process, father involvement, and family structure on 679 urban African-American adolescents, 14-17 year olds (50% female). Findings revealed that involvement of fathers, whether or not they live with their adolescent child, was associated with less substance use and psychological distress. Father effects were mediated by parental support and family conflict. Family structure was not related to any drug use or psychosocial outcome. The results challenge the assumption that nonresident fathers are absent from urban African-American youth's lives and that living in single mother households has adverse effects on youths' development. These findings, which replicate those in another sample, suggest single mother households do not automatically translate into absent fathers, and that interventions that focus on fathers in particular may be a useful approach for drug prevention programs. Salem, D.A., Zimmerman, M.A., Notaro, P.C. Family Relations, 47, pp. 331-341, 1998.

Prospective Study of Tobacco Smoking and Substance Dependencies Among Samples of ADHD and Non-ADHD Participants

This study focused on a group of young adults who as children had attention deficit/hyperactivity disorder (ADHD). The study participants were part of a longitudinal study of the life histories of 492 children, one third who were identified as hyperactive in 1974 and whose childhood symptom ratings and medical histories were used to establish the Diagnostic and Statistical Manual of Mental Disorders (3rd edition., revised DSM-III-R) ADHD diagnoses. The objectives of the study centered on describing (a) develop- mental history of tobacco use among ADHD and non-ADHD participants in a longitudinal sample, (b) the characteristic adult patterns of tobacco use from early adolescence through early adulthood, and (c) the relationship between ADHD status and tobacco and substance dependence outcomes. Adult data were obtained for 81% of the original 492 participants. Lifetime and current tobacco use were assessed from child, adolescent, and adult data, yielding eight measures of smoking status. The study showed that participants with and without ADHD did not differ in age of initiation to smoking, but there was a significant difference in the age smoking regularly began. By age 17, 46% of all participants with ADHD, as

contrasted with 24% of the age-mate controls, reported smoking cigarettes daily. In adulthood, the proportion of participants with ADHD who were current smokers (42%) continued to exceed that of the age-mate controls. There were significantly different lifetime tobacco dependence rates - 40% compared to 19% for age mate controls. The rates for cocaine dependence were 21% for participants with ADHD and 10% for age mate controls. The rates for stimulants were 20% for participants with ADHD and 11% for age mate controls. Results were interpreted to support a possible link between ADHD treatment histories, and levels of tobacco smoking and tobacco dependence in adulthood. Lambert, N. and Hartsough, C. Prospective Study of Tobacco Smoking and Substance Dependencies Among Samples of ADHD and Non-ADHD Participants. Journal of Learning Disabilities. 31(6), pp. 533 - 544, 1998.

Longitudinal Study of Co-Occurring Psychiatric Disorders and Substance Use

To examine temporal priority in the relationship between psychiatric disorders and drug use, researchers completed psychiatric and drug use assessments at three different points in time, spanning nine years. Structured interviews were administered to a cohort of youths and their mothers. Subjects were selected on the basis of their residence in either of two counties in upstate New York. The sample was predominantly white male and female youth, aged 1 through 10 upon initial collection of data. Psychiatric diagnoses were assessed by a supplemented version of the DISC 1, using computer algorithms designed to match DSM-III-R criteria to combine information from mothers and youth. Substance use information was obtained in the interviews. A significant relationship was found to exist between earlier adolescent drug use and later depressive and disruptive disorders in young adulthood, controlling for earlier psychiatric disorders. Earlier psychiatric disorders did not predict changes in young adult drug use. Implications for policy, prevention, and treatment include: (1) more medical attention needs to be given to the use of legal and illegal drugs; and (2) a decrease in drug use may result in a decrease in the incidence of later psychiatric disorders. Brook, J.S., Cohen, P., and Brook, D.W. Longitudinal Study of Co-occurring Psychiatric Disorders and Substance Use. Journal of the American Academy of Child and Adolescent Psychiatry, 37(3), pp. 322-330, 1998.

Marijuana Use and Academic Achievement in Mexican American Students

This study sought to examine the relationship between academic achievement (as measured by standardized achievement scores), substance use, and related psychosocial factors among Mexican American school-age students. Surveys were conducted with 2,165 middle school students who identified themselves as Mexican American. Survey items asked about use of marijuana in the last year, as well as indices of student characteristics (susceptibility to peer influence, dysphoria, school satisfaction, self-esteem, academic achievement). Results of the analyses revealed a complex relationship among risk factors, marijuana use, academic achievement, and gender. One risk factor in particular, peer susceptibility, distinguished marijuana users from non-users, regardless of level of academic achievement for both males and females. In addition, a higher percentage of males than females were found to smoke marijuana, suggesting that, even among students who were academically talented, males were more susceptible to marijuana use than females. The findings suggest that prevention and mediation programs should focus their efforts on risk factors that may be applicable for all students (such as peer susceptibility) in addition to targeting risk factors that are more significant for identified subgroups, such as males and females. In this way, the complex issue of substance use and abuse among our young can be addressed more effectively. Codina, G.E., Yin, Z., Katims, D.S., and Zapata, J.T. Marijuana Use and Academic Achievement Among Mexican American School-Age Students: Underlying Psychosocial and Behavioral Characteristics. J. Child & Adolescent Substance Abuse, 7(3), pp. 79-96, 1998.

Project Towards No Tobacco Use

Project Towards No Drug Abuse (Project TND) is a large-scale indicated drug abuse prevention program for continuation (i.e., alternative) high school youth who are at high risk for drug abuse. The efficacy of a nine-lesson health motivation social skills decision-making curriculum was evaluated in a three-condition experimental design. Twenty-one schools were randomly assigned to one of three conditions: standard care (control), classroom program, and classroom program plus a semester-long school-as-community component. A pretest in all 21 schools was followed by a three week long drug abuse prevention program in the 14 intervention schools. At the completion of the program a post-test was conducted in all 21 schools, and repeated after one year. Changes in use of cigarettes, alcohol, marijuana, and other drugs were assessed in a pretest-one year follow-up time comparison with a follow-up rate of 67% (analysis n=1074). Lower levels of alcohol and other drug use were found for the intervention groups without significant differences between the two program conditions. Project TND is the first limited session school-based model to demonstrate one-year behavioral effects on alcohol and other drug use among older, high-risk youth.

Sussman, S. et al. One-year Outcomes of Project Towards No Tobacco Use. Preventive Medicine, 27, pp. 632-642, 1998.

Self-Initiated Quitting Among Adolescent Smokers

This paper reviews the literature regarding predictors of adolescent self-initiated smoking cessation in a large sample of alternative high school youth in southern California. Youth attend alternative schools due to academic or behavioral problems, and are at relatively high risk for cigarette smoking. Several demographic (e.g., gender), behavioral (e.g., level of smoking), and psychosocial (e.g., risk-taking) predictors of adolescent smoking cessation were investigated. The alternative high school cohort provided a sufficient sample size of quitters (defined as no use in the last 30 days, measured after a 1-year period) to permit a prospective examination of adolescent smoking cessation. Although nine demographic, behavioral, or psychosocial variables discriminated among quitters and nonquitters in univariate analyses, only level of baseline smoking, smoking intention, and perceived stress were predictors in a final multivariable model. Taking results of the literature review and study findings together, smoking cessation programs for adolescents should include counteraction of problem-prone attitudes, support of wellness attitudes, provision of motivation to quit strategies, and assistance with overcoming withdrawal symptoms. Sussman, S. et al. Self-initiated Quitting Among Adolescent Smokers. Preventive Medicine, 27, A19-A28, 1998.

Patterns of Cigarette Smoking in Late Childhood

Early initiation of cigarette smoking so strongly predicts future smoking that several investigators have advocated delaying the age of initiation as a prevention strategy. To complement retrospective studies of early initiation, this study assessed prospectively patterns of smoking behavior in a sample of 401 children who were surveyed in the 4th, 5th and 6th grades. The principal findings were: (1) modeling of smoking by parents and friends is sufficient to influence children to initiate smoking, particularly when children also have low behavioral self-control, and (2) when modeling occurs in combination with poor adjustment to school, low parental monitoring, easy access to cigarettes, and other risk attributes, early initiators are significantly more likely to continue smoking. Jackson, C. et al., A Longitudinal Study Predicting Patterns of Cigarette Smoking in Late Childhood. Health Education and Behavior, 25(4), pp. 436-447, 1998.

Childhood Maltreatment and Pathology among Adult Substance Abusers

The purpose of this study was to examine predictive relationships between types of childhood maltreatment and personality disorders in a substance-abusing population. 339 drug- or alcohol-dependent patients completed a retrospective measure of childhood trauma, the Childhood Trauma Questionnaire (CTQ), and a self-report inventory assessing DSM-III-R personality disorders, the PDQ-R. Structural equation models revealed several significant paths between types of childhood maltreatment and personality disorder clusters and subclusters. Physical abuse and physical neglect were related to a subcluster of "psychopathic" personality disorders, consisting of childhood and adult antisocial personality traits and sadistic traits. Emotional abuse emerged as a broad risk factor for personality disorders within Clusters A, B, and C. Emotional neglect was related to the trait of schizoid personality disorder, which formed its own separate factor. Sexual abuse, which had been expected to predict borderline personality disorder traits, was not significantly related to any disorder cluster. This particular result may be due to the preponderance of males in the sample. These findings support the view that child maltreatment contributes to the high prevalence of co-morbid personality disorders in addicted populations. Bernstein, D., Stein, J.A., and Handelsman, L. Predicting Personality Pathology Among Adult Patients with Substance Use Disorders: Effects of Childhood Maltreatment. Addictive Behaviors, 23, pp. 855-868, 1998.

Role of Fetal Alcohol Exposure in Adult Substance Dependence: Adoption Design

This study used data from a previous adoption study to examine differences in substance use disorder outcomes between adoptees with fetal alcohol exposure and those without. Historical records were used to define fetal alcohol exposure. Results demonstrated that adoptees exposed to alcohol in utero reported higher symptom counts for alcohol, drug and nicotine dependence, and that these relationships held even when several confounding genetic and environmental variables were controlled for. Data was not available to assess the confounding roles of nicotine exposure or other prenatal variables, which may play a role in this relationship. Nonetheless, this study highlights the potential important role of in utero alcohol exposure in the development of later substance abuse and dependence.

Yates, W.R., Cadoret, R.J., Troughton, E.P., Stewart, M., Guinta, T.S. Alcoholism: Clinical and Experimental Research, 22(4), pp. 914-920, 1998.

Parental Substance Use Disorder, Mediating Variables and Adolescent Drug Use

Investigators at the National Opinion Research Center conducted a study to develop and test a non-recursive model that examines the effects of parental psychoactive substance use disorder (PSUD) on the reciprocal relationships among stressful life events, family attachment, peer drug use and adolescent drug use. A 3 yr. prospective cohort study followed 777 10-16 yr-olds who belonged to 3 types of families: 214 who belonged to families in which a parent was diagnosed with PSUD, 181 who belonged to families in which a parent was diagnosed with an affective disorder (but no comorbid PSUD), and 382 who belonged to families in which both parents were free of any diagnosable disorder. Two follow-up interviews of subjects were used to measure stressful life events via the junior High Life Experiences Survey, family attachment via FACES-III (D. H. Olson et al, 1989) and a child-parent strain index, peer drug use, and 2 self-reported drug use scales designed to measure past-year alcohol use and illicit drug use. Findings show that subjects from PSUD families were at heightened risk of stressful life events, peer drug use, attenuated family attachments, and drug use during the 1st follow-up period. In turn, peer drug use was strongly associated with drug use during the 2nd follow-up period. Findings support the non-recursive model. Hoffmann, J.P, Su, S.S. Parental Substance Use Disorder, Mediating Variables and Adolescent Drug Use: A Non-Recursive Model. Addiction, 93(9), pp. 1351-1364, 1998.

Behavioral Family Interventions for Improving Child-rearing

This article reviews evidence that behavioral family interventions are effective at improving child-rearing in distressed families and families with children exhibiting disruptive behavior. Essential behavioral strategies offered within a collaborative therapeutic process and exemplary materials for parents and clinicians are identified. Differences between science-based behavioral family interventions and two popular non-scientific parenting approaches are highlighted. Specifically, the non-scientific programs run counter to the science-based behavioral approaches and lack empirical support. Recommendations are offered for combining behavioral family interventions with other empirically supported approaches, promoting more widespread use of empirically supported interventions, such as behavioral family interventions, and the need for a public health perspective on family functioning, involving collaboration among clinicians, policy makers, and researchers. Taylor, T.K. and Biglan, A. Behavioral Family Interventions for Improving Child-Rearing: A Review of the Literature for Clinicians and Policy Makers. Child and Family Psychology Review, 1(1), pp. 41-60, 1998.

Competence and Drug Use

One construct of the Social Stress Model of Drug Abuse is "competence". This article reviews the empirical evidence for the association of competence with drug use, and describes the preliminary development of a multi-scale instrument designed to assess drug protective competence in low-income Hispanic childbearing women. Hypothesis testing was used to assess construct validity. Four drug protective competence domains (social influence, sociability, self-worth and control/responsibility) were found to be statistically associated with drug use behaviors. The other four domains (intimacy, nurturance, goal directedness and spiritual directedness) while not statistically significant, showed the expected trend relationship with drug use. Lindenberg, C.S., et al. Competence and Drug Use: Conceptual Frameworks, Empirical Evidence and Measurement. Journal of Drug Education, 28(2), pp. 1997-1999, 1998.

Developmental Variations in Factors Related to Initial and Increased Levels of Adolescent Drug Involvement

This study was designed to examine the impact of maternal and adolescent factors on initial and increased levels of adolescent drug use in two groups of adolescents: younger adolescents (ages 12-14 at initial assessment) and older adolescents (ages 15-18). The adolescents and their mothers were interviewed at 2 points in time, 3 years apart. The results indicated that adolescent unconventionality is a crucial determinant for both initial and increased levels of drug use for both age groups, but intrapsychic distress is more important for the younger adolescent's initial use. Lack of maternal attachment and poor control techniques were associated with initial levels of drug use for both groups. However, the mother-child relationship and models of the mother's unconventionality had a greater impact on the older than on the younger group's increased involvement. Interactive results suggest that adolescents from

both age groups who are well adjusted can offset the potential risks of maternal models of drug use. Brook, J.S., Jaeger, L., and Cohen, P. Developmental Variations in Factors Related to Initial and Increased Levels of Adolescent Drug Involvement. Journal of Genetic Psychology, 159(2), pp. 179-194, 1998.

Self and Peer Perceptions in Aggressive and Nonaggressive Boys

In order to examine self and peer perceptions in aggressive and nonaggressive boys during preadolescence and early adolescence, subjects completed differential ratings of themselves and of their peer partners following two brief dyadic discussion tasks with competitive directions and a game-playing task with a cooperative induction. Subjects also rated their expectations for self and peer behavior prior to the two competitive interaction tasks. Researchers later rated videotapes of the interactions. Aggressive boys had more distorted perceptions of dyadic behavior as they overperceived aggression in their partners and underperceived their own aggressiveness. These distorted perceptions of aggression carried over for aggressive boys into the third interactive task with a cooperative induction, indicating these boys' difficulty in modulating these perceptions when the overt demand for conflict is no longer present in the situation. Results also indicated that aggressive boys' perceptions of their own behavior after the first interaction task is substantially affected by their prior expectations, in comparison to nonaggressive boys who rely more on their actual behavior to form their perceptions. Lochman, J.E. and Dodge, K.A. Distorted Perceptions in Dyadic Interactions of Aggressive and Nonaggressive Boys: Effect of Prior Expectations, Context and Boys' Age. Development and Psychopathology, 10, pp. 495-512, 1998.

Pathways to Marijuana Use Among Adolescents: Cultural/Ecological, Family, Peer, and Personality Influences

This study examines the linkages, cultural/ecological factors, and major psychosocial risk factors as they relate to drug use in a sample from Colombia, South America. The participants were 1,687 adolescents living in mixed urban-rural communities in Colombia, South America. An individual interview was administered to youths in their homes by Colombian interviewers. The scales used were grouped into the following risk categories: (1) adolescent personality, (2) family traits, (3) peer factors, and (4) cultural/ecological variables. Results show that each of the domains was related to adolescent marijuana use, with some notable gender differences. Supporting a family interactional theory, the domains of family, personality, and peer factors were found to have a direct effect on the adolescents' marijuana use. Brook, J.S., Brook, D.W., De La Rosa, M., Duque, L.F., Rodriguez, E., Montoya, I.D., and Whiteman, M. Pathways to Marijuana Use Among Adolescents: Cultural/Ecological, Family, Peer, and Personality Influences. Journal of the American Academy of Child and Adolescent Psychiatry, 37(7), pp. 759-766, 1998.

Health Risk Behaviors Among Children and Adolescents

This research focused on authoritative parenting, which previous studies suggest can prevent health risk behaviors among youth. To evaluate the reliability and validity of a new survey measure of authoritative parenting, data from studies of: (1) substance use in a sample of 1,236 4th and 6th grade students; (2) weapon carrying and interpersonal violence in a sample of 1,490 9th and 10th grade students and (3) anger, alienation and conflict resolution in a sample of 224 7th and 8th grade students were analyzed. The Authoritative Parenting Index had a factor structure consistent with other studies, had acceptable validity, and showed grade, sex, and ethnic differences consistent with other studies (e.g., authoritative parenting decreases with age, whites report increased levels of authoritative parenting when compared to than other ethnic groups). In addition, parenting types were identified that varied as hypothesized with multiple indicators of social competence and health risk behaviors among children and adolescents. Jackson, C., et al. The Authoritative Parenting Index: Predicting Health Risk Behaviors Among Children and Adolescents. Health Education and Behavior, 25(3), pp. 319-337, 1998.

Who Responds to Drug Abuse Surveys?

Researchers examined the personality and attitudinal characteristics of eager, reluctant, and nonresponders to a mailed longitudinal survey focusing on substance use through a series of logistic regression analyses. The characteristics that differentiate response patterns in men and women differ in terms of the relative importance of cooperation, behavioral low social conformity (substance use), and support of science/medicine. Socioeconomic status and attitudinal low social conformity did not differentiate among groups of responders, regardless of gender. Ullman, J.B., and Newcomb, M.D. Eager, Reluctant, and Nonresponders to a Mailed Longitudinal Survey: Attitudinal

and Substance Use Characteristics Differentiate Respondents. Journal of Applied Social Psychology, 28, pp. 357-375, 1998.

Further Support for Memory Association as an Important Risk Factor

Previous research on the effect of memory associations has not thoroughly investigated how these associations may combine with personality in the prediction of alcohol and other drug use. Memory associations may interact with personality in these predictive effects, if some personality traits make the individual more susceptible to acting out the cognitive manifestations of these associations. Alternatively, personality and memory associations may be confounded. These alternatives were evaluated in a study of 554 adult men and women from a community sample. In addition, the nature of the effects of memory associations on drinking problems was evaluated. These effects may be indirect, through alcohol consumption, or more direct. The results showed that memory association directly and independently predicted alcohol consumption; these measures indirectly predicted problems from drinking, including drunk driving. None of the assessed personality variables moderated (interacted with) the predictive effects of memory association. The results are consistent with the view that memory associations influence behavior through cognitive processes that are not affected by personality traits or by cognitions emanating from such traits. The results provide further support for the memory association framework in addictive behaviors. Stacy, A.W., and Newcomb, M.D. Memory Association and Personality as Predictors of Alcohol Use: Mediation and Moderator Effects. Experimental & Clinical Psychopharmacology, 6, pp. 280-291, 1998.

Violence-Related Behaviors of Adolescents

This study examined the relations between two dimensions of parenting behavior and violence-related behaviors in 1,221 9th and 10th grade adolescents participating in Kids First. The higher the perceived responsiveness and demandingness of fathers and mothers, the lower the likelihood that adolescents had hit peers, beat peers, threatened a peer with a weapon or carried a weapon to school. Adolescents who perceived low levels of parental responsiveness and demandingness were two to three times as likely to report violence-related behaviors. This effect was stronger in females than males. Jackson, C. and Foshee, V.A. Violence-Related Behaviors of Adolescents: Relations with Responsiveness and Demanding Parenting. Journal of Adolescent Research, 13, pp. 343-359, 1998.

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National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse
February, 1999

Research Findings

Intramural Research

Behavioral Neuroscience Branch

An Effective Treatment for Cocaine Toxicity

Cocaine abuse is a public health concern as seizures and deaths continue to be reported. There were an estimated 150,000 cocaine-related emergency room incidents in 1995 which accounted for 27% of all emergency-department drug-related episodes. These toxicity data represent an increasing trend since 1990. Current emergency treatments for cocaine overdose are not always effective. IRP investigators now report that dopamine D3 receptor agonists dose-dependently and completely block the convulsant and lethal effects of cocaine. In addition to anticonvulsant effects, these compounds also demonstrated antiepileptogenic properties, blocking the development and expression of kindled seizures (increased sensitivity to cocaine-related toxicities) that result from repeated administration of cocaine. These findings implicate dopamine D3 receptors in the acute and chronic toxicity of cocaine and provide a possible alternative medication for the management of cocaine overdose. Gasior, M. and Witkin, J.M. Cocaine-Kindled Seizures: Some Potential Treatment Modalities. Polish Journal of Pharmacology, 50 (suppl): 39, 1998. Witkin, J.M. and Witkin, J.M. Dopamine D3 Receptor Involvement in the Convulsant and Lethal Effects of Cocaine. Polish Journal of Pharmacology, 50 (suppl), pp. 44-45, 1998.

Neuroactive Steroids: Novel Potential Drug Abuse Treatments

Data are beginning to accumulate to suggest a role for neuroactive steroids in certain phases of drug dependence. Drug withdrawal-related anxiety has been treated with benzodiazepines and related compounds in preclinical models and in clinical practice. IRP investigators have shown that some drugs in this class produce effects in animal models that suggest that they may also be useful in the control of anxiety related to cessation of drug abuse. Specifically, neuroactive steroids both prevented and reversed anxiety-like behavioral effects of pentylenetetrazol, a drug used to model drug withdrawal anxiety. These data in conjunction with safety data on neuroactive steroids thus far reported in humans encourages further investigation into the role of this drug class in drug abuse cessation. Beekman, M., Ungard, J.T., Gasior, M., Carter, R.B., Dijkstra, D., Goldberg, S.R. and Witkin, J.M. Reversal of Behavioral Effects of Pentylenetetrazol by the Neuroactive Steroid Ganaxolone. Journal of Pharmacology and Experimental Therapeutics, 284, pp. 868-877, 1998.

Development and Plasticity Section, Cellular Neurobiology Branch

New Oncogene Developed for Producing Neuronal Cell Lines for Drug Toxicity and Gene Expression Testing

Using cell lines can be of great value for evaluating drug-induced neurotoxicity and changes in gene expression

induced by drugs of abuse. Because cell lines are homogeneous, the use of cell lines reduces the complication resulting from the presence of multiple cell types that are present in whole tissue or intact animals. Finding changes in expressed genes can thus be greatly simplified through the use of cell lines. To give an example, drugs of abuse may induce changes in growth factors or adhesion molecules which mediate neuroplastic changes that result in drug adaptation, and thereby contribute to addiction. In addition, the use of human cell lines is the only means of identifying human drug-induced genes, since human subjects cannot be subjected to controlled studies of neurotoxicity. Current methods for generating neural cell lines, however, employ oncogenes which interfere with the development of mature neuronal phenotypic properties, so that model cell lines produced by current cell immortalization techniques are far from ideal for use for in vitro studies of drug effects. The most commonly used oncogene for the generation of neural cell lines is SV40 large T antigen, which has the advantage of effectiveness and well-understood mechanisms of action, but interferes with normal processes related to cell differentiation. A truncated mutant form of SV40 large T antigen, less than one-fourth the size of the intact molecule, and which lacks several of the properties that interfere with normal cellular functions, was developed. This mutant oncogene was able to immortalize mesencephalic cells, and cells produced with this oncogene demonstrated many properties of normal neurons and are sensitive to drug-induced toxicity. This method may be useful for generating neuronal cell lines for examining effects of drugs of abuse in vitro. Truckenmiller, M.E., Tornatore, C., Wright, R.D., Dillon-Carter, O., Meiners, S., Geller, H.M., Freed, W.J. A Truncated SV40 Large T Antigen Lacking the p53 Binding Domain Overcomes p53-induced Growth Arrest and Immortalizes Primary Mesencephalic Cells. Cell and Tissue Research, 291, pp. 175-189, 1998; Dillon-Carter, O., Conejero, C., Tornatore, C., Poltorak, M., and Freed, W.J. N18-RE-105 Cells: Differentiation and Activation of p53 in Response to Glutamate and Adriamycin is Blocked by SV40 Large T Antigen tsA58. Cell and Tissue Research, 291, pp. 191-205, 1998.

Cell Adhesion Molecules in Neuropsychiatric Disorders and Drug Effects

Cell Adhesion molecules are important in the development, maturation, and plasticity of the nervous system. Changes in cell adhesion molecules are also likely to be involved in adaptational changes which occur in response to chronic exposure of the brain to drugs, and may play a role in the establishment of addiction. Neuropsychiatric disorders are also a major risk factor for addictive behavior. We have found changes in two cell adhesion molecules, N-CAM and L1, in the cerebrospinal fluid of patients with schizophrenia, and changes in N-CAM in patients with mood disorders. A novel isoform of N-CAM with a molecular weight of 105-115 kDa has been identified, and is changed in cytosolic fractions of post-mortem brain samples from patients with schizophrenia. A separate isoform of N-CAM, specifically a cytosolic 140 kDa isoform containing the 10 amino acid VASE exon, is changed in the hippocampus of patients with bipolar mood disorder. Interestingly, drug treatment status does not seem to be responsible for these changes; however, similar changes are not seen early in the course of illness. Therefore, it appears that changes in cell adhesion molecules may be linked to long-term chronic drug exposure. The fact that drug treatment produces long-term changes in cell adhesion molecules may be significant in terms of adaptations that occur following chronic exposure to drugs. Such changes, or similar changes, may be important in the establishment or maintenance of addiction. Vawter, M.P., Hemperly, J.J., Hyde, T.M., Bachus, S.E., VanderPutten, D.M., Howard, A.L., Cannon-Spoor, H.E., McCoy, M.T., Webster, M.J., Kleinman, J.E., Freed, W.J. VASE-Containing N-CAM Isoforms are Increased in the Hippocampus in Bipolar Disorder but not Schizophrenia. Experimental Neurology, 154, pp. 1-11, 1998. Vawter, M.P., Cannon-Spoor, H.E., Hemperly, J.J., VanderPutten, D.M., Hyde, T.M., Kleinman, J.E., Freed, W.J. Abnormal Expression of Cell Adhesion Molecules in Schizophrenia. Experimental Neurology, 149, pp. 424-432, 1998. Van Kammen, D.P,. Poltorak, M. Kelley, M.E., Yao, J.K., Gurklis, J.A., Peters, J.L., Hemperly, J.J., Wright, R.D., Freed, W.J. Further Studies of Elevated Cerebrospinal Fluid Neural Cell Adhesion Molecule in Schizophrenia. Biological Psychiatry, 43, pp. 680-686, 1998.

Cellular Neurophysiology Section, Cellular Neurobiology Branch

Transplantation of Fetal Kidney Tissue Reduces Infarction Volume of Cerebral Cortex in Adult Rats

It has been shown that neurotrophic factors have both regenerative and protective actions on neurons in vivo and in vitro. IRP investigators and others recently reported that intracerebral administration of glial cell line derived neurotrophic factor (GDNF) protects against ischemia-induced injury in the cerebral cortex of adult rats. Since fetal kidney tissues contain a number of trophic factors such as GDNF, neurturin, transforming growth factor- b, and OP-1, it is possible that transplantation of fetal kidney tissue could protect brain against ischemia-induced injury by providing these trophic factors. Kidneys from rat embryos, at gestational day of 16, or from adult rats, were dissected and cut into small pieces. Adult male Sprague-Dawley rats were anesthetized with chloral hydrate and placed in a stereotactic apparatus. Kidney tissues were transplanted into 3 cortical areas adjacent to the right middle cerebral artery. Thirty minutes after transplantation, the right MCA was ligated with a 10-O suture and both common carotid arteries were occluded with non-traumatic arterial clips for 90 min. Twenty-four hours after reperfusion, animals were

anesthetized with urethane and perfused intracardially with saline. Brain tissue was removed, sliced, incubated with 2% triphenyltetrazolium chloride for 30 min, and then transferred into 5% formaldehyde solution for fixation. The volume of cortical infarction was measured in each slice and summed using computerized planimetry. Findings indicate that transplantation of either adult kidney tissue or injection of vehicle did not reduce the infarction volume of the cerebral cortex. On the other hand, animals which received fetal kidney transplant showed a significant reduction of infarction volume. Taken together, these data show that fetal kidney transplantation reduces ischemia-induced injury in the cerebral cortex. Authors suggest a release of trophic factors may be involved since adult kidney tissues contain much smaller amounts of these factors. Chiang, Y. H., Chiou, A.L., Lin, S.Z., Hoffer, B. J., and Wang, Y. Transplantation of Fetal Kidney Tissue Reduces Infarction Volume of Cerebral Cortex in Adult Rats. Soc. Neurosci. meeting, 1998.

Co-administration of 1,25(OH)2 Vitamin D3 and Retinoic Acid Attenuates Cortical Infarction Induced by Middle Cerebral Arterial Ligation

IRP investigators have previously reported that intracerebral administration of glial cell line derived neurotrophic factor diminishes middle cerebral arterial (MCA)-ligation-induced cortical infarctions in rats. Recent studies have indicated that application of 1,25(OH)2 Vitamin D3 [1,25(OH)2D3] with retinoic acid enhances GDNF mRNA expression in vitro. The purpose of this study is to investigate if co-administration of 1,25(OH)2D3 and retinoic acid protects against ischemic brain injury. Adult male Sprague-Dawley rats were chronically injected with 1,25(OH)2D3 for 3 days. Animals were later anesthetized with chloral hydrate. Low dosage of retinoic acid was given intraventricularly and directly to the cortex, adjacent to the MCA. Right MCA was temporarily ligated with 10-O suture for 90 minutes. Animals were sacrificed for TTC staining after 24 hour reperfusion. Investigators found that pretreatment of 1,25(OH)2D3 or retinoic acid separately did not attenuate the injury. Co-administration of these two compounds, however, greatly reduced brain infarction. In conclusion, these data suggest that co-administration of 1,25(OH)2D3 and retinoic acid prevents against ischemia-induced brain damage, possibly mediated through the activation of neurotrophic factors. Wang, Y., Lin, S.Z., Chiang, Y. S., and Hoffer, B.J. Co-administration of 1,25(OH)2 Vitamin D3 and Retinoic Acid Attenuates Cortical Infarction Induced by Middle Cerebral Arterial Ligation. Soc. Neuroscience meeting, 1998.

GDNF Protects Against Ischemia-induced Injury in the Cerebral Cortex

Glial cell line-derived neurotrophic factor (GDNF), a recently described and cloned member of the TGF- b superfamily, has been shown to have marked trophic activity on several populations of central neurons. Survival-promoting and injury protectant activity in vitro and in vivo, using several paradigms, has been demonstrated for ventral mesencephalic dopaminergic neurons and spinal cord motoneurons. In view of a proposed commonality of mechanisms, involving intracellular free radical generation, depolarization-induced Ca++ influx, and mitochondrial respiratory enzyme injury, between such GDNF-responsive paradigms and those of ischemia-induced injury, IRP scientists tested the effects of GDNF on the extent of neural degeneration induced by transient middle cerebral artery (MCA) occlusion. Authors now report that intracerebroventricular and intraparenchymal administration of GDNF potently protects the cerebral hemispheres from damage induced by MCA occlusion. In addition, the increase in nitric oxide which accompanies MCA occlusion and subsequent reperfusion is almost completely blocked by GDNF. Thus, this peptide may play an important role in the treatment of cerebrovascular occlusive disease. Wang, Y., Lin, S.Z., Chiou, A. L., and Hoffer, B.J. GDNF Protects Against Ichemia-Induced Injury in the Cerebral Cortex. J. Neurosci., 17, pp. 4341-4348, 1997.

Molecular Neuropsychiatry Section, Cellular Neurobiology Branch

The Role of Reactive Oxygen Species in METH-induced Toxicity

In order to test the idea of the involvement of superoxide radicals in METH-induced toxicity, IRP scientists assessed the effects of toxic doses of the drug on antioxidant defense systems in the brains of mice. Because METH- induced toxicity is attenuated in copper/zinc-superoxide dismutase transgenic (Cu/Zn-SOD-Tg) mice, investigators sought to determine if METH had differential effects on antioxidant enzymes on these mice in comparison to non-Tg mice. A toxic dose of METH caused a significant decrease in Cu/Zn-SOD activity in the cortical region without altering enzyme activity in the striata of non-Tg mice. CuZn SOD activity was not affected in the brains of heterozygous SOD-Tg mice, whereas there was a small increase in the striata of homozygous SOD-Tg mice. In addition, METH caused decreases in catalase (CAT) activity in the striatum of non-Tg mice and significant increases in the cortex of homozygous SOD-Tg mice. METH also induced decreases in glutathione peroxidase (GSH-Px) in both cortical and striatal regions of non-Tg mice and in the striatum of heterozygous SOD-Tg mice, whereas, this enzyme was not affected in the homozygous SOD-Tg mice. Interestingly, lipid peroxidation was markedly increased in both cortices and striata of non-Tg and

heterozygous SOD-Tg mice, but not in the homozygous SOD-Tg. When taken together, these results suggest that the toxic effects of METH involve not only superoxide radicals but a cascade that also includes hydrogen peroxide and hydroxyl radicals. In vitro studies in the laboratory have now documented the production of both superoxide radicals and hydrogen peroxide during exposure of cells to METH. Investigators from other laboratories have reported that hydroxyl radicals are also involved in METH-induced toxicity. Subramaniam J., Ladenheim B, and Cadet J.L. Methamphetamine- induced Changes in Antioxidant Enzymes and Lipid Peroxidation in Copper/Zinc Superoxide Dismutase Transgenic Mice. Ann. NY Acad. Sci., 844, pp. 92-102, 1998.

Superoxide Radicals are Mediators of the Effects of METH on Zif268 (Egr-1, NGFI-A) in the Brain

The cellular effects of exogenous and endogenous ligands are mediated via a molecular cascade that involves the activation of a number of transcription factors. These include the fos and jun families as well as Zif268 (also known as Egr-1, Krox24, or NGFI-A) that have been shown to be rapidly activated by several signaling agents. More recently, the role of dopaminergic agents such as abusable stimulants as activators of these IEGs have begun to be actively studied because of the possibility that they might provide insights into molecular events that lead to stimulant-induced behavioral sensitization in animals. Recent studies aimed at detailing the molecular events involved in the action of stimulant drugs have documented the fact that the amphetamines can activate IEGs such as c-Fos and Zif268. These increases occur very rapidly after drug administration and return to baseline within a few hours. Because of the robustness and consistency of these responses, it has been suggested that IEGs might be important mediators of the neuroplastic adaptation which occurs in the brain during chronic administration of these stimulants. This activation of IEGs cause by these drugs is thought to be mediated mainly through stimulation of D1 receptors. IRP scientists reasoned, however, that redox status might also affect Zif268 expression. As a first step towards assessing a possible role for free radicals in METH-induced changes in IEGs, these investigators used CuZn superoxide dismutase (SOD) transgenic (Tg) mice and quantified the effects of METH on c-Fos and Zif268 mRNAs by in situ hybridization techniques. Mice were injected with 25 mg/kg of METH and sacrificed at various time points afterwards. There were significant METH-induced increases in both c-Fos and Zif268 mRNAs in the frontal cortex and striatum of both strains of animals. Interestingly, the increases in Zif268 were markedly attenuated in the CuZn SOD-Tg mice; the increases in c-Fos were also attenuated, but to a significantly lesser degree. These results indicate that superoxide radicals might play an important role in the activation of Zif268 after METH administration. When taken together with similar findings for AP-1, these results also raise the possibility that oxidative mechanisms might be important factors in neuroadaptive molecular changes caused by stimulant drugs. Hirata H., Asanuma M., and Cadet J.L. Superoxide Radicals are Mediators of the Effects of Methamphetamine on ZIF 268 (Egr-1, NGFI-A) in the Brain: Evidence from Using CuZn Superoxide Dismutase Transgenic Mice. Mol. Brain Research, 58, pp. 209-216, 1998.

Melatonin Attenuates Methamphetamine-induced Toxic Effects on Dopamine and Serotonin Terminals in Mouse Brain

Methamphetamine (METH) is a drug of abuse that causes deleterious effects to brain monoaminergic systems. These toxic effects are thought to be due to oxidative stress. The pineal hormone, melatonin, has been shown to have neuroprotective effects against toxic quinones and oxidative stress produced by catecholamines. The present study was thus undertaken to assess possible protective effects of melatonin against METH-induced neurotoxic effects on the striatum and the nucleus accumbens by using autoradiographic techniques. Four dosages (5, 20, 40, 80 mg/kg) of melatonin were administered to mice intraperitoneally 30 minutes prior to the injections of METH (4 x 5 mg/kg) given at 2- hour intervals. The lowest doses of melatonin (5 mg/kg) had no significant effects against METH-induced toxicity. However, the higher doses (40 or 80 mg/kg) of melatonin significantly attenuated METH- induced toxic effects on both dopamine and serotonin systems. These data provide further evidence for a possible role of oxidative stress in METH-induced toxicity. Hirata H., Asanuma M., and Cadet J.L. Melatonin Attenuates Methamphetamine-induced Toxic Effects on Dopamine and Serotonin Terminals in Mouse Brain. Synapse, 30, pp. 150-155, 1998.

Toxicity of 6-OHDA is Attenuated in SOD Mice

6-Hydroxydopamine is a neurotoxin that produces degeneration of the nigrostriatal dopaminergic pathway in rodents. Its toxicity is thought to involve the generation of superoxide anion secondary to its autoxidation. To examine the effects of the overexpression of CuZn SOD activity on 6-hydroxydopamine- induced dopaminergic neuronal damage, IRP scientists have measured the effects of 6-hydroxydopamine- on striatal and nigral dopamine transporters and nigral tyrosine hydroxylase-immunoreactive neurons in CuZn SOD Tg mice. Intracerebroventricular injection of 6-hydroxydopamine (50 mg) in non-transgenic mice produced reductions in the size of striatal area and an enlargement of the cerebral ventricle on both sides of the brains of mice sacrificed two weeks after the injection. In addition, 6-hydroxydopamine caused marked decreases in striatal and nigral [125I]RTI-121-labelled dopamine transporters not only on the injected side but also on the non-injected side of non-transgenic mice; this was associated with decreased cell number and size of tyrosine hydroxylase-immunoreactive dopamine neurons in the substantia nigra pars compacta on both sides in these mice. In contrast, SOD Tg mice were protected against these neurotoxic effects

of 6-OHDA, with the homozygous transgenic mice showing almost complete protection. These results provide further support for a role of superoxide anion in the toxic effects of 6-OHDA. They also provide further evidence that reactive oxygen species may be the main determining factors in the neurodegenerative effects of catecholamines. These studies document important similarities between the mechanisms involved in catecholamine-induced and METH-induced toxicity. Asanuma M., Hirata H., and Cadet J.L. Attenuation of 6-hydroxydopamine-induced Dopaminergic Nigrostriatal Lesions in Superoxide Dismutase Transgenic Mice. Neuroscience, 85, pp. 907-917, 1998.

Endogenous Opioid Peptide as a Free Radical Scavenger: Prevention of the Neurotoxicity Induced by Methamphetamine ("Ice")

DADLE is a stable analog of the endogenous delta opioid peptide Leu-enkephalin. Over the past few years, IRP researchers in collaboration with scientists from University of Kentucky and University of Michigan have demonstrated the remarkable tissue protective properties of DADLE in extending the survival of isolated peripheral organs. DADLE was found to dramatically enhance the survival of isolated lungs, and isolated hearts, both of which are known to be difficult to preserve. As the survival of tissue depends largely on the oxidative state of the tissue which is linked intimately with the formation of free radicals, the researchers reason that perhaps one of the mechanisms of DADLE in enhancing the tissue survival is to act as a free radical scavenger. As such, it is not unreasonable to speculate that DADLE may act as a tissue protective agent even in the central nervous system. The IRP researchers, in collaboration with intramural scientists from NIMH, demonstrated that indeed DADLE is a free radical scavenger sequestering two of the most reactive free radicals: superoxide anion and hydroxyl radical. Further, given before methamphetamine, DADLE was shown to block the long-term damage of dopaminergic nerve terminals induced by methamphetamine. These data provide a new avenue for understanding the pathobiological damage caused by psychostimulants and the potential treatment strategies thereof. As methamphetamine-induced neurotoxicity is believed to be a potential model system for Parkinsonism, these results suggest that perhaps the endogenous opioid peptides play an important role in the pathogenesis of Parkinsonism. Tsao, L.-I., Ladenheim, B., Andrews, A., Chiueh, C.C., Cadet, J.L. and Su, T.-P. Delta opioid peptide [D-Ala2,D-Leu5] Enkephalin Blocks the Long-Term Loss of Dopamine Transporter Induced by Multiple Administrations of Methamphetamine: Involvement of Opioid Receptors and Reactive Oxygen Species. J. Pharmacol. Exp. Ther., 287, pp. 322-331, 1998.

Sigma Receptor Agonists Potentiate the Action of an Antipsychotic Agent Sulpiride in Primary Cortical Neurons

Sigma receptor agonists have been shown by IRP researchers to play a beneficial role in several animal models of amnesia, including those related to aging and Alzheimer's disease. The underlying mechanism of action of those sigma agonists have been speculated to be related to their ability to potentiate the action of endogenous glutamate on the NMDA receptors which is known to be involved in learning and memory. One of the mechanisms of action of antipsychotic agent sulpiride has been speculated to be related to the NMDA receptors by creating a "hyper-NMDA" state which would benefit the schizophrenic in theory. IRP researchers, in collaboration with Japanese scientists, found that sulpiride can potentiate the NMDA-induced intracellular Ca2+ concentration ([Ca2+]i). Also, they found that sigma receptor agonists, by their own having a tendency to potentiate the action of NMDA, could further enhance the NMDA-potentiating action of sulpiride. Furthermore, they found that this action of sulpiride is mediated by a protein-kinase related intracellular action. These data indicate that antipsychotic sulpiride exerts its therapeutic efficacy via an intra- cellular biochemical action and that sigma agonists, in addition to being antiamnesic, may be beneficial adjunct therapeutic agents for treating schizophrenia. Hayashi, T., Su, T.-P., Kagaya, A., Nishida, A., Shimizu, M. and Yamawaki, S. Neuroleptics with Differential Affinities at Dopamine D2 Receptors and Sigma Receptors Affect Differently the N-methyl- D-aspartate-induced Increase in Intracellular Ca2+ Concentration in Rat Frontal Cortical Neurons: Involvement of Protein Kinase. Synapse, 31, pp. 20-28, 1999.

Chemistry and Drug Metabolism Section, Clinical Pharmacology Branch

Differentiating New Marijuana Use from Residual Drug Excretion in Occasional Marijuana Users

A drug dose is generally excreted in decreasing amounts in sequential urine specimens for only a few days following drug administration. The concentration of the drug in urine may vary considerably due to the amount of urine in the bladder; increases in urine drug concentration may be mistakenly interpreted as new drug use rather than residual drug excretion. Normalization of drug excretion to the urine creatinine concentration reduces the variability of drug measurement due to urine dilution and is suggested for use in treatment and employee assistance programs. A controlled clinical study was recently completed to provide data for the interpretation of urine cannabinoid test results. These data indicate selection of a ratio threshold to evaluate sequential creatinine normalized urine drug concentrations can improve the ability to distinguish residual excretion from new drug usage. The selection of an

appropriate ratio can be made based on the needs of a specific urine drug testing program taking into account sensitivity, specificity, and accuracy data. Huestis, M.A., and Cone, E. Urinary Excretion Half-life of 11-Nor-9-carboxy-delta 9-tetrahydrocannabinol in Humans. Therapeutic Drug Monitoring, 20, pp. 570-576, 1998; Huestis, M.A., and Cone, E. Differentiating New Marijuana Use From Residual Drug Excretion in Occasional Marijuana Users. Journal of Analytical Toxicology, 22, pp. 445-454, 1998. Cone, E.J., Lange, R., and Darwin, W.D. In Vivo Adulteration: Excess Fluid Ingestion Causes False Negative Marijuana and Cocaine Urine Test Results. Journal of Analytical Toxicology, 22, pp. 460-473, 1998.

Saliva and Plasma Testing for Drugs of Abuse: Comparison of the Disposition and Pharmacological Effects of Cocaine

The pharmacological effects and disposition of cocaine in plasma and saliva following subcutaneous drug administration were evaluated. Pharmacological effect data (pupil diameter, heart rate, blood pressure, subject-reported "High") were compared to concurrent cocaine and metabolite concentrations determined by GC-MS. Cocaine was detected in both saliva and plasma within 5-10 min following dosing, and cocaine concentrations in both matrices peaked within 30-60 min. Saliva/plasma cocaine ratios were generally greater than 2 in specimens collected for up to 24 hr following dosing. Pharmacological effects observed after cocaine administration included increases in heart rate, elevations in blood pressure, dilation of pupils, and increases in subject-reported "High". The duration of pharmacological effects was consistently shorter than, or similar to the time course for detection of cocaine in saliva and plasma. These findings suggest that saliva testing may provide valuable insights into the onset and duration of cocaine-induced pharmacological effects and appears to be a useful alternative to plasma testing for cocaine. Cone, E.J., Tsadik, A., Oyler, J. and Darwin, W.D. Cocaine Metabolism and Urinary Excretion Following Different Routes of Administration. Therapeutic Drug Monitoring, 20, pp. 556-560, 1998.

Clinical Psychopharmacology Section, Clinical Pharmacology Branch

GBR12909 Decanoate Affords Long-term Antagonism of Methamphetamine-induced Dopamine Release

Methamphetamine (METH) addiction is a growing health concern worldwide, yet no medicines for this disease are available. Recent findings indicate that DL699, a decanoate analog of GBR12909, can decrease METH self-administration in animals. In the present work, IRP investigators used in vivo microdialysis to evaluate the effect of DL699 pretreatment on METH-induced elevations in extracellular dopamine (DA) in rat nucleus accumbens. Rats received a single im injection of DL699 or its oil vehicle on Day 1; rats were subsequently tested on Days 6 and 13. Microdialysis probes were inserted into previously implanted guide cannulae and perfused with Ringers= solution overnight. In the morning, dialysate samples were collected every 20 min and assayed for DA by HPLC-EC. Basal dialysate DA levels were significantly elevated (2-fold) in the DL699 group on both test days. Moreover, DL699-pretreated rats displayed dramatic and persistent reductions in METH-induced stimulation of DA release when compared to vehicle-pretreated rats. Autoradiographic assessments of [125I]-RTI-55 binding showed the density of DA transporter sites was diminished in the DL699 group. These data suggest that DL699 can antagonize the actions of METH on mesolimbic DA neurons and this effect involves blockade of DA transporters. Thus, DL699 or similar agents might be useful medications for treating METH addiction. Baumann, M.H., Ayestas, M.A., Lewis, D.B., Rice, K.C., and Rothman, R.B. GBR12909 Decanoate Affords Long-term Antagonism of Methamphetamine-induced Dopamine Release. 28th Annual Meeting, Society for Neuroscience, Los Angeles, CA, November, 1998.

Identification of a Novel Cocaine Binding Site in Brain Membranes Prepared from Dopamine Transporter Knockout Mice

Previous work has suggested that the cocaine analog [125I]RTI-55 labels a novel binding site in rat brain membranes, termed DATsite2, which is not associated with the dopamine (DA), serotonin (5-HT) or norepinephrine (NE) transporters (JPET, 274, pp. 385-395, 1995). In this study IRP investigators tested whether DATsite2 is a product of the DA transporter (DAT) gene. A T-antigen knockin at the DAT gene that results in an effective DAT KO, originally developed at NIDA's IRP and now bred at the GRC, were used. Lack of the DAT gene was confirmed by southern blots. Brain membranes were prepared from frozen whole brain minus caudate of swiss-webster (SW) mice, +/+ mice, +/- mice and -/- mice. KO mice were used at approximately 23 days old. Binding surface analysis of [125I]RTI-55 binding to SW membranes, with 100 nM citalopram to block binding to the 5-HT transporter (SERT), revealed two binding sites: DAT (Bmax = 0.63, Kd = 1.8 nM, Ki of RTI-113 = 18 nM) and DATsite2 (Bmax = 1.48, Kd = 28.3 nM, Ki of RTI-113 = 2299 nM), replicating studies conducted with rat brains. [125I]RTI-55 binding blocked with 100 nM citalopram (DAT binding condition) was reduced by 82% in the -/- mice compared to the +/+ mice. [125I]RTI-55 binding in the presence of 100 nM GBR12935 (SERT binding condition) was reduced by 40% in the -/- mice compared to the +/+ mice. With SERT blocked by 100 nM citalopram, 100 nM RTI-113 inhibited [125I]RTI-55

binding by 64% in +/+ mice, 49% in +/- mice and 17% in -/- mice, consistent with an elimination of DAT in the -/- mice. In contrast, the inhibition produced by benztropine (400 nM), which has equal affinity for DAT and DATsite2, was similar in +/+, +/- and -/- mice. Viewed collectively, these data support the hypothesis that DATsite2 is not a product of the DAT gene. The DAT knockout mouse will be a useful system for characterizing DATsite2. Rothman, R.B., Dersch, C.M., Uhl, G.R., Carroll, F.I., Rowley, D.L., and Donovan, D. Identification of a Novel Cocaine Binding Site in Brain Membranes Prepared from Dopamine Transporter Knockout Mice. 28th Annual Meeting, Society for Neuroscience, Los Angeles, CA, November, 1998.

Alterations in Serotonergic Responsiveness during Cocaine Withdrawal in Rats: Similarities to Major Depression in Humans

Withdrawal from long-term cocaine use is accompanied by symptoms resembling major depression. Because acute cocaine affects serotonin (5-HT) neurons, and 5-HT dysfunction is implicated in the pathophysiology of depression, we evaluated the effects to 5-HT agonists in rats withdrawn from repeated injections of cocaine (15 mg/kg i.p., b.i.d., 7 days) or saline. In the first study, prolactin (PRL) responses elicited by the 5-HT-releasing agent fenfluramine, the 5-HT1A agonist (+/-)-8-hydroxy-2-(di-n- propylamino)tetralin (8-OH-DPAT), and the 5-HT2A/2C agonist (+/-)-1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane hydrochloride (DOI) were examined as indices of postsynaptic 5-HT receptor function. In a second study, specific responses induced by 8-OH-DPAT, namely inhibition of brain 5-HT synthesis and stimulation of feeding, were examined as correlates of 5-HT1A autoreceptor function. Prior treatment with cocaine did not modify fenfluramine-evoked PRL release; however, the PRL secretory response to 8-OH-DPAT was blunted and the PRL response to DOI was potentiated after chronic cocaine treatment. Cocaine exposure did not alter the inhibitory effect of 8-OH-DPAT on 5-HT synthesis. 8-OH-DPAT-induced feeding was influenced by prior cocaine, but this effect was secondary to pronounced baseline hyperphagia in the cocaine-treated group. These data indicate that withdrawal from chronic cocaine renders specific subpopulations of postsynaptic 5-HT1A receptors subsensitive and 5-HT2A/2C receptors supersensitive. No evidence for cocaine-induced changes in 5-HT1A autoreceptor responsiveness was found. A survey of the literature reveals similarities in the profile of 5-HT dysfunction between rats withdrawn from cocaine and humans diagnosed with depression. Authors propose that withdrawal from chronic cocaine in rats may serve as a useful animal model of depressive disorders. Baumann, M.H., and Rothman, R.B. Alterations in Serotonergic Responsiveness during Cocaine Withdrawal in Rats: Similarities to Major Depression in Humans. Biol. Psychiatry, 44, pp. 578-591, 1998.

Brain Imaging Section, Neuroimaging Branch

New Compounds with High Affinity for Nicotinic Acetylcholine Receptors Identified as Promising Radioligand Imaging Candidates

3-(2(S)-Azetidinylmethoxy)pyridine (A-85380) has been identified recently as a ligand with high affinity for nicotinic acetylcholine receptors (nAChRs). IRP investigators synthesized a series of ten pyridine-modified analogs of A-85380, featuring a halogen substituent at position 2, 5, or 6 of the 3-pyridyl fragment, and studied their binding to nAChRs in vitro. Authors found that the novel compounds substituted at position 5 or 6, as well as the 2-fluoro derivative, possessed subnanomolar affinity for nAChRs in membranes from rat brain. For these ligands, Ki values ranged from 11 to 210 pM, as measured by competition with (_)-[3H]epibatidine. In contrast, 2-chloro, 2-bromo, and 2-iodo analogs exhibited substantially lower affinities that are likely attributable to their bulkiness at position 2 producing notable changes in the molecular geometry. The high affinity members of the series and (+)-epibatidine displayed a tight fit superposition of low-energy stable conformers. These new high affinity compounds for nAChRs are promising candidates for development as radioligands to study nAChRs both in vitro and in vivo. Koren, A.O., Horti, A.G., Mukhin, A.G., Gundisch, D., Kimes, A.S., Dannals, R.F., and London, E.D. 2-, 5- and 6-Halo-3-(2(S)-azetidinylmethoxy)pyridines: Synthesis, Affinity for Nicotinic Acetylcholine Receptors, and Molecular Modeling. J. Med. Chem. 41, pp. 3690-3698, 1998.

Nicotinic Receptors in the Monkey Brain Successfully Imaged using SPECT -using 5--[123I]iodo-A-85380

The distribution and kinetics of 5-[123I]iodo-A-85380, a novel ligand for brain nicotinic acetylcholine receptors (nAChRs), have been evaluated in the Rhesus monkey using single photon emission computed tomography (SPECT). Peak brain levels of radioactivity were measured in brain at 90 min after injection of the tracer, and radioactivity levels persisted for at least 4 hr. Accumulation of radioactivity was highest in the thalamus, intermediate in frontal cortex and basal ganglia, and lowest in the cerebellum. In other experiments, specific binding was effectively reduced by the subcutaneous injection 1 mg/kg of the nicotinic agonist cytisine 2.25 hr. after radiotracer administration. At 2.5 hr. after cytisine administration, radioactivity in the thalamus was reduced by 84%, in the frontal cortex by 76%, and in the basal ganglia by 57% of the level measured at the time of cytisine administration thereby demonstrating

the reversible nature of the binding. On the basis of these findings, together with other data indicating high affinity, receptor subtype selectivity, low non-specific binding, and lack of toxicity in animals, 5-[123I]iodo-A-85380 appears to be a promising ligand for SPECT imaging of nAChRs in the human brain. Chefer, S.I., Horti, A.G., Lee, K.D., Koren, A.O., Jones, D.W., Gorey, J., Links, J.M., Mukhin, A.G., Weinberger, D.R., and London, E.D. In Vivo Imaging of Brain Nicotinic Receptors with 5-[123I]iodo-A-85380 Using Single Photon Emission Computed Tomography. Life Sci. 63, (25), PL355-PL360, 1998.

A Simple Probe Device has Proven Useful in External Imaging of Cholinergic Activity in Brain

Using radiotracers that bind specifically to receptors for drugs and neurotransmitters, it is possible to monitor the time-course of drug action in brain. Specifically, one can monitor the occupancy of brain receptors by drugs that interact directly with such receptors by determining competition of those drugs with the relevant radiolabeled ligands. In addition, if a drug affects the level of an endogenous neurotransmitter, the time-course of this effect might be charted as the competition of the transmitter with the radioligand. This principle has been demonstrated using [125I]dexetimide, a ligand for muscarinic acetylcholine receptors, and a simple gamma probe to monitor the time-course of increase in brain acetylcholine levels externally in mouse brain following the peripheral administration of physostigmine. The use of such a probe system rather than ex vivo assay allows repeated determinations. This relatively inexpensive and simple technology should be considered for external imaging when anatomical resolution is not essential or when more complicated procedures (e.g., PET, SPECT scanning are not available). Sanchez-Roa, P.M., Wagner Jr., H.W., Villemagne, V.L., London, E.D., and Lever, J.R. Effects of Extracellular Acetylcholine on Muscarinic Receptor Binding Assessed by [125I]dexetimide and a Simple Probe. Eur. J. Pharmacol., 358(3), pp. 207-211, 1998.

Injection of Methylnaloxonium into the Locus Coeruleus of Opiate-dependent Rats Elicits Widespread Changes in Brain Glucose Metabolism Similar to Those of Systemically Administered Naloxone

Previous studies have demonstrated a widespread stimulation of regional cerebral metabolic rate(s) for glucose (rCMRglc) in morphine-dependent rats undergoing precipitated opioid withdrawal following the systemic injection of naloxone. Nonetheless, many of the behavioral signs of opioid withdrawal are produced by intracerebral injections of the opioid antagonist, methylnaloxonium (MN), into the locus coeruleus (LC). The present work determined the extent to which cerebral metabolic alterations in opioid withdrawal could be initiated by a local action in LC. Intracerebral injections of MN into LC increased rCMRglc in morphine-dependent rats, and the anatomical distribution of this effect was similar to that produced by systemic injections of naloxone. These data support the view that LC is a major substrate of opioid withdrawal in the brain, and that the change rCMRglc during precipitated opioid withdrawal is largely due to the effects of antagonists in the LC. Kimes, A.S., Maldonado, R, Ambrosio, E., Koob, G.F., and London E.D. Cerebral Glucose Metabolism during Opioid Withdrawal following Methylnaloxonium Injection into the Locus Coeruleus. Brain Res., 814, pp. 1-12, 1998.

2-[18F]fluoro-A-85380 holds Promise as a Useful Radiotracer for Imaging of Brain Nicotinic Acetylcholine Receptors with PET

The in vivo brain regional distribution of 2-[18F]fluoro-A-85380, a novel tracer for positron emission tomographic (PET), followed the regional densities of brain nicotinic acetylcholine receptors (nAChRs) reported in the literature. Evidence of binding to nAChRs and high specificity of the binding in vivo was demonstrated by inhibition with nAChR selective ligands as well as with unlabeled 2-fluoro-A-85380. A preliminary study of 2-fluoro-A-85380 demonstrated a relatively low incidence of acute biological effects indicative of toxicity. Horti, A.G., Scheffel, U., Koren, A.O., Ravert, H.T., Mathews, W.B., Musachio, J.L., Finley, P.A., London, E.D., and Dannals, R.F. 2-[18F]Fluoro-A-85380, An In Vivo Tracer for the Nicotinic Acetylcholine Receptors. J. Nucl. Med. Biol., 25, pp. 599-603, 1998.

High Affinity N-[11C]methylated Analogs of Epibatidine Developed as PET Radiotracers for Nicotinic Acetylcholine Receptors

Four halogen-substituted analogs of N-methyl-epibatidine, a nicotinic acetylcholine receptor (nAChR) ligand, were synthesized. They were [(_)-exo-N-methyl-2-(2-halogeno-5-pyridyl)-7-azabicyclo[2.2.1]heptanes where halogeno = F (1a), Cl (2a), Br (3a), I (4a)]. (_)-N-Ethyl epibatidine (2b) also was synthesized. The compounds (1a, 2a, 3a, and 4a) and their corresponding normethyl analogs (1, 2, 3, and 4) inhibited the in vitro binding of [3H]epibatidine to nAChRs to a similar degree, with affinities in the 27 - 50 pM range. The binding affinity of N-ethylepibatidine (2b), however, was substantially lower. The N-[11C]methyl derivatives of 1, 2, and 3 were synthesized from high specific radioactivity [11C]methyl iodide using a high temperature/high pressure technique. The pattern of regional distribution of compounds [11C]1a, [11C]2a, and [11C]3a in the mouse brain following intravenous administration matched those of three highly specific nAChR probes, [3H]epibatidine, [3H]norchloroepibatidine and (_)-exo-2-(2-[18F] fluoro-5- pyridyl)- 7-azabicyclo-[2.2.1]heptane ([18F]FPH) demonstrating these high affinity radioligands can

be used with PET (positron emission tomography) to image nAChRs. Horti, A.G., Scheffel, U., Kimes, A.S., Musachio, J.L., Ravert, H.T., Mathews, W.B., Zhan, Y., Finley, P.A., London, E.D., and Dannals R.F. Synthesis and Evaluation of N-[11C] Methylated Analogs of Epibatidine as Tracers for Positron Emission Tomographic Studies of Nicotinic Acetylcholine Receptors. J. Med. Chem., 41(22), pp. 4199-4206, 1998.

Potent Sigma-1 Receptor Ligand Ameliorates Neuronal Ischemic Injury -- Mechanism Involves Modulation of NMDA-evoked Nitric Oxide Production

Previous work by investigators at NIDA's Intramural Research Program and the Johns Hopkins school of Medicine has shown that 4-phenyl-1-(4-phenylbutyl)piperidine (PPBP), a sigma-1 receptor ligand, ameliorates ischemic neuronal injury measured in in vivo and in vitro models. Recently published work demonstrated that PPBP decreased infarction size, but that prolonged treatment with this compound is associated with loss of therapeutic efficacy. Because NMDA-evoked synthesis of nitric oxide (NO) may play an important role in excitotoxic- mediated injury, further studies focused on whether sigma receptor ligands attenuate basal and NMDA-evoked NO production in vivo. Microdialysis studies of rats indicated that PPBP inhibited both basal and NMDA-evoked release of NO in the striatum. The attenuation was reversed by DuP 734, a sigma-1 receptor antagonist, adding credence to the view that the ameliorative actions of PPBP in ischemia models is via sigma-1 receptor interactions. Attenuated NO production by PPBP and like compounds may provide a possible mechanism for protection from focal ischemia. Bhardwaj, A., Sawada, M., London, E.D., Koekler, R.C., Traystman, R.J., and Kirsch, J.R. Potent Final Sigma1-receptor Ligand 4-phenyl-1- (4-phenylbutyl) Piperidine Modulates Basal and N-methyl-D-aspartate-evoked Nitric Oxide Production in Vivo. Stroke, 29(11), pp. 2404-2411, 1998; Harukuni, I., Bhardwaj, A., Traystman, R.J., Crain, B., London, E.D., and Kirsch, J.R., Neuroprotection from Focal Ischemia by 4-phenyl-1-(4-phenylbutyl) piperidine (PPBP) is Dependent on Treatment Duration in Rats. Anesth. Analg., 87(6), pp. 1299-305, 1998.

Clinical Trials Section, Treatment Branch

Broad Beneficial Effects of Two Schedules of Reinforcement for Cocaine Abstinence in Methadone Maintenance Patients

Contingency management, a treatment in which patients receive incentives for cocaine abstinence, is an effective treatment for cocaine abuse, producing significant periods of sustained abstinence in many patients. Patients receive a voucher incentive for each cocaine-free urine; vouchers have monetary values that increase with the number of consecutive cocaine-free urines. Scientists at the Intramural Research Program evaluated two different schedules of reinforcement in an effort to improve abstinence outcomes and identify the most effective procedure. Cocaine abusing methadone patients were randomly assigned to receive vouchers for 12 weeks under an escalating pay schedule, an escalating pay schedule with start-up bonuses, or a noncontingent schedule. The start-up bonuses were designed to provide substantial immediate reinforcement for initiating abstinence. Both contingent voucher interventions significantly increased subjects' longest duration of sustained cocaine abstinence, increased the percent of subjects who were cocaine abstinent and opiate abstinent across the 12 weeks of the voucher intervention, and significantly decreased self reported cocaine craving. Adding start-up bonuses did not improve abstinence outcomes and may have had an adverse effect. These results replicate the efficacy of voucher-based reinforcement of cocaine abstinence, and show that it can have broad beneficial effects as evidenced by its effects on opiate use. Silverman, K., Wong, C.J., Umbricht-Schneiter, A., Montoya, I.D., Schuster, C.R., and Preston, K.L. Broad Beneficial Effects of Two Schedules of Reinforcement for Cocaine Abstinence in Methadone Maintenance Patients. Journal of Consulting and Clinical Psychology, 66, pp. 811-824, 1998.

Cocaine Use Early in Treatment Predicts Outcome in a Behavioral Treatment Program

As part of a project to identify predictors of treatment outcome and improve patient-treatment matching, cocaine use during the first five weeks of treatment (baseline) was compared in methadone maintenance patients who had little or no periods of abstinence versus those with significant periods of sustained abstinence during the following 12 weeks of an experimental treatment. The experimental treatment was voucher-based cocaine abstinence reinforcement. Cocaine use was evaluated by qualitative and quantitative urinalysis and self-report. Abstainers (those who had successful outcomes) used significantly less cocaine in the 5-week baseline than Nonabstainers (those with less successful outcomes). Differences in cocaine use were not evident at the beginning of treatment (the first week of baseline), but Abstainers used significantly less cocaine in the fifth week of baseline compared to Nonabstainers. Qualitative urinalysis was less sensitive to baseline differences than either quantitative urinalysis or self-report. Thus, cocaine use during baseline was a critical predictor of response to the experimental treatment. Preston, K.L., Silverman, K., Higgins, S.T., Brooner, R.K., Montoya, I.D., Schuster, C.R., and Cone, E.J. Cocaine Use Early in Treatment Predicts Outcome in a Behavioral Treatment Program. J. Cons. & Clin. Psych., 66, pp. 691-696, 1998.

Pharmacotherapy Section, Treatment Branch

Cigarette Smoking During Early Cocaine Abstinence

Many cocaine addicts are heavy cigarette smokers, raising the issue of how to deal with their smoking when they enter addiction treatment and abstain from cocaine use. However, little is known about how cigarette smoking might change during early cocaine abstinence. Intramural scientists studied the number of cigarettes smoked daily (measured indirectly by computerized cigarette dispensers) by 12 cocaine-dependent research volunteers during their first 7 full days on the IRP research ward (starting about 1-1/2 days after their last cocaine use). There was no significant difference between the self-reported number of cigarettes smoked before admission and the number dispensed on the ward, nor any significant changes during the week of monitored abstinence. This finding suggests that cigarette smoking does not change significantly during early cocaine abstinence in a residential setting. Radzius, A., Gorelick, D.A. and Henningfield, J.E. Cigarette Smoking during Early Cocaine Abstinence. Am. J. Addict., 7, pp. 305-308, 1998.

Behavioral Pharmacology Section, Preclinical Pharmacology Laboratory

The GABAB Agonist Baclofen Modifies Cocaine Self-administration in Rats

In the search for a pharmacotherapy to treat cocaine addiction, most research has focused on drugs interacting directly with the dopaminergic system. Recent research, however, has indicated that alterations in other neurotransmitter systems may also be effective in altering the behavioral actions of cocaine. For example, research has shown that the GABAB agonist baclofen can alter cocaine self-administration in animals under certain conditions. IRP investigators have recently expanded on this work to show that baclofen can alter cocaine self-administration under a wider range of conditions, and that the effects of baclofen are specific to cocaine. Baclofen does not disrupt responding maintained by food reinforcement at doses that do disrupt responding maintained by cocaine. Further, drugs which affect GABAA function do not alter cocaine self-administration. Finally, authors have shown that the effects of baclofen appear to be mediated by receptors in the nucleus accumbens or ventral tegmental area. These results, along with previous work, suggest that GABAB agonists may be useful in the treatment of cocaine abuse. Shoaib, M., Swanner, L.S., Beyer, C.E., Goldberg, S.R. and Schindler, C.W. The GABAB Agonist Baclofen Modifies Cocaine Self-administration in Rats. Behavioral Pharmacology, 9, pp. 195-206, 1998.

Psychobiology Section, Preclinical Pharmacology Branch

Antagonism of Cocaine Discriminative Effects by D1-Like Dopamine Antagonists in Squirrel Monkeys

The dopamine D1 receptor antagonists have been proposed as potential treatments for cocaine abuse. IRP researchers compared the antagonism by several dopamine D1 antagonists of different behavioral effects of cocaine, each thought to be indicative of abuse liability. All of the antagonists were effective in reversing effects of cocaine, however, their effectiveness depended upon the behavior being examined. These results are consistent with previous suggestions that actions mediated by D1 receptors contribute to the effects of cocaine, and further documents the degree of involvement of D1 receptors in the various effects examined. Importantly, the predicted effectiveness of the D1 antagonists depends on which behavioral effect is examined. Therefore, assessments of treatment efficacy will require studies of the predictive validity of the various preclinical assays that are currently in use. Abstracts of the 28th Annual Meeting of the Society for Neuroscience, 24, p. 1484, 1998.

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National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Program Activities

Program Announcements/RFAs

On September 4, 1998, NIDA, in conjunction with numerous other NIH components, issued a Program Announcement entitled **New Directions in Pain Research: I** (PA-98-102). The purpose of this program announcement is to inform the scientific community of broad, shared interests in pain research encompassing the various components of the NIH, and to stimulate and foster a wide range of basic, translational amd patient-oriented clinical studies on pain.

On September 16, 1998, NIDA, in conjunction with the National Institute of Mental Health (NIMH) and the National Institute of Alcohol Abuse and Alcoholism (NIAAA), issued a Program Announcement entitled **Pathological Gambling: Basic, Clinical and Services Research** (PA-98-106). This program announcement encourages research that builds on extant research findings concerning pathological gambling and research that expands the breadth and depth of scientific knowledge through increased involvement of various disciplines including epidemiology, genetics, neuroscience, developmental psychopathology, and behavioral, cognitive, and social science.

On September 24, 1998, NIDA issued a Program Announcement entitled **Drug Abuse Treatment and Services Dissertation Research** (PA-98-109). Through this program announcement, NIDA announces the availability of small grants (R03) to support doctoral dissertation research in drug abuse treatment and health services research. Grant support is designed to aid the research of new investigators and to encourage doctoral candidates from a variety of academic disciplines and programs to conduct research in these areas of interest to NIDA.

Epidemiologic Research in Drug Abuse (PA-99-002) was issued by NIDA on October 2, 1998. This Program Announcement replaces PA-94-007, "Survey Research on Drug Use and Associated Behaviors" which was published in the NIH Guide, Volume 22, Number 39 on October 29, 1993.

On November 19, 1998, NIDA, in conjunction with NIMH and NIAAA issued the Program Announcement entitled **National Research Service Awards for Individual Predoctoral Fellowships** (PA-99-17). This is a revision of Program Announcement PAR-93-040 that was published in the NIH Guide, Volume 22, Number 12 on March 26, 1993.

NIDA, in conjunction with numerous other NIH components released **Biobehvioral Pain Research** (PA-99-021) on November 27, 1998. The purpose of this biobehavioral pain research program announcement is to inform the scientific community of the interest of the various institutes at the NIH and to stimulate and foster a wide range of basic and clinical studies on pain as they relate to the missions of these institutes.

On December 23, 1998, the Program Announcement **Neuroscience Research on Drug Addiction** (PA-99-033) was released by NIDA and replaces the PA of the same title published in 1993.

On September 15, 1998, NIDA issued an RFA entitled **Genetics of Drug Addiction Vulnerability** (DA-99-003). This RFA solicits investigator-initiated applications for research projects that identify genetic variation that increase vulnerability to addiction, or dependence on stimulants, (E.g., cocaine and amphetamine), narcotics, (e.g., opiates),

nicotine, benzodiazepines, barbiturates, cannabis, hallucinogens and/or multiple drugs of abuse. Letter of Intent Receipt date for this RFA was December 28, 1998, and the Application Receipt date was January 27, 1999.

On September 16, 1998, NIDA issued the RFA entitled **Centers for the Development of Medications to Treat Drug Addiction** (DA-99-005). The purpose of this RFA is to encourage applications for Center Grants to conduct research designed to systematically evaluate the tolerability/safety (Phase I) and efficacy (Phase II or III) of medications in the treatment of addiction to drugs including: cocaine, methamphetamine, opiates, nicotine and marijuana. Letter of Intent receipt date for this RFA was November 4, 1998. Appliction receipt date was December 4, 1998. Strict guidelines were indicated in the RFA emphasizing the importance of conducting rigorous double-blind medications trials. It is hoped that this effort will result in a focused clinical trials effort needed to evaluate medications for drug addiction disorders.

On December 22, 1998, NIDA issued an RFA entitled **Bringing Drug Abuse Treatment from Research to Practice** (DA-99-007). This RFA will support research to improve our knowledge of how to move research-based drug abuse treatment interventions into clinical practice. Practice research is conceptulaized as having three significant aspects: effective transfer of knowledge, changing organizational behavior, and financing new treatments. Letter of Intent receipt date for this RFA is March 29, 1999. Application receipt date is April 29, 1999.

On December 22, 1998, NIDA issed an RFA entitled **Research on Drug Courts** (DA-99-008). The purpose of this RFA is to stimulate research in the evolving area of drug courts. Applications are sought for research to determine the effectiveness of drug court models, to better understand the important components of this systematic integration of criminal justice and drug treatment access, participation and outcomes. Letter of Intent receipt date for this RFA is March 29, 1999. Application receipt date is April 29, 1999.

On December 23, 1998, NIDA issued an RFA entitled **Behavioral Therapy Development and Behavioral Science** (DA-99-009). The purpose of this RFA is to solicit applications for research aimed at the development of behavioral therapies (Stage I research) for drug addiction based upon basic behavioral and cognitive science. This RFA encourages innovative research on the development of new and refinement of existing behavioral interventions for the treatment of drug addiction. The translation of ideas from basic behavioral and cognitive science into novel behavioral interventions for drug addicts is the ultimate goal of this program. Research projects will be considered that integrate basic behavioral and/or cognitive science with behavioral therapy development research, with the aim of developing new or refining existing behavioral therapies for individuals in drug abuse treatment. Letter of Intent receipt date for this RFA is March 29, 1999. Application receipt date is April 29, 1999. Related to this RFA is a special issue of Behavior Therapy (Volume 29, Number 4, Fall 1998) edited by Frank Andrasik and guest edited by Lisa Simon Onken, TRB, NIDA, and Richard R. Bootzin, University of Arizona. This volume is comprised of articles based on the second in a series of NIDA sponsored workshops entitled "Behavioral Therapy Development and Psychological Science". The purpose of this workshop and the resulting document was to reinforce the bond between behavioral therapy development research and other, less applied, areas of psychology and, hopefully, to help inspire more Stage I behavioral therapy development research.

On January 8, 1999, NIDA issued an RFA entitled **National Drug Abuse Treatment Clinical Trials Network** (DA-99-004). Through this RFA, NIDA invites cooperative agreement applications from established clinical investigators to participate in the National Drug Abuse Treatment Clinical Trials Network (CTN). Awardees will conduct and participate in coordinated, multi-site clinical trials of behavioral, pharmacological, and combined behavioral/pharmacological therapies for drug abuse and addiction, and condiuct research on practices, i.e., studies of factors that impact upon successful adoption of new treatments. CTN research is carried out in community-based treatment settings, in collaboration with other awardees and with NIDA. Each awardee will function as a CTN Research Node, consisting of a Regional Research and Training Center (RRTC) that is linked in partnership with community-based treatment programs (CTPs). The CTN will consist of multiple Nodes and each Node will work in concert with other Nodes and NIDA to conduct multi-site and cross-regional (nationwide) clinical trials research. The Letter of Intent receipt date for this RFA is March 13, 1999. Application receipt date is April 13, 1999.

On December 11, 1998, the RFA **Transdisciplinary Tobacco Use Research Centers (TTURCs)** (CA-98-029) was released. Applications are due April 12, 1999. Program contacts are Jaylan Turkkan, Ph.D. at NIDA and Glen Morgan, Ph.D. at NCI. A dedicated website with the RFA and additional information and resources can be found at http://www.nida.nih.gov/tturc.html. NIDA and NCI are jointly sponsoring this nationwide Centers initiative in fiscal year 1999. Collaborations with other agencies and private foundations such as the Robert Wood Johnson Foundation are planned. Each TTURC will consist of scientists drawn from diverse disciplines who will work collaboratively to solve problems in tobacco use. Research themes may include, for example, the neurobehavioral underpinnings of nicotine addiction, impact of advertising and marketing, prevention of tobacco use, addiction to tobacco, treatment of tobacco use, the identification of biomarkers of tobacco exposure, and the identification of genes related both to addiction and susceptibility to harm from tobacco.

Under the **HBCU Research Scientist Award** RFA (DA-98-005), jointly supported by NIDA and the NIH Office of Research on Minority Health, four Historically Black Colleges and Universities were funded. Florida A&M, Howard, Morgan, and North Carolina Central Universities will recruit research scientists to establish drug abuse research programs on their campuses in the following respective areas: pharmacology, epidemiology, prevention and cellular biology. On November 6, 1998, the first meeting of the HBCUs was held in Bethesda, Maryland to discuss development and recruitment plans.

Dr. Coryl Jones, ERB and Dr. Vince Smerglio, CAMCODA, NIDA representatives to the NIH Child Abuse and Neglect Workgroup, participated in the development of an **Interagency RFA on Child Neglect** issued February 1, 1999 for award April 4, 2000 with co-funding provided by NIDA, NIMH, NINDS, NICHD, NIAAA, ACF and NIJ.

Drug Interaction Studies

A meeting with expert consultants on cardiovascular interactions between cocaine and potential medications was held by MDD on December 1, 1998 in Rockville. The consultants enthusiastically approved the validation of the model and directed MDD to proceed with testing of compounds selected for upcoming clinical studies. The results of the drug interaction studies will be critical in supporting clinical pharmacology studies with cocaine and new chemical entities. They indicated that the methodology was state-of-the-art and comparable to drug safety programs at major pharmaceutical companies. The first compound to be tested along with cocaine will be GBR 12909.

Clinical Pharmacology Unit

NIDA's Medications Development Division has opened a new Clinical Pharmacology Unit at the former Neonatal ICU at the National Naval Medical Center in Bethesda, MD. Dr. Louis Cantilena is the principal investigator. The renovations are complete and on November 29,1998 the first clinical trial was initiated. The study title is: A Multiple Dose, Open Label, Fixed Order, Dose Escalating Study with Four Dosages of GBR 12909 in Normal Volunteers.

National Youth Anti-Drug Media Campaign Evaluation

In support of a special collaboration with the White House Office of National Drug Control Policy (ONDCP), NIDA has awarded a contract to conduct an independent, scientifically based impact evaluation of the National Youth Anti-Drug Media Campaign, sponsored by ONDCP. The contract was designed in collaboration with leading experts in statistical sampling, design, and measurement, and in drug abuse prevention and communications research. In September, NIDA awarded the contract to WESTAT, Inc., a nationally recognized survey company, to conduct the 4-year study to measure the effectiveness of the campaign in changing the attitudes and behaviors of youth (age 9-18) and their parents. The evaluation project consists of national cross-sectional household surveys of parents and youth conducted twice a year, which will track more immediate campaign effects; and longitudinal surveys conducted once a year in four local communities, which will track the cumulative effects of the campaign on families.

Drug Abuse Prevention and Communications Research

Also with funding by the ONDCP, NIDA released an RFA, "Drug Abuse Prevention and Communications Research (DA-98-006)" in February 1998. NIDA received 23 applications, which proposed to study the influences of the media on drug use, and the use of the mass media as a prevention intervention. NIDA awarded five grants that have the potential to provide guidance to the national campaign on the most effective messages and approaches to discourage drug use among youth. The grants are geographically diverse, address urban, suburban and rural populations, compare racial and ethnic groups in terms of media message effectiveness, and include the range of age groups targeted in the national campaign.

Interagency Task Force on Child Abuse and Neglect

NIDA participates in the Interagency Task Force on Child Abuse and Neglect which involves 22 Federal agencies involved in child research. At the 5th Federal Forum on Child Abuse and Neglect held in March 1998, NIDA continued to be second in level of Federal funding of research on child abuse and neglect (Compendium of grants available from National Center on Child Abuse and Neglect). The 6th Federal Forum will meet in March 1999.

NIDA/IRP Summer Research Program for Students

Since 1986, the IRP has had a summer research program for students. During the summer of 1998, a total of 41 students representing 35 high schools, colleges, and medical and graduate schools participated in the program through either the NIH Summer Internship Program or the Minority Research and Training Program. Each student participant was assigned to work with an IRP scientist on a research project. The students' training program is

individually developed and includes directed readings, tutorials, attendance at seminars, and actual laboratory experience under the direction of the scientist. The culmination of the summer program is the students' presentation of their research at the NIH Student Poster Session held at the Bethesda campus in early August. Because of outstanding contributions and effort, some students will be co-authors on published papers or abstracts. The NIH Summer Internship Program is coordinated by Dr. Stephen Heishman, and the Minority Research and Training Program is coordinated by Dr. Jean Cadet and Ms. Mary Affeldt.

NIDA's New/Competing Awards Since September 1998

Adams, Catherine --- University of Colorado Health Sciences Center
Nitric Oxide Mediation of Hippocampal Nicotine Effects

Alterman, Arthur I. --- University of Pennsylvania
Validity of Original and New ASI Summary Indices

Crits-Christoph, Paul --- University of Pennsylvania
Further Data Analysis on the NIDA CCTS

Epstein, Elizabeth E. --- Rutgers/State University of New Jersey
Adapting Behavioral Marital Therapy to Treat Drug Abuse

Fava, Maurizio --- Massachusetts General Hospital
Bupropion as an Adjunct to the Nicotine Patch Plus CBT

Glick, Stanley D. --- Albany Medical College
The Archer Conference on Drug Abuse: New Medications

Gorbach, Sherwood L. --- Tufts University School of Medicine
Nutritional Status in HIV-Positive Hispanic Drug Abusers

Guydish, Joseph R. --- Institute for Health Policy Studies
Drug Abuse Treatment on Demand Impacts in San Francisco

Hyler, Steven E. --- Columbia University
Drug Addiction Treatment: New Research Findings On-Line!

Karler, Ralph --- University of Utah-Department of Pharmacology
Behavioral Sensitization: Cocaine and Amphetamine

Kornetsky, Conan --- Boston University School of Medicine
Brain Stimulation Models of Drug Abuse

Mannheimer, Sharon Beth --- Harlem Hospital Center
The Harlem Adherence with Retroviral Therapy Study

Mello, Nancy K. --- McLean Hospital
Biobehavioral Studies of Substance Abuse

Niaura, Raymond --- Miriam Hospital
Motivation and Patch Treatment for HIV-Positive Smokers

Rawson, Richard A. --- Friends Research Institute, Inc.
Psychosocial Treatment Dose: A Prospective Study

Reith, Maarten E. --- University of Illinois at Chicago
The Dopamine Transporter and Cocaine

Rosenberg, Howard C. --- Medical College of Ohio
Pharmacology of Benzodiazepine Tolerance and Dependence

Schneider, Nina G. --- UCLA
Nicotine Dependence: Tailoring and Preference Research

Siegel, Ralph M. --- Rutgers State University
Norepinephrine and Attentional Modulation of Cortex

Stitzer, Maxine L. --- Johns Hopkins Bayview Medical Center
Behavior Therapy for Inner-City IV Heroin Abusers

Svingos, Adena L. --- Cornell University Medical College
Structural Sites for Opiate Modulation of Frontal Cortex

Taxman, Faye S. --- University of Maryland
An Evaluation of the HIDTA Seamless System for Offenders

Weiss, Roger D. --- McLean Hospital
Relapse Prevention Group for Bipolar Substance Abusers

Wells, Elizabeth A. --- University of Washington
Brief Motivational HIV Risk Reduction Among IDUs

Wong, Mamie M. --- Wested
Conference on Drug Use and Outcomes in Mixed Race Youth

Review Activities

Staff Development

Dr. Teresa Levitin, Director, OEPR, Dr. William C. Grace, Deputy Director, OEPR, and Ms. Diana Souder, Training GTA, OEPR, presented a training seminar "NIDA Research Center Grants" to NIDA staff in October to acquaint them with changes in NIDA's Centers program.

Ms. Jackie Porter, Special Assistant to the Director, OEPR and Ms. Pam Stokes, Grants Systems Specialist, OEPR presented a training session to the Division of Basic Research, NIDA on the use of the electronic council book. This training was similar to that presented to the Council in September.

Dr. Mark Swieter, SRA, presented at a training session jointly sponsored by OEPR and the Office of Science Policy and Communications. The session, 'NIDA's K Awards and Training Program', was attended by staff from NIDA and other NIH components.

[Home Page][Office of the Director][Report Index][Previous Report Section] [Next Report Section]

Archive Home | Accessibility | Privacy | FOIA (NIH) | Current NIDA Home Page

National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Congressional Affairs

Presidential Action - Bills of Interest

P.L. 105-277 -- The Omnibus Consolidated and Emergency Supplemental Appropriations Act, 1999 (H.R. 4328). After enactment of six continuing resolutions, on October 20, 1998, the House, by a vote of 333-95, passed H.R. 4328. This measure provides appropriations funding for eight spending bills, including the Labor, HHS, Education Appropriation, through September 30, 1999. On October 21, the Senate passed the measure by a vote of 65 to 29, and the President signed the bill as P.L. 105-277.

Selected provisions of interest

NIH Appropriations - The bill provides an increase of $1.990 billion for NIH, or a 14.6 percent increase over the FY 98 level, for a total of $15.612 billion, plus $40 million (available in October 1999) for the clinical research center. NIDA funding for FY 99 was $603,274,000 or 14.4% over FY 98.

Alternative Medicine - establishes in statute a National Center for Complementary and Alternative Medicine (NCCAM); repeals the authority of the current Office of Alternative Medicine (OAM); provides NCCAM with grant-making authority and an advisory council; requires establishment of a clearinghouse; and requires a full-time CAM coordinator in each ICD.

Human Embryo Research - prohibits the use of funds in the bill to create human embryos for research purposes, or for research in which a human embryo or embryos are destroyed, discarded or knowingly subjected to risk of injury or death greater than that allowed under current law for research on fetuses in utero.

Needle Exchanges - bans the use of funds in the bill to carry out any program to distribute sterile needles or syringes for the injection of any illegal drug. Prohibits Promoting Legalization of Controlled Substances - except where there is evidence of therapeutic advantage or that federally sponsored clinical trials are being conducted to determine advantage.

Bioterrorism - concerned that civilian health authorities are ill prepared for bioterrorist attack, Congress provided close to $150 million to several government agencies - mainly CDC and NIH - to stockpile vaccines, develop response plans and study new methods of detecting and treating biological and chemical agents. The funds were included in the DHHS appropriations provisions of the Omnibus bill.

National Foundation for Biomedical Research - $500,000 for the Foundation and continuation of the authority for the Foundation to transfer funds to NIH. The name of the Foundation was changed by the Health Professions Education Partnerships Act of 1998 to the National Foundation for the NIH.

Release of Research Data under FOIA - requires the OMB (Office of Management and Budget) to amend Circular A-110 to ensure that all data produced under research awards be made available to the public through procedures established under the Freedom of Information Act (FOIA).

P.L. 105-248 -- On October 9, 1998, H.R. 4382, the Mammography Quality Standards Reauthorization Act, was signed into law. This legislation, among other things, reauthorizes through FY 2002 such sums as may be necessary for the award of grants for breast cancer screening surveillance research.

P.L. 105-276 - H.R. 4194 -- On October 21, 1998, the President signed H.R. 4194 the Departments of Veterans Affairs and Housing and Urban Development, and Independent Agencies Appropriations Act, 1999, as P.L. 105-276. This bill contains funding for NIEHS through Superfund for research and for worker training.

P.L. 105-305 - H.R. 3332 -- On October 28, 1998, the President signed the Next Generation Internet Research Act of 1998, becoming P.L.105-305. This legislation amends the High-Performance Computing Act of 1991 to authorize appropriations for FY 1999 and FY 2000 for government-funded research into high-capacity, high-speed computer networks. NIH becomes one of five agencies authorized to receive funds ($5 million for FY 1999 and $7.5 million for FY 2000) for this purpose. The law directs the President's Information Technology Advisory Committee to report annually to Congress and the President regarding the progress of the NGI program. H.R. 3332 passed the House on September 14, 1998, and the Senate on October 8, 1998.

P.L. 105-340 - S. 1722 -- On October 31, 1998, the President signed into law S. 1722, the Women's Health Research and Prevention Amendments of 1998 (P.L. 105-340). This legislation extends and/or amends various NIH authorities related to women's health research including the following: the drug DES; osteoporosis, Paget's disease, and related disorders; breast cancer and ovarian and related cancers; heart attack, stroke, and other cardiovascular diseases in women; aging processes in women; and the Office of Research on Women's Health. This legislation also extends and/or amends a variety of CDC authorities regarding women's health.

P.L. 105-362 -- On November 10, 1998, the President signed into law S. 1364, the Federal Reports Elimination Act of 1998. This legislation eliminates numerous NIH reports to Congress, including the Report of the Council on Alzheimer's Disease; Report on the U.S.-Japan Cooperative Medical Science Program; Report of the Interagency Coordinating Committee on Arthritis and Musculoskeletal and Skin Diseases; Report on Family Planning and Population Research; Report of the NICHD Associate Director for Prevention; Report on Health Services Research (Report to Senate and House authorizing committees by NIDA, NIAAA, & NIMH); the Annual Reports of the National Diabetes Advisory Board, the National Digestive Diseases Advisory Board, the National Kidney and Urologic Diseases Advisory Board; the Public Health Service Report; the Annual Report on Disease Prevention; and the Annual Report on Administrative Expenses.

P.L. 105-392 - S. 1754 - Health Professions Education Partnership Act, sponsored by Sen. Bill Frist (R-TN), reauthorizes federal health professions education programs and consolidates the 37 programs that currently assist minority and disadvantaged students pursuing health care careers into seven clusters.

Anti-Drug Bill

H.R. 4550 - On September 16, 1998, by a vote of 396 to 9 the House passed a wide-ranging anti-drug bill, H.R. 4550, introduced by Rep. Rob Portman (R-OH) that would have authorized numerous drug prevention and treatment programs. By a voice vote, the House adopted a substitute amendment to alter parts of the bill as introduced. The most significant change deleted a provision that aimed to encourage drug companies to develop anti-addiction medications by extending a company's exclusive right to market certain other drugs. The provision would have allowed pharmaceutical companies that develop and market anti-addiction medications for cocaine or methamphetamine to extend the time during which they are protected from competition under the FDA approval process for a qualifying on-market drug. Other provisions from this bill, such as the National Youth Anti-Drug Media Campaign and Drug Free Prisons and Jails, were eventually swept into the Omnibus Consolidated and Emergency Supplemental Appropriations Act (P.L. 105-277) under Division D-Drug Demand Reduction Act.

Other Items

Tobacco Settlement

In November 1998, all 46 states that had not previously settled with the tobacco industry signed on to a $206 billion, 25-year agreement that resolves their claim against the tobacco companies for tobacco-related health expenditures under Medicaid. Senator Hatch has agreed to Senator Feinstein's request to hold a hearing on the new tobacco settlement early in the 106th Congress. Senator Feinstein promised to consult with many interested parties, including public health groups and the FDA and review what the settlement between the states and tobacco industry has accomplished.

GAO Review

Senators Campbell (R-CO) and Kohl (D-WI), Chairman and Ranking Minority of the Senate Appropriations Subcommittee on Treasury and General Government, requested a General Accounting Office (GAO) review of ONDCP's Anti-Drug Media Campaign. Plans are to complete the study by June 1999.

NIH Officials Brief Senate Budget Committee Staff

On December 22, 1998, NIH Director, Dr. Harold Varmus, and five institute directors briefed staffers from the Senate Budget committee on how NIH would handle increases that advocates are seeking for NIH in FY 2000. Institute Directors who accompanied Dr. Varmus included Dr. Alan I. Leshner, Director, NIDA; Dr. Francis Collins, Director, NIHGR; Dr. Anthony Fauci, Director, NIAID; Dr. Steven Hyman, Director, NIMH; and Dr. Gerald Fischback, Director, NINDS. Also attending the meeting were NIH Deputy Director, Ruth Kirschstein, NIH Budget Director, Francine Little, and Acting Associate Director for Legislative Policy and Analysis, Roz Gray.

NIDA Officials Brief House Commerce Committee Majority Staff

On November 3, 1998, at the request of majority staff of the House Committee, Dr. Frank Vocci, Director, Medications Development Division (MDD), National Institute on Drug Abuse (NIDA), provided an update on the status of current research on anti-addictions medications. Dr. Timothy Condon, Associate Director, NIDA, and Mary Mayhew, NIDA Legislative Contact, accompanied Dr. Vocci.

[Home Page][Office of the Director][Report Index][Previous Report Section] [Next Report Section]

Archive Home | Accessibility | Privacy | FOIA (NIH) | Current NIDA Home Page

National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

International Activities

NIDA sponsored several international activities during the American Methadone Treatment Association meeting in New York in September 1998. An international research workgroup session, chaired by International Program Director Dr. M. Patricia Needle, attracted methadone treatment practitioners and researchers from 14 countries who discussed NIDA research on pharmacotherapies and behavioral therapies for opiate, cocaine, and methamphetamine addiction. NIDA staff participating in the session included Dr. Frank Vocci, MDD, and Drs. Robert Battjes, James Cooper, and Dorynne Czechowicz, DCSR.

The 1998-1999 Hubert H. Humphrey Drug Abuse Fellows began their study program at The Johns Hopkins University in August. There are 4 NIDA-supported Fellows in this year's group of 11 Fellows; they are Drs. Amany El Mougy, Egypt; Gabor Kelemen, Hungary; Leonardo Estacio, The Philippines; and Gennadiy Novitskiy, Russia. Other Fellows are from China, Egypt, Ghana, Myanmar, Panama, Paraguay, and Saudi Arabia. NIDA sponsored an introductory meeting October 1, 1998 in Baltimore and a NIDA research orientation meeting in Rockville on November 6, 1998 for Fellows and program staff.

On September 25, 1998, Richard A. Millstein, Deputy Director, NIDA, and Dr. M. Patricia Needle, met with Dr. Yasuhiro Suzuki, new Executive Director for Social Change and Mental Health, World Health Organization, to discuss NIDA-WHO cooperation in the area of drug abuse. Mr. Suzuki was in the Washington area for the regional WHO meeting at the Pan American Health Organization and to meet with NIH and other U.S. government officials.

NIDA welcomed Secretary Herbert Schaepe and board members Dr. Hamid Ghodse and Mrs. Elba Torres Graterol of the International Narcotics Control Board (INCB) on October 7, 1998 as part of their first official visit to the U.S. Attending for the United States were NIDA Deputy Director, Richard A. Millstein, Dr. James Cooper, DCSR, M. Patricia Needle, Dr. Stuart Nightingale, Associate Commissioner for Health Affairs, Food and Drug Administration, and Mr. Thomas Coony, Department of State.

On November 13, 1998, M. Patricia Needle met with Dr. B@rbel K`ster, Coordinator of International Relations of the German Federal Ministry for Education, Science, Research and Technology, to discuss a possible U.S.-German research seminar on drug abuse and related health consequences to be held in 1999.

On November 17, 1998, Dr. Peter A. Bootsma, incoming Counselor for Health and Welfare of the Royal Netherlands Embassy, visited NIDA with Mr. Herbert P. Barnard, outgoing Counselor who has worked with NIH on health issues for the past several years.

On November 22-23, 1998, Dr. Robert Battjes participated in the health services research task force meeting of the World Health Organization-NIH Joint Project on the Assessment of Disablement, held in Seattle, WA.

Dr. Robert Battjes, along with NIDA grantee Dr. Bruce Rounsaville of Yale University School of Medicine, traveled to St. Petersburg and Moscow, Russia, December 4-12, 1998, visiting drug abuse treatment programs, the Pavlov State Medical University, the (national) Research Center on Addictions, and the Ministry of Health. The purpose of the visit was to gather information on drug abuse treatment within Russia and to facilitate planning for an upcoming NIDA training workshop which will be held in the St. Petersburg area in May 1999.

Ann Blanken, DEPR, made a presentation on qualitative research on drug abuse in the United States at the European Monitoring Center's seminar entitled "Qualitative Research - Knowledge for Effective Action, Lisbon, Oct. 29-31, 1998.

Ann Blanken and Elizabeth Robertson, DEPR, and M. Patricia Needle, International Program met on November 16, 1998 with representatives Kwan-Shik Min, LL.D. and K.T. Moon of the Korean anti-drug effort.

Dr. Richard Needle and Helen Cesari, CRB, organized and hosted a planning meeting for the 1999 Global Research Network on HIV Prevention in Drug-Using Populations in Rockville, MD, in October 1998. Participants included international and U.S. researchers and representatives from NIDA, the NIH Office on AIDS Research, the World Health Organization/Programme on Substance Abuse (WHO/PSA), the Joint United Nations Programme on HIV/AIDS (UNAIDS), the Centers for Disease Control and Prevention, and the DHHS Office of International and Refugee Health.

Drs. Elizabeth Robertson, Kathy Etz, and Larry Seitz, DEPR, met with Dr. Matthew Sanders, Director, Parenting and Family Support Center and Associate Professor, Clinical Psychology, University of Queensland, Australia, to discuss family-based prevention interventions in Australia and the United States on November 3, 1998. Following this, Dr. Sanders led a seminar on Positive Parenting Program, a universal, selected and indicated intervention program.

On October 20, 1998, Drs. Elizabeth Robertson and M. Patricia Needle met with a group of scientists from South America to discuss NIDA's research portfolio, international activities, and prevention programming.

Dr. Larry Seitz briefed Mr. David Teeman, Research Officer at the University of Essex Health and Social Services Institute, United Kingdom, who visited the Prevention Research Branch (PRB) on November 9, 1998 regarding NIDA's prevention research program and the many aspects of good prevention interventions. PRB also developed an itinerary for Mr. Teeman to visit with senior prevention researchers in the Washington/Baltimore metropolitan area.

Dr. Elizabeth Robertson was a member of the planning committee for the International Classification of Prevention Trials meeting, co-sponsored by NIDA and held on December 10 and 11, 1998 in Washington, D.C.

William J. Freed, Ph.D., of the Intramural Research Program, was invited to speak at the Ninth Biennial Winter Workshop on Schizophrenia in Davos, Switzerland, on "N-CAM Abnormalities in Schizophrenia".

Dr. Marilyn A. Huestis of the NIDA intramural program presented the plenary lecture at the International Congress on Clinical and Analytical Toxicology held in Liege, Belgium in October 1998, where she spoke on "Recent Advances in Human Kinetics and Disposition of Marijuana". She also was a plenary speaker for the AUSTOX meeting in Sydney, Australia where she presented three lectures entitled "Safety of Buprenorphine: Ceiling Effect for Physiologic & Subjective Measures at High Intravenous Doses", "Pharmacokinetics of Cannabinoids in Urine", and "Raising the Opiate Cutoffs".

[Home Page][Office of the Director][Report Index][Previous Report Section] [Next Report Section]

Archive Home | Accessibility | Privacy | FOIA (NIH) | Current NIDA Home Page

National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Meetings/Conferences

NIDA organized a Town Meeting in Des Moines, Iowa entitled **"Understanding Drug Abuse and Addiction: Myths versus Reality"** on October 14, 1998. NIDA Director Dr. Alan I. Leshner and NIDA researchers discussed ways that state policy makers, organizations, schools and communities can utilize the latest scientific research to assess state and local drug problems and tailor programs to meet these needs. Dr. Timothy Condon gave a presentation entitled "Focus on Methamphetamine," addressing a drug problem particular to the region.

NIDA hosted its **Fifth Annual Constituent Conference** on December 1-2, 1998 at the Lansdowne Conference Center in Lansdowne, Virginia. NIDA Director, Dr. Alan I. Leshner presented the 'NIDA Report Card' highlighting specific actions taken by the Institute in response to constituent group recommendations and needs.

NIDA sponsored a **Drug Abuse Track at the Community Anti-Drug Coalitions of America Annual National Leadership Forum** in Washington, D.C., November 18-21, 1998.

The National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), and the Office of Medical Applications of Research (OMAR) sponsored a 3-day **NIH Consensus Development Conference on Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder** in November, 1998. After hearing presentations by national and international medical research and health care experts in the fields and public testimony from interested organizations and individuals, an independent, non-Federal consensus panel chaired by Dr. David Kupfer, Thomas Detre Professor and Chair, Department of Psychiatry, University of Pittsburgh, weighed the scientific evidence and wrote a draft consensus statement. Among the findings the panel made were: 1) careful therapeutic use of stimulants is effective in treating the core symptoms of ADHD, 2) although increased risk of drug abuse and cigarette smoking is associated with childhood ADHD, existing studies come to conflicting conclusions as to whether exposure to psychostimulant medication increases or decreases the subsequent risk of abuse, and 3) while increased availability of stimulant medications may pose risks for society, there is little evidence that current levels of production have had a substantial effect on abuse. The full draft NIH Consensus Statement on Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder is available by calling 1-888-NIH-CONSENSUS (1-888-644-2667) or by visiting the NIH Consensus Development Program Web site at http://consensus.nih.gov.

NIDA sponsored a **Drug Abuse track at the annual conference of the New York State Alcoholism and Substance Abuse Programs Associations** in Saratoga Springs, New York, on October 27, 1998. NIDA Director, Dr. Alan Leshner, was the keynote speaker at this event.

NIDA sponsored a **mini-town meeting in conjunction with the University of Buffalo**, in Buffalo, New York, on October 28, 1998.

On December 1, 1998 the Medications Development Division held a quarterly meeting with its participating **Department of Veterans Affairs Medications Development Research Units (MDRUs)**. The meeting focused on changing certain administrative aspects of the MDRU program and transferring the VA's locus of administrative oversight from its Medical Research to its Cooperative Studies Program in order to promote management efficiencies.

On July 29, 1998, NIDA's Medications Development Division held a review of **Alpha-2 Adrenergic Agonists:**

Feasibility of Inpatient v. Outpatient Efficacy Studies Directions. This meeting of internationally recognized leaders in the field concerning the use of alpha-2 agonists as treatments for opiate withdrawal was convened to review evidence and formulate optimal research strategies for evaluating relatively novel medications in this class as treatments for opiate withdrawal. Participant reviewers included G.E. Bigelow, Ph.D., Johns Hopkins University School of Medicine, C. Gorodetzky, M.D., Ph.D., Hoechst Marion Roussel, H. D. Kleber, M.D., Columbia University, T. R. Kosten, Yale University School of Medicine, L. McNicholas, M.D., Ph.D., University Pennsylvania School of Medicine, J. Myles, M.D., Avon Drug Problem Team, UK, S. A. Reines, M.D., Ph.D., Merck Research Laboratories, and J.A. Renner, Jr., M.D., Boston VA MDRU. Other Presenters were G. Gerra, M.D., Az. USL, Distretto "Parma Citta", Italy, M.S. Gold, M.D., University of Florida Brain Institute, D.R. Jasinski, M.D., Johns Hopkins University School of Medicine, and P.G. O'Connor, M.D., M.Ph., Y. Shaham. The focus was the feasibility of conducting inpatient versus outpatient studies.

NIDA's Medications Development Division held a **Lofexidine Project Review: Ad Hoc Consultants Meeting on Future Directions** on July 30, 1998, at the Hyatt Regency Hotel in Bethesda, MD. Lofexidine is an alpha-2 adrenergic agonist that has previously been shown in open studies and recently (1996-1998) in double-blind trials to have similar efficacy but significantly less hypotensive effects than clonidine in the treatment of opiate withdrawal. As there is no FDA approved non-opiate medication for opiate withdrawal in the U.S., MDD, NIDA has been exploring lofexidine to fill this gap. Clonidine is an approved medication in the U.S. for the treatment of hypertension, but it is not approved for the treatment of opiate withdrawal. Lofexidine (up to 2.4 mg/day) is approved for opiate withdrawal in the UK where over 45,000 doses have been administered to date. The meeting was convened to evaluate results of completed two site Phase I tolerability/preliminary efficacy trial (evaluating highest dose: 4.0 mg/day) conducted at the Philadelphia VA Medications Development Research Unit (MDRU) and at the Los Angeles (now Long Beach) VA MDRU to provide external peer review evaluation as to whether MDD, NIDA should move forward to an inpatient double-blind pivotal multi site Phase II/III trial. Results of this meeting: All 7 consultants indicated that MDD, NIDA should go forward with the proposed Phase II/III study.

On August 13-18, 1998, NIDA's Special Populations Office cosponsored **"Diversity 2000"** at the annual convention of the American Psychological Association in San Francisco, California. This program encourages minority community college students to develop leadership skills and pursue advanced degrees and research careers.

Dr. Alan I. Leshner, NIDA Director, presented the keynote address at the "Primary Care/Behavioral Healthcare Summit," held in St. Louis, Missouri, November 3-6, 1998.

Dr. Timothy Condon, Associate Director, NIDA and Director, Office of Science Policy and Communications (OSPC), attended the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, held October 28 - November 1, 1998 in Anaheim, California.

Dr. Timothy Condon, Dr. Andrea Baruchin, and Dr. Cindy Minor of OSPC attended the Society for Neuroscience Annual Meeting in Los Angeles, California, November 9 - 13, 1998. Dr. Baruchin presented at the 'Survival Skills Workshop on Job Hunting' and Dr. Baruchin and Dr. Minor participated in a trans-NIH research training session.

Dr. Timothy Condon traveled to Omaha, Nebraska to represent NIDA at the Second Meeting of the Methamphetamine Interagency Task Force Federal Advisory Committee held October 5-6, 1998.

Dr. Timothy Condon presented the keynote address "Drugs and The Brain: Can Science Replace Ideology?" at the meeting of Join Together National Leadership Fellows held in Hilton Head, South Carolina on September 17, 1998.

Dr. Andrea Baruchin, OSPC Science Policy Branch Chief, attended the "Community and Science: Models for Success" meeting, a bioethics workshop held in Tuskegee, Alabama on November 19-20, 1998.

Dr. Cindy Miner conducted a grant writing workshop at the American Academy of Child and Adolescent Psychiatry held in Anaheim, California on October 28, 1998.

Drs. Cindy Miner and Cathrine Sasek, OSPC, gave a presentation entitled "The Effects of Drugs on the Brain" on November 20, 1998 at the CADCA National Leadership Forum in Washington D.C., November 18-21, 1998.

On September 23, 1998, Dr. Timothy Condon, Associate Director, NIDA, and Beverly Jackson, Chief, Public Information and Liaison Branch, OSPC, attended the NIH meeting hosted by Dr. Varmus, "Enhancing Public Participation in NIH Activities."

On November 6, 1998, Beverly Jackson participated in the planning meeting for the 1999 Recovery Month activities, organized by the Center for Substance Abuse Treatment.

On November 12, 1998, Dr. Timothy Condon and Beverly Jackson participated in a day-long conference on outreach to the entertainment industry held in Los Angeles, CA.

On November 19-20, 1998, Drs. Alan Leshner and Lula Beatty chaired the Addictions Panel at the NIH sponsored "Community and Science: Models for Success" conference held at Tuskegee University in Tuskegee, Alabama. This conference was a follow-up activity in response to the President's apology for the PHS syphilis study conducted in Tuskegee. Addictions Panel members included Dr. Leshner and past/current NIDA Council members, Drs. Lawrence Brown, Kathy Sanders-Phillips, and Andrea Barthwell.

On September 18-20, 1998, as a part of the semiannual meeting of governance boards and committees, Dr. Lula Beatty participated in the American Psychological Association's Committee on Women's meeting.

On October 1, 1998, Dr. Lula Beatty attended the Advisory Board meeting of the Office of Research on Minority Health.

On October 15, 1998, Dr. Lula Beatty attended a conference on Racial Trends sponsored by the National Academy of Science.

On September 16-19, 1998, Ana Anders, Senior Advisor on Special Populations, Special Populations Office, chaired a workshop entitled "Impact of Welfare Reform on Substance Abuse: Requirements on Latino Families and Community" at the NIDA cosponsored Latino Behavioral Health Institute Conference in Los Angeles, California. Dr. Alan Leshner, Director, NIDA, was a keynote speaker at this conference.

On October 8, 1998, Ana Anders participated in a daylong retreat with Hispanic colleagues from other NIH institutes in order to review the charter on responsibilities of the Hispanic Task Force.

On October 13, 1998, Ana Anders represented NIDA on the MADD diversity Committee at a planning meeting for the upcoming National Diversity Forum.

On October 14, 1998, Ana Anders represented NIDA at the NIH Hispanic Task Force meeting with Dr. Ruth Kirchstein, Deputy Director, NIH. They met to review and recommend actions for the Hispanic Agenda at NIH.

As a representative of NIDA, Ana Anders has attended ongoing meetings with multiple federal agencies hosted by ONDCP. They have met to finalize the U.S./Mexico Demand Reduction portion of the Binational Drug Strategy document and to design a Web page to allow better avenues of communication between the two countries.

On December 8, 1998, Pamela Goodlow, Special Populations Office, presented an overview of NIDA's minority supplements program to NIDA staff. Topics covered included history of the program, policy and review procedures for minority supplements, and eligibility concerns.

Dr. Frank Vocci, Director, MDD, and Dr. Walter Ling briefed the California Research Advisory Panel on the development of buprenorphine and buprenorphine/naloxone on September 23, 1998.

Dr. Frank Vocci and Mr. Joel Egertson, MDD, briefed the Board of Directors of the American Methadone Treatment Association at their annual meeting held in New York City on Sept 28, 1998.

Drs. Tim Condon and Frank Vocci, and Ms. Mary Mayhew briefed Mr. Mark Wheat on the development of medications for the treatment of addictive disorders on October 6, 1998.

Barbara H. Herman, Ph.D., MDD, chaired a meeting of the P50 Medications Centers Grantees entitled Interim Center Grant Update on Medications for Cocaine, Opiate, and Nicotine Abuse/Addiction on March 4-5, 1998, in Washington, D.C. Principal Investigators (PIs) and Co-Investigators from the five P50 medications center grants were asked to present interim update on medications for addictive disorders from each center, and to encourage interaction and scientific exchange among the center participants. PIs of these centers include:

J. Grabowski, Ph.D., University of Texas (Houston); Dorothy Hatsukami, Ph.D., University of Minnesota; Herbert D. Kleber, M.D., Columbia University; Thomas R. Kosten, M.D., Yale University and VA Connecticut Health Care System; Walter Ling, M.D., UCLA and Los Angeles (now Long Beach) VAMC. In addition to presentations by the PIs there were 15 presentations by co-investigators from these sites.

Stephen R. Zukin, M.D., Director, Division of Clinical and Services Research (DCSR), was a speaker at the 10th Annual St. Thomas Hospital Conference on Addictions in Akron, Ohio on November 4, 1998. Dr. Zukin's speech was entitled Progress in Treatment: From Research to Practice.

Jack Blaine, M.D., Chief of the Treatment Research Branch, DCSR, was the keynote speaker at the Community Forum on November 16, 1998 sponsored by the San Francisco Treatment Research Center on "Bridging the Gap Between Drug Abuse Treatment and Research."

Jack Blaine, M.D., participated in a symposium on Contingency Management Approaches to the Treatment of Drug Abuse at the 9th Annual Meeting of The American Academy of Addiction Psychiatry, December 3-6, 1998 in Amelia Island, FL. He also participated in the Biopsychosocial Research Committee and the Multi-Treatment Committee, and participated in a "lunch with experts" discussion on developing a substance abuse research career.

Drs. Harold Gordon and Steven Grant, ECNB, DCSR, attended the annual meeting of the Society for Neuroscience in Los Angeles, November 1998.

Arthur MacNeill Horton, Jr., Ed.D., ECNB, DCSR, represented NIDA at the HIV/CNS Tissue Network, Steering Committee Meeting, held at the Natcher Conference Center on December 1-2, 1998.

Dr. Harold Gordon, ECNB, DCSR, chaired and co-organized with Jonathan Pollock, Ph.D. as part of the Genetics Workgroup, a NIDA-sponsored Satellite Symposium entitled "Prospects for the Molecular Genetics of Drug Abuse" held in conjunction with the annual meeting of the American Society of Human Genetics in Denver, CO on October 27, 1998.

Dr. William Cartwright made a presentation on pharmacoeconomics at the 38th Meeting of New Clinic Drug Evaluation Unit on June 12, 1998, entitled "Which Drug Shall Die?"

Dr. Bennett Fletcher spoke on improving drug abuse treatment and NIDA's treatment and health services research agenda at the North Carolina Council of Community Programs held in Pinehurst, North Carolina on December 7, 1998.

Richard H. Needle, Ph.D., M.P.H., Chief, CRB, DEPR, was an invited keynote speaker at the "Opening Event" of the Center for Drug Use and HIV Research, held September 28, 1998 at National Development and Research Institutes (NDRI), Inc., in New York City. Dr. Needle's presentation addressed the origins, evolution, and current status of NIDA's HIV prevention research and intervention programs. The event represented the Center's formal establishment at NDRI, made possible by a NIDA Core Center grant award to the Center's Director, Sherry Deren, Ph.D.

Dr. Elizabeth Robertson presented a workshop titled "Methamphetamines and Other Drugs in Rural America" in conjunction with Drug Enforcement Agency (DEA) staff at the Community Anti-Drug Coalitions of America (CADCA) National Leadership Forum on November 20, 1998 in Washington, D.C.

Richard H. Needle, Ph.D., M.P.H., Chief, CRB, DEPR, participated as a Special Discussant in a panel on "Needle Exchange Programs: Roles in HIV Prevention and as Conduits to Substance Abuse Treatment," at the 126th Annual Meeting of the American Public Health Association, on November 16, in Washington, D.C. Dr. Needle's presentation was entitled "The Importance of Research on Sterile Syringe and Needle Exchange Programs."

Drs. Elizabeth Robertson and Kathy Etz, DEPR, participated in a Performance Enhancement Protocol System (PEPS) planning group meeting convened by CSAP on October 5-6, 1998. The planning group reviewed the status of current PEPS documents and discussed future guidelines, documents and dissemination and evaluation plans.

Richard H. Needle, Ph.D., M.P.H., Chief, CRB, DEPR, served as discussant for a panel session at the Annual Meeting of the American Anthropological Association, held in Philadelphia in December 1998. Dr. Needle's presentation described the history and importance of ethnography in the conduct of community-based HIV and drug abuse prevention research.

Peter Hartsock, Dr.P.H., CRB, DEPR, represented NIDA at Yale University's historical research conference, "100 Years of Heroin," held September 18-20, 1998 in New Haven, CT. This year marks the 100th anniversary of the development of "medicinal" heroin by the Bayer Corporation. ale University's Dr. David Musto, a widely renowned drug abuse historian and NIDA grantee, chaired the conference. Participants included scholars as well as former and current government officials who have made significant contributions to the development of drug abuse intervention strategies, many of which are in use today. Senator Daniel Patrick

Moynihan of New York was the Conference's keynote speaker. Dr. Hartsock gave a presentation on historical research opportunities at NIDA.

Arnold Mills, CRB, DEPR, represented NIDA at the Native American Symposium held in Tucson, Arizona, October 21 - 22, 1998. The Symposium focused on issues related to the conduct of research in Native American communities, including Institutional Review Board (IRB) concerns, the identification and development of effective strategies for involving Native Americans in drug abuse research, and funding mechanisms for collaborative research on drug abuse and its consequences in Native American communities.

Jacques Normand, Ph.D., CRB, DEPR, gave a briefing on findings from the NIDA-sponsored NRC/IOM report, "Under

the Influence? Drugs and the American Workforce," at the meeting of the Committee on Data and Research for Policy on Illegal Drugs, held by the National Research Council of the National Academy of Sciences on November 20, 1998 in Irvine, CA.

Jacques Normand, Ph.D., of CRB, DEPR, served as discussant for a panel session on "The Effectiveness of HIV Interventions for Out-of-Treatment Drug Users: Main Findings of the 1993-1997 NIDA Cohort," held at the 126th Annual Meeting of the American Public Health Association, on November 17, 1998 in Washington, D.C.

Dr. Kathy Etz, DEPR, participated in an ONDCP working group, Prevention Principles and Policies, that developed logic models and glide paths and determined data issues and resources to assist ONDCP in refining the Performance Measure of Effectiveness System. After multiple meetings, the working group made their recommendations to the steering group in October 1998.

Dr. Kathy Etz, DEPR, participated as NIDA's representative in the Join Together Information Exchange, October 15, 1998. The exchange provides an opportunity for those working in the public and private sectors to share information on preventing and reducing substance abuse.

On November 18, 1998, Dr. Kathy Etz, DEPR, represented NIDA at CADCA's National Leadership Forum, participating in workshops on Prevention Principles when Dealing with Youth and Strategies for Environmental Change.

Dr. Kathy Etz, DEPR, represented NIDA at the American Society of Criminology's annual meeting held November 11-14, 1998 in Washington, D.C. The meeting provided a unique opportunity to meet with criminologists who focus on interventions and outcomes for substance abusers.

On November 5-6, 1998, Drs. Kathy Etz and Elizabeth Robinson, DEPR, represented NIDA at NIH's conference on Preventive Intervention Research at the Crossroads: Contributions and Opportunities from the Behavioral and Social Sciences. The conference showcased examples of NIH supported prevention intervention research, highlighted contributions of behavioral and social science to prevention research and provided recommendations for opportunities in prevention research.

Dr. Rita Liu, Receipt and Referral Officer for NIDA, conducted a training session with staff from the Division of Basic Research and other NIH components at the Society for Neuroscience annual meeting in Los Angeles, November 7, 1998. The session entitled Grantsmanship for New Investigators Workshop, was sponsored by the Society and organized by NIMH.

Mr. Richard Harrison, Chief, Contracts Review Branch, represented the NIH at the National Congress of American Indians Annual Conference in Myrtle Beach, SC in October 1998. He also participated in an NIH panel to discuss employment, training, and internship opportunities at NIH during the American Indian Science & Engineering Society Annual Conference in Denver, November 18 - 21, 1998.

Mr. Eric Zatman, Contracts Review Branch, has represented NIDA at the NIH Worksite Health Promotion Action Committee, which is charged with creating and implementing health enhancement programs and establishing NIH as a national leader in worksite health promotion. In November, he was made Chair of the Physical Fitness Subcommittee.

Dr. Teresa Levitin evaluated scientific projects submitted for the fifty-eighth annual Science Service competition for high school students. This competition, which was formerly sponsored by Westinghouse and is now sponsored by Intel, took place in December 1998 at the Science Service offices in Washington, DC.

Mr. Richard Harrison represented NIH on the Interagency American Indian/Alaska Native Committee to coordinate activities related to the American Indian/Alaska Native Heritage Month celebrations in November 1998. In December 1998, he met with the Federal Interagency Committee on Alcohol and Substance Abuse in Indian Country, chaired by the Assistant Secretary for Indian Affairs, Department of the Interior.

Dr. Kenzie Preston, IRP, presented "Combined Behavioral and Pharmacological Treatment of Opioid Dependence" at the annual scientific meeting of the International Council of Alcoholism and Addiction in St. Julians, Malta, in September, 1998.

Dr. Roy Pickens, IRP, presented papers on "Genetics of Drug Abuse: Effects of Parental Substance Abuse on Methadone Maintenance Outcome" and "Cost Effectiveness of Treatment for Pregnant Drug Dependent Women" at the annual scientific meeting of the International Council of Alcoholism and Addiction in St. Julians, Malta, in September, 1998.

Nine members of the Intramural Research Program's Chemistry and Drug Metabolism Branch presented their

research findings at the Society of Forensic Toxicology/The International Association of Forensic Toxicologists meeting in Albuquerque, NM in October 1998.

Dr. David A. Gorelick of the Treatment Branch of the intramural program presented Psychiatry Grand Rounds on "Pharmacological Treatment of Cocaine Addiction" at the West Los Angeles VA Medical Center, Los Angeles, CA on August 20, 1998.

Drs. Masato Asanuma and Jean Lud Cadet, IRP, presented "Attenuation of Methamphetamine- induced Increase in Striatal NF-KB Activity in Superoxide Dismutase Transgenic Mice" at the Society for Neuroscience's annual meeting held in Los Angeles, CA, November 7-12, 1998.

Dr. Jean Lud Cadet, IRP, presented "Dopamine-induced Apoptosis is Abrogated in Immortalized Neural Cells Overexpressing Bcl-2" at the Society for Neuroscience's annual meeting held in Los Angeles, CA, November 7-12, 1998.

Drs. Teruo Hayashi, Hiroshi Hirata, Masato Asanuma, Li-I Tsao, Tsung-Ping Su, and Jean Lud Cadet, IRP, presented "Induction of p53 mRNA by Methamphetamine (METH) is Blocked by [D-ALA2, D-LEU5]Enkephalin (DADLE) Via Nonopioid Action: Potential Mechanism Underlying the Protective Effect of DADLE against METH-induced Neurotoxicity" at the Society for Neuroscience's annual meeting held in Los Angeles, CA, November 7-12, 1998.

Mike McCoy and Dr. Jean Lud Cadet, IRP, presented "Differential Display Evidence for Increased Vimentin Expression during Methamphetamine-induced Apoptosis in Vitro" at the Society for Neuroscience's annual meeting held in Los Angeles, CA, November 7-12, 1998.

Dr. Roman Stefanski, Bruce Ladenheim, Dr. Jean Lud Cadet and Dr. Steven Goldberg, IRP, presented "Neuroadaptations to Methamphetamine Self-administration in Rats: Contingent vs. Noncontingent Infusions of Drug" at the Society for Neuroscience's annual meeting held in Los Angeles, CA, November 7-12, 1998.

Dr. Subramanian Jayanthi, Bruce Ladenhiem, Dr. Anne Andrews, and Dr. Jean Lud Cadet, IRP, presented "Overexpression of Human Copper/Zinc-Superoxide Dismutase in Transgenic Mice Attenuates Oxidative Stress Caused by Methylenedioxy-methamphetamine (MDMA, Ecstasy)" at the Society for Neuroscience's annual meeting held in Los Angeles, CA, November 7-12, 1998.

Drs. Li-I Tsao, C. Chiueh, Jean Lud Cadet and Tsung-Ping Su presented "[D-ALA2,D-LEU5] Enkephalin (DADLE) is a Free Radical Scavenger in Vitro: Implications for DADLE's Protective Action against Methamphetamine (METH)-induced Neurotoxicity" at the Society for Neuroscience's annual meeting held in Los Angeles, CA, November 7-12, 1998.

Dr. David A. Gorelick, IRP, presented an invited lecture on "The Neurobiology of Addiction and its Implications for Medical Practice," at the American Osteopathic Academy of Addiction Medicine annual meeting, New Orleans, LA on October 6, 1998.

Dr. D. Bruce Vaupel, IRP, presented "5-[123I]iodo-A-955380: A Promising Radiotracer for SPECT Imaging of Nicotinic Acetylcholine Receptors (nARChRs)" at The NIH Research Festival held in Bethesda, MD, October 7-9, 1998.

Dr. Katherine Bonson, IRP, presented "Validation of an Analytic Method of Calculating Cerebral Glucose Metabolism Using PET" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12, 1998.

Dr. Daniella Gundisch, IRP, presented "Evaluation of High Affinity [3H] Epibatdine Binding in Rat Brain" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12, 1998.

Ms. Geraldine Hill, IRP, presented "Acute and Chronic Effects of Methamphetamine on Cerebral Glucose Metabolism" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12, 1998.

Dr. Alane S. Kimes, IRP, presented "Ex Vivo and In Vitro Autoradiographic Analysis of Nicotinic Acetylcholine Receptors Using 5-[125I]iodo-A-85380" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12, 1998.

Dr. Andrei Koren, IRP, presented "Synthesis and Evaluation of Halogenated Analogs of A-85380 as Ligands for Nicotinic Acetylcholine Receptors" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12, 1998.

Dr. John Matochik of the intramural program presented "Age-Related Decline in Striatal Volume in Monkeys as Measured by MRI" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12,

1998.

Dr. Alexey Muhkin, IRP, presented "5-iodo-A85380-a Novel Highly Selective Ligand of a4b2 Subtype of Nicotinic Acetylcholine Receptors" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12, 1998.

Dr. Monique Ernst, IRP, presented "Nicotine and Cerebral Blood Flow During a Working Memory Task" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12, 1998.

Dr. D. Bruce Vaupel, IRP, presented "5-[125I]iodo-A-85380: Evaluation as a Radiotracer for the In Vivo Imaging of Nicotinic Acetylcholine Receptors in the Mouse" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12, 1998.

Dr. Svetlana Chefer, IRP, presented "In Vivo Imaging of Brain Nicotinic Acetylcholine Receptors with 5-[123]iodo-A-85380 Using Single Photon Emission Computed Tomography" at the 27th Annual Meeting of the Society for Neuroscience, Los Angeles, CA, November 7-12, 1998.

Dr. Aviv Weinstein, IRP, presented "Activation of Craving in Cocaine Abusers While Performing the Continuous Performance Task-Can Cocaine Abusers Divide their Attention?" at the 37th Annual American College of Neuropsychopharmacology Meeting, Las Croabas, Puerto Rico, December 14-18, 1998.

Drs. Edythe D. London and Monique Ernst, IRP, co-chaired a panel, entitled "Cerebral Responses to Nicotine: From the Perspectives of Neuroimaging and Receptor Dynamics" and Dr. London participated in a study group entitled "Measurement of Alcohol and Other Drug Reactivity and Craving in the Animal and Human Laboratory: Issues of Design, Ethics, and Interpretation" at the 37th Annual American College of Neuropsychopharmacology Meeting, Las Croabas, Puerto Rico, December 14-18, 1998.

[Home Page][Office of the Director][Report Index][Previous Report Section] [Next Report Section]

Archive Home | Accessibility | Privacy | FOIA (NIH) | Current NIDA Home Page

National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Media and Education Activities

NIDA Goes to School

NIDA's new national science education initiative, **NIDA Goes To School**, was launched on November 21, 1998 at the National Leadership Forum of the Community Anti-Drug Coalitions of America, Washington, D.C. NIDA Goes To School is designed to bring to the Nation's educators the latest scientific information about how drugs of abuse affect the brain and to give them effective, accurate tools to use in teaching their students. As part of the initiative, an initial mailing sent to every public and private middle school in the country (nearly 19,000), including American schools at military bases overseas, featured NIDA's award-winning MIND OVER MATTER materials. NIDA has also created a NIDA Goes To School website featuring information specially geared to students and teachers. As new science education materials are developed, they will be added to this website.

Awards

NIDA's Nicotine Conference materials won a Silver Certificate in the Mercury Awards given by MerComm, Inc., for excellence in public relations and corporate communications. The Nicotine Conference materials package was put together for the national conference, "Addicted to Nicotine, a National Research Forum," held on July 27-28, 1998.

Media Activities

September 23 & 24, 1998 - **Emotional Memory and Drug Addiction, Molecular and Cellular Basis of Emotional Memory**, Bethesda, MD. Conducted outreach for selected press to attend the Emotional Memory meeting -- Denise Grady of The New York Times and Beth Azar of the APA Monitor attended and the agenda and papers were sent to other journalists.

October 14, 1998 - Iowa Town Meeting, Des Moines, Iowa. NIDA experienced the most press coverage of any town meeting. Crews from ABC and CBS affiliates and Iowa Public TV were among the eight broadcast venues at the meeting. Print reporters represented The Des Moines Register, the Associated Press, the Omaha World Herald, and local Illinois papers.

October 20 and November 9, 1998 - **Why Do Sally and Johnny Use Drugs?**, a bylined piece by NIDA Director, Dr. Alan Leshner, appeared in the Washington Times and the Los Angeles Times. In addition, Dr. Leshner was interviewed by Abby Trafford, editor of the Washington Post's Health Section, for her December 15, 1998 column. The original article has also been distributed via a syndicated editorial service to over 1,000 small newspapers throughout the country and will start appearing in January 1999.

November 2, 1998 - Dr. Leshner was invited back to Des Moines by Iowa Public TV producers to participate in the award-winning series, **Student Voices**. This show was broadcast live to students through the State of Iowa's

communications network with schools.

November 22, 1998 - A letter by Dr. Leshner to the Editor of the Boston Globe appeared in rebuttal to a previous letter about the effects of using marijuana.

Dr. Frank Vocci, Director, MDD, was interviewed for an article **"Seeking Ways to Crack Cocaine Addiction"**, that appeared in the October 17, 1998 issue of The Lancet.

Dr. Barbara Herman, MDD, was pictured and quoted in Szalavitz, M. **"Brain Power. Memory Research Could Help Addicts and Stroke Victims."** Newsday, December 8, 1998. This article related to research indicating the role of glutamate and excitatory amino acids in a variety of brain disorders including addictive disorders and stroke, and how medications development may assist in the treatment of these disorders (cf. Science, June 26, 1998).

Press Releases

September 29, 1998 - New Research Helps Explain Ritalin's Low Abuse Potential when Taken As Prescribed. Individuals taking therapeutic doses of methylphenidate rarely abuse it or become addicted, even though it is a stimulant with properties similar to those of cocaine and amphetamines. Ritalin, an oral form of methylphenidate, is the drug prescribed most frequently for children, adolescents, and adults diagnosed with Attention Deficit Hyperactivity Disorder (ADHD). As a result of this news release, an article was distributed by Reuters.

October 22, 1998 - Prevention Could Save $352 Million Annually, New Study Clarifies Effects of Prenatal Exposure To Crack and Cocaine. Researchers at Brown University estimate that subtle deficits in IQ and language development will occur in up to 80,550 cocaine-exposed children. Although the developmental effects are subtle, special education to prevent these children from failing in the school environment will cost up to $352 million per year nationwide. As a result of this news release, articles appeared in The Washington Times and were distributed through Reuters, AP, and the BBC News.

November 5, 1998 - Different Treatment Strategy May Be Required For HIV Positive Women Who Have Used Injection Drugs. According to a study published in the November 7, 1998 issue of The Lancet, HIV-1-positive women who have used injection drugs may need a different schedule for anti-AIDS therapy from current practice. Among study subjects who developed AIDS, levels of HIV were significantly lower in the women than in the men, suggesting that rates of disease progression are more rapid in HIV-infected women who have used injection drugs than in men with the same viral load. As a result of this news release, articles appeared in The New York Times, The Washington Post, USA Today, and the online Doctor's Guide to Medical & Other News.

November 12, 1998 - Individuals Who Abuse Any One Type of Drug Are at Serious Risk of Abusing All Other Types of Drugs. New research on pairs of male twins who had abused an illicit drug at some time in their lives shows a common vulnerability to co-occurring drug abuse, and a significantly increased risk of abusing every other category of illicit drug. Researchers found evidence that this common or shared vulnerability underlies abuse of a wide range of illicit drugs, including marijuana, sedatives, opiates, stimulants, and psychedelics. As a result of this news release, an article was distributed by Reuters.

November 18, 1998 - Every Middle School Nationwide to Receive Award-Winning, Science-Based Drug Education Materials. A new science education initiative for middle school students, teachers, and counselors was launched by NIDA, at the November 21, 1998 National Leadership Forum of the Community Anti-Drug Coalitions of America. NIDA Goes To School is designed to bring to the Nation's educators the latest scientific information about how drugs of abuse affect the brain and to give them effective, accurate tools to use in teaching their students.

November 18, 1998 - NIH Consensus Panel Statement Cites Inconsistencies In Care For Children With ADHD. Children with attention deficit hyperactivity disorder (ADHD) often receive an inconsistent level of care from a fragmented system that consumes a large share of health care dollars, according to a consensus panel convened by NIH. The problem is compounded by the fact that an accurate diagnosis for ADHD remains elusive and controversial yet continues to be a commonly diagnosed behavioral disorder of childhood. As a result of this press release, articles appeared in The Washington Post, USA Today, The Washington Times, The New York Times, Time magazine, U.S. News & World Report, Newsday (New York, NY), Pittsburgh Post-Gazette, The Buffalo News, New Scientist, and in distribution by the Associated Press and PR Newswire. CBS News, CNN Today, and NPR also covered the conference.

November 19, 1998 - Comprehensive Research Effort Advanced on Tobacco Use. The National Cancer Institute (NCI), following the recommendations of its Tobacco Research Implementation Group, is advancing a plan to

expand and accelerate tobacco research that can prevent cancers associated with tobacco use. In the first initiative, which creates a collaborative Transdisciplinary Tobacco Research Centers program, NCI will commit $50 million and the National Institute on Drug Abuse will commit $20 million over 5 years. As a result of this press release, an article was distributed through the Associated Press.

December 7, 1998 - Drug Abuse Costs Society $97.7 Billion and Climbing. The latest issue of NIDA NOTES, Vol. 13, No. 4, and a Media Advisory highlighting articles from the newsletter were sent to science and general interest press.

December 8, 1998 - Panel Urges Broadened Access, Insurance Coverage for Methadone Treatment Nationwide. An independent panel convened for a NIH Consensus Development Conference came out firmly in favor of methadone treatment for all heroin addicts who might benefit from it. The panel on "Effective Treatment of Opiate Addiction" met in November 1997 and its report is published in full in the Journal of the American Medical Association. As a result of this press release, articles appeared in The Atlanta Journal and Constitution, Chicago Tribune, The Deseret News, The Detroit News, The Herald Sun (Durham, NC), The New York Times, the Philadelphia Inquirer, USA Today, the Nando Times, The Stuart News/Port St. Lucie News, the Press Journal (Vero Beach, FL), Fox News Online, CNN.com, NBC.com, Agence France Presse, and were distributed through the Associated Press.

December 11, 1998 - Emerging Drug Trends Meeting To Be Held In Miami, Researchers Discuss U.S. Metropolitan Area Trends and International Data. Current and emerging patterns and trends in drug abuse were discussed at the 45th meeting of the Community Epidemiology Work Group (CEWG) held December 15-18, 1998 at the Wyndham Hotel, Miami, Florida. This meeting included international findings from members of the International Epidemiology Work Group on Drug Abuse. As a result of this press release, the meeting was covered by AP Miami and the Miami Herald.

December 18, 1998 - Drug Use Eases Among Teens For Second Consecutive Year, Secretary Shalala Also **Announces NIDA Goes To School Initiative**. The 1998 survey of drug use among adolescents found general stability among the proportion of 12th graders using most illicit drugs in the past year or past month, including the most frequently used drug, marijuana. There were also important decreases this year in 10th graders' use of marijuana, alcohol and cigarettes, and among 8th graders, the survey indicates evidence of a gradual decline in drug use over the past two years. As a result of this press release, articles appeared in USA Today, The Washington Times, The New York Times, The Washington Post, The Buffalo News, The Detroit News, Deseret News, The Milwaukee Journal Sentinel, the Baltimore Sun, the San Jose Mercury News, the Chicago Tribune, the Dayton Daily News, Agence France Presse, United Press International, The Atlanta Journal and Constitution, the Los Angeles Times, the Omaha World-Herald, the Philadelphia Inquirer, and the San Antonio Express-News, and were distributed by Associated Press, UPI, Knight-Ridder, and Cox. CNN also covered this announcement.

December 21, 1998 - Popular Rave Drug "Ecstasy" Impairs Memory, Apparently Related to Brain Damage. Heavy use of the drug Ecstasy, or MDMA, can lead to persistent problems in remembering what is seen and heard, according to a study appearing in the December issue of Neurology. According to researchers from Johns Hopkins University, the memory impairment increases with the amount of drug taken and lasts at least two weeks after stopping use. These memory problems appear to be related to the damage Ecstasy does to particular brain cells that use the chemical serotonin for communication. As a result of this press release, an article appeared in The Independent (London), and an article was distributed through Reuters.

Video

A new video, "Treatment Solutions," was launched at NIDA's 5th Annual Constituency Conference at Lansdowne, VA in December 1998 and received an enthusiastic response from the meeting's participants. Marketing and distribution plans include mailings to interested groups who have requested copies, distribution via NCADI, and placement of stories about its availability in constituent newsletters and other targeted publications.

Web Site

The NIDA web site continues to be updated. Two new initiatives recently added include information on the Clinical Trials Network and a NIDA Goes To School page that features an interactive site based on the Mind Over Matter series.

NIDA Exhibits Program

The fall season is one of the busiest for NIDA. The following are meetings where NIDA recently exhibited its publications and program announcements:

October 9-10, 1998	Society for Advancement of Chicanos and Native Americans in Science
October 14, 1998	Iowa Town Meeting
October 18-21, 1998	American Psychiatric Nurses Association
October 19-21, 1998	National Corrections Conference
October 25-27, 1998	New York State Association of Alcoholism & Substance Abuse Providers
October 27-Nov 1, 1998	American Academy of Child & Adolescent Psychiatry
October 28, 1998	Buffalo Mini Town Meeting
October 29-Nov 1, 1998	U.S. Conference on AIDS
November 4-6, 1998	Primary Care
November 5-8, 1998	Association for Advancement of Behavior Therapy
November 7-12, 1998	Society for Neuroscience
November 15-19, 1998	American Public Health Association
November 19-21, 1998	Community Anti-Drug Coalitions of America
November 20, 1998	Parklawn Health Fair
November 21-24, 1998	Minority Research Symposium
December 1-2, 1998	NIDA Annual Constituent Meeting
December 9-12, 1998	American Indian Science & Engineering Society

46,000 attendees were present at these conferences.

[Home Page][Office of the Director][Report Index][Previous Report Section] [Next Report Section]

Archive Home | Accessibility | Privacy | FOIA (NIH) | Current NIDA Home Page

National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Publications

Research Monographs

Drug Abuse Prevention Through Family InterventionÑRM 177--NCADI #M177
NIH Pub. No. 99-4135
This monograph is based on a scientific meeting that was sponsored by NIDA. It consists of scientific papers presented at the meeting on state-of-the-art family-based drug abuse prevention research; synopses of panel and workshop discussions; and recommendations for future NIDA research in the area of family focused drug abuse prevention interventions.

Other Publications

Epidemiologic Trends in Drug Abuse: Community Epidemiology Work Group, June 1998: Volume II -- NIH Pub. No. 99-4301

NIDA Community Drug Alert Bulletin - Methamphetamine -- NCADI MS709

NIDA NOTES, Vol. 13, Issue No. 4 -- NCADI NN0032
The lead story for this issue is about the cost to society of drug abuse. Two articles discuss gender differences in drug abuse and in HIV prevention efforts. The Director's Column discusses the importance of tailoring intervention efforts to include gender as a component of the interventions. The affect of prenatal cocaine exposure on elementary-children is the subject of another article. Winners of the Prism Awards and increased neuroscience research in NIDA's Division of Intramural Research were also covered.

Preston, K.L., and Walsh, S.L. Evaluating Abuse Liability: Methods and Predictive Value. In: Drug Abuse Handbook, ed. by S. B. Karch, CRC Press LLC, Boca Raton, FL, pp. 276-306, 1998.

Shoaib, M., Swanner, L.S., Beyer, C.E., Goldberg, S.R. and Schindler, C.W. The GABAB Agonist Baclofen Modifies Cocaine Self-administration in Rats. Behavioral Pharmacology, 9, pp. 195-206, 1998.

Hoffman, J.A., and Moolchan E.T. The Phases of Treatment Model of Methadone Treatment. Euro-Methwork, 13, pp. 7-9, 1998.

Radzius A., Gorelick, D.A., and Henningfield, J.E. Cigarette Smoking During Early Cocaine Abstinence. The American Journal on Addictions, 7(4), pp. 305-308, 1998.

Huestis, M.A. and Cone, E. Alternative Testing Matrices. In Karch, S. (ed.) Handbook of Drug Abuse, CRC Press, (Boca Raton, FL), pp. 799-857, 1998.

Huestis, M.A., and Cone, E. Urinary Excretion Half-life of 11-Nor-9-carboxy-D9- tetrahydrocannabinol in Humans. Therapeutic Drug Monitoring, 20, pp. 570-576, 1998.

Huestis, M.A., and Cone, E. Differentiating New Marijuana Use From Residual Drug

Excretion in Occasional Marijuana Users. Journal of Analytical Toxicology, 22, pp. 445-454, 1998.

Cone, E.J., Tsadik, A., Oyler, J. and Darwin, W.D. Cocaine Metabolism and Urinary Excretion Following Different Routes of Administration. Therapeutic Drug Monitoring, 20, pp. 556-560, 1998.

Cone, E.J., Lange, R., and Darwin, W.D. In Vivo Adulteration: Excess Fluid Ingestion Causes False Negative Marijuana and Cocaine Urine Test Results. Journal of Analytical Toxicology, 22, pp. 460-473, 1998.

Soderstrom, C.A., Dischinger, P.C., Kerns, T.J., Kufera, J.A., McDuff, D.R., Gorelick, D.A, and Smith, G.S. Screening Trauma Patients for Alcoholism According to NIAAA Guidelines with Alcohol Use Disorders Identification Test Questions. Alcoholism: Clinical and Experimental Research, 22, pp. 1470-1475, 1998.

Radzius, A., Gorelick, D.A., and Henningfield, J.E. Cigarette Smoking during Early Cocaine Abstinence. American Journal on Addictions, 7, pp. 305-308, 1998.

Singleton, E.G. and Gorelick, D.A. Mechanisms of Alcohol Craving and their Clinical Implications. In Galanter, M. (Ed.), Recent Developments in Alcoholism, Vol 14, (New York, Plenum), pp. 177-195, 1998.

Gorelick, D.A., Pickens, R.W., and Bonkovsky, F.O. Clinical Research in Substance Abuse: Human Subjects Issues. In Pincus, H.A., Lieberman, J.A., and Ferris, S. (Eds.), Ethics in Psychiatric Research: A Resource Manual for Human Subjects Protection, (Washington, D.C., American Psychiatric Association), pp. 177-218, 1998.

Gorelick, D.A. Pharmacologic Therapies for Cocaine and Other Stimulant Addiction. In Graham, A.W. and Schultz, T.K. (Eds.), Principles of Addiction Medicine, 2nd edition, (Chevy Chase, MD: American Society of Addiction Medicine), pp. 531-544, 1998.

Wilkins, J.N., Gorelick, D.A., and Conner, B.T. Pharmacologic Therapies for Other Drugs and Multiple Drug Addiction. In Graham, A.W. and Schultz, T.K. (Eds.), Principles of Addiction Medicine, 2nd edition, (Chevy Chase, MD: American Society of Addiction Medicine), pp. 583-592, 1998.

Wilkins, J.N., Conner, B.T., and Gorelick, D.A. Management of Stimulant, Hallucinogen, Marijuana and Phencyclidine Intoxication and Withdrawal. In Graham, A.W. and Schultz, T.K. (Eds.), Principles of Addiction Medicine, 2nd edition, (Chevy Chase, MD: American Society of Addiction Medicine), pp. 465-486, 1998.

Liu, X., Matochik, J.A., Cadet, J.L., and London, E.D. Smaller Volume of Prefrontal Lobe in Polysubstance Abusers: A Magnetic Resonance Imaging Study. Neuropsychopharmacology, 18, pp. 243-252, 1998.

Subramaniam, J., Ladenheim, B., and Cadet, J.L. Methamphetamine-induced Changes in Antioxidant Enzymes and Lipid Peroxidation in Copper/Zinc-Superoxide Dismutase Transgenic Mice. Annals of NY Academy of Science, 844, pp. 92-102, 1998.

Asanuma, M., Hirata, H., and Cadet, J.L. Attenuation of 6-hydroxydopamine-induced Dopaminergic Nigrostriatal Lesions in Superoxide Dismutase Transgenic Mice. Neuroscience, 85, pp. 907-917, 1998.

Hirata, H., Asanuma, M., and Cadet, J.L. Melatonin Attenuates Methamphetamine-induced Toxic Effects on Dopamine and Serotonin Terminals in Mouse Brain. Synapse, 30, pp. 150-155, 1998.

Hirata, H., Asanuma, M., and Cadet, J.L. Superoxide Radicals are Mediators of the Effects of Methamphetamine on ZIF 268 (Egr-1, NGFI-A) in the Brain: Evidence from Using CuZn Superoxide Dismutase Transgenic Mice. Molecular Brain Research, 58, pp. 209-216, 1998.

Vawter, M.P., Hemperly, J.J., Thomas, M.H., Bachus, S.E., VanderPutten, D.M., Howard, A.L., Cannon-Spoor, H.E., McCoy, M.T., Webster, M.J., Kleinman, J.E., and Freed, W.J. VASE-containing N-CAM Isoforms are Increased in the Hippocampus in Bipolar Disorder but not Schizophrenia. Experimental Neurology, 154, pp. 1-11, 1998.

Bergman, J. and Katz, J.L. Behavioral Pharmacology of Cocaine. In: Higgins, S.T. and Katz, J.L. (Eds.). Cocaine Abuse Research: Pharmacology, Behavior, and Clinical Applications. San Diego: Academic Press, pp. 51-79, 1998.

Higgins, S.T. and Katz, J.L. (Eds.) Cocaine Abuse Research: Pharmacology, Behavior, and Clinical Applications. San Diego: Academic Press, 1998.

Husbands, S.M., Kline, R.H., Allen, A.C., and Newman, A.H. A Diastereospecific Synthesis of 2-Methyl-5-b-phenyl-5-a-carboethoxy-2-azabicyclo[2.2.1]heptane: A Ring Constrained Analog of Meperidine. J. Org. Chem., 63, pp. 418-419, 1998.

Lomenzo, S.A., Izenwasser, S., Katz, J.L., and Trudell, M.L. The Effects of Alkyl Substituents at the 6-position of Cocaine Analogues on Dopamine Transporter Binding Affinity and Dopamine Uptake Inhibition. In: Newman, A.H. (Ed.) The Dopamine Transporter as a Molecular Target for the Development of Cocaine Abuse Therapeutics, Medicinal Chemistry Research, 8, pp. 35-42, 1998.

Newman, A.H. Novel Dopamine Transporter Ligands: The State of the Art. Med. Chem. Res., 8, pp. 1-11, 1998. (Invited Guest Editorial - Special Issue).

Newman, A.H., and Agoston, G.E. Novel Benztropine [3?-(Diphenylmethoxy)tropane] Analogs as Probes for the Dopamine Transporter. Current Medicinal Chemistry, 5, pp. 301-315, 1998. (Invited Review).

Zhang, C., Izenwasser, S., Katz, J.L., Terry, P., and Trudell, M.L. Synthesis and Dopamine Transporter Affinity of the Four Stereoisomers of (")-2-methoxycarbonyl-7-methyl-3-phenyl- 7-azabicyclo[2.2.1] heptane. Journal of Medicinal Chemistry, 41, pp. 2430-2435, 1998.

Women, Drug Use, and HIV Infection (Haworth Press, 1998). Edited by Sally J. Stevens, Stephanie Tortu, and Susan L. Coyle. This volume, co-published simultaneously as Women & Health, Vol. 27, Numbers 1-2, brings together 13 papers from NIDA's Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program. Cooperative Agreement data are presented at the local and national level and examine women's individual HIV risks as well as social/contextual variables that affect risk taking behaviors.

Coyle, S.L., Needle, R.H., Normand, J. Outreach-Based HIV Prevention for Injecting Drug Users: A Review of Published Outcome Data. Public Health Reports, 113 (Supp. 1), pp. 19-30, 1998.

Needle, R.H., Coyle, S.L., Normand, J., Lambert, E., Cesari, H. HIV Prevention with Drug-Using Populations--Current Status and Future Prospects: Introduction and Overview. Public Health Reports, 113 (Supp. 1), pp. 4-18, 1998.

Cost-Benefit and Cost-Effectiveness Analysis of Drug Abuse Treatment Services. The foundations of cost-benefit and cost-effectiveness analysis (CB/CEA) for drug abuse treatments are developed. An economic model of addict choice and drug markets is presented. This model is synthesized with the current "cost-of-illness" methods used to measure the burden of the disease on society. The problem of doing cost-effectiveness studies in the presence of large nonhealth benefits is examined, and guidance is offered to clinical studies with a cost-effectiveness component or to stand alone cost-effectiveness studies. References and an extensive bibliography on drug abuse treatment related CB/CEA studies are appended. Cartwright, W.S. Evaluation Review, 22(5), pp. 609-636, 1998.

[Home Page][Office of the Director][Report Index][Previous Report Section] [Next Report Section]

Archive Home | Accessibility | Privacy | FOIA (NIH) | Current NIDA Home Page

National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

February, 1999

Staff Highlights

Honors and Awards

1998 NIDA Director's Award

Individual Awards

Carol B. Hubner, Ph.D., MDD
Mark Swieter, Ph.D., OEPR
Cikena V. Reid, OEPR
Jacqueline R. Porter, OEPR
Katherine Davenny, M.P.H., CAMCODA
Jagjitsing H. Khalsa, Ph.D., CAMCODA
Debra S. Grossman, M.A., DCSR
David Shurtleff, Ph.D., DBR
Nancy S. Pilotte, Ph.D., DBR
Joyce A.Williams, DBR
David A.Thomas, Ph.D., DBR
Pushpa V. Thadani, Ph.D., DBR
Jack R. Manischewitz, Ph.D., OPRM
David C. Jones, OPRM

Group Award: National Conference on Drug Addiction Treatment Planning

Stephen R. Zukin, M.D., DCSR
Lisa S. Onken, Ph.D., DCSR
Andrea Baruchin, Ph.D., OSPC
Robert J. Battjes, D.S.W., DCSR
Jack D. Blaine, M.D. , DCSR
L. Jeanne Borger, OSPC
Mona Brown, OSPC
Timothy P. Condon, Ph.D., OSPC
Dorynne J. Czechowicz, M.D., DCSR
Bennett W. Fletcher, Ph.D., DCSR
Jan W. Lipkin, OSPC
Joan D. Nolan, OSPC
Susan Schlossberg, OD
Jack B. Stein, OSPC
Beverly Jackson, OSPC
Carol C. Sneeringer, IRP

Jonathan L. Katz, Ph.D., IRP

Group Award: Brain Imaging Center, IRP

Edythe D. London, Ph.D.
Andrew G. Horti, Ph.D.
Andrew Koren, Ph.D.
Daniela Gundisch, Ph.D.
Alane S. Kimes, Ph.D.
Donald B. Vaupel, Ph.D.
Andrea Baruchin, Ph.D., OSPC
Joan D. Nolan, OSPC

Group Award: Desktop Software Transition Team, OPRM

Tina McDonald-Bennett
Constance E. Latzko

EEO Awards

Individual Awards

Carol Cushing, MDD
Melanie Pickett, DEPR

Group Award: IRP

Jean Lud Cadet
Lena Eads
Angela McLeod
Brian Alston

30 Years Length of Service

Suzanne M. Cole, OPRM
Jose A. Prada, IRP
Thomas R. Vischi, DCSR
Susan L. David, DEPR
Richard A. Millstein, OD

Commissioned Corps Awards

Unit Commendations

Anthony J. Brooks, IRP
Paul J. Na, IRP
Thomas P. Bridge, MDD
Chung-Yui B. Tai, MDD
Steven P. Sparenborg, MDD

Commendations

Steven P. Sparenborg, MDD
Kesinee C. Nimit, DEPR
Chung-Yui B. Tai, MDD
Peter J. Delaney, DCSR

NIH Director's Award

Henry Francis, OoA
Susan Herbert, MDD
Mary Affeldt, IRP

Quality of Worklife Award

Ann Gupman, IRP

1998 Blue Cross Blue Shield Federal Employee Program Award

Charles Sharp, DBR
Ann Montgomery, MDD

Other Honors and Awards

Dr. Alan I. Leshner, Director, NIDA, was elected as a member of the National Academy of Science's Institute of Medicine in October 1998.

Dr. Alan I. Leshner, received the American Academy of Addiction Psychiatry's (AAAP) Founders Award in December 1998 "in recognition of his outstanding national presence, leadership, creativity, and tireless efforts to place drug abuse on the national agenda in a positive manner utilizing the brain disease concept" and "for his ability to build alliances and clearly translate complex research findings to clinicians, the public, and policy makers."

Dr. Arthur M. Horton was presented with an award for his "Contributions to the Development of Professional Neuropsychiatry" by the American Board of Professional Neuropsychiatry at the Board's Annual membership meeting in Washington, DC on November 5, 1998.

Dr. Arthur M. Horton has also been elected to Fellow status in the American Psychological Association (APA) through the Division of the Psychology of Addictive Behaviors (50).

In November, 1998 **Dr. Amy H. Newman** of the NIDA intramural program was announced as the recipient of the 1998 Sato International Memorial Award. This is an early career award in Medicinal Chemistry, awarded by the Pharmaceutical Society of Japan. It will be presented at the 119th Annual Scientific Meeting of the Pharmaceutical Society of Japan, in Tokushima, Japan on March 28, 1999.

Newman, A.H., Allen, A.C., Kline, R.H., Izenwasser, S., Katz, J.L., 3a-Diphenyl-methoxytropane Analogs as Cocaine Therapeutics, U.S. Patent #5,792,775, Awarded August 11, 1998.

On October 19, 1998, **Dr. Katherine Bonson**, an IRTA Post-Doctoral fellow working with Dr. Edythe London of the NIDA Brain Imaging Center, was honored as a recipient of a Fellows Award for Research Excellence in Biomedical Research at a ceremony held in Lipsett Amphitheater, Bethesda, MD. Dr. Bonson was honored for her work in validating an analytic method of calculating cerebral glucose metabolism using PET. As an alternative to the traditional numeric integration procedure, the analytic method simplifies PET experimental procedures without a loss of accuracy.

Staff Changes

Dionne Jones, Ph.D., formerly with the Lewin Group of Fairfax, VA and Howard University in Washington, D.C., recently joined the Community Research Branch, DEPR, as a Health Scientist Administrator.

Dr. Jerry Flanzer has recently joined the Services Research Branch, DCSR, as a Social Science Analyst. Dr. Flanzer received his D.S.W. from the University of Southern California and was a professor of social work at both University of Wisconsin and Arkansas-Little Rock. During his academic tenure, Dr. Flanzer directed several projects geared toward integrating practice and research and taught in the areas of research, group work and human development. For the last 10 years, Dr. Flanzer has directed Recovery and Family Treatment, a clinical substance abuse program, and has taught research, human development and group work/organizational change courses as a visiting professor at the graduate programs of Catholic, Virginia Commonwealth, and Howard Universities. Dr. Flanzer comes to NIDA with a background in services research with a primary interest in the areas of adolescent substance abuse and the relationship between substance abuse and family violence.

Elizabeth Cooper officially joined NIDA as the Prevention Research Branch secretary on January 3, 1999.

Tracy Catron joined NIDA's EEO office on September 27, 1998. Ms. Catron was formerly with the National Institute of Nursing Research.

Debra Yarrick joined NIDA's Executive Secretariat on September 27, 1998.

Michelle Scala, formerly with the National Cancer Institute, joined NIDA's Contracts Management Branch on December 20, 1998 as a Contract Specialist.

Frenda Lundmark, formerly with the private sector, joined NIDA's Office of Science Policy and Communication (OSPC) on November 8, 1998.

Gwendelyn Jones joined NIDA's OSPC on September 22, 1998. Ms. Jones was formerly with the Health Services

and Resources Administration.

Dr. Charlene Woodard joined the Science Policy Branch of the Office of Science Policy and Communications on October 13, 1998. Dr. Woodard is a clinical psychologist who came from Virginia Commonwealth University's Medical College of Virginia (VCU/MCV) where she was an assistant professor of Human Genetics, Psychiatry, Preventive Medicine & Community Health. She was affiliated with the Virginia Institute for Psychiatric and Behavioral Genetics where she worked on adolescent twin studies of substance abuse. Her background includes a two-year post-doctoral fellowship in substance abuse medicine focusing on perinatal addicted women and chronic pain. Dr. Woodard maintained a clinical practice focusing on chronic pain and addiction during her tenure at VCU/MCV. She received her doctoral degree from the University of Georgia in clinical psychology in 1992.

NIDA has established a public liaison office within the Office of Science Policy and Communications. The Public Information Branch was renamed the Public Information and Liaison Branch (PILB), and **Beverly Jackson**, Chief of PILB, has been designated as the public liaison contact.

Grantee Honors

Lisa Najavits, Ph.D. of McLean Hospital in Massachusetts was presented with the Early Career Contribution to Research Award of the Society for Psychotherapy Research in Salt Lake City in June 1998.

Dr. Howard Liddle of the University of Miami School of Medicine, Department of Psychiatry, Center for Family Studies, was the recipient in October of the 1998 American Association for Marriage and Family Therapy (AAMFT) Award for "Cumulative Contribution to Family Therapy Research." The AAMFT is the largest family therapy professional association in the world.

After reviewing programs from all universities across the state, the Colorado Commission on Higher education recently named the NIDA funded **Tri-Ethnic Center for Prevention Research** as a Program of Excellence. In addition, Colorado State University recently selected the Tri-Ethnic Center for the second consecutive five-year period, as a Program of Research and Scholarly Excellence. This competitive award carries with it an honoria and partially accounts for the selection of the Center to receive a newly renovated, larger building.

[Home Page][Office of the Director][Report Index][Previous Report Section]

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