National Institute on Drug Abuse

Director's Report

to the
National Advisory Council on Drug Abuse

May, 1996

Index

[Home Page][Office of Director] [First 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

May, 1996

Research Findings

Basic Research

Common Intracellular Mechanisms in Morphine Tolerance and Thermal Hyperalgesia

Dr. Jianren Mao of Virginia Commonwealth University, in his investigation of neural and molecular mechanisms of hyperalgesia, discovered that morphine tolerance and hyperalgesia have in common certain neural substrates such as activation of N-methyl-D-aspartate (NMDA) receptor and the subsequent intracellular activation of protein kinase and nitric oxide and that these cellular and intracellular commonalities result in interactions between morphine tolerance and thermal hyperalgesia, i.e., thermal hyperalgesia develops when animals are made tolerant to the antinociceptive effects of morphine, a phenomenon that may have significant clinical implications for the treatment of painful conditions such as neuropathic pain, postoperative pain, and cancer pain.

NMDA Receptor Antagonists

NIDA grantee Dr. Charles Inturrisi and his coworkers have identified two NMDA antagonists (dextromethorphan and ketamine) with well established clinical safety and shown that both can attenuate morphine tolerance and inflammatory (formalin) pain. This "dual action" could provide an important nonopioid adjunct for use in the management of patients with combined nociceptive and neuropathic pain.

Opioid Receptor Splice Variant

NIDA grantee Dr. Charles Inturrisi and his coworkers, using RNase protection technique, PCR and Southern blot analysis have provided evidence for a mouse mu opioid receptor splice variant missing exons 2 and 3. Using a riboprobe obtained from the cloned splice variant they are comparing the distribution of this splice variant and the MOR-1 mRNA in selected regions of mouse CNS. This finding is of particular interest since it may provide an explanation for the pharmacologically defined mu receptor subtypes.

Paternal Opiate Exposure and Offspring Development

NIDA-supported researchers, Drs. Theodore Cicero, Bruce Nock and their associates from Washington University School of Medicine, St. Louis, have recently reported that acute paternal morphine exposure just before breeding with drug-naive females had no effect on fertility, but exerted negative effects on the viability and development of their offspring. These findings represent the most compelling evidence to date that paternal opiate exposure can adversely

affect fetal outcome and are particularly striking as they were produced by a single injection of morphine. Cicero, T.J., Nock, B. et al., J Pharmacol Exp Therap 273: pp. 386-392, 1995.

Buprenorphine and Brain Opioid Receptor Adaptation

Recently, Dr. Carmine Coscia and his associates have found that administration of buprenorphine to rats induces a brain-regionspecific down and up regulation of opioid sites. Based on these findings, the investigators suggest that buprenorphine is a useful tool to study brain opioid receptor adaptation *in vivo* and the information accrued may be relevant to the mode of action of this drug in the treatment of heroin and cocaine abuse. Belcheva, M.M. et al., J Pharmacol Exp Therap, In Press, 1996.

A Novel, Rapid Method for the Determination of Anandamide Amidase Activity in Tissues

Anandamide amidase is an enzyme involved in the hydrolytic degradation of anandamide, an endogenous ligand for the brain cannabinoid receptor (CB1). Anandamide amidase is distributed in the regions of the brain where the CB1 receptors exists and can therefore serve as a marker for the presence of CB1. The amidase is also found in other organs and can be used as a marker for the presence of anandamide.

A good analytical method for the determination of the activity of amidase is currently not available. The existing methods rely on the separation and measurement of radioactive hydrolysis products. Very recently a novel, rapid, and sensitive method was developed by Dr. Markriyannis and colleagues at the University of Connecticut. The new method is based on HPLC separation and does not use radioactive substrates and extensive extraction procedures are not involved. The assay could be utilized for measuring the enzyme activity in different cells and also for determining the metabolic stability of novel anandamide analogs. This method has been further extended to the measurement of anandamide levels in different tissues. One important application for the method is that this could be adapted for high throughput screening for the discovery of anandamide amidase inhibitors. Lang et al. Analytical Biochemistry, In Press.

1-Deoxy HU-210: A Very Potent Cannabinoid with High Affinity for the CB2 Receptor

Dr. Huffman and colleagues have recently synthesized the deoxy analog (this compound lacks the phenolic -OH) of the very potent cannabinoid HU-210. The synthesis was carried out following methodology developed earlier by Dr. Huffman. The biological evaluation is carried out by Dr. Billy Martin and his colleagues. The compound exhibited unexpected potency and CB2 selectivity. The CB2 selectivity is around 30 fold. Deoxy HU-210 was also very potent in vivo in the mouse model (spontaneous activity, tail flick, and rectal temperature) and was also active in the rat drug discrimination model.

Orphanin FQ: Receptor Binding and Analog Structure Activity Relationships in Rat Brain

Dr. Houghten and colleagues have reported the preparation of a tritiated form of orphanin FQ (also known as nociceptin). This radioligand was used to develop a radioreceptor assay using rat brain homogenates. Initial kinetic studies identified a single high affinity binding site. Specific binding was found in all parts of rat brain tested. Binding was observed in the caudate nucleus, a region reported not to have expression of the mRNA of the orphanin FQ receptor.

Thirty four analogs of orphanin FQ were synthesized and tested. The loss of activity upon Nterminal truncation and the relatively unchanged affinities observed for C-terminal truncation analogs indicate that the N-terminal plays a crucial role in binding. The data supports the view of Meunier et al. that orphanin FQ binding to its receptor is analogous to dynorphin binding to the kappa receptor, with N-terminal Phe-Gly-Gly-Phe representing the "message" portion of the molecule and the C-terminal amino acids representing the "address." The binding capability of the pentapeptide analog of orphanin FQ is also similar to that seen in the opioid system, in which the pentapeptide representing the N-terminal of a longer sequence (e.g. beta-endorphin or dynorphin) is found to bind to the receptor with high affinity.

Prenatal Cocaine

Dr. Jerrold Myer of the University of Massachusetts has been studying the effects of prenatal cocaine in rats. In a series of experiments, he has determined the characteristics and localization of fetal and adult brain recognition sites labeled with [125I][RTI-55, a potent cocaine congener. His results, "Characterization and Localization of [125I]RTI-55-Labeled Cocaine Binding Sites in Fetal and Adult Rat Brain". J. Pharmac. Exp. Ther. In Press, 1996, apparently represent the first visualization of cocaine's sites of action in the fetal brain and thus provide strong evidence that cocaine can interact directly with fetal brain neurons.

Cocaine and Reward

Cocaine effects on reward mechanisms have been studied by several grantees. Drs. Friebert Weiss and Athena Markou at the Scripps Research Institute in La Jolla and Roger Spealman at the New England Regional Primate Center in Boston have been concentrating on dopaminergic mechanisms in rats and monkeys. Dr. Weiss' work with the D1, D2 and D3 agonists and antagonists has implicated the D1 binding site as particularly sensitive for cocaine "craving", while all three sites appear equally effective for cocaine "seeking" behaviors. "Effects of Dopamine Agonists and Antagonists on Cocaine-Induced Operant Responding for a CocaineAssociated Stimulus". Psychopharmacology, In Press, 1996.

Dr. Weiss has also compartmentalized cocaine self-administration in the rat to "cocaine-seeking", "operant responding", "extinction", and "reinstatement" behaviors which can be separately identified and measured. These tests may provide useful tools for the assessment of potential treatment drugs for the various parts of cocaine abuse in humans. "Measures of Cocaine-Seeking Behavior Using a Multiple Schedule of Food and Drug Self-Administration in Rats". Drug and Alcohol Dependence 38: pp. 237-246, 1995.

Dr. Markou has developed the microdialysis techniques for studying monoamine levels in the amygdala. She has reported that both dopamine and serotonin are detectable in the dialysate, although serotonin levels were not increased in response to KCl stimulation, while dopamine levels were increased. Most investigators have used the microdialysis technique exclusively in the striatum. Studies on the amygdala are particularly important because of new information that this brain structure is important in mediating drug hunger or relapse. Furthermore, the amygdala is thought to be critical in the formation of associations to the drug experience. These data will expand our overall knowledge of monoamine involvement in other brain areas. "Basal Extracellular Dopamine Levels in the Nucleus Accumbens are Decreased During Cocaine Withdrawal after Unlimited-Access Self-Administration". Originally discussed in Brain Research 593: pp. 314318, 1992.

Dr. Spealman's self-administration and discrimination work in monkeys has concentrated on the D1, D2 and D3 receptor agonists, and the development of newer D3 compounds that may have less extrapyramidal side effects than existing compounds. His work on the D1 agonists have led him to postulate that this binding site will maintain cocaine self-administration, depending on the schedule of reinforcement and the pharmacological properties (selectivity, intrinsic efficacy) of the particular drug.

"Differential Effects of D1 and D2 Receptor Agonists on Schedule-Controlled Behavior of Squirrel Monkeys. J. Pharmac. Exp. Ther. 273: pp. 40-48, 1995; "Self-Administration of D1 Receptor Agonists: Comparison Under Different Schedules of Reinforcement. NIDA Res. Monograph Series, In Press.

Other grantees have concentrated on serotonergic involvement in cocaine's rewarding effects. Dr. Nissar Darmani at the Kirksville College of Osteopathy and Medicine has been studying cocaine's effect on the rat "head-twitch" response (HTR) evoked by serotonergic drugs (5-HTP, fenfluramine, sertraline, etc.). His data suggests that 5HT-1A and 5-HT2A receptor supersensitivity results from chronic cocaine administration, resulting in marked increases in the HTR. "The Mechanism by Which the Selective 5-HT1A Receptor Antagonist S-(-)UH 301 Produces Head-Twitches in Mice. Pharmac. Biochem. Behav. In Press, 1996; "The Stimulatory and Inhibitory Components of Cocaine's Actions on the 5-HTP-Induced 5-HT2A-Receptor Response. Pharmac. Biochem. Behav. In Press, 1996.

Dr. George King of the Duke University Medical Center, has a FIRST award to study the contribution of the 5-HT3 receptor on cocaine sensitization and tolerance in rats. In the past year, he has shown that the co-administration of 5-HT3 antagonists and cocaine block the development of sensitization and tolerance. His data suggest that 5-HT3 receptor stimulation is critical for the development of sensitization and tolerance. Furthermore, his research indicates that continuous cocaine administration induces a functional down-regulation of 5-HT3 receptors in the nucleus accumbens. Since the nucleus accumbens is thought to be critical in mediating reinforcement processes in general, this down-regulation may be critical in our understanding of the consequences of cocaine abuse.

Neurotensin Modulates DA Activity

While NIDA neuroscience is focused on the dopamine (DA) systems in brain, attention is being broadened to the role in drug abuse of the systems that modulate DA function and are affected by DA release. The group headed by Glen R. Hanson, Ph.D., DDS at the University of Utah College of Pharmacy has focused on the neurotensin (NT) system. In rats, removal of extracellular NT by infusion of NT antibody into the brain, or blockade of the NT receptor by SR-48692, caused a large increase (5-fold in the case of the antibody) in the DA released in the nucleus accumbens after sc injection of a low methamphetamine dose (0.5 mg/kg), accompanied by dramatic enhancement of locomotion and rearing. These findings suggest that the endogenous NT system is activated by low doses of methamphetamine, and serves to restrain the dopamine response. In conscious, freely moving rats, in both the nucleus accumbens and striatum, NT release was increased by a DA D2 receptor agonist (quinpirole) and decreased by a D2 antagonist (eticlopride), demonstrating for the first time that D2 receptors are important in the regulation of extrapyramidal and limbic NT release. Wagstaff, Gibb & Hanson, Brain Res., 1996; The release of NT by low dose methamphetamine was blocked by both D1 and D2 antagonists in the striatum, but only by the D2 antagonist in accumbens. Wagstaff, Gibb & Hanson, J. Pharmacol. Exp. Ther., 1996.

Regulation of Opiate Receptors

NIDA MERIT awardee Dr. Robert Elde from the University of Minnesota has made great gains in defining the spatial relations between opioid peptides and their receptors. In some instances, opioid immunoreactive dendritic processes interdigitate with opioid immunoreactive terminals. In other instances (e.g. nucleus accumbens and interpeduncular nucleus) nerve terminals containing opioid peptides form networks and occur in adjacent regions to neuronal elements containing opioid receptors. These later findings suggest the possibility that opioid neurotransmission may occur over significant volumes. The use of high magnification confocal and preliminary electron microscopic studies have also suggested that a great fraction of opioid receptors are not on the plasma membrane of axons or their terminals, but rather are intra-axonal in association with vesicles, perhaps awaiting exteriorization in response to stimulation. Dado, et al. NeuroReport 5: pp. 341-344, 1993; Arvidsson, et al. J. Neuroscience 15: pp. 1215-1235, 1995; Arvidsson, et al. J. Neuroscience 14: pp. 3328-3341, 1994; Arvidsson, et al. Proc. Natl. Acad. Sci. 92: pp. 5062-5066, 1995.

[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

May, 1996

Research Findings

Behavioral Research

Exposure to Pain Modulates Morphine's, But Not Butorphanol's Subjective Effects

In this study with human volunteers, and in contrast to animal research, a painful stressor does attenuate the subjective effects of the mu agonist morphine, but stress does not modulate the effects of the mixed kappa agonist-antagonist butorphanol. These results have clinical implications in that patients receiving morphine under painful, stressful conditions may be less "intoxicated" than those receiving morphine in the absence of stress. In contrast, butorphanol may be a more effective analgesic in patients under stress. Zacny, J. P. Effects of Cold Water Immersion on Subjective and Psychomotor Effects of Opiates in Healthy Volunteers, Experimental and Clinical Psychopharmacology, In Press.

Transnasal Butorphanol Alters Mood and Psychomotor Function in Normal Volunteers: Implications for Ambulatory Patients

Butorphanol is effective in treating migraine headache and post operative pain. Although butorphanol has been reported to have a low potential for abuse in opioid abusers, this study is the first to demonstrate that butorphanol also has significant effects on psychomotor function and mood in normal volunteers. Ambulatory patients, therefore, should use caution when taking this prescribed medication. It is noteworthy, however, that in the present study clinically-relevant doses of butorphanol did not increase drug-liking ratings in normal volunteers. Zacny, J. P. et al., The Effects of Butorphanol on Mood and Psychomotor Functioning in Healthy Volunteers. Anesthesia & Analgesia, In Press.

Food Deprivation Increases Crack Smoking in Rhesus Monkeys

Rhesus monkeys under short-term food deprivation worked harder in an instrumental task to gain access to cocaine base (1 mg/kg per delivery) than when they were food-satiated. These results and others demonstrate that food deprivation increases self-administration for some abusable substances, and may indicate that increasing appetitive motivation may generalize to a variety of reinforcers including drugs of abuse. Comer, S.D., Lac L.T., Wyvell, C.L., Curtis, L.K. & Carroll, M.E. Effects of Food Deprivation on Cocaine Smoking in Rhesus Monkeys. Psychopharmacology, 119, pp. 127-132, 1995.

Amphetamine Alters the Contribution of Macronutrients to Total Caloric Intake

Food intake of research volunteers was measured during lunch after they were administered either amphetamine (30mg/70kg, QID) or placebo. Amphetamine decreased intake of all macronutrients relative to placebo. However, amphetamine resulted in a relative increase in carbohydrate intake and a decrease in fat and protein intake. That is, the relative contribution of macronutrients to total caloric intake was changed following amphetamine ingestion. These results raise issues concerning the effects of phentermine (a new weight-loss drug) on macronutrient selection given it has neurochemical effects that are similar to d-amphetamine. Foltin, R.W., Kelly, T.H. & Fischman, M.W. Effect of Amphetamine on Human Macronutrient Intake. Physiology & Behavior, 58, pp. 899-907, 1995.

Extending the Release of Alprazolam Reduces its Abuse Liability

Researchers at the Johns Hopkins University School of Medicine assessed the behavioral, subjective and stated preference for immediate- (1 and 2 mg) vs extended-release (2 and 3 mg) alprazolam. Subjects with a history of sedative abuse participated. Plasma alprazolam concentrations peaked, on average, 1.7 and 9.2 hours after IR alprazolam and ER alprazolam, respectively. IR alprazolam impaired cognitive and psychomotor function, while ER alprazolam reduced only a single measure of motor performance, and only at the highest dose examined. In terms of subjective effects, IR alprazolam increased all positive drug effect measures, while effects of the higher ER dose on positive effect measures was mixed. Also, subjects were willing to pay significantly more money for either IR alprazolam dose than the ER doses. These data suggest that extended-release alprazolam has a much lower abuse potential then immediate-release alprazolam. Mumford, G.K., Evans, S.M., Fleishaker, J.C. & Griffiths, R.R. Alprazolam Absorption Kinetics Affects Abuse Liability. Clin Pharmacol Ther, 57, pp. 356-365, 1995.

Alcohol Hangover and Managerial Effectiveness

Dr. Siegfried Streufert and colleagues at Pennsylvania State University studied the effects of alcohol hangover on managerial effectiveness in subjects who held managerial positions. Twenty-two male managers who normally drink moderate amounts of alcohol participated in a placebo-controlled, double-blind, cross-over experiment. Subjects consumed either placebo or alcoholic drinks to attain a breath alcohol level of 0.10 during the evening before participation in Strategic Management Simulations. By the time of arrival at the simulation laboratory on the following morning, breath alcohol levels were measured at 0.00. Questionnaire responses indicated considerable hangover discomfort. Responses to semantic differential evaluative scales suggested that research participants evaluated their own managerial performance in the simulation setting as impaired. However, multiple (validated) measures of decision-making performance obtained in the simulation task did not show any deterioration of functioning. Previous research had shown considerable performance decrements in the same task setting, while blood/breath alcohol levels ranged from 0.05 through 0.10%. Apparently, complex decision-making competence by persons who normally consume moderate amounts of alcohol may not be impaired by hangover caused by intoxication during the previous evening that remains at or below a blood alcohol level of 0.10. Streufert et al., Alcohol Hangover and Managerial Effectiveness. Alcohol Clin Exp Res, 19, pp. 1141-1146, 1995.

Caffeine Deprivation and Managerial Effectiveness

In another study by Dr. Siegfried Streufert and colleagues, 25 male and female managers who reported an average daily caffeine consumption of 575 mg participated in two complex simulations. A double-blind cross-over design was employed to assess the effects of normal caffeine consumption versus caffeine deprivation upon seven validated measures of managerial effectiveness. Data from a Caffeine Withdrawal Questionnaire indicated discomfort upon deprivation. Systolic blood pressure increased during normal caffeine consumption levels but fell quickly and remained lower during deprivation. Several measures of managerial performance indicated decreased effectiveness upon caffeine deprivation. In contrast to prior research from simpler task settings, cognitive effectiveness during complex task performance was diminished. However, a measure of strategic performance which requires a relatively high level of cognitive effort showed no impact of caffeine deprivation. Streufert S. et al, Effects of Caffeine Deprivation on Complex Human Functioning. Psychopharmacology, 118, pp. 377-84, 1995.

Behavioral Pharmacology of Phencyclidine (PCP)

Dr. Robert Balster of the Medical College of Virginia, has used the drug discrimination procedure and other behavioral measures to evaluate drugs acting on the N-methyl-D-aspartate (NMDA) receptor complex. The NMDA receptor is the target of much pharmaceutical research because compounds acting at this receptor complex have been shown to be

useful therapeutically, but the utility of some of these compounds, e.g. phencyclidine (PCP), is limited because of abuse potential. PCP is a non-competitive NMDA antagonist that blocks the calcium channel site of the receptor complex, and Dr. Balster has shown that all compounds acting at the PCP binding site in the NMDA channel produce PCP-like behavioral effects which differ only in potency. For example, memantine, a low potency antagonist at this site, has similar reinforcing and discriminative effects to PCP. Competitive antagonists bind to the NMDA excitatory amino acid binding site and can serve as training drugs in the drug discrimination procedure. Competitive antagonists have been shown to have unique discriminative stimulus effects for which PCP-like non-competitive agents do not fully substitute. Recent studies in rats using NMDA as the training drug in drug discrimination studies indicated that a number of excitatory amino acids (EAA) could partially substitute for NMDA but only the novel EAA agonist LY 285265 fully substituted with a potency 100 times that of NMDA. Thus, LY 285265 should be a useful agent for in vivo studies of the NMDA receptor Discriminative Stimulus Effects of Excitatory Amino Acid Agonists in Rats, Neuropharmacology, 34, pp. 55-62, 1995.

Other studies from Dr. Balster's laboratory demonstrated that two novel agents which act as antagonists at the glycine modulatory site of the NMDA receptor complex differ markedly from PCP in their behavioral actions. These compounds are devoid of PCP-like discriminative stimulus properties, do not antagonize PCP discrimination, and do not serve as a discriminative stimulus. Behavioral Pharmacology of Two Novel Substituted Quinoxalinedione Glutamate Antagonists, Behavioral Pharmacology, 6, pp. 577-589, 1995.

Mu Opioid Agonists and Tolerance

Dr. Linda Dykstra has investigated the role of intrinsic efficacy in determining cross-tolerance to the rate-decreasing effects of mu agonists on food maintained responding. Tolerance and Cross-Tolerance to the Response Rate-Decreasing Effects of Mu Opioids in Morphine-Maintained Squirrel Monkeys, Behavioral Pharmacology, 6, pp. 776784, 1995. Based on a hypothesis proposed by Paronis and Holtzman (Psychopharmacology 114, pp. 601-610, 1994), mu agonists with higher intrinsic activity than morphine such as etorphine, l-methadone, and sufentanil would be expected to exhibit less cross-tolerance to these rate decreasing effects than the tolerance observed with morphine itself. Buprenorphine, a mu agonist with low intrinsic activity would be expected to exhibit greater cross-tolerance. The degree of cross-tolerance between morphine and drugs with high intrinsic efficacy was as predicted. The dose-effect curves of l-methadone, etorphine, and sufentanil were shifted less far to the right than that for morphine itself. However, buprenorphine exhibited smaller than predicted cross-tolerance; the buprenorphine dose-effect curve was shifted rightward to the same degree as high efficacy agonists.

[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

May, 1996

Research Findings

Clinical and Services Research

Mortality Following Inpatient Addictions Treatment: Role of Tobacco Use in Community-Based Cohort

In a population-based retrospective cohort study, Hurt et al. examined the medical records of 845 residents (mean age of 41.4 years, 35% women) of Olmstead County (Rochester, Minnesota) from the time they were admitted to Mayo's inpatient alcoholism treatment unit (between 1972 and 1983) through 1994. The underlying cause of death was classified as alcohol, tobacco related, both, or neither based on the classification from the CDC. About 75% of those admitted for alcoholism treatment were long-term heavy smokers. The investigators found that 222 patients died (death certificates were available for 214) at a death rate 2.5 times greater than what would be expected in a group of people at this age and sex. Of the deaths, 51% were due to tobacco-related causes, most notably heart disease, emphysema and lung cancer; and 34% (73) deaths were due to alcohol-related causes, including accidents, liver disease and suicide. The authors conclude that patients previously treated for alcoholism and/or other non-nicotine drug dependence had an increased cumulative mortality that was due more to tobaccorelated than to alcohol-related causes and that nicotine dependence treatment is imperative in such high-risk patients. Richard D. Hurt, Kenneth P. Offord, Ivana T. Croogan, Leigh Gomez-Dahl, Thomas E. Kottke, Tobert M. Morse, and L. Joseph Melton, JAMA, 275(14): pp. 1097-1108, April 10, 1996.

Diagnosis and Clinical Assessment

Drs. Chung, Langenbucher, Labouvie, and Morgenstern have reported on the results of their large scale diagnostic project at the Rutgers University Center of Alcohol Studies. In a sample of 295 substance users seeking treatment, data on symptomatology associated with DSM-IV substance use disorders were collected by administering the Comprehensive International Diagnostic Instrument-Expanded Substance Abuse Module (CIDI-SAM) and used to determine, by gender, the developmental sequence of symptoms for cannabis, cocaine, and alcohol. Results indicated important differences in the sequential development of dependence symptoms as they related to drug-of-choice and gender. Males acquired fewer symptoms of dependence than did women during an equal period of time. Results also suggested that a distinct sequence of symptoms of cocaine dependence emerges for men and for women, unlike the moderately correlated order in which symptoms appear in men and women for cannabis and alcohol dependence. In summary, cocaine dependence may present a unique problem, emerging with more malignancy than marijuana and alcohol and following a different developmental pattern for males and females.

Smoking Cessation and Heart Disease

Dr. Joy Schmitz from the University of Texas Health Science Center at Houston is studying two treatments for tobacco dependence in women with heart disease: 1) a coping-skills relapse prevention (RP) intervention; or 2) an educational intervention based on the health belief model (HBM). Pretreatment measures are also being examined to determine whether they predict differential response to the two interventions. Results to date show a significant reduction in mean smoking rate and CO level in both treatment conditions across sessions, with a non-significant trend favoring RP treatment over HBM. There is early evidence of important differential treatment effects as a function of patient characteristics, such as age and baseline level of self-esteem. For older subjects, the probability of quitting smoking is higher when receiving RP rather than HBM. For younger subjects, the probability of quitting smoking is relatively equal for the two treatments. Subjects with high self esteem respond better with RP, and those with low self-esteem respond relatively equally to the two treatments. Schmitz, J.M., Bordnick, P.S., & Le, T. Smoking Cessation in Women with Heart Disease Risk: A Preliminary Comparison of Two Treatment Models. Presented at the Society for Research on Nicotine and Tobacco Annual Meeting, Washington, D.C., March, 1996.

Treatment of Smokeless Tobacco Users

Dr. Dorothy Hatsukami from the University of Minnesota examined the effects of group behavioral treatment versus minimal contact and of nicotine versus placebo gum on cessation of smokeless tobacco use in a 2x2 study. Participants were randomly assigned to one of the four treatments. Dr. Hatsukami concludes that 2 mg nicotine gum is not more successful than placebo gum with either minimal intervention or as an adjunct to behavioral treatment. However, withdrawal symptoms were significantly reduced by nicotine gum, compared with placebo during the initial phases of cessation. The ineffectiveness of nicotine gum on treatment outcome may be attributed to the relatively low level of nicotine gum or its similarity with smokeless tobacco. Secondly, behavioral treatment with and without the use of 2 mg nicotine gum produced continuous abstinence rates comparable to minimal contact without active nicotine gum. However, when point-prevalence data were analyzed, behavioral treatment demonstrated greater treatment success than minimal contact, both during and shortly after treatment. Thus it may be that smokeless tobacco users are more likely to be able to return to abstinence after a lapse if they are involved with a more intensive treatment approach. Hatsukami, D., Jensen, J., Allen, S., Grillo, M., & Bliss, R. Effects of Behavioral and Pharmacological Treatment on Smokeless Tobacco Users. Journal of Consulting and Clinical Psychology, 64, pp. 153-161, 1996.

Smoking Cessation

Cinciripini et al. have recently published results showing the effects of smoking schedules on cessation outcome. Several procedures for smoking prior to quitting were compared to determine which would produce the highest abstinence rates one year later.

All procedures had a preestablished quit date and a standard behavioral intervention, including the contingent return of a $110 deposit depending on attendance, compliance with instructions, and abstinence. However, the procedures differed in having a particular schedule of smoking for the five weeks prior to the quit date. Four groups were set up to compare 1) gradual reduction by smoking at prescheduled times, 2) smoking usual amount at prescheduled times, 3) gradual reduction by smoking at self-selected times, and 4) smoking usual amount at self-selected times. Abstinence at one year was 44%, 32%, 18%, and 22% for the four groups, respectively. The highest abstinence rates were found in the two groups that were allowed to smoke at prescheduled times only. For example, in the group that had gradually reduced smoking at prescheduled times, abstinence was 44%--a remarkably high rate, considering that the nicotine patch was not used. In contrast, the worst results were found with the group which reduced smoking by lighting up at self-selected times. The abstinence in this group was only 18%. Apparently, these smokers were choosing optimal times and situations for enjoyment--and subsequently had a very high relapse rate. In comparison, the prescheduling of cigarettes meant that smoking occurred at times unrelated to critical events, such as a cup of coffee, a meal, or a period of boredom. As a result, much of the enjoyment was taken out of smoking, the stimulus control ("triggering") by critical events was disrupted, and the opportunity to learn how to cope with smoking urges was increased. The results of this research are particularly important since many smokers who try to quit choose the "common sense" procedure of cutting down at self-selected times-one of the worst procedures they could devise. Cinciripini, P. M., Lapitsky, L., Seay, S., Wallfisch, A., Kitchens, K., and Vunakis, H. V. The Effects of Smoking Schedules on Cessation Outcome: Can We Improve on Common Methods of Gradual and Abrupt Nicotine Withdrawal? Journal of Consulting and Clinical Psychology, 63, pp. 388-399, 1995.

Multisystemic Therapy for Delinquents

Dr. Scott Henggeler of the Medical University of South Carolina has recently reported that with home-based multisystemic therapy it is possible to virtually eliminate treatment dropout in delinquents. He reports that of 118 delinquents randomly assigned to either home-based multisystemic therapy or usual community services, 98% in the multisystemic therapy completed the full 5-month treatment. However, 78% of those assigned to usual community services received no substance abuse or mental health treatment in the 5 months after referral. Multisystemic therapy is a comprehensive therapy approach offering individualized treatment, the use of multiple strategies, unlimited availability of therapists, and increased accessibility of services. Henggeler, S. W., Pickrel, M. P., Brondino, M. J., Crouch, J. L. Eliminating (Almost) Treatment Dropout of Substance Abusing or Dependent Delinquents Through Home-Based Multisystemic Therapy. Am J Psychiatry 153:3, March 1996.

Retaining Cocaine-Abusing Women in a Therapeutic Community

Researchers found that cocaine abusing women whose children were living with them during residential treatment remained in the programs significantly longer than women whose children were not living with them at the facility. Some 77% of women in the Demonstration Group (with their children living in the facility) were still in the program at 3 months, compared to 45% of the Standard Group (i.e., without their children); at 6 months, the corresponding figures were 65% vs. 18%, and at 12 months 29% vs. 5% ($p<.05$). The average length of stay for women in the demonstration group was 300.4 days, compared to 101.9 days for women in the standard group ($t=2.83$, $p<.05$). The clear implication is that providing facilities to accommodate children is a major factor in improving retention and outcome for drug abusing mothers in treatment. In addition, having the children in the facility provides opportunities to assess and meet their needs which may, in turn, affect the mother's prognosis. Hughes, P.H., Coletti, S.D., Neri, R.L., Urmann, C.F., Stahl, S., Sicilian, D.M., Anthony, J.C. Retaining Cocaine-Abusing Women in a Therapeutic Community: The Effect of a Child Live-In Program, American Journal of Public Health, 85(8), pp. 1149-1152, 1995.

Postpartum Women in Outpatient Drug Abuse Treatment

This study compared a sample of post-partum crack-abusing women randomly assigned to an intensive day treatment program (DT) and a traditional outpatient program (OP). DT subjects were significantly more likely to remain in treatment beyond 4 months than women in the OP group (60.2% versus 46.1%; $z=2.17$, $p=.02$). The completion rate was significantly higher for DT (45%) as compared to the OP (21%) ($z=3.4$, $p=.000$). Barriers to treatment that correlated most significantly ($p<.01$) with retention focus on what the authors identify as personal feelings or conditions and problem denial. These include: a desire to be in another program correlated significantly (-.33); having a relapse (-.25); believing they could manage recovery on their own (-19); child's medical problems (.19); and attitudes of program staff (-.18). Strantz, I.H. and Welch, S.P. Postpartum Women In Outpatient Drug Abuse Treatment: Correlates of Retention/Completion, Journal of Psychoactive Drugs, 27(4), pp. 357-73, 1995.

[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

May, 1996

Research Findings

AIDS Research

Maternal Antibodies in HIV-Uninfected Infants

The presence of human immunodeficiency virus (HIV)-specific maternal antibodies bound to the peripheral blood mononuclear cells (PBMCs) was observed in 39 uninfected infants born to HIV-infected women. Such antibodies were not observed on PBMCs of 13 infants in whom maternal-child transmission of HIV had occurred. These results suggest that PBMC-bound maternal antibodies might have a protective role in the transmission of HIV from mothers to infants. Wang X-P, Oyaizu N, and Pahwa S. Pediatric Research, 38: pp. 384-389, 1995.

Neuropsychological Effects of Non-IV Drug Use and HIV Status

Research conducted by Dr. Robert A. Bornstein of Ohio State University examined the neuropsychological performance of HIV+ symptomatic, HIV+ asymptomatic, and HIV- individuals who had never abused drugs, had past histories of drug use, or currently abused drugs. The results revealed that with increasing proximity to time of drug use, HIV+ groups began to have worse performances than the HIV- group. There were no differences between the HIV-, HIV+ asymptomatic, and HIV+ symptomatic groups who had never abused drugs. The findings suggest that drug use may potentiate the expression of cognitive deficits in HIV infection.

Correlates of Hepatitis C Virus Infections Among Injection Drug Users

Recent analysis of the correlates of Hepatitis C infection from a long-term cohort study of the natural history of HIV infection among active IDUs found a very high prevalence of infection. HCV antibodies were detected in 89% of the participants (N=1356), and prevalence increased with age and with the duration of drug use: anti-HCV was present in 94% of those who had injected over 10 years. Prevalence was also higher in those who injected at least daily, among those sharing needles, and among those injecting cocaine. Prevalence was also significantly higher in those also HIV infected (93%) compared with HIV negatives (87%). No evidence for sexual acquisition of HCV was found. This study demonstrated that HCV infection occurs rapidly after the initiation of illicit drug injection: 78% of study participants were anti-HCV positive after 2 years of injecting. Thomas D, Vlahov D, Solomon L, Cohn S, Taylor E, Garfein R, Nelson K, Medicine, In Press, 1995.

Detection of HIV-1 DNA in Needle/Syringes, Paraphernalia, and Washes from Shooting Galleries in Miami: A Preliminary Report

With support from NIDA grants, Drs. Shah, Shapshak, Rivers, Stewart, Weatherby, Page, Chitwood, Mash, Vlahov, and McCoy conducted a study to detect the presence of HIV-1 DNA in injection paraphernalia and wash waters obtained from shooting galleries in Miami. Antibodies to HIV-1 proteins were detected in 52% of the visibly contaminated needles, 18% of the cottons, 14% of the cookers, and 6.0% of the washwater samples. HIV-1 DNA (gag, envelope) was detected in 84% and 85%, respectively, of the contaminated needles, 27% and 36% of the cottons, 46% and 56% of the cookers, and 38% and 67% of the washwater samples. The authors conclude that HIV-1 might be present in contaminated cottons, cookers, and washwater as well as in contaminated needle/syringes in shooting galleries. A key implication from these findings is that infection risks may reside in the behaviors of IDUs, independent of the effects of needle/syringe exchange programs. Reduction of Risks of Exposure to HIV-1 Among IDUs May Require Modification of Behaviors that are Ancillary to the Act of Injection, Such as the Use of Common Cookers, Cottons, and Washwater. JAIDS, 11: pp. 301-306, 1996.

Linked HIV Epidemics in San Francisco

Drs. Susan Service and Sally Blower assessed linkages between the first wave of HIV infection through the gay community in San Francisco in the early 1980s and the second wave that is now occurring among young gay men in the city. HIV seroprevalence is extremely age stratified in the gay community of San Francisco (42% of gay men >age 30 vs 18% of gay men

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[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

May, 1996

Research Findings

Epidemiology, Etiology and Prevention Research

Drug Use and Violence

Data was analyzed from two waves (7th grade and young adulthood) of a multiwave longitudinal study to examine the moderating influence of levels of self derogation and antisocial personality on the relationship between early drug use and later violence among subjects who were free of violence at the earlier time of measurement (N=4,536). Using logistic regression techniques, a significant main effect between drug use and later violence was observed, controlling for gender, race/ethnicity, father's education, other forms of deviance, and antisocial personality. Adolescent drug use increased the likelihood of later deviance for subjects exhibiting high derogation, but not for those exhibiting low derogation. The effect of drug use on later violence for low derogation subjects was suppressed by countervailing effects of antisocial personality. Among subjects with low levels of self derogation who have low levels of antisocial personality, drug use leads to higher levels of violence, but for those who have low levels of self derogation and high levels of antisocial personality, drug use decreases the probability of later violence. Among low-self derogating individuals, drug use seems to have a suppressing effect on violence for those prone to violence, while having a disinhibiting effect on those not prone to violence. These findings suggest a positive relationship between drug use and violence for well socialized individuals, and a negative relationship between drug use and later violence for those who are not well socialized and are prone to violence. Kaplan, and Damphouse, "Self-Attitudes and Antisocial Personality as Moderators of the Drug Use-Violence Relationship" in Drugs, Crime and Other Deviant Adaptations: Longitudinal Studies, edited by H.B. Kaplan. Plenum Press, New York, 1995.

Gene Variants Associated with Dopamine Have Additive Effects on ADHD Symptoms

David Comings and colleagues at the City of Hope (Duarte, CA) have been studying variants of a variety of genes associated with the dopamine system and their association with disorders and behaviors comorbid with drug abuse. In one study, it was found that individuals who possessed all three of the rarer alleles--*Taq* A1 of the dopamine D2 receptor gene, *Taq* B1 of the dopamine ß-hydroxylase gene, and the 10/10 (repeats) of the dopamine transporter gene--had the most Attention Deficit Hyperactivity Disorder symptoms. Those with two of the three alleles had fewer symptoms but still clinically labeled with the disorder. One allele yielded a borderline ADHD score; none of the alleles yielded a normal score. Comings, D.E., Wu, H., Chiu, C., Ring, R.H., Gade, R., Ahn, C., MacMurray, J.P., Deitz, g., Muhleman, D. "Polygenic Inheritance of Tourette Syndrome, Stuttering, Attention Deficit Hyperactivity, Conduct and Oppositional Defiant Disorder: The Additive and Subtractive Effect of Three Dopaminergic Genes-- DRD2, DßH, DAT1, American Journal of Medical Genetics (Neuropsychological Genetics. These findings along with several others nearing completion contribute to the notion of a genetic basis for a "reward deficiency syndrome" consisting of addictive, impulsive, and compulsive behavior, and personality disorders. Blum, K., Cull, J.G., Braverman, E.R., & Comings, D.E. "Reward Deficiency Syndrome," American Scientist, 84, pp, 132-145, 1996.

Substance Abuse and Gender Differences

In a study exploring the effect of gender on circumstances surrounding initiation and escalation of binge drinking, marijuana use, and the use of other illicit drugs, support was found for literature regarding differential motives and consequences as a result of differential socialization. Surrounding literature asserts that gender affects the relevance of peer influence, need to enhance self-importance and sense of power, conflictive consequences, sensation seeking as a motive, and reduction of distress in initiation and escalation of the use of alcohol and drugs. The study examined young adults' self reported circumstances surrounding initiation and escalation of alcohol and other substances. The sample consisted of 6,074 subjects from a longitudinal study that began in 1971 with a random 50% sample of Houston Independent School District 7th grade students (in 1971, N=9,335), who were re-interviewed in 1980. Respondents were asked if they had ever consumed alcohol and each of a list of drugs, and were further asked about heavy use of drugs and alcohol. Respondents were also asked about general circumstances (motives, expectations, and perceived consequences) before initial use and later abuse of drugs and alcohol, situations one week prior to initial drug and alcohol use and later abuse. Logistic regression controlled for race, socioeconomic status, and tendency to over or under endorse items.

General findings show that males are more likely than females to enhance their sense of self importance through the use of alcohol and illicit drugs, and are more likely than females to feel powerful and important through drug and alcohol use. Males are also more likely than females to engage in alcohol and drug use to gain peer approval and as a means of social bonding with peers. Males are more likely than females to be motivated to use alcohol and drugs for personal problems and in circumstances of low self-worth and depression. Other gender effects were substance specific or contingent upon socioeconomic status. This is attributable to the differential effects and social contexts of alcohol and drug use.

Liu and Kaplan, Gender Related Differences in Circumstances Surrounding Initiation and Escalation of Alcohol and Other Substance Use/Abuse. Deviant Behavior: An Interdisciplinary Journal, 17; pp. 71-106, 1996.

Childhood Irritability and Liability to Substance Use in Early Adolescence

Irritability may be a factor predicting the liability for psychoactive substance use disorder (PSUD), according to investigators at the Center for Education and Drug Abuse Research (CEDAR) at the University of Pittsburgh. Sons of substance abusing fathers (n=40) and non substance abusing fathers (n=56) were studied when they were 10-12 years old and again at age 12-14. Assessments included an assay of cortisol concentration (a measure of stress reactivity); amplitude and latency of the N1, N2, N3, P1, P2, and P3 event-related potentials; psychomotor indicators of behavioral control; a family disruption index; an irritability scale; and drug use items. After modeling using hierarchical regression analysis, the results indicate that family dysfunction, stress state of the child, and low behavioral self-control additively account for a significant proportion of variance on irritability scores 2 years later, and that this trait, in conjunction with family discord, is associated with substance use as a coping response by early adolescence. These findings suggest that (1) drug seeking may be associated with attempts to stabilize affective dysregulation by pharmacological means, assuming that adolescents with such regulation problems would find the "normalizing" effect of psychoactive compounds especially reinforcing; or (2) adolescents with affective dysregulation concomitant to dispositional irritability may be marginalized by peers, leading them to socialize with more deviant and similarly marginalized individuals, who exhibit and tolerate non-normative behavior such as alcohol and drug use. Tarter, Blackson, Brigham, Moss, and Caprara. The Association Between Childhood Irritability and Liability to Substance Use in Early Adolescence: a 2-Year Follow-Up Study of Boys at Risk for Substance Abuse. Drug and Alcohol Dependence, 39, pp. 253-261, 1995.

Paternal Alcoholism Predicts Rate of Growth of Adolescent Substance Use

Adolescents with alcoholic fathers not only are more likely to use drugs and alcohol, but their substance use increases at a more rapid rate than that of their non-children-of-alcoholic (COA) peers. These findings are based on a 3-year longitudinal study of 246 male and female COA's with at least one biological alcoholic parent who was also a custodial parent and 208 controls, with no alcoholic biological or custodial parents. Subjects were 10.5 to 15.5 years of age at initial recruitment, and computer-assisted interviews were administered annually to the adolescents and parents to ascertain measures of parental monitoring, association with drug-using peers, adolescent life stress, adolescent negative affect, emotionality and sociability, and adolescent substance use. Structural modeling and latent growth curve modeling showed that adolescents with alcoholic fathers were significantly more likely to use drugs and alcohol

and also had a higher rate of growth of substance use. Maternal alcoholism was associated with elevated initial levels of adolescent substance use but did not predict the rate of growth. Hierarchical modeling also confirmed that parental monitoring, elevated environmental stress and negative affect, and elevated emotionality and sociability mediated the effects of parental alcoholism. Diminished paternal monitoring, for example, appeared to mediate the effects of the fathers' alcoholism on growth of substance use. Paternal alcoholism also was associated with higher environmental stress and resultant negative affect, which in turn was associated with affiliation with drug-using peers, providing another pathway. Despite these indications of mediators, paternal alcoholism retained significant direct effects. Chassin, Curran, Hussong, and Colder. The Relation of Parent Alcoholism to Adolescent Substance Use: A Longitudinal Follow-Up Study. Journal of Abnormal Psychology, 105(1), pp. 70-80, 1996.

Parent Drug Use, Parent Personality, and Parenting

This study examined the relationship of parent drug use and specific parent personality traits with four indicators of the parent-child bond: affection, child-centeredness, involvement, and nonconflictual relations. The participants (N = 71) were young mothers or fathers who have participated in a longitudinal study of 1,000 children and their parents from 1975 to the present. They answered a self administered questionnaire about themselves and their oldest child. Regression analyses indicated that the domains of parent drug use and parent personality had independent effects on most of the parentchild variables. Specific parent personality traits buffered the effect of drug use on aspects of the bond. The implications of these findings are that reducing parental drug use can have direct and positive effects on the parent-child bond and can enhance some parent personality traits, thus strengthening the bond. Protective personality characteristics can mitigate the impact of drug use on the bond. Brook, Whiteman, Balka, & Cohen, Parent Drug Use, Parent Personality and Parenting. Journal of Genetic Psychology, 156(2), pp. 137-151, 1995.

Aggression, Intrapsychic Distress, and Drug Use: Antecedent and Intervening Processes

The interrelation of childhood aggression, early and late adolescent intrapsychic distress, unconventionality, and drug use were explored. Data were obtained from the subjects when they were 5 to 10 years old. Follow-up interviews were conducted when the subjects were between 13 and 18 years old and again when they were 15 to 20 years old. A LISREL analysis indicated that childhood aggression was related to later intrapsychic distress, unconventionality, and drug use. There were significant pathways (1) from childhood aggression to drug use at 15 to 20 years of age with mediation through intrapsychic distress and unconventionality and (2) during adolescence there is a pathway from intrapsychic distress to unconventionality that leads to legal and subsequently illegal drug use. There was also considerable stability in intrapsychic distress, unconventionality, and drug use. Intrapsychic distress and unconventionality are important mediators of childhood aggression and adult drug use. Brook, Whiteman, Finch, & Cohen, Aggression, Intrapsychic Distress and Drug Use: Antecedent and Intervening Processes. Journal of the American Academy of Child and Adolescent Psychiatry, 34(8), pp. 1076-1083, 1995.

Longitudinally Predicting Late Adolescent and Young Adult Drug Use: Childhood and Adolescent Precursors

The childhood and adolescent personality determinants of young adult drug use were examined. Data were obtained on children when they were approximately 5.5 (Tl), 14 (T2), 16 (T3), and 22 (T4) years of age. T2-T4 interviews of subjects and their mothers assessed child personality and behavior. At Tl, 976 mothers were interviewed. The analysis was based on 734 subjects. Specific childhood and adolescent personality traits were related to stage of drug use in young adulthood. Regressions showed that (1) traits at T2 and T3 mediated the effect of traits at earlier ages on T4 drug use and (2) stage of drug use was stable from T3 to T4 despite controlling for personality. Significant interactions revealed two buffers weakening the effect of T3 drug use on T4 drug use. Many more Tl-T3 personality traits, particularly low aggression, enhanced the effect of low T3 use on T4 use. Earlier findings that childhood personality is related to adolescent personality and then to drug use were extended to young adulthood. This mediational model indicates the stability of personality across development. Sources of this stability and that of drug use are discussed. Despite this stability, other results suggest ways to modify drug use. Brook, Whiteman, Cohen, Shapiro, & Balka, Longitudinally Predicting Late Adolescent and Young Adult Drug Use: Childhood and Adolescent Precursors. Journal of the American Academy of Child and Adolescent Psychiatry, 34(9), pp. 1230-1238, 1995.

Psychosocial Risk and Protective Factors, Multiple and Specific Drug Use and Needle Sharing in Male IVDAs

Only a few authors have examined the influences of multiple and specific drug use on needle sharing in IVDAS. The authors studied the influences of multiple and specific drug use on needle sharing in a cohort of male IVDAS. Subjects were 294 male intravenous drug abusers, 35% of whom were in methadone treatment, and 41% of whom were HIV positive. Subjects were given individually administered interviews using structured questionnaires. Using logistic regression analysis, the authors found that cocaine and heroin use, including that given by non-parenteral routes of administration, were the most important individual drug correlates distinguishing needle sharers from non-needle sharers. As the total number of drugs used increased from one to five, the risk of needle sharing with both familiar people and strangers increased. This effect of the number of drugs used was modified by family protective factors, such as parental support, significant other support, own childhood warmth and identification, and family conflict. Heroin and cocaine use, and multiple drug use, are risk factors for needle-sharing behavior among male IVDAS. Brook, Brook, Wynn, Masci, Roberto, & de Catalogne, J. Psychosocial Risk and Protective Factors, Multiple and Specific Drug Use and Needle Sharing in Male IVDAS. American Journal on Addictions, 4, pp. 118-126, 1995.

The Reciprocal Influence of Punishment and Childhood Behavior Disorder

This paper examines the nature of the linkages between punishment and conduct problems. In this study children were originally sampled in 1975 (Tl) when they were ages 1 to 10. A second follow-up series of interviews completed in 1985-86 (T3) included 96% of those seen in the first follow-up, as well as about half of those who were located but with whom we were not able to schedule interviews in 1983. In each family, interviews were carried out with one parent, usually the mother, and, for the follow-up interviews, the study child. Mothers and children were interviewed simultaneously but separately in their homes by two trained interviewers. Psychiatric diagnoses including conduct disorder were assessed by structured diagnostic interviews of mother and youth using the Diagnostic Interview Schedule for Children (DISC) (Costello, Edelbrock, Dulcan, & Kalas, 1984), as modified and supplemented by this group. Investigators first obtained the measure of punishment in the interviews of mothers when the children were ages 1 to 10. Mothers indicated which of a series of power-assertive techniques of controlling or disciplining the child they had employed during the previous month. The authors concluded that the causal effect of punishment on conduct disorder is real. Although the frequency of use of coercive methods is undoubtedly substantially influenced by the operant behavior of the child during early childhood, on the whole, the magnitude of the estimates and the fact that the influence begins so early in life led the authors to conclude that the predominant influence is from punishment for conduct problems. Once begun, punishment has a more potent negative effect on the temperamentally vulnerable. Results of this study indicate that punishment practices take on a stability during later childhood and adolescence that is uninfluenced by the level of the child's problem behavior. However, they continue to have a negative influence on the child's behavior. Cohen, & Brook, The Reciprocal Influence of Punishment and Childhood Behavior Disorder. In J. McCord (Ed.), Coercion and Punishment in Long-Term Perspectives (pp. 154-164). Cambridge, MA: Cambridge University Press, 1995.

Childhood Aggression and Unconventionality: Impact on Later Academic Achievement, Drug Use, and Workforce Involvement

The interrelation of childhood aggression, unconventionality, academic orientation, work involvement, and drug use was explored. Data was obtained for the subjects when they were 5-10 years old. Follow-up interviews were conducted when the subjects were 15-20 years old and again at 21-26 years old. Using latent variable causal analysis, the findings revealed long-term relations between early childhood aggression and adolescent problem behavior in the academic and occupational areas. The findings also indicated that adolescent drug use generates an early involvement with adult role behaviors, such as work at the expense of further education. Implications of the findings for prevention are discussed. Brook & Newcomb, Childhood Aggression and Unconventionality: Impact on Later Academic Achievement, Drug Use, and Workforce Involvement. Journal of Genetic Psychology, 4, pp. 393-410, 1995.

Effects of Parent Drug Use and Personality on Toddler Adjustment

This study is an attempt to examine the interrelation between parent drug use and parent personality on their 18month-old children's adjustment. Data on the parents were available at four points in time. Time 1 (Tl) at mean age 6.1, Time 2 (T2) at mean age 13.7, Time 3 (T3) at mean age 16.4, and at Time 4 (T4) at mean age 22.2. Data on their toddlers at 18 months old were also available. The subjects were given structured interviews assessing their personality and drug use and their toddler's adjustment. T3 parent personality traits were related to T4 personality

traits which in turn were related to the toddler's adjustment. The influence of parent alcohol involvement (T3) in the toddler's adjustment was mediated by parent personality (T3, T4) and parent alcohol problems (T4). Interactive effects demonstrated that protective parent personality traits (non-drug conducive) enhanced the effects of low parent drug use resulting in the highest amounts of toddler adjustment. There are significant pathways between parent personality and drug use and toddler adjustment. Parent protective factors enhance parent low drug use on toddler adjustment. Brook, Whiteman, Shapiro, & Cohen, Effects of Parent Drug Use and Personality on Toddler Adjustment. Journal of Genetic Psychology, 157(1), pp. 19-35, 1996.

A Multiple Risk Interaction Model: Effects of Temperament and Divorce on Psychiatric Disorder

Effects of family status on the trajectory of problematic temperament adjustment at one to 10 years of age and associated psychiatric disturbance eight years later were examined in an epidemiological sample of 648 children. After adjusting for predivorce temperament-adjustment and background factors, logistic regression yielded independent effects of single custodial mother (SCM) family status for increased risk of disruptive and anxiety disorders, and of stepfamily status for increased risk of disruptive disorders. Increased risk of psychiatric disorder was more pervasive for SCM family boys versus intact family boys than for SCM family girls versus intact family girls, however only significantly more so for depression. No significant gender interaction was observed for stepfamily status. When girls and boys were treated independently, pattern of family status and outcomes of internalizing disorders varied. In step families, an elevated risk of depression and anxiety disorder was observed in girls but not boys, whereas in SCM families an elevated risk of depression was observed in boys but not girls. Within each family status group there was support for an altered risk of later psychiatric disorder given specific problematic predivorce temperament-adjustment characteristics. Kasen, Cohen, Brook, & Hartmark. A Multiple Risk Interaction Model: Effects of Temperament and Divorce on Psychiatric Disorder in Children. Journal of the American Academy of Child and Adolescent Psychiatry, In Press.

The Relation of Parent Alcoholism in Adolescent Substance Use: A Longitudinal Follow-Up Study

Researchers tested parent alcoholism effects on growth curves of adolescent substance use, and whether parent and peer influences, temperamental characteristics, and stress could explain parent alcoholism effects. Participants were 316 families from a 3-year longitudinal study of children of alcoholics (COAs) and demographically matched controls. Adolescents (mean age = 12.7 at Time 1) and their parents received 3 computer-assisted interviews at annual intervals. Latent growth curve modeling showed that COAs, boys, and adolescents with drug-using peers showed steeper growth over time in substance use than did non-COAs, those without drug-using peers, and girls. Data was consistent with father's monitoring, stress, and peer drug use as mediators of COA risk, but these factors did not completely account for paternal alcoholism effects. The findings underscore the importance of parental alcoholism risk because the environmental socialization factors could not entirely explain why adolescent COAs are at increased risk. Chassin, Curran, Hussong, Colder. The Relation of Parent Alcoholism to Adolescent Substance Use: A Longitudinal Follow-Up Study. Journal of Abnormal Psychology, 105, 1996.

The Patterns and Predictors of Smokeless Tobacco Use Onset Among Urban Public School Teenagers

This study describes the patterns and predictors of smokeless tobacco (ST) use in large sample of urban public school students (grades 7 and 8) in Los Angeles and San Diego counties. The use of ST is more common among men than women and among Caucasians than African Americans, Hispanics and others. Approximately 20% of the male respondents and 5% of the female respondents reported use of ST at least once, and 10.1% of male students and 3.1% of female students who had never tried ST by seventh grade started to use it by eighth grade. Among Caucasians, about 30% of boys reported trying ST at least once and 13.7% of those who had never used ST by seventh grade initiated experimentation by eighth grade. These data were used to examine the family, peer, and intrapersonal predictors of ST use onset. The family risk factors for ST onset included living with a single parent, parent-child conflict, and parental alcohol use. The peer risk factors for ST use included peer drug use and activities with friends, such as parties and participation in sports. The intrapersonal risk factors included poor grades in school, risk taking, and stress. The study also shows that those who use cigarettes, alcohol, or marijuana are at highest risk of using ST and vice versa. This study supports a problem-prone behavior perspective of ST use and cigarette smoking suggesting that both products be targeted by prevention programs that counteract risk factors for problem-prone behavior. Hu, F.B., Hedeker, D., Flay, B.R., Susman, S., Day, L.E., Siddiqui, O. The Patterns and Predictors of Smokeless Tobacco Onset Among Urban Public School Teenagers. American Journal of Preventive Medicine,

12(1), pp. 22-28, 1996.

The Relationship Between Parent and Offspring Comorbid Disorders

Data concerning alcohol and drug abuse and dependence, depression, and anti-social behaviors among both subjects and their parents were obtained from a community sample of 1,201 young adults. Although 35% of the sample exhibited alcohol abuse or dependence, 14% marijuana or cocaine abuse or dependence, and 22% reported a parent positive for alcoholism, evidence of comorbidity with depression or antisocial personality was generally rare among both parents and subjects. Over one third of the subjects were negative both for family history and any disorder of their own and 20% reported a problem in both themselves and in one or both parents. These findings lend only partial support for Winokur's depression spectrum disease hypothesis, in that diagnosed children of depressed-only families have a 30% chance of exhibiting substance abuse or dependence alone, whereas diagnosed children of alcoholic-only families have only a 7% chance of exhibiting depression alone. Johnson, V. The Relationship Between Parent and Offspring Comorbid Disorders. Journal of Substance Abuse, 7, pp. 267-280, 1995.

The Relationship Between Sensation Seeking and Delinquency: A Longitudinal Analysis

A sample of 584 male and female adolescents were studied at two points in time to determine the relationship between self-reported delinquency and sensation seeking. Analyses of variance and covariance were used to test the effect of delinquency status and frequency of minor delinquent activity on sensation seeking at Time 1 and on changes in sensation seeking from Time 1 to Time 2. Results indicated that delinquency and sensation seeking are related in adolescence regardless of sex: those adolescents who are delinquent score significantly higher on the Disinhibition scale. This finding was not obtained for experience seeking. One implication of the findings is that rates of minor delinquency could be lowered by providing high sensation seekers with socially approved opportunities for meeting their sensation-seeking needs. White, H.B., Labouvie, E., Bates, M. The Relationship Between Sensation Seeking and Delinquency: A Longitudinal Analysis. Journal of Research in Crime and Delinquency, 22(3), pp. 197-211, 1995.

Cessation of Cocaine Use

This study explores factors that are related to cessation of cocaine use versus continued use in a non-clinical sample of adolescents and young adults. Data was collected as part of the Rutgers Health and Human Development Project, a prospective longitudinal study of 1,380 New Jersey adolescents who were tested initially at the ages of 12, 15, and 18 years and retested on two occasions until the ages of 18, 21, and 24 years (92% follow-up rate across the three measurement occasions). Cocaine stoppers (N=104) and current users (N=267) were compared in terms of age and sex, patterns of contemporary and prior drug use, life style characteristics, and a selected group of social learning variable. Cocaine stoppers and users had similar patterns of drug use at early points in time, but users had higher current frequencies of all types of drug use. In addition, those youth who stopped using cocaine were more likely to be married and have children than those who currently used, but the two groups did not differ in terms of career/school status. The data lent partial support to a social learning perspective and indicated that differential associations and punishments were most strongly related to cessation. In addition, users reported more dependency symptoms than did stoppers. Overall, the results suggested that friends' use, negative physical consequences of cocaine, and life style changes were factors that contributed most to cocaine use cessation. White, H.R., Bates, M.E. Cessation from Cocaine Use. Addiction, 90, pp. 947-957, 1995.

Young Adult Substance Use - Predictors and Consequences

Longitudinal data on substance use of 345 adolescents, from five overlapping age cohorts (11-15) in the Pacific Northwest, measured at four annual time points, were analyzed using Latent Growth Modeling (LGM). An associative cohort-sequential model was tested for alcohol, cigarette, and marijuana use. Hypotheses concerning the shape of the growth curve, the extent of individual differences in the common trajectory over time, and the influence of family cohesion, peer encouragement, and gender on initial substance use and shape of the growth curve were tested. Results indicated similar upward trends in the initial use and development of alcohol, cigarettes, and marijuana, the greatest increase occurring between 13-14 years. Peer encouragement influenced the developmental trajectories. Females were higher than males in initial status and developed less rapidly in their use of the substances than did males. The similar developmental trajectories across substances and the contradictory influences of family and peers

suggest early intervention efforts aimed at both domains are necessary. Duncan, T.E., Tildesley, E., Duncan, S.C., Hops, H. The Consistency of Family and Peer Influences on the Development of Substance Use in Adolescence. Addiction, 90, pp. 1647-1660, 1995.

Drugs and Homicide by Women

Data from 215 female homicide offenders incarcerated or on parole in New York were examined for subjects' drug use prior to and at the time of the homicide, their victims' drug use, and their perceptions as to the drug-relatedness of the homicides. Semistructured, conversational interviews we conducted in order to obtain detailed quantitative and qualitative data focusing on drug use histories and the homicide events for which respondents were incarcerated. Approximately 7 out of 10 respondents had been regular users at some point in their lives prior to their incarceration, while over half had been addicted to a substance. Over one-third of the respondents who were present at the scene were high on a drug at the time, while about half of the victims of these homicides used drugs before the homicide. Almost two-thirds of the homicides committed by respondents who were present at the scene were perceived to be drug-related. Alcohol, crack, and powdered cocaine were the drugs most likely to be related to these homicides. Many respondents acknowledged the need for alcohol and drug programs and comprehensive aftercare programs. Spunt, B.I., Brownstein, H.M., Cammins, S.M. and Langley, S. Drugs and Homicide by Women. Substance Use and Misuse, 31 (7), pp. 825-845, 1996.

Drug Use by Homicide Offenders

Interviews were conducted with 268 homicide offenders (97% of whom were male) incarcerated in New York State correctional facilities to examine their drug use prior to and at the time of the homicide, and their perceptions as to whether and how the homicides were related to their drug use. Most respondents who used a drug were not hardcore users of that drug. About one in five of the respondents could be considered polydrug abusers. Thirty percent of the sample believed that the homicide was related to their drug use. Alcohol was the drug most likely to be implicated in these homicides. This research suggests that the common wisdom that violence primarily occurs either when people are seeking drugs or as a result of buying or selling drugs need to be reconsidered. Spunt, Brownstein, Goldstein, Fendrich, Liberty. Drug Use By Homicide Offenders. Journal of Psychoactive Drugs, 27 (2), pp. 122-134, 1995.

Understanding the Effects of Adolescent Drug Use Prevention Interventions

While outcome research has shown that drug prevention programs based on theories of social influence may prevent the onset of adolescent drug use, little is known empirically about the processes through which they have their effects. The purpose of this study was to evaluate intervening mechanism theories of two program models for preventing the onset of adolescent drug use: normative education and resistance training. Analyses of 3077 fifth graders participating in the Adolescent Alcohol Prevention Trial revealed that both normative education and resistance training activated the causal processes they targeted. While beliefs about prevalence and acceptability significantly mediated the effects of normative education on subsequent adolescent drug use, resistance skills did not significantly predict subsequent adolescent drug use. More impressively, this pattern of results was virtually the same across sex, ethnicity, context (public verses private school students), drugs (alcohol, cigarettes, marijuana), and levels of risk; and, was durable across time. These findings strongly suggest that successful social influence-based prevention programs may be driven primarily by their ability to foster social norms that reduce an adolescent's social motivation to begin using alcohol, cigarettes, and marijuana. Donaldson, S.I., Graham, J.W., & Hansen, W.B. Testing the Generalizability of Intervening Mechanism Theories: Understanding the Effects of Adolescent Drug Use Prevention Interventions. Journal of Behavioral Medicine, 17(2), pp. 195-216, 1994.

The Effect of a Multi-Dimensional Anabolic Steroid Prevention Intervention

A team-based educational intervention to reduce adolescent athletes' intent to use anabolic androgenic steroids (AAS) was tested using a randomized, prospective trial. Thirty-one high school football teams involving 547 adolescent football players at schools whose students received an intervention and 696 players at control schools participated in the study. Experimental subjects were given seven weekly 50-minute class sessions delivered by coaching staff and student team leaders which addressed AAS effects, sports nutrition and strength training alternatives to AAS use, drug refusal role play, and anti-AAS media messages. Seven weightroom sessions were taught by research staff. A pre- and post-intervention questionnaire assessed intent to use AAS, knowledge, attitudes

and behaviors regarding drug use and diet, exercise, and risk factors for adolescent AAS use. Compared to controls, experimental subjects had significantly reduced post-intervention intent to use AAS, improved eating habits, increased exercise behavior, greater understanding of AAS effects, greater belief in personal vulnerability to AAS, more anti-AAS attitudes, reduced impulsivity and hostility, improved perception of athletic abilities, stronger belief that coaches and parents were against AAS use, more competent drug refusal skills, and less belief in media messages. A team-based approach to improve other adolescent behaviors and risk factors warrants strong consideration. Goldberg, L. et al. The A.T.L.A.S. (Adolescents Training and Learning to Avoid Steroids) Program: The Effect of a Multi-Dimensional Anabolic Steroid Prevention Intervention, JAMA Olympic Edition, In Press, July 1996.

Dropouts and Drug Use

Problem prone behaviors of White American, Mexican American, and American Indian high school dropouts, students in good academic standing and students in poor academic standing were surveyed. Generally, dropouts were most involved with drugs, perpetration of violence, and being victimized by violence with students in poor standing the next most involved and students in good standing the least. Ethnicity did not interact with academic status, suggesting differences between dropouts and students were similar across ethnic groups. Some ethnicity and gender main effects were found. Findings were related to Jessor's theory of problem prone behaviors, to peer cluster theory and to intervention design. Beauvais, F, et al. Drug Use, Violence and Victimization Among White American, Mexican American, and American Indian Dropouts: Students with Academic Problems, and Students in Good Academic Standing, Journal of Counseling Psychology, In Press.

Anger Reduction

High anger 6-8th graders received cognitive-relaxation coping skills (CRCS) social skills training (SST) or no treatment. Compared to the control, CRCS and SST were equally effective in reducing trait, general, and personal-situational anger, and outward negative anger expression as well as increasing controlled anger expression. On some variables regarding shyness and one measure of anxiety, CRCS showed some superiority. No between group differences were found on self-esteem, alcohol consumption, or intoxication. Deffenbacher, J. et al. Anger Reduction in Early Adolescents, Journal of Counseling Psychology, In Press.

Perceptions of Social Pathology and the Etiology of Drug Addiction

Dr. David Nurco and associates surveyed three groups of adult males (drug addicts, peer controls, and community controls) about their perceptions of the neighborhoods where they lived at ages 12 through 14. Clear differences arose, with addicts perceiving the greatest amount of deviance and community controls the least. These findings raise questions about attitudes and events that take place in early adolescence and subsequent addiction. Nurco, D. N., T. Kinlock,
K. O'Grady, M. Lerner, and T. E. Hanlon. Perceptions of Social Pathology in the Neighborhood and the Etiology of Narcotic Addiction: A Retrospective Study, Journal of Nervous and Mental Disease, 184(1), pp. 35-42, 1996.

[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

May, 1996

Research Findings

Intramural Research

Psychobiology Section, Preclinical Pharmacology Laboratory, DIR

Benztropine Analogs Lack Cocaine-like Behavioral Effects Benztropine analogs bind to the dopamine transporter and inhibit dopamine uptake but do not produce behavioral effects similar to those of cocaine. It has been suggested that these compounds lack cocaine-like behavioral effects. Recent studies conducted in the Psychobiology Section show conclusively that antimuscarinic actions potentiate rather than interfere with the expression of cocaine-like behavioral effects. Therefore, the lack of cocaine-like effects of the benztropine analogs is not due to antimuscarinic actions, and may better be accounted for by an action at the dopamine transporter that is distinct from that of cocaine.

Brain Imaging Section, Neuroscience Branch, DIR

NOS Inhibitors as Potential Treatment Medications for Opiate Withdrawal Nitric oxide synthase (NOS) inhibitors and clonidine were compared for their effectiveness in attenuating signs of opiate withdrawal and affecting blood pressure in rats. Several signs of opiate withdrawal reduced by the NOS inhibitors were similarly attenuated by clonidine, which is used clinically to treat heroin withdrawal. Three NOS inhibitors, L-nitroarginine, L-nitroarginine methyl ester and LN(5)-(1-iminoethyl)-L-ornithine increased mean arterial pressure in awake morphine-naïve and morphine-dependent rats. 7-Nitroindazole, a selective inhibitor of neuronal NOS, did not elevate blood pressure and attenuated more withdrawal signs than other NOS inhibitors. Because hypertension is a component of opioid withdrawal in humans, the effectiveness of 7-nitroindazole to attenuate signs of morphine withdrawal without affecting blood pressure suggests that this drug may have human therapeutic potential.
DB Vaupel, AS Kimes, and ED London, Nitric oxide synthase inhibitors. Preclinical studies of potential use for treatment of opioid withdrawal. Neuropsychopharmacology 13: pp.315-322, 1995.

Interaction Between NMDA Antagonists and Opioids Studies utilizing the isolated spinal cord of the neonatal rat examined the role of glutamate in opioid tolerance. MK-801, a noncompetitive antagonist of the NMDA subtype of glutamate receptor, did not prevent the development of opioid tolerance. The results demonstrate that glutamate receptor antagonists act synergistically to enhance the potency of opioids, thus masking tolerance. JA Bell and CL Burgess, MK-801 blocks the expression but not the development of tolerance to morphine in the isolated spinal cord of the neonatal rat. Eur. J. Pharmacol. 294: pp.289-296, 1996.

Presynaptic Glutamate Receptors Contribute to Opiate Withdrawal The isolated spinal cord of the neonatal rat and intact adult rats were used to examine the role of glutamate in the expression of opioid dependence. Chronic MK-801, a noncompetitive antagonist, enhanced withdrawal signs. MK-801, given acutely, diminished withdrawal in the isolated cord, but disrupted the behavioral expression of withdrawal in intact rats. The results demonstrated that a

component of the opiate withdrawal syndrome is due to hyperactivity of presynaptic glutamatergic neurons. JA Bell and CL Burgess, Co-treatment with MK-801 potentiates naloxone-precipitated morphine withdrawal in the isolated spinal cord of the neonatal rat. Eur. J. Pharmacol. 294: pp. 297-301, 1996.

New 18F-labeled Ligand for PET Imaging of Nicotinic Acetylcholine Receptors A new radiotracer for the nicotinic acetylcholine receptor, (+/-)-exo-(2-[18F]fluoro-5-pyridyl)-7azabicyclo[2.2.1]heptane, was synthesized by Kryptofix(r) 222 assisted nucleophilic no-carrieradded [18F]fluorination of (+/-)-exo-(2-bromo-5-pyridyl)-7-azabicyclo[2.2.1] heptane. The 18Flabeled tracer may be developed for the noninvasive visualization of central nicotinic receptors using positron emission tomography (PET). A Horti, HT Ravert, ED London, and RF Dannals, Synthesis of a radiotracer for studying nicotinic acetylcholine receptors: (+/-)-exo-2-(2[18F]fluoro-5-pyridyl-7)-azabiocyclo[2.2.1]heptane. J Labeled Compds Radiopharm 38: pp.355366, 1996.

Cocaine Sensitization is Prevented by *K*-opioid Agonists Studies conducted in the rat demonstrated that *K*-opioid receptor agonists prevented sensitization to the conditioned rewarding effects of cocaine. TS Shippenberg, A Le Fevour, and C Heidbreder. K-opioid agonists prevent sensitization to the conditioned rewarding effects of cocaine. J Pharmacol Exp Ther, 276: pp. 545554, 1996.

Molecular Neuropsychiatry Section, Neuroscience Branch, DIR

Chronic Cocaine Use as a Neuropsychiatric Syndrome In humans, chronic cocaine abuse is associated with neuropathological changes in the central nervous system. Acute administration of cocaine is associated with acute psychoactive episodes and paranoid states, while withdrawal from the drug is often associated with depressed mood. DIR investigators propose that the chronic, heavy use of cocaine may result in a neuropsychiatric syndrome, the disconnection syndrome, which because of its subtlety may have deleterious effects on both the acute and longterm therapeutic interventions with these subjects. JL Cadet and KI Bolla, Chronic cocaine use as a neuropsychiatric syndrome: a model for debate. Synapse 22: pp. 28-34, 1996.

A Role for Superoxide Radicals in the Chronic Effects of Methamphetamine Methamphetamine (METH)-induced neurotoxicity is thought to involve release of dopamine (DA) in presynaptic DA terminals, which is associated with increased formation of oxygen-based free radicals. In CuZn-superoxide dismutase expressing transgenic mice, the loss of DA terminals caused by METH was attenuated in a gene dosage-dependent manner, with female mice being more resistant than male mice against the deleterious effects of METH. These results suggest a role of superoxide radicals in the long-term effects of METH. H Hiroshi, B Ladenheim, E Carlson, E Epstein, and JL Cadet, Autoradiographic evidence for methamphetamine-induced striatal dopaminergic loss in mouse brain: attenuation of CuZn-superoxide dismutase transgenic mice. Brain Research 714: pp. 96-103, 1996.

Sigma Ligand PRE-084 as an Anti-Amnesic Agent In both long-term and short-term memory retrieval tests in mice, a selective sigma receptor ligand PRE-084, identified at the DIR, NIDA, was found to block the impairment of learning and memory induced by MK-081, mecamylamine, and nimodipine. PRE-084 may have a unique property to act as a anti-amnesic agent. T Maurice, T-P Su, DW Parish and A Privat, Prevention of nimodipine-induced impairment of learning by the F selective phencyclidine derivative PRE-084. J. Neural Transmission, 102: pp.1-18,1995.

Lung Survives Longer with Delta Opioid Peptide DADLE Delta opioid peptide DADLE worked in an as yet to be investigated manner to prolong lung preservation. In this study DIR investigators demonstrated that the DADLE-preserved lung functioned perfectly when transplanted into the host animal. PR Oeltgen, ND Horton, SF Bolling and T-P Su, Extended lung preservation with the use of hibernation trigger factors. The Annuals of Thorac. Surg., In Press.

A Hibernation Specific Protein is Purified and Partially Sequenced A protein enriched in winter-hibernating animal has been purified and partially sequenced. It is a 88 kDa protein with a sequence which does not exhibit homology with any known protein. ND Horton, PR Oeltgen, DJ Kaftani, T-P Su, DS Bruce, AS Krober and JF Jones, Biochemical characterization of a hibernation-specific 88 kDa protein derived from the plasma of deeply hibernating woodchucks. In: "Adaptations to the Cold - Tenth International Hibernation Symposium", Ed: F. Geiser, Univ. New England Press, Armidale, Australia, In Press.

An Original Opioid/Sigma Receptor? In an attempt to purify non-opioid sigma receptors, we have instead purified a protein which resembles the opioid/sigma receptors originally proposed by Martin and coworkers. This protein binds benzomorphans, naloxone, morphine, and haloperidol with high affinities. The protein showed three bands in SDS/PAGE. L-I Tsao and TP Su, A naloxone-sensitive, haloperidol-sensitive, [3H](+)SKF-10047-binding protein partially purified from rat liver and rat brain membranes: An opioid/sigma receptor? Synapse, In Press, 1996.

Sigma Ligand PRE-084 as an Anti-Amnesic Agent for Aging and Alzheimer's Patients? Scientists at DIR

found that PRE-084 reverses the amnesia in Senescence Accelerated Mice (SAM) both in short-term memory and long-term memory tests. Sigma ligands may represent a new class of drugs for targeting amnesia due to aging or Alzheimer's disease. T Maurice, FJ Roman,,T-P Su and A Privat, Beneficial effects of sigma ligands on the age-related learning impairment in the senescence accelerated mouse (SAM). Brain Res., In Press.

[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

May, 1996

Program Activities

Program Announcements/RFAs

A new prevention research announcement, **"Drug Abuse Prevention Intervention Research for Women and Minorities"**, program announcement PA-96-018, was issued by NIDA on February 2, 1996. The purpose of this program announcement is to solicit research to develop, refine, and test the efficacy and effectiveness of theory-based, universal, selective and indicated drug abuse prevention interventions for minorities and women. The intent is to support research which seeks to combine what is known from drug abuse prevention research with what is known about culturally diverse and/or gender specific experiences.

The Division of Epidemiology and Prevention Research issued an amendment to its current program announcements to include research on **the Co-Occurrence and Health Consequences of Violence, Drug Abuse, and HIV/AIDS.** The amendment appeared in the NIH Guide, Vol 25., No. 6, March 1, 1996. Its purpose is to encourage a range of research on (1) the co-occurrence of these behaviors, (2) their common and distinct correlates and public health consequences, and (3) community-based interventions to prevent and reduce their incidence, prevalence, and adverse health outcomes.

Eighteen proposals have been received thus far in response to MDD's RFA DA 96-003, **"Novel Pharmacotherapies for Treatment of Cocaine and Other Psychostimulant Dependence".** The emphasis is on non-dopaminergic approaches to pharmacotherapy. Proposals will be reviewed in July/August for funding in September.

On March 14, 1996, MDD issued RFA 96-002 **"Strategic Program for Innovative Research on Cocaine Addiction Pharmacotherapy (SPIRCAP),"** a U-19 Cooperative Agreement mechanism. This mechanism is being utilized to encourage expedited transition of ground-breaking research from advanced preclinical findings to applied clinical mode, specifically to (1) interface between innovative, advanced preclinical research of sound scientific rationale and clinical proof-of-concept of an identified cocaine addiction therapeutic strategy; and (2) implement pilot clinical studies in volunteers or cocaine addicts to validate the therapeutic modality. This mechanism requires applicants to foster multi-party collaborations among universities, research institutes and the pharmaceutical/biotechnology industry. Letters of intent are due 5/13/96 with a submission deadline of 6/13/96.

Health Services Research Database Catalogue

The Services Research Branch, DCSR, through NIDA's Health Services Research Resource Center, is undertaking the development of a data base catalogue that critically assesses the major features and usefulness of existing governmental and non-governmental data bases available for drug abuse health services research.

University of Miami -- Health Services Research Center

The University of Miami's Health Services Research Center, directed by Dr. Clyde McCoy and funded under a NIDA grant, was officially dedicated April 3, 1996.

NIDA/VA Medications Development Research Units (MDRU) Meeting

On February 26-27, 1996, the first quarterly meeting of the principal investigators and select senior staff from the NIDA/VA MDRU network was held. This was primarily an organizational and orientation meeting. MDD staff and incumbent investigators (Philadelphia and Los Angeles) presented background information and data on compounds for testing, summary of the outside consultants clinical cocaine program meeting in January 1996 and data from ongoing/completed research. A second meeting is scheduled for June. It is expected that each of the three new NIDA/VA MDRUs will have two studies of potential treatments for cocaine dependence/relapse underway by mid-summer. A cocaine clinical trials database is under development so that information from all NIDA sponsored clinical trials in this area can be accessed and such parameters as design, outcome, pharmacokinetics, etc., can be made available to scientists.

Evaluation of NIH AIDS Research

On March 14, 1996 the Office of AIDS Research at NIH issued the report of a year-long evaluation of the entire AIDS research portfolio of the NIH. The panel of scientists and community advocates that conducted the evaluation was established by the Office of AIDS Research Advisory Council and was chaired by Dr. Arnold Levine of Princeton University. Scientific area subpanels were established in the areas of Etiology and Pathogenesis; Drug Discovery; Clinical Trials; Vaccine Research and Development; Behavioral and Social Sciences and Prevention Research; and Natural History, Epidemiology, and Prevention Research. The subpanels identified the scientific priorities within each area, evaluated the current research portfolio, and developed recommendations to improve, enhance, and streamline AIDS research. The subpanel reports were subsequently summarized in the March 14 report in 14 overarching recommendations. Individual subpanel reports will also become available sometime late this spring.

[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

May, 1996

Congressional Affairs

NIH Reauthorization

Dr. Harold Varmus and heads of selected NIH institutes testified before the Senate Labor and Human Resources Committee during hearings on the reauthorization (or "revitalization") of the agency on March 6 and 7. Committee Chairman, Senator Nancy Kassebaum (R-KS), said the government and NIH should work together to assure a more efficient conversion of research breakthroughs into practical applications and called the reauthorization of NIH a high priority.

Dr. Varmus described the organization and mission of NIH and stressed the many commonalities of the numerous Institutes and Centers. He gave a preview of the NIH budget priorities for 1997, including neuroscience, computer science technology, genetics, and applications related to degenerative diseases. Dr. Varmus also said that NIH should have "greater flexibility in setting its own priorities ... priority setting is best done in an atmosphere in which scientists who manage scientific programs are given maximum flexibility to choose those that show the greatest interest and the greatest importance."

Later the same day, NIDA Director Dr. Alan Leshner testified before this committee as a member of the Neuroscience Panel. Others on this Panel were Dr. Hall, Director, NINDS, and Dr. Kupfer, Director, NEI. In his oral statement, Dr. Leshner not only discussed neuroscience research as a central and critical component of NIDA's research portfolio, but he also emphasized that much of the basic brain research that is supported by other NIH Institutes is also of great interest and use to NIDA. Dr. Leshner stated that "... although we each have our own missionspecific portfolios, we also collaborate a great deal." He gave examples of how this cooperation and collaboration has already provided important information for multiple areas. He also pointed out that addiction is not just a brain disease but is one expressed in behavioral ways and in a social context. Further, all aspects of that complex relationship are critical to understanding and treating addiction. Therefore, NIDA's research spans a wide range of disciplines, from molecular and cellular biology, through the behavioral and social sciences. Neuroscience and addiction research are inextricably linked. As we move into the 21st century, our increasing knowledge of the brain and behavior will allow us to respond to the new challenges posed by new mind-altering drugs.

House Appropriations Hearings on the President's FY 1997 Budget Request

On Monday, April 22, Dr. Alan Leshner, Director, NIDA, testified before the Labor HHS/Education Subcommittee of the House Appropriations Committee. In his testimony, Dr. Leshner discussed the role of the brain in drug addiction and emphasized the importance of dissemination of research advances on drug addiction to the families, communities, practitioners, and policy makers who need it.

Dr. Leshner emphasized that major basic science advances are helping move us much more quickly toward NIDA's top priority goal of developing effective treatment medications for cocaine addiction. He said that these kinds of findings are a major breakthrough because they provide clear biological targets at which to direct anti-cocaine medication development efforts. As one example, Dr. Leshner mentioned that this year NIDA-supported researchers

had successfully immunized animals against the stimulant effects of cocaine. As another example, he said that NIDA-supported researchers have recently shown that activation in the brain of one type of dopamine receptor, the D1 receptor, suppresses drug-seeking behavior, whereas activation of the D2 receptor stimulates drug seeking. Thus, he explained, D1 agonist compounds may be good candidates as anti-cocaine medications.

Dr. Leshner also told subcommittee Members that significant progress in identifying effective nonpharmacological behavioral treatments continues to be made. And he spoke of NIDA's substantial efforts devoted to the intersection between drug abuse and HIV/AIDS. As just one example, Dr. Leshner said, NIDA-supported researchers have developed outreach and intervention strategies that are very effective in changing risk behaviors associated with the spread of HIV, even among those drug users not in treatment.

President's FY 1997 Budget Request

It is estimated that in FY 1996, NIH will receive $11.939 billion dollars. For FY 1997 the President has requested $12.424 billion dollars for NIH. It is estimated that $18.0 million of this amount will be in third party payments for patient care costs at the clinical center, if this authority is granted. The authority to collect and keep third-party reimbursements for care provided at the NIH Clinical Center is sought in the President's budget request, with such payments being credited to the NIH Management Fund where they would remain available for one fiscal year after the fiscal year in which they are deposited.

It is estimated that in FY 1996, NIDA will receive $458.441 million (of which $153.3 million is part of the AIDS distribution). For FY 1997, the President has requested $466.3 million (of which $154.3 million is part of the AIDS distribution).

Excluding the increase for the new clinical center, the President's budget requests a 1.6% increase for NIH. This amounts to a $193 million dollar increase in program costs over FY 1996. Most of the boost will target research project grants. "NIH's highest priority continues to be funding investigator-initiated, peer-reviewed research project grants (RPGs)," the agency's budget documents state.

Faced with a modest increase of $166 million dollars in research project funding, NIH has revised its financial management plan to increase the total number of grants. Budget documents state: "Average direct cost increases for RPGs will be revised to 2% in 1997, down from previous annual increases of 4% in part to reflect the declining inflation rates for biomedical research."

At a March 19, 1996 HHS press conference, Dr. Varmus noted that "through my consultations with extramural investigators, its very clear that they would rather have a slight reduction in the increase in noncompetitive awards to allow us to increase the number of new competing awards." He predicted that the FY 1997 RPG success rate will be 24% under the President's plan.

Research training is also slated for an increase in the FY 1997 request. Support for NIH training activities would increase 2.4% or $15 million dollars, to a $404 million dollar total under the President's plan.

One of President Clinton's high priority research areas for FY 1997 is research on "the biology of brain disorders." In budget documents, NIH says: "This research employs animal models, neuroimaging, and clinical studies in an effort to understand many disorders such as pain, addiction, mental illness, neurodegenerative disease, diseases of the aging brain, such as Alzheimer's and damage to the sensory system."

CRADAs

The President signed H.R. 2196, National Technology Transfer Improvements Act, into law on March 7. Introduced by Representative Connie Morella (R-MD), the new law P.L. 104-113 is designed to make it easier for the federal government to enter into CRADAs with private industry. Such agreements allow government and industry to work together to develop science projects and spell out how to distribute royalties among the creative team. It allows a private company to secure the exclusive license for one kind of use for any product that is the result of any such agreement. In return, the federal government is entitled to royalties from the product.

Methamphetamine Control Act

On March 12, Senators Charles Grassley (R-IA) and Dianne Feinstein (D-CA) introduced S. 1607, Methamphetamine

Control Act of 1996. This bill would increase the regulation of precursor chemicals necessary to produce methamphetamine and increase the penalties for possession of controlled chemicals or paraphernalia used to make methamphetamine.

Briefings/Meetings

NIDA Director's Meeting with Senator Levin

At his request, Senator Carl Levin (D-MI) was briefed on March 28, 1996, by Dr. Alan Leshner, Director, NIDA, on cocaine medications and research advances in this area.

Briefing for Senate Minority Staff on Medications Development

At the request of Senator Moynihan's staff, Dr. Alan Leshner, NIDA Director; Dr. Frank Vocci, Acting Director, MDD, NIDA; and Dr. Tim Condon, Acting Deputy Director, OSPC, NIDA briefed staff to Senators Moynihan, Biden, and Kennedy on progress on medications development and related research issues. This briefing was held on April 11, 1996 in Senator Moynihan's office.

Other Items of Interest

GOP Releases Drug Strategy

On March 28, 1996, the Republican Leadership released a report by the Task Force on National Drug Policy entitled "Setting the Course: A National Drug Strategy." The report states that treatment must remain an important element, but more needs to be done to eliminate duplication and waste. A renewed strategy needs to look at establishing more effective evaluation techniques to determine which treatment programs are most successful, with accountability the key element. Research is not addressed in any depth, but is mentioned in the section "Focus on Treatment Programs that Work" with the following language:
"Another major component in pursuing effective treatment alternatives is basic and applied research into the causes of drug abuse and methods for treating or preventing addiction. In addition to current efforts, one contribution that major pharmaceutical companies can make in this area, in addition to efforts to control the diversion of legal drugs with high abuse potential, would be to support research efforts on drug addiction."

The President's New National Drug Control Strategy

President Clinton and General Barry R. McCaffrey, the new Director of the Office of National Drug Control Policy (ONDCP), released the new National Drug Control Strategy on April 29 in Miami, Florida. General McCaffrey said that the first of the five goals of the 1996 strategy is to motivate America's youth to reject illegal drugs and substance abuse. He emphasized that this is a strategy oriented to youth. The second goal is to reduce drug related crime and violence. Other goals include reducing the health, welfare, and crime costs from illegal drugs; shielding America's frontiers from the threat of drugs; and breaking foreign and domestic sources of supply.

The strategy discusses emerging drugs, including methamphetamine, "...a dangerous drug bringing about violence and loss of physical and mental control." A separate methamphetamine strategy was released the same day to increase penalties, stop the sale of component chemicals, and increase DEA agents assigned to stop trafficking. The budget to implement the overall strategy is $15.1 billion.

[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

May, 1996

International Activities

NIDA Director Alan Leshner addressed the Secretary of State's Open Forum at the Dean Acheson Auditorium of the Department of State on May 15, on "Technological Advances in the Prevention and Treatment of Drug Abuse." The Open Forum provides an opportunity for members of the Foreign Affairs community, from the Department of State and other foreign affairs agencies, as well as foreign science counselors stationed in Washington, to attend presentations on key issues, particularly those with foreign policy implications. Dr. Leshner informed the group about NIDA's research perspective on the public health consequences of drug abuse, the relationship between drug abuse and HIV/AIDS, and the Institute's international strategy for disseminating NIDA research and for building targeted research collaboration between the U.S. and selected regions of the world.

1996-97 will be the ninth year of NIDA participation in the Hubert H. Humphrey International Fellowship Program in Drug Abuse. The Institute will sponsor three fellows, from Peru, Bulgaria and Egypt, to study and initiate research projects as part of the program at the Johns Hopkins University. In addition to academic course work at Johns Hopkins, the experience of the NIDAsponsored Fellows includes a research mentorship visit of 8-10 weeks with a NIDA grantee.

NIDA has also selected three INVEST International Research Fellows for 1996-1997. Sylvia Cruz, Ph.D. of Mexico will work at Virginia Commonwealth University with Dr. Robert Balster on the molecular and neurochemical events associated with the acute depressant effects of organic solvents. Danxin Wang, Ph.D. of China, will join Professor Wolfgang Sadee at the University of California San Francisco to study the effects of dihydroetorphine. Raka Jain, Ph.D. of India will work with Professor Stephen Holtzman of Emory University on abuse liability, tolerance, and dependence potential of various psychotropic drugs.

The U.S.-India Workshop on Behavioral and Social Research Methodologies for Prevention of Drug Abuse and HIV/AIDS was held in New Delhi during March. NIDA grantees Sherry Deren, Don Des Jarlais and Robert Trotter, Judith Auerbach of the NIH Office of AIDS Research and NIDA staff Drs. Don Vereen, Richard Needle and Patricia Needle, accompanied by Science Attache Gray Handley of the U.S. Embassy, met for four days of presentations and discussion combined with individual meetings with Indian researchers to assist in finalizing proposals for submission to the U.S.-India Fund. Following the New Delhi workshop, Drs. Vereen and Patricia Needle traveled to Imphal for a two-day conference on establishing research priorities in drug abuse and HIV/AIDS, hosted by the Commissioner of Health of Manipur State. The India visit was supported through a Letter of Agreement with the Department of State. It is anticipated that there will be 4-5 Indo-U.S. collaborative behavioral research proposals submitted in time for funding before the termination of the Fund in 1997.

NIDA's International Program is serving as the coordinating office for a satellite meeting to the annual meeting of the College on Problems of Drug Dependence in San Juan. The meeting, "Building International Research in Drug Abuse," scheduled for Saturday, June 22, will bring NIDA-trained visiting scientists and foreign fellows from the Hubert H. Humphrey and INVEST Research Fellowship Programs together with U.S. researchers to explore aspects of implementing international research collaboration and to share research findings. Support for the satellite meeting has been provided through a Letter of Agreement with the Department of State.

During March, Dr. Robert Battjes (DCSR) participated in the Steering Committee meeting for the WHO/NIH Joint

Project on Assessment and Classification of Disablements. This new initiative, which involves WHO, NIDA, NIMH and NIAAA, will develop cross-cultural instruments addressing impairments, disabilities, and handicaps, building upon previous collaborative work that developed instruments for diagnosis of mental and substance use disorders, i.e., the Composite International Diagnostic Interview (CIDI) and the Schedules for Clinical Assessment in Neuropsychiatry (SCAN).

The third meeting of the International Drug Abuse Epidemiology Work Group (IEWG) is scheduled for July at WHO Headquarters in Geneva. The IEWG is composed of officials and researchers from international organizations, such as WHO, the United Nations Drug Control Programme, the Council of Europe Pompidou Group, the Commission of the European Communities, the European Monitoring Centre for Drugs and Drug Addiction and the Organization of American States, among others. IEWG participants also include researchers and officials from national agencies, institutions and universities, including staff from NIDA's Division of Epidemiology and Prevention Research, the Mexican Secretariat of Health, the University of Chile, the Malaysian University of Science and the South African Medical Research Council. The purpose of the meeting is to provide a forum for representatives from epidemiology surveillance networks from around the world to discuss the objectives and logistics of establishing an international network for the presentation and discussion of epidemiologic data on drug abuse on an ongoing basis; for developing an infrastructure for identifying and promoting epidemiologic and other drug abuse research; and for linking research findings to community and national public health policy.

Ann Blanken (DEPR) represented NIDA at the 24th meeting of the Pompidou Group in Athens, Greece, during April. The Pompidou Group is a consortium of European drug abuse epidemiology experts.

Karol Kumpfer, former NIDA Prevention Research Branch grantee and member of the IRG, will be in Australia for six weeks as a consultant to train social service and health care workers on her Strengthening Families Program model which was developed through NIDA and CSAP grants. The Strengthening Families Program (SEP) is a 16-week selective prevention intervention program designed for elementary school age children living in high risk families. The program includes separate interventions for the child, the parents, and the family.

Shunzo Abe, Planning Director for the Tokyo-based Drug Abuse Prevention Center (DAPC) visited NIDA in April. DAPC is under joint jurisdiction of the National Police Agency and the Japanese Ministry of Health and Welfare and serves as the national coordinator for a drug abuse prevention and education campaign. Mr. Abe was briefed on NIDA's research programs, international opportunities, program announcements, and publications.

[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

May, 1996

Meetings/Conferences

On January 25-26, 1996 an ad hoc scientific consultant group reviewed the MDD clinical cocaine treatment program. Representatives of MDD, DCSR, IRP, and the VA MDRUs were present. The group reviewed currently available clinical and preclinical information and made recommendations regarding pharmacologic methods, clinical trial methods, and categories of compounds to be considered.

On March 18, 1996, NIDA Deputy Director, Mr. Richard A. Millstein convened a joint all-day meeting of Parklawn staff and ARC staff involved in HIV/AIDS research. The purpose of the meeting was to provide overviews of the Institute's AIDS initiatives and to discuss how the intramural program could be better integrated into the NIH/NIDA research planning efforts in this area. Representatives from the Office on AIDS and each of the Extramural Program Divisions, Dr. George Uhl, Acting Director, IRP, and staff members from the IRP's Treatment Branch, Molecular Neurobiology Branch, Neuroscience Branch, Clinical Pharmacology Branch, and Preclinical Pharmacology Laboratory participated.

Consultant meetings were held to review the Medication Development Division's two preclinical discovery programs--the Cocaine Treatment Discovery Program on March 7-8, 1996, and the Opiate Treatment Discovery Program on March 19, 1996. Both meetings involved NIDA staff, NIDA contractors, NIDA grantees, and experts from the pharmaceutical industry. Specific recommendations were obtained for future compound screening efforts and a number of follow-up subcommittee/workgroup meetings will be held to address critical issues raised during the meetings. One of the most important follow-up efforts will be to establish a detailed information template to be used in recommending compounds for advancement from preclinical to clinical development.

On April 15, 1996, an expert panel was convened to address special issues concerning **"Research on the Role of Childhood Trauma in the Etiology of Drug Abuse."** This meeting in which 15 national experts discussed the impact of child abuse trauma on the developmental trajectory of children, possible sequelae and outcomes including PTSD and drug abuse was organized by Dr. Coryl Jones, DEPR, and Ms. J.C. Comolli, OSPC, and chaired by NIDA Director Dr. Alan Leshner, and later, by NIDA Deputy Director Mr. Richard A. Millstein. Special issues concerned research on vulnerabilities and individual responsivities to trauma, risk and protective factors, and cross-cutting issues and related research activities within NIH and other Federal agencies and departments. Steps and barriers for prospective studies and the problems inherent in developing an epidemiologic data base were identified. These included a range of problems which must be addressed with regard to human subject concerns. Recommendations will be used for program development and review of applicable policies.

On April 17, 1996 the Satellite Wellness Action Network (SWAN) and The Frost Foundation, Ltd. in partnership with the Metropolitan Washington Council of Governments (COG), Georgetown University, the Center for Substance Abuse Prevention (CSAP) and the National Institute on Drug Abuse (NIDA) sponsored a live interactive teleconference titled **"Pathways to Prevention"**.

A **NIDA/University of Puerto Rico Research Development Seminar** on Increasing Drug Abuse Research by Hispanic Investigators was held in San Juan, Puerto Rico April 17-19, 1996. The workshop provided technical assistance, mentoring, and grants development assistance to new Hispanic investigators interested in drug abuse research.

The NIDA Resource Center for Health Services Research held a meeting focusing on **Database Management and Archiving** on April 18, 1996.

A **NIDA/Howard University Drug Abuse Research Technical Assistance Project (DARTAP) HBCU Administrators Meeting** was held in Bethesda, MD on April 30, 1996. Over 30 administrators and faculty members from Historically Black Colleges and Universities participated in an intensive grants development workshop which focused on infrastructure development needs and designs.

On May 14 and 15, 1996, Drs. Lisa Onken and Jack Blaine launched the first in a series of meetings attempting to enrich NIDA's behavioral therapy development efforts by linking therapy development with basic behavioral science. The meeting was entitled **"Behavioral Therapy Development and Psychological Science."**

NIDA's Services Research Branch staff worked with the Secretary of Health and Human Services' staff to develop the national conference, **"Access and Opportunity: A National Leadership Conference on Managed Behavioral Health Care,"** which was held May 14 and 15, 1996, in Arlington, VA.

Dr. Dorynne Czechowicz, Division of Clinical and Services Research (DCSR), and Joel Egertson, Medications Development Division (MDD), organized a symposium entitled **"New Medications for Treating Cocaine Abuse and Dependence: Bench to Bedside"** conducted at the 27th Annual Medical-Scientific Conference of the American Society of Addiction Medicine (ASAM) on April 20, 1996 in Atlanta Georgia. This day long symposium, co-sponsored by NIDA with the Medications Development Committee of ASAM, presented research on the neurobiology of cocaine addiction: the search for cocaine treatment medications, progress to date and future directions. The symposium was co-chaired by Dr. Frank Vocci, Acting Director MDD, and Dr. Stephen Zukin, Director, DCSR and featured NIDA's Dr. David Gorelick, Chief, Treatment Research Branch, Intramural Research Program, Dr. Peter Cohen, Special Expert, MDD, along with Dr. Donald Wesson, Chairman of the ASAM Medications Development Committee, Dr. David Smith, ASAM President, and several speakers from the research community and pharmaceutical industry.

Dr. Jaylan Turkkan gave the keynote address at a conference at the City University of New York on May 3, 1996. The conference title was **"Categorization and Concept Formation: Same Topic, Different Perspectives".**

Drs. Chiiko Asanuma, Joseph Frascella, Harold Gordon, and Mac Horton, of the Etiology and Clinical Neurobiology Branch/DCSR, attended a meeting on **Current and Emerging Techniques for Monitoring Brain Structure & Function** held in Bethesda, MD on March 28-29, 1996.

Dr. Chiiko Asanuma of the Etiology and Clinical Neurobiology Branch/DCSR attended the FASEB meeting in Washington D.C., April 1996.

Dr. Joseph Frascella of the Etiology and Clinical Neurobiology Branch/DCSR was a faculty participant in a **NIDA Special Populations Research Development Training Seminar** held in San Juan, Puerto Rico, April 17-19, 1996.

Gary Palsgrove, SRB, DCSR, served as reactor to a panel presentation of the UCLA/RAND Corporation research findings at the **National TASC Conference on Drugs and Crime** held in Chicago on April 1, 1996.

Dr. William Cartwright, SRB, made a presentation entitled **"Managed Care, Government, and Science"** to the NIH Workgroup on Economics on April 4, 1996.

Dr. William Cartwright participated in an Institute for Health, Health Care Policy and Aging Research, Rutgers University workshop entitled, **"Direct Contracting and Managed Mental Health Care from the U.S. and U.K. Perspective,"** May 9 and 10, 1996 in New Brunswick, New Jersey. The workshop explored U.K. and U.S. experiences with public sector contracting in the private sector for mental health services.

Dr. Meyer Glantz presented a paper entitled "**The Application of Etiology Research Data to Substance Abuse Prevention"** at the International Congress of Behavioral Medicine joint meeting with the Society for Behavioral Medicine in Washington, D.C. March 14, 1996.

On March 10, 1996, Dr. Elizabeth Robertson, DEPR, presented a paper at the Society for Research on Adolescence entitled **"Trends in Adolescent Drug Use: Comparisons of Metropolitan and Nonmetropolitan Areas of the United States."**

Dr. Elizabeth Robertson of DEPR, represented NIDA at the **Sixth Biennial Meeting of the Society for Research on Adolescence** to discuss research opportunities with meeting attendees.

Dr. Meyer Glantz represented NIDA at the **Scientific Advisory Board of the NIMH Depression/Awareness, Research & Treatment (D/ART) Planning Board Meeting** on a new D/ART program focusing on comorbidity

issues.

On March 28, 1996, Dr. William Bukoski and Cathrine Sasek joined a group of experts from the Department of Health and Human Services to provide guidance and scientific input to Disney Animation Studios in their efforts to develop a drug abuse prevention video for middle school students, parents and teachers.

Richard H. Needle, Ph.D., M.P.H., conducted a workshop on grantsmanship on March 29, 1996 at the annual meeting of the **Society for Applied Anthropology**, held in Baltimore, Maryland.

Dr. Coryl Jones, ERB/DEPR, served on the steering committee and participated in the **Federal Forum on Childhood Research on Child Abuse and Neglect** involving 22 Federal programs held April 16, 1996, in Bethesda, Maryland. Her presentation outlined the NIDA portfolio on studies of child abuse and neglect, domestic violence, and victimization.

Dr. Peter Hartsock represented the Department at the annual conference of the **Arctic Research Council of the U.S. (ARCUS)** on March 26-27, 1996.

Dr. Peter Hartsock represented NIDA at the **NIMH AIDS Cost Effectiveness Analysis Meeting** on March 21-22, 1996 and described NIDA-supported economic modeling efforts related to drug abuse, AIDS, and other infectious diseases.

Dr. Peter Hartsock represented NIDA at the March 12, 1996 meeting of the **NIH Task Force on Emerging and Reemerging Infectious Diseases (EREIDS)**. The Task Force met to review new EREID initiatives by the World Health Organization and opportunities for NIH support of EREID research.

On April 25-26, 1996, Dr. William Bukoski, Chief, Prevention Research Branch was a panelist for an NIAAA workshop entitled **"Research on Alcoholism in the Workplace."** The meeting was held in Washington, D.C. Dr. Bukoski presented NIDA's latest prevention research findings and discussed current program initiatives.

Dr. William J. Bukoski, Chief of the Prevention Research Branch served as panelist and resource person to the **Fifth Annual National Conference on Prevention Research**, sponsored by the National Institute of Mental Health, which was held on May 9-11, 1996 in Washington, D.C. The meeting presented an overview of prevention research findings and discussed salient recommendations for future research.

On March 6, 1996 Dr. Peter Cohen, MDD, presented a talk entitled **"Science and Law as Alternative Approaches to Reality"** to anesthesia residents at the Georgetown University Medical Center.

On March 16, 1996 Dr. Frank Vocci spoke at the **Society for Research on Nicotine and Tobacco** in Washington, D.C. Dr. Vocci spoke on new findings in the nicotine field as they related to medications development leads.

On March 28, 1996 Dr. Frank Vocci spoke at an FDA/ NIMH/ NIDDK sponsored symposium on "Current and Emerging Techniques for Monitoring Brain Structure and Function". The title of his talk was **"Assessment of Neurotoxicity Caused by Drugs of Abuse and Potential Treatment Agents**.

Dr. Cora Lee Wetherington, NIDA's Women's Health Coordinator, gave an invited plenary session presentation, **"Women and Gender Differences: Research Opportunities"** at the annual North Carolina Governor's Institute on Alcohol and Substance Abuse, February 14-16, 1996 in Greensboro, NC. Dr. Wetherington also led a workshop, **"Research Priorities, Training and Development."**

Dr. Lula Beatty presented a seminar on drug abuse research careers at the Psychology Department at **George Washington University**, Washington, DC on February 29, 1996.

Dr. Lula Beatty, Chief of NIDA's Special Populations Office, was the Keynote Speaker at the **University of Arkansas at Pine Bluff's Annual Student-Faculty Research Forum** held March 19-22, 1996.

Dr. Lula Beatty served as discussant on the panel **"Ethnographic Methods for Community Health"**, at the **Society for Applied Anthropology**, in Baltimore, MD on March 28, 1996.

Dr. Lula Beatty moderated a session on drug abuse research at HBCUs at the **Center for Substance Abuse Prevention (CSAP) Conference**, held in New Orleans, LA, April 1-4, 1996.

Dr. Lula Beatty, Chief, SPO, presented NIDA's HBCU Initiative before the Twenty-First National Conference on Blacks in Higher Education, sponsored by the **National Association for Equal Opportunity in Higher Education (NAFEO)** on April 18, 1996.

Dr. Lula Beatty presented a session on research at the **NIDA Leadership Seminar for Asian Pacific Islanders** on April 22, 1996.

On February 1, 1996, Dr. Harry Haverkos made a presentation entitled, **"National Trends of HIV Infection Among Minorities"** at a conference on "Drug Abuse, HIV and Minorities" at the University of Miami, Coral Gables, Florida.

Dr. Harry W. Haverkos served as the Katharine Rosenbaum Boucot Sturgis Visiting Professor at the Medical College of Pennsylvania and at Hahnemann University, Philadelphia, PA, March 6-7, 1996. He met with medical students, researchers, clinicians, and drug abuse service providers. He presented Infectious Diseases Grand Rounds at Hahnemann University on **"Kaposi's Sarcoma: A Multifactorial Hypothesis,"** and Infectious Diseases Grand Rounds at the Medical College of Pennsylvania on **"Trends of AIDS and Drug Abuse."**

Dr. Jonathan L. Katz, DIR, was invited to present a paper entitled **"Dopaminergic Mechanisms Underlying Cocaine Effects and Cocaine Abuse"** at a plenary session entitled "Ethanol, Cocaine and Opioids: Common CNS Substrates of Action and Addiction" held at the Seventh Annual Spring Brain Conference, March 1996.

Drs. Amy H. Newman and Jonathan L. Katz, both of DIR, were invited to co-present a paper entitled **"Novel Benztropine Analogs: Potent Dopamine Uptake Inhibitors that are Behaviorally Distinct from Cocaine"** at the NIDA/MDD Meeting entitled "Cocaine Medications -- Better Treatment Through Chemistry", held April 29-30, 1996.

Students from the National Association of Academies of Sciences and American Junior Academy of Sciences visited the Intramural Research Program on February 8, 1996. The visit was hosted by Dr. Edythe D. London and coordinated by Dr. Rebeca Soria.p> Dr. Edythe D. London, DIR, presented a lecture entitled, "**FDG and PET Studies Comparing Brain Metabolism and Volumetric MRI Analysis in Substance Abusers and Controls**" at the European Winter Conference on Brain Research held in Serre-Chevalier, France on March 16-23, 1996.

Dr. Steven J. Grant, DIR, presented a lecture entitled, "**Activation of a Cortical Memory Circuit is Related to Cue-Elicited Cocaine Craving: A Positron Emission Tomographic Study**" at the Cognitive Neuroscience Society Third Annual Meeting held in San Francisco, CA on March 31 - April 2, 1996.

Drs. Toni Shippenberg and Bruce Vaupel, both of DIR, participated in the **Opiate Treatment Development Program Consultants Meeting** held by the Medications Development Division, NIDA in Bethesda, MD on March 19, 1996.

Dr. Jean L. Cadet, DIR, presented a lecture entitled, "**Superoxide Radicals Mediate the Biochemical Effects of MDMA**" at the Gordon Conference held in Ventura California on February 11-16, 1996.

Dr. Jean L. Cadet presented a keynote address entitled, "**Substance Abuse in the Elderly**" at the Bethune Cookman College Gerontology and 4th Annual Substance Abuse Conference held in Daytona Beach, Florida on March 28-30, 1996.

Dr. Jean L. Cadet attended the **Coppin State College 10th Annual Substance Abuse Conference** held in Baltimore, Maryland on April 24-27, 1996.

[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

May, 1996

Media and Education Activities

Secretary's Marijuana Prevention Initiative Support

In support of the Secretary's Initiative, NIDA conducted a series of meetings in San Francisco, Albuquerque, Bozeman, and Memphis, and at several U.S. Army installations. The purpose of the meetings was to encourage the attendees and the media to reach large numbers of the general public with the message that "there is clear scientific evidence that marijuana is a dangerous drug that can impair learning and affect memory, perception, judgment, and complex motor skills such as those needed to drive."

The meetings typically included community leaders, teachers and counselors. After the Memphis meeting, Viacom Cable reached 125,000 viewers with the Marijuana video and an interview with Mike Herman, Director of Safe and Drug Free Schools in Tennessee. The Nashville Banner, News Examiner, and Hendersonville Star reached 78,000 readers with related stories.

Press Conference at the Center on Addiction and Substance Abuse

On February 28, 1996, Dr. Alan Leshner participated in a press conference sponsored by the Center on Addiction and Substance Abuse to release a study of substance abuse and urban America. Dr. Leshner presented a statement addressing the need to look at drug abuse and addiction as a major health problem that dramatically affects both the health of individuals and that of the public, and the need for continued research.

Media Advisories

All NIDA Media Advisories are available under the Communications and Documents section of NIDA's Home Page.

February 20, 1996: **Attention and Memory Impaired in Heavy Users of Marijuana.** The Media Advisory highlights a new, NIDA-funded study conducted by researchers at McLean Hospital in Belmont, Massachusetts which shows that critical skills related to attention, memory, and learning are impaired among heavy users of marijuana, even after discontinuing use for at least 24 hours.

March 14, 1996: **Scientists Moving Closer to Identifying Compounds to Treat Cocaine Addiction.** Yale University School of Medicine researchers, funded by NIDA, report important findings that have significant implications for the development of medications to treat cocaine addiction. Researchers found that activation of the brain's D1 dopamine receptor system can suppress cocaine seeking in drug-experienced animals, whereas activation of the D2 dopamine receptor system can trigger cocaine seeking.

March 15, 1996: **NIDA Director to Discuss Behavioral Science Research In Drug Abuse.** Alan I. Leshner, Ph.D., Director, NIDA, presented a keynote address, "Drug Abuse Is a Health Issue and Why Does It Matter?" to the

Fourth International Congress of Behavioral Medicine in Washington, D.C. Dr. Leshner discussed the importance of drug abuse and addiction as a major avenue for increased morbidity and mortality of the nation.

March 21, 1996: **Town Meeting to Promote Understanding and Dispel Myths About Drug Abuse and Addiction.** NIDA and the University of Miami announced joint sponsorship of a Town Meeting to promote public understanding of what research has shown about drug abuse and addiction, and to help community drug abuse prevention and treatment programs fully utilize science-based information in their own work.

April 15, 1996: **National Teleconference Highlights Drug Abuse Prevention Video.** NIDA's video "Coming Together on Prevention" was featured in a live, nationwide teleconference on April 17, providing a forum for sharing effective approaches to drug abuse prevention. Dr. J. David Hawkins and NIDA grantee Dr. Mary Ann Pentz presented findings from their studies and participated in roundtable discussions.

April 18, 1996: **NIDA-ASAM Symposium Focuses on Treatment for Cocaine Addiction.** On April 20, NIDA and the American Society of Addiction Medicine (ASAM) cosponsored a one-day symposium on "New Medications for Treating Cocaine Abuse and Dependence: Bench to Bedside." Several NIDA and other experts in the field of addiction research presented findings on the neurobiology of cocaine addiction, treatment medications, and integrated treatment approaches.

NIDA Exhibits

In the past several months, NIDA has exhibited at the following:

International Congress of Behavioral Medicine
March 13-16, 1996
Washington, D.C.

Society for Adolescent Medicine
March 22, 1996
Crystal City, Virginia

NIDA/NIH and University of Miami
Understanding Drug Abuse and Addiction: Myths vs. Reality
April 1-2, 1996
Miami, Florida

National Association for Equal Opportunity in Higher Education (NAFEO)
April 17-20, 1996
Washington, D.C.

American Society of Addiction Medicine (ASAM)
April 18-21, 1996
Atlanta, Georgia

Community Epidemiology Work Group (CEG) Internet Home Page

The National Institute on Drug Abuse (NIDA) Division of Epidemiology Services and Prevention Research (DESPR) has developed a CEWG Home Page. The Home Page is currently under Institute review and is expected to be installed as a link to the Home Page in the near future. The CEWG Home Page includes the Advance Report and Volume I and II from the most recent biannual meeting. It also includes reports from State Epidemiology Work Groups and from pilot ethnographic research which has been sponsored by DEPR during the past several years. The reports can be read and/or downloaded. In addition, the Home Page has a listing of members of the CEWG, staff associated with the project and links to other related World Wide Web sites.

Planned Meetings

On May 21 to 23, 1996 NIDA will sponsor a symposium entitled **"Perspectives on Rural Drug Abuse"** in Ames, Iowa. This meeting will build on the work of State Epidemiology Work Group (SEWG) meetings held in rural and

frontier states in the past two years and the research review on rural alcohol and drug abuse held in Washington in April 1994. The goal of the symposium is an open exchange of information and views on the issues associated with rural drug use and abuse including: research-based findings on drug patterns and the processes that lead to drug use and abuse; the effects and implications of federal, state and local programs and policies; and access to and appropriateness of prevention and treatment interventions for rural areas. Panel discussions featuring Federal, state, and local policy makers and practitioner and presentations by researchers who study rural substance abuse will inform the development of recommendations for future policy, intervention, and research directions.

The **20th Meeting of the Community Epidemiology Work Group (CEWG)** is scheduled to be held in New York City on June 4-7, 1996. The CEWG was established by the National Institute on Drug Abuse in November 1976 and is composed of researchers from 20 selected metropolitan areas of the United States who meet semiannually to report on patterns and trends of drug abuse in their respective areas; emerging drugs of abuse; vulnerable populations and factors that may place people at risk for drug use and abuse; and, negative health and social consequences. Reports are based on drug abuse indicator data, such as morbidity and mortality information, treatment data and local and State law enforcement data. Additional sources of information include criminal justice, correctional, medical and community health data, local and State survey information, and research findings from ethnographic studies.

Cornell Medical College's Prevention Center will host a conference titled **"Multi-Ethnic Drug Abuse Prevention Research Findings: Implications for Practice"**. Topics/presentations will include (1) Theoretical Connections in ATOD Prevention, (2) Wellness In a Multi-Ethnic Society, (3) School-Based ATOD Prevention Strategies, (4) Family Interventions, (5) Reconnecting At-Risk Youth to Prevent Drug Abuse, School Dropout & Suicide Risk Behaviors, (6) Gaining the Excellent Edge with Successful Diversity Strategies, and (7) ATOD Prevention in Community Settings. This conference is sponsored by NIDA and CSAP and will be held June 6-8, 1996 .

The National Institute on Drug Abuse (NIDA) and the American Psychological Association (APA) Science Directorate are collaborating to cosponsor a **Conference on Drug Abuse (CODA)**. The conference will be held in conjunction with the 1996 APA Convention in Toronto. The goals of this conference are to focus attention on drug abuse and drug abuse research, to disseminate the latest and most important research findings, to encourage new research, researchers and research collaborations, and to stimulate communication among researchers in different areas and other professionals who are involved with the issues of drug abuse. A variety of activities are being planned including 15 keynote presentations, and over one hundred symposia, education workshops, papers, poster sessions and other special activities. Training and informational sessions with NIDA staff and opportunities to find out about research activities, support and professional development will also be part of the conference. Approximately 15,000 to 20,000 people are expected to attend the APA convention including clinicians, researchers, educators, policy and planning professionals and graduate students. APA has 51 different interest oriented divisions focusing on a vast range of psychological, psychiatric, behavioral, neuropsychological, social, and developmental areas. The latest information about the Conference will be available through NIDA's home page on the internet (http://www.nida.nih.gov) and through APA publications. Drs. Meyer Glantz (NIDA/DEPR), Timothy Condon (NIDA/OSPC) and Christine Hartel (APA/SD) are the co-chairs of the Conference.

Dr. Jaylan Turkkan will be chairing a symposium on June 25, 1996 at the annual meeting of the College on Problems of Drug Dependence titled **"Self-Control and Decision Making: Applications to Drug Abuse".** Presentations will cover self-control, impulsivity, risktaking, and decision-making relating to drug abuse. Speakers are: Dr. Howard Rachlin, Dept. of Psychology, State University of New York at Stony Brook. "Behavioral Patterning and SelfControl". Dr. George Loewenstein, Dept. of Social and Decision Sciences, Carnegie Mellon University. "Out of Control: Decision Theory and the Limits of Volition". Discussant: Dr. Thomas Crowley, Dept. of Psychiatry, University of Colorado School of Medicine.

Dr. Frank Tims, Chief, SRB, will chair a NIDA workshop on **"Managed Care Research and Institutional Change,"** at the annual meeting of the Association for Health Services Research, June 19, 1996 in Atlanta, Georgia.

[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

May, 1996

Publications

National Pregnancy and Health Survey: Drug Use Among Women Delivering Livebirths: 1992 -- NCADI #BKD192

The National Pregnancy and Health Survey provides extensive information on the nature and extent of substance abuse among women delivering live-born infants in the U.S. The survey found that 5.5 percent of the 4 million women who gave birth, used some illicit drug during pregnancy.

National Survey Results from the Monitoring the Future Survey, 1975-1994: Vol II College Students and Young Adults.
This report presents the results of the 1977 through 1994 follow-up surveys of the graduating classes of 1976 through 1994 as respondents have progressed through young adulthood. It provides information on the prevalence of drug use among American young adults and college students, trends of use, distinctions among important demographic subgroups in these populations, the intensity of drug use, and their attitudes and beliefs concerning various types of drug used.

Research Monographs

Individual Differences in the Biobehavioral Etiology of Drug Abuse - **Research Monograph 159 (1996)** -- NCADI #M159

Explores new directions for research development in the biobehavioral etiology of substance abuse. Addresses the genetic bases, neurophysiological correlates, and neurochemical factors underlying drug abuse risk and resistance.

Molecular Approaches to Drug Abuse Research Volume III: Recent Advances and Emerging Strategies - Research Monograph 161 (1996) -- NCADI #M161

Presents the cutting-edge research of NIDA's Molecular Biology and Genetics program. Presents studies on the transgenic models and other genetic approaches, the fast growing field of opioid receptors, and three families of transporters. Explores future directions in understanding the molecular mechanisms underlying drug addiction.

Problems of Drug Dependence, 1995. Proceedings from the 57th Annual Scientific Meeting of the College on Drug Dependence, inc.- **Research Monograph 162 (1996)** -- NCADI #M162

Contains papers adapted from the symposium meetings and plenary sessions held at the 57th Annual Scientific Meeting and offers the state-of-the-art on a wide variety of areas encompassing many disciplines in drug abuse research. Abstracts on various research-in-progress are also included, permitting readers to be informed of the latest research developments in the drug abuse field.

Neurotoxicity and Neuropathology Associated with Cocaine/Stimulant Abuse - **Research Monograph 163 (1996)** -- NCADI #M163

Describes clinical, biochemical, physiological, and psychological aspects of neurotoxicity and neuropathology associated with abuse of cocaine and other psychostimulants and proposes placing stimulant dependence in the category of neurological disorders in addition to the class of psychiatric disorders. Discusses the significance of neuropathologies in phenomenology of drug dependence and their relevance in developing successful treatment strategies.

Behavioral Studies Of Drug-Exposed Offspring: Methodological Issues in Human and Animal Research - Research Monograph 164 (1996) -- NCADI #M164

Discusses the possible adverse behavioral effects of prenatal drug exposure on the neonate and the developing child and addresses the complex methodological issues that challenge research in this field.

Treatment for Drug-Exposed Women and Children: Advances in Research Methodology - Research Monograph 166 (1996) -- NCADI #M166

Presents experiences, products, and procedures associated with the NIDA-supported Perinatal-20 Treatment Research Demonstration Program projects. Describes their efforts to expand clinical sites and implement services research protocols. Discusses issues associated with subject selection, recruitment, and retention, clinical assessment and program evaluation, data management and analyses.

NIDA NOTES

Volume 10, No. 6 (November/December 1995)-- NCADI #NN0011
The lead article in this issue reports that researchers have demonstrated that marijuana may cause drug dependence in animals. Other articles report on other marijuana research. A special report highlights the 60th anniversary of NIDA's Addiction Research Center.

Other Publications

A NIDA Conference report entitled **"Cardiopulmonary Complications of Crack Cocaine Use-Clinical Manifestations and Pathophysiology"** edited by Pushpa V. Thadani and the participants of the NIDA workshop has been accepted for publication in CHEST.

Gary Palsgrove was a co-author with P.M. Flynn, J.W. Luckey, and B.S. Brown, of an article entitled **"Relationship Between Drug Preference and Indicators of Psychiatric Impairment,"** American Journal of Drug and Alcohol Abuse, 21(2), pp. 153-166, 1995.

Ingster, L.M. and Cartwright, W.S., **"Drug Disorders and Cardiovascular Disease: The Impact on Annual Hospital Length of Stay for the Medicare Population."** American Journal of Drug and Alcohol Abuse, 21(1): pp. 93-110, 1995.

[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

May, 1996

Staff Highlights

Awards

Dr. Alan I. Leshner, Director, NIDA received an award from the Society for Applied Anthropology on March 28, 1996 in recognition of "exceptional leadership, resourcefulness, and vision in supporting and significantly furthering the work of anthropology in applied research on substance abuse and AIDS."

Dr. Jack E. Henningfield, Chief, Clinical Pharmacology Branch, DIR received the 1996 ASAM Annual Award "for expanding the frontiers of the field of Addiction Medicine and broadening our understanding of the addictive process, through research and innovation."

Dr. Edward J. Cone, Chief, Chemistry and Drug Metabolism Section, DIR has been selected by the U.S. Public Health Service Commissioned Officers Association to receive the 1996 SciPAC Career Scientist of the Year award for "his pioneering research on the detection of psychoactive drugs in humans and for the broad implications of his discoveries to improve drug abuse prevention and treatment."

Dr. Roger Brown, Chief, BNRB, DBR was elected to membership in the International Behavioral Neuroscience Society.

Dr. Rao S. Rapaka, Chief, Basic Neurobiology and Biological Systems Branch, DBR, was selected by the organizers of the Cyprus conference on "New Methods in Drug Research" as the recipient of the "1996 Award for Distinguished Service in Drug Abuse Research". The award recognizes Dr. Rapaka's long-standing efforts in promoting drug abuse research, drug supply system, medications development, and drug discovery.

Dr. Edythe D. London, DIR, was appointed as member of the Graduate Faculty, Graduate School, University of Maryland.

Dr. Toni Shippenberg, DIR, was appointed to the Executive Committee of the European Behavioral Pharmacology Society.

Dr. Stephen Husbands, DIR, received a Travel Award to attend the 1996 Annual Meeting of the College on Problems of Drug Dependence.

Staff Changes

Effective April 15, 1996, **Dr. Charles Grudzinskas**, Director, Medications Development Division (MDD), left Government service to become Vice President for Medications Development, G.D. Searle Company. Dr. Grudzinskas served as division director for five years during MDD's critical formative period, and from June 1993 to February 1994, served as NIDA's Acting Deputy Director. **Dr. Frank Vocci** is now serving as MDD's Acting Division Director.

Ms. Marge Hutton, Chief of NIDA's Personnel Management Branch, OPRM, retired after 20 years of Federal service on March 1, 1996.

Henry L. Francis, M. D. was appointed Chief, Clinical Medicine Branch, DCSR, effective April 29, 1996. Dr. Francis comes to NIDA from Johns Hopkins University School of Medicine and the Baltimore City Health Department. He was previously employed by the National Institute of Allergy and Infectious Diseases, including an assignment conducting AIDS research in Kinshasa, Zaire. Dr. Francis received his M.D. from Howard University College of Medicine and is board certified in internal medicine.

Joseph Frascella, Ph.D. has been appointed Chief, Etiology and Clinical Neurobiology Branch, DCSR, effective May 12. Dr. Frascella joined NIDA in December 1988 as a program official in the Neuroscience Research Branch, DBR, and has been serving as Acting Chief, ECNB, since February 1995. He holds a Ph.D. in neuroscience from Brown University.

David Thomas, Ph.D. and **Thomas Aigner, Ph.D.** joined the Behavioral Neurobiology Research Branch of the Division of Basic Research in October, 1995. Dr. Thomas received his doctorate from The American University in Washington, D.C. and was most recently a Research Associate fellow at the University of Chicago. Dr. Aigner received his Ph.D. from the Medical College of Virginia in Richmond, and spent the last 13 years in the intramural research program of NIMH on the Bethesda campus.

Nancy Pilotte, Ph.D. joined the Behavioral Neurobiology Research Branch of the Division of Basic Research in March, 1996. Dr. Pilotte, who received her degree from Florida State University, transferred from the Medications Development Division of NIDA to DBR.

Leslie Cooper, Ph.D., a Commissioned Officer, joined NIDA's Epidemiology Branch on April 1, 1996. Prior to coming to NIDA, Dr. Cooper was stationed at the NIH from June 1983 until May 1995 primarily assigned to NICHD, and the last three years at the NINR and the NHLBI. From May 1995 to April 1996, she worked at the Maternal and Child Health Bureau within the Health Resources Services Administration. Dr. Cooper is an epidemiologist with the majority of her experience focusing on the maternal and child health population.

Dr. Peter Delany, Services Research Branch, DCSR, has been detailed part-time to the Office of the Assistant Secretary for Planning and Evaluation to coordinate HHS's efforts on the National Survey of Homeless Assistance Providers and Clients.

Grantee Honors

NIDA grantees David Paschane, Dennis Fisher, Henry Cagle, and Andrea Fenaughty, of the University of Alaska at Anchorage, were awarded the 1996 Award for Excellence by the Center for Substance Abuse Treatment and the National Rural Institute on Alcohol and Drug Abuse. The award was in recognition of their work on drug use, sexually transmitted diseases, and sex-related risk behaviors in Alaska. The award will be formally presented at the 12th Annual National Rural Institute on Alcohol and Drug Abuse to be held at the University of Wisconsin-Eau Claire, Eau Claire, Wisconsin, June 9-13, 1996.

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

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