National Institute on Drug Abuse

Director's Report

to the

National Advisory Council on Drug Abuse

May, 1998

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Research Findings

Basic Research

Acetylcholine Receptors Containing the Beta-2 Subunit are Involved in the Reinforcing Properties of Nicotine

Using knockout mice lacking the beta2 subunit of the neuronal nicotinic acetylcholine receptor (nAChR), but preserving expression of all other subunits of the neuronal nAChR, NIDA grantee Dr. Marina Picciotto and her colleagues at Yale University have uncovered evidence that the beta2 subunit is a necessary component of the receptor that mediates the reinforcing properties of nicotine in the brain. Each of the steps in the pathway leading to nicotine addiction has been examined in these animals: high affinity nicotine binding is completely absent in the mesolimbic system of mice lacking the beta2 subunit; both the electrophysiological response to nicotine of dopaminergic neurons, as well as nicotine-induced dopamine release, were absent in beta2 mutant mice; and beta2 mutant mice will self-administer cocaine, but extinguish self-administration behavior when nicotine is substituted for cocaine, implying that these animals cannot experience the reinforcing properties of nicotine in this paradigm. These experiments identify binding of nicotine to nAChRs containing the beta2 subunit as the first step in the pathway toward nicotine addiction. Future experiments using mice deficient in various other subunits of the nAChR will allow identification of the other subunits that make up this receptor. Picciotto, M.R., Zoli, M., Rimondini, R., Lena, C., Marubio, L.M., Merl, E., Pich, K. Fuxe, Changeux, J.P. Nature. 391(173), 1998.

An Ultra Sensitive Method for the Detection of Vesicular Components

One of the principal way cells communicate with each other is through the secretion of chemical signals known as hormones and neurotransmitters. These hormones and neurotransmitters are stored in vesicles that have volumes as small as a zeptoliter (10-12 liter), and are released in response to physiological stimuli. Dr. Richard Zare and his colleague at Stanford University have developed and perfected a technique that permits the chemical characterization of the contents of a single vesicle. In the February 20, 1998 issue of *Science* Dr. Zare reported that secretory vesicles isolated from the atrial gland of the sea snail Aplysia Californica were chemically analyzed individually. A single vesicle, having a volume of an attoliter (10-18 liter) was introduced into the tapered inlet of a separation capillary using a technique called optical trapping and lysed. The components of the vesicles were fluorescently labeled with napthalene-2, 3 dicarboxaldehye. The fluorescently labeled contents of the synaptic vesicle were then separated with capillary electrophoresis and analyzed with a laser-induced florescence technique. The amino acid, taurine, was detected in some vesicles but not in others. Standard biochemical techniques that examine the contents of a population of a vesicle would have failed to reveal the variations in vesicle content. This breakthrough will enable scientists to elucidate the cellular mechanisms used to package and sort chemical messengers into vesicles, and provides a precision previously unattainable for identifying types of secreted bioactive products from single vesicles. Chiu, D.T., Lillard, S.J., Scheller, R.H., Zare, R.N., Rodriguez-Cruz, S.E., Williams, E.R., Orwar, O., Sandberg, M.,

Lundqvist, J.A. Probing Single Secretory Vesicles with Capillary Electrophoresis. Science. 279(5354), pp. 1190-1193, Feb. 20, 1998.

Amphetamine Release of Dopamine by Reversal of Transport and Displacement

Mark Wightman, of the University of North Carolina at Chapel Hill, and his colleagues at Duke recently published data on the intraneuronal regulation of monoaminergic transmitters. The intracellular and extracellular concentrations of monoaminergic neurotransmitters are regulated by two types of transporters. Na+/Cl- -dependent plasma membrane transporters terminate neurotransmission by removing transmitters from the extracellular space, while vesicular transporters move the monoamines from the cytoplasm into vesicles, a process critical for stimulated release of transmitter. The plasma membrane transporters are the initial cellular targets of cocaine, and both transporters are targets of amphetamine. Wightman and his colleagues used fast-scan voltammetry to measure extracellular dopamine in the striata of mice lacking the plasmalemmal dopamine transporter to elucidate the mechanism of action of amphetamine. They demonstrated that amphetamine releases dopamine by two separate mechanisms, through reversal of transport (movement of dopamine out of the cell via the dopamine transporter) and by displacement of vesicular dopamine into the cytoplasm of the terminal. Mice lacking the dopamine transporter do not show the typical increase in locomotor activity to an injection of cocaine. Mice that lack the vesicular transporter (VMAT2), in contrast, are not viable, but heterozygotes, which show a 50 percent decrease in the VMAT2, respond vigorously with increased motor activity in response to amphetamine. However, they do not appear to develop behavioral sensitization to repeated injections of amphetamine. These mice also have lower tissue content of dopamine and decreased basal dopamine extracellularly relative to control animals. The significance of this observation is to suggest that one role of the VMAT2 may be to calibrate the capacity of neuron to store the appropriate monoamine intracellularly. Accordingly, either the size of the releasable pool or transmitter or the amount of transmitter stored in each vesicle may be regulated by VMAT2. Jones, S.R., Gainetdinov, R.R., Wightman, R.M., Caron, M.G.. Mechanisms of Amphetamine Action Revealed in Mice Lacking the Dopamine Transporter. J. Neuroscience. 18, pp. 1979-1986, 1998. Wang, Y-M., Gainetdinov, R.R., Fumagalli, F., Xu, F., Jones, S.R., Bock, C.B., Miller, G.W., Wightman, R.M., Caron, M.G. Knockout of the Vesicular Monoamine Transporter 2 Gene Results in Neonatal Death and Supersensitivity to Cocaine and Amphetamine. Neuron, 19, pp. 1285-1296, 1997.

Cocaine & Female Reproductive Function

NIDA supported research findings published in the January 1998 issue of *The American Journal of Obstetrics and Gynecology* which reported on the cocaine-induced disruption in menstrual and ovarian cyclicity in monkeys. These physiological changes were observed in monkeys following daily administration of cocaine during the normal cycling (follicular-phase) period. The disruption in menstrual cyclicity and folliculogenesis were independent of weight loss, caloric intake, or basal gonadotropin levels. Potter, D.A., et al, Amer. J. Obstet. Gyn. 178, pp. 118-125, 1998.

Analgesic Activity of Orphanin FQ2, Murine Prepro-Orphanin FQ141-157 in Mice

Orphanin FQ/Nociceptin (OFQ/N) is generated from a larger precursor peptide, prepro-orphanin FQ (ppOFQ). Dr. Gavril W. Pasternak and his research team at the Memorial Sloan-Kettering Cancer Center have discovered another putative heptadecapeptide within the sequence of murine ppOFQ, orphanin FQ2 (OFQ2), corresponding to murine ppOFQ141-157. OFQ2 was a potent analgesic given either supraspinally (ED50 0.5 g, i.c.v.) or spinally (ED50 0.7 g, i.t.). As with opioids and OFQ/N, OFQ2 analgesia was enhanced by blockade of sigma receptors with haloperidol, which increased the potency of the peptide over 10-fold. Supraspinal OFQ2 analgesia was readily reversed by the opioid antagonist naloxone, implying that OFQ2 activated opioid systems. Spinal OFQ2 analgesia was insensitive to naloxone. OFQ2 also inhibited gastrointestinal transit. Together, these studies suggest that OFQ2 may be a useful neuropeptide with important physiological actions. Rossi, G.C., Mathis, J.P., Pasternak, G.W. NeuroReport, In Press.

High Concentrations of Nicotine Inactivate Nicotinic Receptor Function in Vitro

Acetylcholine receptors (nAChRs) exposed to brief pulses of nicotine results in the release of dopamine, whereas prolonged exposure with low concentrations of nicotine (approximately 10 nM) produces a reversible blockade of a subsequent nicotine challenge (i.e., nAChRs desensitization). Dr. Peter Rowell of the University of Louisville School of Medicine and others have observed that, following prolonged exposure with a stimulating (M) concentration of nicotine, there is incomplete recovery from desensitization. In a recent study, Dr. Rowell and his research team

investigated this nonrecoverable phenomenon by characterizing the ability of nicotine to stimulate [3H]dopamine release from rat striatal synaptosomes following recovery from nicotine-induced desensitization. Brief (12 seconds) exposure to 30 M nicotine, or longer exposure (Æ5 minutes) to 0.3 M nicotine, produced a long-lasting decrease in nAChR function with an apparent IC50 of 0.7 M. The maximum inactivation achieved was approximately 50 percent. Recovery of nAChR function did not return even after five hours, whereas recovery from desensitization occurred within 20 minutes. Determinations of the con-centration of nicotine in the superfusate indicated that residual nicotine could not account for the observed decrease in response as a consequence of desensitization. These results indicate that high concentrations of nicotine can produce a long-lasting nAChR inactivation which can be distinguished from reversible nAChR desensitization. The phenomenon may have important implications for the use of nicotinic agonists as therapeutic agents or in smoking cessation programs. Rowell, P.P., Duggan, D.S. Neuropharmacology. 37(1), pp. 103-111, 1998.

Highly Delta-Receptor Selective Peptides Useful as Chemical Probes

A recent report has described the preparation and pharmacological properties of several cyclic enkephalin peptide analogs, having the structure Tyr-c[D-Pen-Gly-Phe(p-X)-Pen]-Phe-OH, which show high potency at the delta receptor in the rat brain. In addition, when part of the chemical structure (the 4-X-phenylalanine (p-X)) is substituted for iodine, chlorine, or fluorine, very high selectivity ratios of 10000-45000 for delta opioid versus mu opioid binding were found. H-Tyr-c[D-Pen-Gly-Phe(p-F-Pen]-OH, exhibited an exceptionally low IC50 value of 0.016 nM. These peptides may serve as potentially useful probes in opioid research. Hruby, et al. J. Medicinal Chemistry. 40, pp. 3957-3962, 1997.

Extraordinary Potency of a Novel Delta Opioid Receptor Agonist

A new cyclic opioid peptide Tyr-D-Pen-Gly-Phe-Cys-Phe (HBP2) was evaluated for its delta-receptor interaction. HBP2 was approximately 160 times as potent as a standard delta-opioid ligand, DPDPE. Estimation of the affinity and efficacy of the peptide revealed that the higher potency of HBP2 was due to a 5.3-fold increase in efficacy and 37-fold increase in affinity. This compound may serve as a good receptor probe. Kramer, et al. Life Sciences. 61(2), pp. 129-135, 1997.

Dopamine Transmission in the Nucleus Accumbens as a Function of Free-Choice Novelty

To assess dopamine efflux during novelty-seeking behavior in rats, fast-scan cyclic voltammetry in the nucleus accumbens was combined with free-choice entry into a novel environment. Cyclic voltammograms, confirmed by in vitro testing, revealed that entry into novel, but not familiar, surroundings increased dopamine efflux in a regionally and temporally distinct pattern. Whereas dopamine failed to change in the core region of the accumbens and overlying neostriatum, an abrupt increase occurred in accumbal shell, a limbic-related area implicated in goal-directed behavior. Although the dopamine response was confined to the brief period of entry into novelty (approximately 8 s duration), a less rapid and more persistent dopamine change (> 20 s duration) occurred in the shell-core transition zone. These results suggest that novelty mimics other positively reinforcing stimuli in enhancing dopamine transmission in the nucleus accumbens, but the regional and temporal heterogeneity of this effect may represent different aspects of accumbal dopamine function. Rebec, G.V., Christensen, J.R., Guerre, C. & Bardo, M.T. Regional and Temporal Differences in Real-Time Dopamine Efflux in the Nucleus Accumbens During Free-Choice Novelty. Brain Research. 776(1-2), pp. 61-67, 1997.

Repeated Amphetamine Produces Persistent Structural Changes in Nucleus Accumbens and Prefrontal Cortex Neurons

Terry E. Robinson and Bryan Kolb at the University of Michigan found that repeated administration of amphetamine produces morphologic changes lasting more than a month in neurons in the nucleus accumbens and prefrontal cortex in rats. The exposure to amphetamine produced an increase in the length of dendrites, in the density of dendritic spines, and in the number of branched spines on the medium spiny neurons of the accumbens, and similar effects on the apical, but not basilar, dendrites of layer III pyramidal neurons in the prefrontal cortex. The ability of amphetamine to alter patterns of synaptic connectivity in these brain structures may contribute to some of the long-term behavioral consequences of repeated amphetamine use, including amphetamine psychosis and addiction. Robinson, T.E., Kolb, B. J. Neurosci. 17, pp. 8491-8497, 1997.

Catecholaminergic Activity in the Forebrain During Exposure to Novelty

Voltammetric recordings with electrochemically modified carbon-fiber electrodes were obtained from specific regions of the forebrain in rats given free-choice access to a novel environment. Entry into novelty increased the catechol signal in the medial prefrontal cortex and shell of the nucleus accumbens by more than 100%, but had no consistent effect in either the neostriatum or accumbal core. In both the medial prefrontal cortex and accumbal shell, moreover, the novelty-induced increase in catecholaminergic activity was detectable only during the initial entry into the novel compartment and did not reappear when animals returned to the familiar environment. These results support increasing evidence for a functional distinction between the accumbal core and shell, with the latter having been linked to brain reward mechanisms. The results also indicate that novelty activates some of the same neurochemical systems believed to play a critical role in the reinforcing effects of certain drugs of abuse. Rebec, G.V., Grabner, C.P., Johnson, M., Pierce, R.C., & Bardo, M.T. Transient Increases in Catecholaminergic Activity in Medial Prefrontal Cortex and Nucleus Accumbens Shell During Novelty. Neuroscience. 76(3), pp. 707-714, 1997.

Reviewing the Neuropharmacologic Mechanisms of Drug Reward

Multiple lines of research have implicated the mesolimbic dopamine system in drug reward measured by either the drug self-administration or conditioned place preference paradigm. The present review summarizes recent work that examines the neuropharmacological mechanisms by which drugs impinge on this dopaminergic neural circuitry, as well as other systems that provide input and output circuits to the mesolimbic dopamine system. Studies examining the effect of selective agonist and antagonist drugs administered systemically have indicated that multiple neurotransmitters are involved, including dopamine, serotonin, acetylcholine, glutamate, GABA, and various peptides. Direct microinjection studies have also provided crucial evidence indicating that, in addition to the mesolimbic dopamine system, other structures play a role in drug reward, including the ventral pallidum, amygdala, hippocampus, hypothalamus, and pedunculopontine tegmental nucleus. GABAergic circuitry descending from the nucleus accumbens to the pedunculopontine tegmental nucleus via the ventral pallidum appears to be especially important in directing the behavioral sequelae associated with reward produced by various drugs of abuse. However, activation of the reward circuitry is achieved differently for various drugs of abuse. With amphetamine and cocaine, initiation of reward is controlled within the nucleus accumbens and prefrontal cortex, respectively. With opiates, initiation of reward involves the ventral tegmental area, nucleus accumbens, hippocampus, and hypothalamus. It is not clear presently if these multiple anatomical structures mediate opiate reward by converging on a single output system or multiple output systems. Bardo, M.T. Neuropharmacological Mechanisms of Drug Reward: Beyond Dopamine in the Nucleus Accumbens. Critical Reviews in Neurobiology. 12(1-2), pp. 37-67, 1998.

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Research Findings

Behavioral Research

Anti-Craving Medications and Incentive Motivation

Environmental cues associated with drugs of abuse may elicit craving and contribute to relapse. A 'reinstatement' model of self-administration with cocaine has been proposed to mimic the incentive motivational properties of these cues. In phase I of the experiment rats were trained to press a lever to receive a cocaine infusion in the presence of certain environmental cues. In phase II, in the absence of the previously paired environmental cues, these rats continued to press the lever but were not given cocaine and eventually bar pressing stopped. In phase III, however, when the original environmental cues were re-introduced, control rats began to bar press again wheras experimental rats chronically administered DMI, a noradrenergic reuptake blocker, did not return to bar pressing. This suggests that these cues activate motivational processes which drive drug-seeking behavior. Dr. Janet Neisewander at Arizona State University recently reported that chronic treatment with a noradrenergic reuptake blocker, desmethylimipramine (10 mg/kg DMI/day), attenuated responses made on the drug lever following cue presentation in extinction. As DMI has been demonstrated to possess 'anti-craving' properties in some patient populations, this observation suggests that a possible mechanism for this anti-craving effect may be the blockade of incentive motivational properties associated with drug-related stimuli. Fuchs, R.A., Tran-Nguyen, T.L., Specio, J.E., Groff, R.S., Neisewander, J.L. Psychopharmacology. 135, pp. 151-160, 1998.

Cocaine Effects on Cocaine Versus Food-Maintained Responding

This project by Dr. J.R. Glowa is examining the effects of continuously infusing cocaine on cocaine- versus food-maintained operant responding in rhesus monkeys. When animals worked to self-administer low doses of cocaine (10 &g/kg/injection), additional non-contingent continuous cocaine infusion decreased such responding in a dose-related manner but without affecting food-maintained responding. In contrast, when animals self-administered at higher doses of cocaine (56 &g/kg/injection), additional cocaine infusion decreased both cocaine- and food- maintained responding. These data show that long-acting agonist approaches to pharmaco-therapy of cocaine are viable, but are dependent on dose and the event that maintains responding. Glowa, J.R., Fantegrossi, W.E. Drug and Alcohol Dependence.45, pp.71-79, 1997.

Establishing Preference for Oral Cocaine

In prior research, Dr. John L. Falk has shown in rats that preference for oral cocaine, as well as preference for non-reinforcing lidocaine, can be established by pairing it with a highly palatable vehicle such as dilute ethanol or a glucose/saccharin solution which is then slowly faded out. Dr. Falk has now reported that preference for cocaine can also be established by exposing the rats to a history of choosing cocaine in preference to lidocaine. This work along

with the prior work suggest that two kinds of historical associations may be involved in the establishment of drugs as reinforcers: Drug preference can be acquired, on the one hand, by the avoidance of an aversive alternative; and, it can also result from a past association with a positively reinforcing social context. This work makes it clear that pharmacological consequences often may not be the major factor initiating and sustaining chronic drug-taking. The person's history of an association of drug-taking with the satisfaction of other motives allows drug-seeking and drug-taking behavior to be maintained at a high level long after the original motives are no longer operative. Falk, J.L., Lau, C.E. Establishing Preference for Oral Cocaine Without an Associative History with a Reinforcer. Drug and Alcohol Dependence. 46, pp. 159-166, 1997.

Morphine's Immunosuppressive and Analgesic Effects: Time Course Comparison

The possibility of a relation between morphine's immunosuppressive effects and its analgesic effects was examined by comparing the time courses of these two measures. Following a subcutaneous injection of morphine (15 mg/kg), immune system measures (i.e., NK activity, proliferation of T- and B-cells and cytokine production) and antinociception (using the tail-withdrawal assay) were assessed across a 24-hr period. Maximal suppression occurred after 1 hr with recovery complete within 24 hours, while morphine-induced antinociception occurred in 30 minutes to 2 hours, with recovery complete within 6 hours. These results suggest that different mechanisms may be modulating morphine's immunosuppressive effects and its analgesic effects. Nelson, C.J., Dykstra, L.A., Lysle, D.T. Anesthesia and Analgesia. 85, pp. 620-626, 1997.

Effects of Rearing on Morphine-Induced Behavior and Neurology

Rats were raised from weaning (21 days old) to young adulthood (50-60 days old) in either an enriched or impoverished stimulus environment. In the enriched condition (EC), rats were group-housed with various novel objects that were re-arranged daily. In the impoverished condition (IC), rats were housed individually without any objects. As adults, a four-trial conditioned place preference (CPP) test was used to assess locomotor activity and reward produced by morphine (0, 0.1, 1 or 10 mg/kg). On morphine conditioning day 1, both EC and IC rats displayed an inverted U-shaped dose-effect curve for locomotor activity and the locomotor stimulant effect of acute morphine was greater in IC than EC rats. Across morphine conditioning days 1-4, both EC and IC rats displayed locomotor sensitization; the locomotor sensitization following repeated morphine injections was greater in IC than EC rats. In contrast to the enhanced locomotor stimulant effect of morphine observed in IC rats, morphine-induced CPP was attenuated in IC rats relative to EC rats, indicating that the locomotor and rewarding effects of opioids depend upon different neural substrates. Measurement of mu opioid receptor density and rates of morphine-stimulated dopamine synthesis in the mesolimbic and nigrostriatal systems of EC and IC rats revealed no reliable differences between groups. Therefore, the ability of mu opioid receptors to modulate mesolimbic dopamine neurotransmission does not account for the differential behavioral effects of morphine in EC and IC rats. Bardo, M.T., Robinet P.M., & Hammer, R.F., Jr. Effect of Differential Rearing Environments on Morphine-Induced Behaviors, Opioid Receptors and Dopamine Synthesis. Neuropharmacology. 36(2), pp. 251-259, 1997.

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Research Findings

Clinical and Services Research

Neuroimaging and Episodic Memory Retrieval

Fred L. Bookstein, Ph.D. at University of Michigan and colleagues have explored interactions between brain areas that may be determinates of cognitive and behavioral operations. They used positron emission tomography (PET) regional cerebral blood flow (rCBF) to study patterns of episodic memory retrieval. Subjects were presented words lists and were asked to process different types of information, reflecting differential levels of processing. Functional connectivity of voxels located within Brodmann areas 10 and 45/47 in the right prefrontal cortex and the left hippocampus with the rest of the brain. Area 10 and left hippocampus showed an opposite pattern of functional connectivity, with a large expanse of bilateral limbic cortices that was equivalent in all tasks. However, during high retrieval, area 45/47 was included in this pattern. The results suggest that activity in portions of the right prefrontal cortex reflects either memory retrieval mode or success, depending on other brain regions that are functionally linked. As researchers parse the concept of emotional memory and the implications of emotion and memory for brain models of addiction, a focus upon systems-level interactions will be crucial. McIntosh, A.R. et al., Human Brain Mapping, 5(4), pp. 323-327, 1997.

Marijuana Intoxication and Disturbed Time Sense

Roy J. Mathew, M.D. and collegues at Duke University Medical Center studied the effects of THC infusion on brain activation in 46 marijuana smokers with regional cerebral blood flow (CBF) measured with positron emission tomography (PET) and magnetic resonance imaging (MRI). This group found, consistent with previous reports, a significant increase in cortical and cerebellar blood flow following THC, but not all subjects showed this effect. Those who showed a decrease in cerebellar blood flow also had a significant alteration in time sense. Alteration in time sense, as demonstrated with these THC results, can cause a distortion in the subjective framework through which an individual views and orients himself/herself, and has implications for episodic memory formation, cognitive thought processes and goal-directed behaviors. The relationship between decreased cerebellar flow and impaired time sense is of particular interest because the cerebellum has been linked to an internal timing system. Brain Research, In Press.

Attention Deficit Disorder among Substance Abusers

Howard Schubiner, M.D. and his colleagues at Wayne State University School of Medicine have been studying the prevalence of Attention Deficit Hyperactivity Disorder (ADHD) in a cross-section sample of adults seeking substance abuse treatment. ADHD is considered to be a genetic and neurobiological disorder with a 5% prevalence rate in all

children within the U.S. In a sample of 201 adult substance abusers (106 males and 95 females) 24% were found to meet DSM-IV clinical criteria for ADHD (as a child and as an adult). The gender prevalence in males was 28% and 19% in females, a non-significant difference. Overall, substance abusers with ADHD (compared to substance abusers without ADHD) were more likely to have conduct disorder and antisocial personality disorder (ASPD) and more motor vehicle accidents. Gender effects were noted. While the use of specific types of drugs was not significantly different between the groups of substance abusers with and without ADHD, female substance abusers with ADHD had an increased number of treatments for alcohol abuse and dependence. (The above findings were presented at the at the *Fifth Annual Conference on Behavior, Neurobiology, Substance Abuse, and Culture*, on October 16, 1997, in Los Angeles, California).

Computerized Scheduling of Nicotine Gum Use

Dr. Albert Jerome from PICS, Inc. in Reston, VA, has received SBIR funding from NIDA to conduct smoking cessation research with a product his company developed called LifeSign. LifeSign is a credit card-sized computer that uses a scheduled, gradual reduction protocol to help smokers quit. Their most recent work combines a customized version of LifeSign with nicotine gum. A randomized outcome study was conducted to collect preliminary data on effectiveness. The experimental group (LS-N), used computer prompts to determine when to begin and stop chewing each piece of nicotine gum. The computer gradually increased intervals between gums until gum use was eliminated completely. The comparison group was standard ad lib gum users in an eight-week self-help study. Findings indicated significantly better treatment outcomes for the LS-N group than for the gum only group across a variety measures. More subjects in the LS-N condition were abstinent at posttreatment (29% vs. 11%); and the percentage of subjects who quit for at least 24-hours was greater in the LS-N condition (76% vs. 39%). Analysis of self-reported gum use showed that the LS-N group used more gum during the first week following a quit attempt and that the amount of gum used during the first week was positively related to abstinence at posttreatment. A recently completed one-year follow-up showed that the relative advantage of the LS-N program was maintained (17% vs. 5% abstinent).

Menstrual Cycle Effects on Tobacco Cessation Symptoms

Dr. Sharon Allen at the University of Minnesota, has conducted a study to examine the effects of the menstrual cycle on smoking behavior in women during continued smoking and quit smoking status. Withdrawal and premenstrual symptomatology during phases of the menstrual cycle were investigated. Preliminary analysis indicated that there were no significant differences in withdrawal symptom scores across menstrual cycle phases in both the continued smoking and quit smoking groups. As expected, premenstrual symptom scores tended to be higher in the late luteal phase compared to the follicular phase in both the continued smoking ($p=.03$) and quit smoking ($p=.0014$) groups. Although total withdrawal symptom scores do not differ significantly across cycle phases, these findings suggest that smoking cessation may be more difficult in the late luteal phase due to increased premenstrual symptoms. Christianson, D., Allen, S., Hatsukami, D., Nelson, D. Smoking Withdrawal and Premenstrual Symptomatology Across Menstrual Cycle Phases. Presented at the Society for Research on Nicotine and Tobacco. March, 1998.

Efficacy of Lithium Treatment for Adolescents With Bipolar Disorders and Secondary Substance Dependency

Dr. Barbara Geller and colleagues at the Washington University School of Medicine conducted a 6-week double-blind, placebo-controlled, parallel group clinical trial to assess the efficacy of lithium for 16 male and 9 female adolescents (12-18 years) with a primary DSM-III-R bipolar disorder and secondary substance dependency disorder. Results indicate lithium to be an efficacious treatment for both disorders in terms of concurrently reducing symptoms of psychopathology (e.g., improved mood) and the use of illicit substances. No gender differences were noted. Geller, B., Cooper, T.B., Sun, K., et al. Journal of the American Academy of Child and Adolescent Psychiatry, 37(2), pp. 171-178, 1998.

Efficacy of Imipramine Treatment for Opiate-Dependent Patients With Depressive Disorders

Drs. Nunes, Quitkin, Donovan and colleagues at the New York State Psychiatric Institute and Columbia University conducted a single-blind, placebo-controlled clinical trial to assess the efficacy of imipramine hydrochloride for opiate-dependent patients with a DSM-III-R depressive disorder receiving treatment at community-based methadone maintenance clinics. One hundred and thirty-seven patients were randomized to a 12-week trial. Of these, 53

dropped out (non-compliance did not differ between the imipramine-treated and placebo-treated groups) and 84 completed a minimum adequate trial of at least 6 weeks. Of the 84, 57% receiving imipramine were rated as responders (i.e., reduced substance use and reports of craving; improved mood) compared with 7% receiving the placebo ($p<.001$). Nunes, E.V., Quitkin, F.M., Donovan, S.J., et al. Archives of General Psychiatry, 55(2), pp. 153-160, 1998.

Progression From Conduct Disorder to Antisocial Personality Disorder Following Treatment for Adolescent Substance Abuse

Drs. Mark Brown, Sandra Brown and colleagues at the University of California, San Diego, conducted a prospective longitudinal study of 137 substance-abusing adolescents (mean age at intake 15.9 years) who met DSM-III-R criteria for Conduct Disorder. Subjects (39% female) recruited from two adolescent inpatient drug treatment programs were interviewed at intake and again 4 years later. Results indicate that four years after treatment 61% (N=84) of the study group met DSM-III-R criteria for Antisocial Personality Disorder (APD), of which males were disproportionately represented (N=60) compared to female subjects (N=24; $p<.005$). Pretreatment clinical characteristics which predicted post-treatment APD include deviant behavior at or before age 10, greater diversity of deviant behaviors independent of substance use during childhood and early adolescence, and more extensive drug, but not alcohol use during the 30 days before admission to the program. These findings suggest a poorer prognosis for adolescents when conduct disorder is diagnosed independent of drug use, whereas more favorable drug treatment outcomes might be achieved with adolescents whose pretreatment diagnosis of conduct disorder occurred primarily in the context of or subsequent to their use of illicit substances. Myers, M.G., Stewart, D.G., and Brown, S.A. American Journal of Psychiatry, 155(4), pp. 479-485, 1998.

Validity of Substance Use Self-Reports in Dually Diagnosed Outpatients

Dr. Roger Weiss and colleagues at the Department of Psychiatry, Harvard Medical School compared the self reports of substance use with supervised urine samples collected on the same day for subjects participating in two separate studies, each designed to test a new group psychotherapy for patients with coexisting substance use disorder and with either PTSD or bipolar disorder. The mean age of the subjects was 35.2 years. All subjects in the PTSD group were women, by design, and 53.8% of the subjects in the bipolar group were men. Most patients, 69% had both alcohol and drug dependence and 95.6% were dependent on more than one drug. Marijuana and cocaine were the most common primary drugs of abuse. Results indicate that self reports were highly valid. Only 4.7% of cases involved subjects not reporting substance use detected by urine screens. Weiss, R., Najavits, L., Greenfield, S., Soto, J., Shaw, S., Wyner, D. American Journal of Psychiatry, 155, pp. 127-129, 1998.

Association of Antibody to GB Virus C (Hepatitis G Virus) with Viral Clearance and Protection from Reinfection

GB virus C (GBV-C) RNA and envelope antibody (anti-GBV-C) were assessed in samples collected over 6.5 years among injection drug users (IDUs). A marker of GBV-C infection was detected in 110 (94.8%) of 166 IDUs. GBV-C RNA was detected at all visits in 32 IDUs, was never detected in 70 IDUs, was acquired in 7 and was cleared in 8 IDUs. The odds of detecting anti-GBV-C were 103-fold higher in participants without detectable RNA (64/70) than in IDUs with persistent RNA (3/32). Antibody was detected in all 8 instances of viral clearance. GBV-C RNA did not reappear once cleared and no new infections occurred in 61 anti-GBV-C positive IDUs followed for 382 person years, although all reported ongoing drug use. The study findings suggest that RNA testing alone may significantly underestimate the occurrence of GBV-C infection and demonstrate that anti-GBV-C is highly associated with viral clearance and protection from reinfection. Thomas, D.L., Vlahov, D., Alter, H.J., Hunt, J.C., Marshall, R., Astemborski, J., Nelson, K.E.. J Infect Dis, 177, pp. 539-542, 1998.

Amount of Prenatal Cocaine Exposure and Birth Outcomes

Two recent publications from researchers at the University of Florida add to the growing body of evidence for the importance of studying the amount of exposure when examining developmental outcomes associated with use of drugs during pregnancy. In this prospective, longitudinal project, 154 women were identified during pregnancy as using cocaine, and 154 comparison women as not using cocaine, but matched on race, parity, socioeconomic status,

and location of prenatal care (which related to level of pregnancy risk). Data analyses included control for marijuana, alcohol, and tobacco use. Although there were no overall differences between the two groups on gestational age, birth weight, or birth length, there was a significant relationship between the amount of cocaine used in the third trimester, and newborn length and head circumference. Similarly, the reported amount of cocaine use in the third trimester was negatively associated with measures of state regulation, alertness, and the ability of the infant to orient to the environment. These findings raise concerns about later developmental abilities of these infants. The researchers are continuing to follow the development of these children. Eyler, F.D., Behnke, M., Conlon, M., Woods, N.S., Wobie, K. Birth Outcome from a Prospective, Matched Study of Prenatal Crack/Cocaine Use: I. Interactive and Dose Effects on Health and Growth. Pediatrics, 101, pp. 229-237, 1998; Eyler, F.D., Behnke, M., Conlon, M., Woods, N.S., Wobie, K. Birth Outcome from a Prospective, Matched Study of Prenatal Crack/ Cocaine Use: II. Interactive and Dose Effects on Neurobehavioral Aassessment. Pediatrics, 101, pp. 237-241, 1998.

Cocaine-Induced Cerebral Vasoconstriction Detected in Humans with Magnetic Resonance Angiography

In a double-blind randomized controlled trial, Mendelson and his colleagues at Harvard Medical School have shown that cocaine is associated with cerebrovascular complications in humans. Twenty-four healthy neurologically normal men (av.age 29 yrs; reporting median cocaine use of 8 lifetime exposures [range, 3 to >40]) were administered iv cocaine 0.4 or 0.2 mg/kg, or placebo. The cerebral magnetic resonance angiography was performed at baseline and 20 min following infusion. Results showed that cocaine induced cerebral vasoconstriction in a dose-related fashion ($p=0.03$), with angiograms indicative of vasoconstriction in 5/8 and 3/9 subjects at 0.4 or 0.2 mg/kg, cocaine, respectively, compared with 1/7 injected with placebo. These changes occurred at low cocaine doses and in the absence of other risk factors, including polydrug abuse, hypertension, or cerebrovascular disease. Outcome stratification by prior use of cocaine (3-10, 11-40 times, or >40 times) statistically strengthened the relationship between cocaine administration and vasoconstriction in a dose-related manner ($p<0.001$), further suggesting that cocaine may have a cumulative residual effect in promoting cerebrovascular dysfunction. Kaufman, M.J., Levin, J.M., Ross, M.H., Lange, N., Rose, S.L., Kukes, T.J., Mendelson, J.H., Lukas, S.E., Cohen, B.M., and Renshaw, P.F. JAMA, 279 (5), pp. 376-380, 1998.

Why Different Rules are Required for Polygenic Inheritance

Controversy continues to rage over the best methodology for studying the molecular genetics of drug abuse and addiction. David Comings at the City of Hope Medical Center delineates the issues, arguing that drug abuse like other complex disorders is likely to be polygenic with many genes contributing 5% of the variance or less. Furthermore, he suggests that if, for example, 24 genes are associated with the disorder, it may be that one needs only a fraction of them, say 8, to precipitate the phenotype as defined by diagnostic techniques. But due to heterogeneity, the same 8 or more genes may not be present in everyone with the disorder, and many without the disorder will have a proportion of the purportedly causative genes. Accordingly, some of the more popular methodology for finding these genes, such as *haplotype relative risk* or *sib-pair* analyses lose considerable power. In addition, the concept of *heterosis* is ignored. Heterosis is the situation where the heterozygote is either the causative or protective genotype (cf. Hybrid corn) rather than the homozygote with or without two copies of the mutant allele. The article concludes that both heterogeneity and especially the polygenic nature of the disorders under study need to be considered rather than a more traditional one gene-one disease approach. Comings, D.E. Alcohol, 15(5), pp. 1-10, 1998.

Comparative Treatment Effectiveness: Effects of Program Modality and Client Drug Dependence History on Drug Use Reduction

. This study examined treatment outcome as a function of program modality, clients' lifetime patterns of drug dependence, and their interaction, controlling for current level of drug use at treatment intake. Data were based on almost 3,000 clients who were interviewed at intake and one-year follow-up as part of the national Drug Abuse Treatment Outcome Study (DATOS). Subjects' lifetime patterns of drug dependence were classified into nine groups according to the Diagnostic and Statistical Manual of mental Disorders (DSM-III-R; American Psychiatric Association; 1987) diagnostic criteria and time of onset of drug use career. Outcome measure was the reduction of heroin use or cocaine use. The presence of dependence diagnosis was associated with less improvement when current use level at intake was controlled. Clients dependent on heroin but not currently daily users benefited most from inpatient and residential programs. Methadone programs were also relatively ineffective in reducing cocaine use. Characteristics of the client's drug dependence history, in addition to the current or presenting drug problem, should be assessed to

guide treatment planning. The high rate of cocaine dependence among methadone clients, most of whom were dependent on heroin, poses considerable challenge to contemporary opiate substitution treatments. Hser, Y.I., Anglin, M.D., and Fletcher, B. Journal of Substance Abuse Treatment, 15(1), pp. 1-11, 1998.

ERP Amplitude Anomalies in Children at Risk for Substance-use Disorders

Previous research has considered event-related potentials (ERPs) in relation to liability for alcohol and other substance use. This study explored ERPs in preadolescent boys at elevated risk for substance use due to paternal history of substance abuse or dependence. Sons (age 10-12) of fathers with an alcohol-use disorder (ALC, n = 29) were matched by age, IQ, education and parental alcohol use with sons of fathers with a polysubstance abuse or dependence diagnosis (POLY, n = 37). These two groups were matched with a low-risk comparison group (LOW, n = 29) of boys whose fathers had no substance-use disorder diagnosis. No boy in the study met criteria for a substance-use disorder. ERPs were collected from midline (Fz, Ct, Pt) and parietal (P3, P4) electrode leads during an auditory oddball task. ERPs of boys from the ALC and POLY groups showed a slow negative shift prominent at Ct and Pz. This negative shift, evident by 100 ms post-stimulus and lasting for the duration of the 1000-ms recording period, overlapped temporally with N1, N2 and P3 amplitude differences distinguishing the ALC and POLY groups from the LOW group. The ALC and POLY groups differed from each other in N2 amplitude at Ct, which was larger for ALC subjects. These findings offer a possible alternative explanation for previously observed amplitude anomalies noted in children at risk for substance-use disorders and suggest new avenues of inquiry. Brigham, J., Moss, H.B., Murrelle, E.L., Kirisci, L., and Spinelli, J.S. Psychiatry Research, 73(3), pp. 133-146, 1997.

A Discrete Choice Model of Drug Abuse Treatment Location

Goodman and his associates used three years of insurance claims for 9,878 individuals representing 10 large self-insured firms to examine determinants of inpatient care for disorders related to drug abuse. In addition to examining the effects of individual characteristics on treatment utilization, the research focused on the ways in which differences among firms affect the choice of treatment location. The probability of inpatient drug treatment was found to be related to diagnosis of a cocaine problem (abuse or dependence), a diagnosis of drug *dependence* (versus abuse), and a diagnosis of psychosis. Men were more likely to be hospitalized than women. Controlling for patient risk factors, where patients are employed and have insurance made a substantive difference in the probability of receiving inpatient treatment, with the firm-specific probability varying by as much as 87 percent. Over time, a trend toward more use of outpatient treatment was observed. Goodman, A.C., Nishiura, E. & Hankin, J.R. A Discrete Choice Model of Drug Abuse Treatment Location. Health Services Research, In Press.

Costs and Utilization of Short Term Drug Abuse Treatment

This paper investigates three aspects of drug abuse treatment costs emphasizing systematic differences among employers: predictors of costs, differentials in costs across employers, and differential effects of patient and employer characteristics on treatment costs. The study uses insurance claims data from ten large self-insured employers over a three-year period starting January 1989. Principal findings are (1) marginal inpatient costs generally exceed average costs, implying increasing cost per day as utilization increases; (2) for outpatient treatment, marginal costs are slightly less than average costs, implying outpatient drug treatment maintains slightly decreasing costs as utilization increases; and (3) analyses of cost differences among employers suggest that observed differences among employers and/or their carriers and providers appear to be at least as important as the characteristics of the people covered or the care provided. In summary, policies aimed at reducing drug treatment costs are likely to have differing impacts on different employers. Goodman, A.C., Nishiura, E. & Hankin, J.R. Short Term Drug Abuse Treatment Costs and Utilization: A Multi-Employer Analysis. Medical Care, In Press.

Cost and Usage Impacts of Treatment Initiation

Using insurance claims data from 10 large self-insured firms, a study was carried out to explore the impact of alcohol and drug abuse treatment on subsequent alcohol, drug abuse, and medical treatment utilization and costs. The study provides an analysis of the relationship between type (inpatient or outpatient) and intensity of utilization and costs. Findings indicate that treatment cost models may differ from treatment usage models. For example, inpatient drug treatment was negatively associated with medical treatment in the 6 months following drug treatment initiation, but longer inpatient drug abuse treatment was associated with increasingly higher costs. The cost and utilization models

for drug abuse treatment were very similar to those for alcohol treatment. For both, the largest costs of coincident and subsequent treatment were for (1) inpatient treatment, and (2) treatment occurring within 6 months of initiation of drug or alcohol treatment. Goodman, A.C., Nishiura, E., and Humphreys, R.S. Cost and Usage Impacts of Treatment Initiation: A Comparison of Alcoholism and Drug Abuse Treatments. Alcoholism: Clinical and Experimental Research, 21, pp. 931-938, 1997.

Drug Treatment Outcomes and Physical and Sexual Abuse

Relationships between psychopathology, drug treatment outcomes, and history of physical or sexual abuse were examined in a longitudinal study of 330 patients in 26 outpatient programs. Both forms of abuse were found to be associated with higher levels of psychopathology, but with significant gender differences. For women in the study, sexual abuse was associated with higher levels of psychological disturbance, while physical abuse was associated with less disturbance. The inverse relationship was found for men: physical abuse was associated with several types of psychological disturbances, while sexual abuse was associated only with anxiety disorder. The study points to the need to assess histories of sexual and physical abuse in assessing and treating co-occurring psychopathology. Gil-Rivas, V., Fiorentine, R., Anglin, M.D., and Taylor, E. Sexual and Physical Abuse: Do they Compromise Drug Treatment Outcomes? Journal of Substance Abuse Treatment, 14, pp. 351-358, 1997.

Costs and Incentives in A Behavioral Health Carve-Out

A carve-out of mental health and substance abuse services initiated in 1993 by the Group Insurance Commission (GIC) of the Commonwealth of Massachusetts resulted in changes in the costs of those services. Those changes were related to incentives in the contract between the GIC and its managed behavioral health vendor. Total and plan costs were reduced by 30-40 percent after adjusting for trends. Incentives to produce savings of this magnitude not only were a consequence of the payer/ vendor contract but also appeared related to the growth potential of companies in the managed behavioral health care market. Ma, C. and McGuire, T.G. Health Affairs, 17, p. 54, 1998.

Drug Treatment Careers, A Conceptual Framework and Existing Research Findings

While outcomes for any single intervention are important to determine, the treatment careers perspective provides a useful framework to evaluate the long-term effects of multiple sequential interventions, leading to a better understanding of drug dependence and its treatment. The analytic model involves a longitudinal dynamic approach to identify and understand key factors in drug abuse treatment, including treatment seeking, utilization and resistance, entry and reentry, engagement and retention, client treatment matching, and outcomes. Key findings include high resistance to entering treatment by many drugs users, late development of treatment careers relative to addiction and criminal careers, short durations of most treatment episodes, cumulative and facilitative effects of treatment experiences, and beneficial effects of matching clients to treatment. Hser, Y-I., Anglin, M.D., Grella, C., Longshore, D. and Prendergast, M. J of Subs Abuse Treatment, 14(6), pp. 543-558, 1997.

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National Institute on Drug Abuse

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

May, 1998

Research Findings

AIDS Research

Vitamin A Supplementation and Human Immunodeficiency Virus Load in Injection Drug Users

The use of vitamin A therapy in HIV infection has been under investigation for its potential efficacy in modulating replication of HIV. A randomized, double-masked, placebo-controlled clinical trial was performed in drug users to determine the impact of a single high-dose vitamin A supplementation, 60-mg retinol equivalent (200,000 IU), on HIV viral load and CD4 count. One hundred-twenty HIV-infected injection drug users were randomly assigned to receive vitamin A or placebo. Plasma vitamin A levels, CD4 lymphocyte counts, and HIV viral load were assessed at baseline and at 2 weeks and 4 weeks post-treatment. Vitamin A supplementation had no significant impact on viral load or on CD4 count at 2 weeks or at 4 weeks post-treatment. Study results indicate that high-dose vitamin A supplementation does not influence viral load in HIV infection. Semba, R.D., Lyles, C.M., Margolick, J.B., Caiaffa, W.T., Farzadegan, H., Cohn, S., and Vlahov, D. J Infect Dis, 177, pp. 611-616, 1998.

Prognostic Indicators for AIDS and Infectious Disease Death in HIV-Infected Injection Drug Users: Plasma Viral Load and CD4+Cell Count

Plasma HIV viral load and CD4 count, markers used to predict prognosis in HIV-infected individuals, were analyzed to determine whether these markers in combination improve prognostic accuracy and whether they predicted prognosis in a predominantly African-American population of HIV-infected IDUs. Plasma HIV RNA and CD4 cell count were measured at baseline and compared with time to first clinical AIDS diagnosis and time to death due to an infectious disease in 522 subjects (96% African-American, 80% male, median age 33, 96% active injectors in prior 6 months). A total of 146 cases of AIDS and 119 infectious disease deaths occurred during a median follow-up period of 6.4 years. Baseline levels of viral load and CD4 cell count were independent predictors of progression to AIDS and infectious disease deaths, but in proportional hazards models, viral load had better predictive value than CD4 cell count. Analysis of time to AIDS and to infectious disease deaths by viral load categories (<500; 500-9999; 10,000-29,000; >=30,000 copies/mL) at 3 levels of CD4 cell count (<200; 200-499; >=500/mm^3) was reduced to a 5-stage classification scheme. The 5-year cumulative probabilities for AIDS and infectious disease deaths ranged from 0% and 0%, respectively, for those with viral load <500 copies/mL and CD4 count >=500/mm^3 (stage 1) to 81% and 76%, respectively, for those with viral load >=10,000 copies/mL and CD4 cell count 200-499/mm^3 (stage 5). This study demonstrated that plasma HIV viral load independently and in combination with CD4 cell count measurements provided powerful prognostic information for progression to AIDS and to death caused by infectious disease in this population of IDUs. Combining categories of both markers provided a simple method for prognostically staging HIV disease. Vlahov, D., Graham, N., Hoover, D., Flynn, C., Bartlett, J.G., Margolick, J.B., Lyles, C.M., Nelson, K.E., Smith, D., Holmberg, S., and Farzadegan, H. JAMA, 279, pp. 35-40, 1998.

Temporal Trends in the Progression of HIV Disease in a Cohort of Drug Users

Changes over time in rates of progression to AIDS, mortality, and distribution of AIDS-defining illnesses were evaluated in a prospective cohort of HIV+ drug users. Study participants attended a methadone maintenance program with on-site primary care and were enrolled between 1986 and 1995. Data were analyzed among 524 HIV-infected drug users (42% female, 64% Hispanic, 23% black, 14% white); 92% reported illicit drug use during follow-up and 77% reported injection. No specific drug or route of administration was prominently associated with progression to AIDS. AIDS-defining illnesses occurred in 98/524 persons (18%), an overall rate of 5.5/100 person years (PY). Among those with an initial CD4 cell count <=200/mm^3, the AIDS rate was 17.5/100 PY vs. 3.8/100 PY in those with initial CD4 cell count >200/mm^3. Those who enrolled after 1990, compared to earlier enrollees, demonstrated greater AIDS-free time: progression to AIDS declined from 19.9/100 PY to 15.0/100PY for those with CD4 cell count <=200 vs. 4.7/100PY to 2.5/100PY for those with CD4 cell count >200). The proportionate morbidity due to Pneumocystis carinii pneumonia (PCP) as the initial AIDS-defining illness declined from 33% of AIDS cases before 1990 to 17% after 1990. TB also declined, from 20% to 13% after 1990, while recurrent bacterial pneumonia increased from 10% to 20% after 1990. Recent enrollees (1994-95) had approximately one-fifth the hazard ratio (HR) of progression to AIDS compared with the reference group of participants enrolled between 1986 and 1987, after controlling on CD4 cell count and age. Overall mortality, however, did not differ significantly by year of study entry (8.9/100 PY before 1990 to 8.5/100PY after 1990). The mortality HR did not differ by year of study enrollment, controlling on age and CD4 cell count. The reduction in morbidity and greater AIDS-free time was associated with implementation of a comprehensive on-site primary care program. Webber, M.P., Schoenbaum, E.E., Gourevitch, M.N., Bouno, D., Chang, C.J., Klein, R. Epidemiology, In Press.

Assessing the Impact of HIV Risk Reduction Counseling

Changes in cognitive, psychological, and risky behavior latent variables after Traditional or Specialized AIDS education was assessed after two years using structural equation modeling (SEM) in a sample of impoverished at-risk African-American women (N=300). Both groups reported significant improvement at 2 years in their Self-Esteem and Social Resources. They also reported less Threat Perception, Avoidant Coping, Emotional Disturbance, HIV Risk Behavior, and Drug Use Behavior. There was an advantage to Specialized group membership. When compared to the Traditional group at two years, women in the Specialized group reported enhanced social resources, reduced emotional distress, less use of an avoidant coping style and less drug use. Advantages of culturally sensitive HIV risk reduction program and the importance of connecting women with social services available in their communities is discussed. Nyamathi, A.M., and Stein, J.A. AIDS Education and Prevention, 9(3), pp. 253-273, 1997.

Study Identifies Sexual Risk Behaviors among Native American Drug Users

This study describes patterns of sexual behavior and condom use in a sample of Native American drug-using men and women (N=114). Data were collected on self-reported sexual behaviors in the past 30 days, including descriptions of the most recent sex partners (up to five partners). There were 157 sex partner pairs, of which at least one partner was a drug user. Native American women (55%) were more likely than Native American men (23%) to report never using condoms for vaginal and anal sex in the last 30 days. Compared with other ethnic pair combinations, sex partner pairs composed of Native American women and white men (n=18) were least likely to use condoms (6% of pairs) and the most likely to report an injection drug user sex partner (33% of pairs). These results suggest a potential vector of HIV and other STDS between white male IDUs and Native American women and highlight the need for further qualitative and quantitative research to examine the factors underlying this pattern of sexual risk behavior. Fenaughty, A.M., et al. Sex Partners of Native American Drug Users. Journal of AIDS & Human Retrovirology, 17(3); pp. 275-282, 1998.

HIV-Risk Behaviors and Mental Health Characteristics Among Homeless or Drug Recovering Women and their Supportive Person

This paper describes risky drug and sexual behavior and mental health characteristics in a sample of 240 homeless or drug-recovering women and their most immediate source of social support. Women and their closest support sources both reported a great deal of recent non-injection drug use (56% and 52%, respectively) and lesser, though similar, amounts of recent injection drug use (12% and 14%, respectively). Over a third of both groups reported a history of

a STD and sexual activity with multiple partners. Fifty one percent of the women and 31% of their companions had CES-D scores of 27 or greater, suggesting a high level of depressive disorders in both samples. Similarly, 76% of the women and 59% of their friends had psychological well-being scores below a standard clinical cutpoint. These data suggest that homeless and impoverished women are turning to individuals who are themselves at high risk for emotional distress and risky behaviors as their main source of support. Implications relating to the importance of integrating the dyad in interventions and introducing alternate sources of support are discussed. Nyamathi, A., Flaskerud, J., and Leake, B. Nursing Research, 46(3), pp. 133-137, 1997.

Relative Impact of Two AIDS Education Programs among High-Risk Women on Cognitive, Behavioral, and Psychosocial Variables

Changes in cognitive, psychological, and risky behavior latent variables were assessed after traditional or specialized AIDS education after 2 years using structural equation modeling in a sample of impoverished at-risk African American women (N = 300). The traditional group watched an AIDS videotape and received a 1-hour basic AIDS education program. In addition to the videotape, the specialized group received a 2-hour program in which they received a demonstration of risk-reducing behaviors, discussion of problem-focused coping, and techniques to enhance self-esteem. Also, they received individualized responses to their concerns such as referrals to drug rehabilitation programs or shelters. Both groups reported significant improvement at 2 years in their self-esteem and social resources. They also reported less threat perception, avoidant coping, emotional disturbance, HIV risk behavior, and drug use behavior. When compared with the traditional group at 2 years, women in the specialized group reported more social resources, more reduced emotional distress, less use of an avoidant coping style, and less drug use. The advantages of culturally sensitive HIV risk reduction programs and the importance of connecting women with social services available in their communities is discussed. Nyamathi, A.M., and Stein, J.A. AIDS Education and Prevention, 9, pp. 253-273, 1997.

Ethnographic Study Characterizes HIV Risk Behaviors of High Risk Men

An exploratory ethnographic study was conducted in Seattle, Washington to characterize the drug use and sexual risk behaviors, social and ecological contexts, and service needs of men who use drugs and who have sex with men (DUMSM). Three ethnographic methods were used for this research: unobtrusive observations, focus group interviews, and individual interviews. Thirty DUMSM ranging between 20 to 56 years of age were interviewed for the study, 80% of whom were white, and 20% of whom were Native American, Latino, African American, and multi-racial. Nearly all of the men were HIV positive or had an AIDS diagnosis, and almost all identified themselves as gay or bisexual. A number of common themes emerged from the interviews: almost all of those interviewed injected methamphetamine and used other drugs (cocaine, MDMA, alcohol, marijuana, and heroin); almost all described an intense association between methamphetamine use and sex; and some of the men said they had moved to Seattle specifically because it had a reputation as "the hot spot" for DUMSM. Although some respondents had completed treatment and remained abstinent from methamphetamine for a period of time, most had also relapsed, explaining that they were unable to enjoy sex without it. Abstaining from methamphetamine was perceived as equivalent to abstaining from sex, and therefore made treatment entry and compliance options of last resort. The authors learned that methamphetamine was sometimes used by respondents to manage the depression they felt from being HIV positive or having AIDS. At the same time, they learned that needle sharing and unprotected sex were common among the men who reported being HIV seropositive or having AIDS, either because they assumed their injecting drug and sexual partners were also HIV positive, or because they would become so intoxicated that they'd forget they were HIV positive. Gorman, M.E., et al. Speed, Sex, Gay Men, and HIV: Ecological and Community Perspectives. Medical Anthropology Quarterly, 11(4), pp. 505-515, December 1997.

Longitudinal Theory-Based Study Predicting Needle-Disinfection by IVDUs who Share Needles

Working from the AIDS risk reduction model (ARRM) and other theories of behavior change such as the theory of reasoned action, the authors tested psychosocial antecedents of needle/syringe disinfection by 136 injection drug users who admitted sharing needles in both waves of a longitudinal study. Latent variables were developed as predictors. High perceived self-efficacy for risk reduction had a positive effect on needles/syringe disinfection attempts one year later. Self-efficacy was, in turn, related to less perceived infection risk, peer norms more favorable to risk reduction, and greater knowledge of AIDS. Behavioral intention had no significant effect on subsequent disinfection attempts. These results suggest that disinfecting needles/syringes is partly nonvolitional, that high perceived infection risk may be counter- productive to injection risk reduction, and that perceived self-efficacy, but

not intention to change behavior, may be a useful leverage point for AIDS preventive intervention. Longshore, D., Stein, J.A., and Anglin, M.D. AIDS Education and Prevention, 9, pp. 443-460, 1997.

Study Provides Guidance on Interpreting Indeterminate HIV Test Results in Prisoners

A study was conducted in Rhode Island to evaluate the significance of indeterminate HIV test results in the prison setting and to develop specific information and guidelines to direct HIV counseling of incarcerated persons with an indeterminate test result. Medical chart review was conducted for all prisoners incarcerated at the Rhode Island State Prison who had received indeterminate HIV test results between the inception of mandatory testing of inmates in 1990 and October 1996. There were 35 inmates who had an indeterminate HIV Western blot result and 31 who had follow-up HIV testing. Of the 31 with follow-up testing, 23 (74%) seroconverted. Factors strongly associated with seroconversion were drug/alcohol use, including crack cocaine and injection drug use, as well as injection drug use only. Of research studies on seroconversion rates among persons with indeterminate HIV test results, this is the highest rate ever reported. The authors suggest that many of the behaviors that put people at risk of HIV also put them at risk of incarceration, particularly drug-related activities and prostitution. In addition, many people may become infected near the time of incarceration when HIV risk behaviors are escalating. The findings indicate that indeterminate HIV test results taken on entrance to correctional institutions are more likely to represent true HIV infections in prison populations than in other groups. For this reason, counseling of prisoners with indeterminate test results should acknowledge the likelihood of seropositivity and encourage immediate confirmatory viral loading tests. Rich, J.D., et al., Interpretation of Indeterminate HIV Serology Results in an Incarcerated Population. Journal of AIDS and Human Retrovirology, 17 (4), pp. 376-379, 1998.

Needle Sharing and Sexual Risk Behaviors Among IDUs in Rio de Janeiro

This paper characterizes HIV seroprevalence and risk behaviors of IDUs in Rio de Janeiro, Brazil between 1990 and 1996. Three separate cross-sectional samples of IDUs in Rio de Janeiro were compared on the basis of demographic characteristics, HIV risk behaviors, and HIV seroprevalence, and combined analyses were performed to determine the factors associated with injection drug use risk behaviors, sexual risk behaviors, and HIV seropositivity. There were a total of 727 IDUs from the three samples, and the overall HIV seroprevalence among the combined samples was 25%. Persons recruited in the latest years (1995-1996) had lower levels of needle sharing and lower HIV seroprevalence in one of the three samples composed mainly of less educated, poorer IDUs living in deprived neighborhoods. There were no trends toward safer behavior for sexual risk, however, with younger age being the primary factor associated with high risk. The study shows that levels of needle sharing and sexual risks among IDUs in Rio de Janeiro remain high, demonstrating an urgent need to increase the limited preventive measures undertaken so far. Seroprevalence levels for HIV remain significantly lower in the most deprived sample, arguing for the fundamental importance of prompt and effective HIV prevention strategies to keep infection rates from rising among the poorest and largest population strata of Rio's IDUs. Telles, P.R., et al., Risk Behavior and HIV Seroprevalence Among IDUs in Rio de Janeiro, Brazil. AIDS, 11(suppl 1), pp. S35-S42, 1997.

Determinants of Syringe Sharing in Communities With Illegal/ Underground Needle Exchange Programs

Between 1992-1995, researchers administered the NIDA Cooperative Agreement Risk Behavior Assessment and Follow-Up Assessment instruments to 1,304 IDUs in Oakland, California. To determine the factors related to syringe and injection supply sharing among the IDUs, who lived in a community with an illegal/underground needle exchange program (NEP), researchers recently re-examined seven semi-annual waves of interviews from both the baseline and follow-up assessments. Since some of the respondents were interviewed on more than one occasion, the researchers statistically adjusted for correlations between multiple observations on the same person. They also controlled for several potentially confounding variables, including drug treatment, marital status, gender, and income, as well as for possible temporal trends in use of NEPs and syringe sharing (i.e., "calendar time" or interview "waves"). There were substantial declines in syringe sharing over the seven waves of interviews: in 1992, 52% of respondents shared syringes compared to only 28% in 1995. Conversely, use of the NEP increased from 5% of the IDUs at Wave 1 (in 1992) to 36% in 1995 despite arrests of program volunteers during the study period. When temporal trends in behavior were controlled, researchers were able to distinguish the independent impact of a temporal trend toward less syringe sharing over the study period from the significant impact of the NEP on syringe sharing among study participants. They also found an individual protective effect from use of an NEP on needle sharing among consumers of an illegal/underground NEP. The data from this analysis indicate that use of an illegal/underground NEP is

associated with lower rates of syringe sharing, suggesting that, regardless of legal status, NEPs can be effective for HIV prevention among IDUs. Bluthenthal, R.N., Kral, A.H., Erringer, E.A., and Edlin, B.R. Use of an Illegal Syringe Exchange and Injection-Related Risk Behaviors among Street-Recruited Injection Drug Users in Oakland, California, 1992-1995. Journal of AIDS and Human Retrovirology, In Press.

An Examination of Substance Abuse, HIV Seropositivity, and the Role of Partner Notification

In this article, researchers discuss a recent pilot study on partner notification with drug users and the social policy implications of implementing notification programs to inform HIV positive drug-using and sexual partners of drug users about their potential exposure to HIV. The pilot study was conducted in Washington, D.C., with 53 out-of-treatment injecting drug users (29 males, 24 females) between 30 and 49 years old. About 75% of the respondents were sexually active and about 33% of persons being sexually active also reported being the sexual partner of an IDU. More than one in six had tested positive for HIV. A questionnaire was given to each respondent concerning 4 types of partners: close drug using, casual drug using, close sexual, and casual sexual. The majority of respondents said they would desire to disclose their HIV positive serostatus to all 4 types of partners (96% for close drug using, 78% for casual drug using, 100% for close sexual, and 86% for casual sexual). Most also preferred to self-notify than to have outreach worker or provider assistance, with 72% saying this for close drug using partners, compared to 67% for casual drug using partners, 71% for close sexual partners, and 55% for casual sexual partners. Only 2% said they would fear being harmed if they disclosed their status to close drug users, but 19% said they would fear harm in telling casual drug using partners; 10% feared harm from close sexual partners compared to 31% for casual sexual partners. The findings from this pilot suggest that partner notification by self-disclosure is preferred for close drug using and sexual partners, but less so for casual partners and that self-disclosure is preferred over and above outreach/ provider-assisted notification. While these findings are generally favorable for partner notification, there are difficult barriers that must be addressed before a partner notification program could be implemented. These include personal issues such as fear of losing the partner, fear of losing support, and not knowing how to initiate the conversation, as well as legal and ethical concerns about confidentiality, the extent to which contacts should be traced, and the types of information, services, and support that should be available once a person learns about his/her potential exposure. Hoffman, J.A. and Klein, H. Social Policy Implications of Partner Notification for Substance Abusers Who Test HIV Positive. Research on Social Policy, 6, May 1998.

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National Institute on Drug Abuse

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

May, 1998

Research Findings

Epidemiology, Etiology and Prevention Research

The Effect of Home Environment on Adolescent Substance Use and Depressive Symptoms

Researchers at the National Opinion Research Center (NORC) used data from the screening phase and first two waves of a panel study to compare the home environments of families with a substance abusing parent, families with a depressed parent, and families in a comparison group. They diagnosed substance use disorder and affective disorder by administering the Structural Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders (3rd edition, revised) to each participating parent.The data suggested that families in which parents display a substance use disorder are very similar to those in which parents suffer from affective disorder, in terms of negative life events and lower family cohesion. The results of structural equation modeling indicated that parental substance use disorder and parental affective disorder influence adolescent substance use and depressive symptoms. In addition, parental substance use disorder were found to have a direct influence on adolescent substance use at the time the first-wave data were collected, but this effect does not persist over time. Su, S.S., Hoffman, J.P., Gerstein, D.R., and Johnson, R.A. J of Drug Issues, pp. 851-878, 1997.

Early Stages of Drug Use: Transitions from Opportunity to Use

In research at Johns Hopkins University focusing on the earliest stages of drug involvement investigators studied the transition from an initial opportunity to try marijuana to the subsequent use of this drug through secondary analysis of self-report interview data gathered from nationally representative samples of the United States National Household Surveys on Drug Abuse, 1979-1994. The evidence indicates that the estimated prevalence of an opportunity to try marijuana has been rather stable for 15 years. However, there are recent increases in the probability of rapidly progressing from first marijuana opportunity to first marijuana use, among persons given an opportunity to use. In addition, the transition from first marijuana opportunity to eventual marijuana use seems to depend upon age at first opportunity. This epidemiological evidence on the transition from marijuana opportunity to marijuana use, the first to be published based on a nationally representative US sample, highlights directions for future research and a focus for prevention efforts. Van Etten, M.L., Neumark, Y.D., Anthony, J.C. Drug and Alcohol Dependence., 49(1), pp. 1-7, 1997.

Adolescent Versus Adult Onset and the Development of Substance Use Disorders in Males

While the adolescent onset of substance use disorders has been thought to be characterized by specific features, previous studies on the importance of age of onset have not distinguished adolescent from early-adult onset. Drs. Clark, Kirisci and Tarter of CEDAR examined the influence of adolescent age of onset on the development of

substance use disorders by comparing adolescents with substance use disorders and adults divided into three groups by age of onset: adolescent, early-adult and late-adult. Adolescent-onset groups, compared with adult-onset groups, had higher lifetime rates of cannabis and hallucinogen use disorders, shorter times from first exposure to dependence, shorter times between the development of their first and second substance dependence, and higher psychopathology rates, including conduct disorder and major depression. The results suggest that adolescent-onset SUD is a distinct subtype involving different substances and more rapid development than adult-onset SUD. Clark, D.B., Kirisci, L., and Tarter, R.E. Drug and Alcohol Dependence, 49, pp. 115-121, 1998.

Association Between a Microsatellite Polymorphism at the DRD5 Gene and the Liability to Substance Abuse

This population-based study of the relationship between the risk for substance abuse and the dopamine D5 receptor locus (DRD5) was conducted in a sample of adult males and females with a DSM-III-R diagnosis of substance dependence (SD) or without any psychiatric disorder who are participants in a longitudinal family/high-risk study of substance abuse (Center for Education and Drug Abuse Research, CEDAR). To lessen the potential influence of the stratification bias, only European-American subjects' DNA samples were used in this pilot study. To maximize the phenotypic differences for the liability to substance abuse between the affected and nonaffected subsamples, the control subjects were selected to be older than 35 years of age (males' age range, 35-64; females', 35-52), and thus had predominantly been beyond the age of risk for development of SD. The data showed an increased frequency of the modal, 148 base pairs repeat length, allele of a dinucleotide polymorphism (allele 9) among SD males. This finding was reproduced in females with even greater contrast between affected and nonaffected individuals. The association was also found to be significant when all the alleles of the polymorphism were taken into account in a likelihood ratio test. The case-control and sex differences were also observed for genotypes coded in accordance with the number of alleles 9 (0 to 2). It is noteworthy that none of the SA females had the non-9/non-9 genotype, while the frequency of this genotype among control females was 37%; among males, the respective frequencies were 25 and 47%. The genotype was also found to be associated with novelty seeking in females, but not in males, in whom even a trend for such an association was absent. Interestingly, there were no sex differences in novelty seeking among substance abusers or controls, while the relationship between this temperament/personality trait and the risk for SD was more pronounced in males than females. The findings suggest that the DRD5 locus is involved in the variation and sex dimorphism of the liability to substance abuse and related traits. Vanyukov, M.M., Moss, H.B., Gioio, A.E., Hughes, H.B., Kaplan, B.B., and Tarter, R.E. Behavior Genetics, 28, pp. 75-82, 1998.

School Differences in Rates of Substance Use

Previous research has noted that schools vary in substance use prevalence rates, but explanations for school differences have received little empirical attention. This article assesses variability across elementary schools (N=36) in rates of early adolescent alcohol, cigarette, and marijuana use. Characteristics of neighborhoods and schools were measured using student, parent, and archival data. Findings show substantial variation across schools in substance use. Attributes of neighborhoods and schools are statistically significant related to school rates of lifetime alcohol use, lifetime cigarette use, and current cigarette use. Contrary to expectations, lifetime alcohol and cigarette use rates are higher in schools located in neighborhoods having greater social advantages as indicated by the perceptions of residents and archival data. Neighborhood effects are expressed both directly and indirectly through school characteristics. Ennett, S.T., Flewelling, R.L., Lindrooth, R.C. & Norton, E.C. School and Neighborhood Characteristics Associated With School Rates of Alcohol, Cigarette, and Marijuana Use. Journal of Health and Social Behavior, 38, pp. 55-71, 1997.

Students Who Bring Weapons to School and Drug Use

Social, demographic, and behavioral characteristics and self-reported carrying of a weapon to school among middle school students provide a statistical profile of youth most likely to bring weapons to school and help to identify characteristics that are only spuriously related to this behavior. Study respondents were part of an ongoing randomized evaluation of a school-based drug use prevention program in Illinois. Self-administered questionnaires were completed by 1,503 seventh and eight graders. Fifteen percent of respondents brought some type of weapon to school in the past month. Weapon carrying was significantly associated with being male, not living with both parents, not feeling close to parents, heavy drinking, participating in fights, damaging school property, and perceiving that at least a few other students bring weapons to school. Victimization and fear for safety in school were not significantly associated with weapon carrying. Study results suggest that the structure and the dynamics of the family and

perceived normative influences play important roles in weapon carrying behavior. Weapon carrying also appears to cluster with other deviant behaviors including drug use. Bailey, S.L., Flewelling, R.L., Rosenbaum, D.P. Characteristics of Students Who Bring Weapons to School. Journal of Adolescent Health, 20, pp. 261-270, 1997.

African-American and Puerto Rican Drug Use: A Longitudinal Study

The objective of this study was to examine the interrelationship of acculturation, family, personality, ecology, and peer domains measured in adolescence as they impact drug use 5 years later and to assess the role of family variables as buffers against personality risks. Youths completed questionnaires in classrooms at T1 and were individually interviewed at T2 (mean age = 20 years). Data were analyzed separately for African-American and Puerto Ricans using correlations, hierarchical multiple regressions, and two-way interactions. Most results were similar or both ethnic groups. Eighty percent of the T1 variables significantly related to T2 stage of drug use. A mediational model of the path to drug use was supported. Acculturative influences were associated with family relations, which in turn were related to personality attributes. A reciprocal relationship emerged between the personality and peer domains in their impact on drug use. Family variables primarily enhanced the effect of protective personality traits on drug use. Results suggest that the stability of drug use alone cannot explain the relationship between the earlier domains and later drug use. Specific adolescent risks have long-lasting effects. The personality domain has a direct effect on later drug use despite a benign picture in the acculturation, family, and peer domains. Brook, J S., Whitemans, M., Balka, E.B., Win, P.T., and Gursen, M.D. Journal of American Academy of Child Adolescent Psychiatry, 36(9), pp. 1260-1268, 1997.

Jump Start: A Targeted Anti-Drug Prevention Program

A substance abuse prevention and life skills program for economically disadvantaged, high sensation seeking African American teens was developed and tested. Formative research was conducted to determine program content and format. Over two implementations, 289 individuals in the target population were recruited as participants for the field test of the program. For the first implementation, participants were randomly selected from a summer youth employment program. For the second, a media campaign was designed to recruit participants. Participants evaluated the program extremely positively. Analysis indicated that the significant pretest difference in liquor and marijuana use between high and low sensation seekers was neutralized in both years of the program as were attitudes toward drugs in the first year of the program. These results suggest that sensation seeking is a useful message design and audience-targeting variable for substance abuse prevention program design. Harrington, N.G., & Donohew, L. Jump start: A Targeted Substance Abuse Prevention Program. Health Education and Behavior. 24(5), pp. 568-586, 1997.

The Association of Early Risk Factors to Opiate Addiction and Psychological Adjustment

Family/parental, peer and individual risk factors that appear early in life contribute to increased susceptibility to addiction. This study aimed to determine the relationship between risk factors, the development of opiate addiction, and the development of psychological maladjustment in addicts. A total of 252 addict subjects, age 12-39 years at the onset of opiate addiction and 342 nonaddict controls from the same neighborhood, matched for age, race and place of residence were selected. Ten risk factors related to family disruption, peer deviance, personal deviance and psychological symptoms were studied. White addicts scored significantly higher than African American addicts on all of the risk factors, whereas African American addicts scored significantly higher than African American nonaddicts on risk factors. Addicted individuals with a diagnosable psychiatric disorder on a standardized psychological instruments as young adults had also experienced related symptoms during the adolescent years prior to addiction. Thus, in addition to problems directly attributable to addiction, there were many problems that either coincided with, or pre-dated, severe drug abuse. Nurco, D.N., Hanlon, T.E., O'Grady, K.F., & Kinlock, T.W. Risk Factors for Opiate Addiction. Criminal Behavior and Mental Health, 7, pp. 213-228, 1997.

A County Survey of Mental Health Services in Drug Treatment Programs

Forty-five administrators from randomly selected drug treatment programs in Los Angeles County were surveyed between December 1994 and October 1995 about the adequacy of mental health services within their program and the drug treatment system. Approximately half agreed that dually diagnosed clients are not served within the system, and the majority (about 70%) noted that their programs restrict admission of such clients. Agreement was highest among administrators of residential and day treatment programs and lowest among administrators of outpatient

drug-free programs and methadone maintenance programs. Administrators of outpatient drug-free programs and methadone maintenance programs were more likely to characterize their mental health services as inadequate or unavailable than were administrators of other types of programs. Yet, despite this poor assessment, administrators expressed only mild support for providing additional training in this area either for themselves or for their counselors. Administrators may not perceive a need to enhance their mental health services if severely mentally ill clients are restricted from entering their programs. Grella, C.E., and Hser, Y.I. A County Survey of Mental Health Services in Drug Treatment Programs. Psychiatric Services, 48(7), pp. 950-952, 1997.

Association between Attention Deficit Hyperactivity Disorder (ADHD) and Cigarette Smoking

In a follow-up study of siblings of ADHD and control probands, it was found that found that ADHD in probands increased the risk for cigarette smoking in siblings regardless of the sibling's own ADHD status or the presence of other psychiatric conditions. Moreover, ADHD in the siblings was associated with higher rates of cigarette smoking along with a significantly younger age at onset. In like manner, conduct disorder, major depression and drug abuse were associated with high rates of cigarette smoking. In addition, cigarette smoking appeared to be familial among the ADHD families but not the control families. Finally, male gender did not appear to be a risk factor for cigarette smoking in the sample. Using DSM-III-R structured diagnostic interviews and blind raters, we conducted a four-year follow-up of siblings from ADHD (N=149) and control families (N=117). The mean age of the siblings was 17.2 (range 9 to 41) and roughly half were males. First we analyzed the data using univariate methods (i.e., Chi-square tests) which were followed by multivariate logistic regression models which simultaneously controlled for confounding variables such as high risk status (i.e., whether a sibling of an ADHD or normal control proband), socioeconomic status, age, IQ, gender and psychiatric disorders. Since ADHD is a prevalent, childhood onset disorder that is often characterized by impulsive behavior, it could represent a large group of youth at high risk for smoking, illicit drug use, medical morbidity and premature mortality. Since ADHD children and their siblings comprise a large portion of the population at high risk for smoking, they may represent an excellent group to be targeted for prevention programs. Further Evidence of an Association between Attention Deficit Hyperactivity Disorder (ADHD) and Cigarette Smoking: Findings from a High Risk Sample of Siblings. Milberger, S., Biederman, J., Faraone, S.V., Chen, L., and Jones J. American Journal on Addictions, 6, pp. 205-217, 1997.

Using the National Youth Survey Data Socioeconomic Status Has a Nonlinear Relationship with Marijuana Use

This may account for many null findings that used linear methods to describe the relationship. This study also found that predictors for females were substantially different from males. However, weekly alcohol use was the strongest predictor for both groups (both odds ratios greater than 11.0). Other predictors for both sexes included having a job, having friends who use marijuana and having used some alcohol in the past year. For females, prior victimization and low school aspirations were also significant. For males, GPA, commitment to friends, urbanicity, time spent with friends and peer strain were also significant predictors. Miller, D.S., and Miller, T.Q. Addictive Behaviors, 22(9), pp. 479-489, 1997.

Similar and Different Precursors to Drug Use and Delinquency Among African-Americans and Puerto Ricans

Correlational and net regression techniques were used to examine the commonalities and differences in adolescent risks for later drug use and delinquency among African-Americans and Puerto Rican youths. Eighty-eight percent of the risks were significantly related to both problem behaviors. Within the personality, family, peer, ecology, and acculturation domains many risks independently contributed to the prediction of each problem. Only three risks had a significantly stronger relationship to one of the problem behaviors than to the other. Finding so many common intrapersonal and interpersonal predictors supports a general dimension of problem behavior. The commonalities suggest that interventions targeting these adolescent risks might reduce both problem behaviors. Brook, J.S., Whiteman, M., Balka, E.B., Win, P.T., and Gursen, M.D. Journal of Genetic Psychology, 159 (1), pp. 13-29, 1998.

Tobacco Use Among Mexican American Youth

Increases in smoking/tobacco-related diseases among the Hispanic population call for an examination of tobacco use among this population. This study examined the relationship between gender, level of cultural identification, migrant

status, grade level, tobacco use, and perception of harm among Mexican American youth. Results showed males were more likely to use cigarettes (occasional and daily) and smokeless tobacco than females when grade, cultural identification, and migrant status of parent are held constant. No gender effect was found for lifetime cigarette use. The odds of using cigarettes and smokeless tobacco were found to increase substantially across grades. Effects were found for Mexican American/Spanish and Anglo/White American cultural identification and daily cigarette use. Youths who belonged to nonmigrant families or who identified with a traditional Mexican American/Spanish culture were more likely to consider the regular use of tobacco harmful. Casas, M.J., Bimbela, A., et. al. Cigarette and Smokeless Tobacco Use Among Migrant and Nonmigrant Mexican American Youth. Hispanic Journal of Behavioral Sciences, 20(1), pp. 102-121, 1998.

A Regression Analysis Estimating the Number of Drug-using Arrestees in 185 U.S. Cities

A prevalence model for drug-using arrestees was developed by relating selected social indicators from 1990 Census data and drug use rates from Drug Use Forecasting data using logistic regression analysis. An estimation of the total arrestee population was based upon the FBI's Uniform Crime Reports (UCR). Of the originally selected 200 largest cities (indicated by total population size), 16 did not report to UCR; arrest data for Chicago were obtained separately from local officials. Thus, 185 cities were included in the present analysis. A separate logistic regression was conducted for each of the following dependent variables: the urine positive rates for cocaine, opiates, amphetamines, intravenous drug users, and any drug, for each of the eight subgroups defined by the cross-combination of gender and offense type (violent, drug-related, income-generating, and others). Predictors were five social indicators from Census data hypothesized to be associated with drug use levels in different cities: Census population, and percentages of unemployment, poverty, high school graduates, and youths. It was estimated that in 1990, about 925,000 arrestees used cocaine; 317,000 used opiates; 213,000 used amphetamines; 389,000 were drug injectors; and 1,296,000 used some illicit drug. This approach represents a cost-efficient method for prevalence estimation that is based on empirically demonstrable relationships between social indicators and drug use rates. Hser, Y.I., Prendergast, M.L., Anglin, M.D., Chen, J., and Hsieh, S. American Journal of Public Health, 88(3), pp. 487-490, 1998.

Tobacco Policy Effects on Youth

Tobacco policy may be differentially enforced with youth, depending on their risk for school failure and other problem behavior. An analysis of the policy change component of a multi-component community intervention for adolescent drug abuse prevention was conducted. Effects of the community intervention (program or control) on tobacco policy change and tobacco were assessed, as well as effects of policy (level of restrictiveness) on tobacco use were evaluated. Results showed that intervention decreased tobacco use over the study period and had an effect on changing tobacco policy toward more restrictiveness. However, existing level of policy restrictiveness (prior to and independent of intervention) was associated with higher tobacco use, suggesting that schools adopt more restrictive policies on their own in reaction to a greater tobacco use problem. Pentz, M.A., Sussman, S., & Newman, T. The Conflict Between Least Harm and No Use Tobacco Policy for Youth: Ethical and Policy Implications. Addiction, 92(9), pp. 1165-1173, 1997.

Ethnicity and Gender in Adolescent Drug Resistance

While ethnic and gender differences have been reported in the amount and type of drug use, little is known about how drugs get offered to adolescents and how members of different cultural groups respond to those offers. Interviews (30-40 minutes) were conducted with 158 middle school students. Adolescent "near-peer" interviewers were trained for this project and matched to participants by ethnicity and gender. Data were content analyzed and results showed that for all groups, simple offers were more likely than complex, pressure-filled strategies, and these offers were typically resisted through simple refusals (i.e., "no") rather than more complex techniques (e.g., explanations). Drugs tended to be most frequently offered to all groups at home or in public rather than at school or parties. Gender and ethnic differences were observed in other areas. Latinos/Latinas were significantly more likely to experience drug offers than other males and females. Hecht, M., Trost, M., Bator, R., & MacKinnon, D. Ethnicity and Gender Similarities and Differences in Drug Resistance. Journal of Applied Communication Research, 25, pp. 1-23, 1997.

Parental and Family Risk Factors for Substance Use in Inner-City African-American Children and Adolescents

The purpose of this study was to develop and test a multi- dimensional model of parental and family influences on risk for substance use in inner-city African-American primary grade children and their adolescent siblings. The risk factors investigated were conceptually grouped into three broad domains of family influences and the respective indices computed: parental risk attributes, family risk attributes, and parenting styles. Parenting styles were captured as indicators of a latent construct, "poor parenting." In study 1, it was hypothesized that the parental and family risk variables would be mediated through parenting styles to predict intentions to use drugs, actual drug use, positive drug attitudes, and negative drug attitudes in a sample of 455 inner-city African-American families and their primary-grade children. In study 2, the substance use risk model was tested on a sample of 59 adolescent siblings to determine whether the pattern of parental and family factors that contributed to early high-risk attitudes and behaviors in children would predict drug attitudes and behaviors in teen siblings. The results confirmed expectations that parental and family risks were important predictors of children's negative drug attitudes and intentions to use drugs in the future and that positive parental and family characteristics would protect against future risk by enhancing negative drug attitudes. Also, substance use attitudes and behaviors in teen siblings were predicted primarily by family risk characteristics. The family risk index also predicted frequency of use of hard drugs, but only when mediated through poor parenting. The implications of these results for future research are discussed. Newcomb, M.D. Journal of Psychopathology and Behavioral Assessment, 19(2), pp. 369-400, 1997.

Longitudinal Study of Co-occuring Psychiatric Disorders and Substance Use

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

Adolescent School Experiences and Dropout, Adolescent Pregnancy, and Young Adult Deviant Behavior

Predictive effects of school experiences were studies over a 7-year interval in a random community sample of 452 adolescents, 12 through 18 years of age. Outcomes examined included dropping out of school, adolescent pregnancy, engaging in criminal activities, criminal conviction, antisocial personality disorder, and alcohol abuse. Logistic regression showed academic achievement, academic aspirations, and learning-focused school settings to be related to a decline in deviant outcomes independent of the effects of disadvantaged socioeconomic background, low intelligence, childhood conduct problems, and having deviant friends during adolescence. Associations between school conflict and later deviancy were mediated by deviant peer relationships in adolescence and other school characteristics. Prior research reporting continuity of childhood conduct problems and the influence of adolescent affiliations with deviant peers on negative outcomes was supported. Implications for using the school context in risk factor research and the practical applications of such research for intervention are discussed. Kasen, S., Cohen, P., and Brook, J.S. Journal of Adolescent Research, 13(1), pp. 49-72, 1998.

Self-Reported Drug Use: Results of Selected Empirical Investigations of Validity

This article reviews the literature and discusses two series of empirical studies. The literature shows some evidence that drug abusers self-reports are generally reliable and accurate, but the studies are more strikingly marked by findings of wide variations in accuracy and in the samples and procedures used to obtain them. In the authors first study, data from 323 narcotics addicts were collected through two interviews held 10 years apart. This set of analyses examined the quality of the longitudinal retrospective self-report from narcotics addicts, including validity of

recent narcotics use, reliability of various measures, stability of relationships among these measures, and pattern reliability among latent constructs. Results contribute strongly to confidence in the validity of the relationships among these data derived from addicts self-report. The second set of analyses focused on validity of self-reported drug use among 3,493 clients from Los Angeles County sexually transmitted disease clinics, hospital emergency rooms, and jails. Results suggest that the accuracy of self-report of recent drug use varies by the sample sources, drug types, and subject characteristics. Targeting these high-risk groups may improve prevalence estimation. The article concludes that empirical validation of self-report is always necessary to enhance the utility of collected self-report data and provide means of controlling for potential biases. Hser, Y.I. Self-Reported Drug Use: Results of Selected Empirical Investigations of Validity. In L. Harrison and A. Hughes (Eds.), The Validity of Self-Reported Drug Use: Improving the Accuracy of Survey Estimates (NIDA Research Monograph 167, pp. 320-343). Washington, DC: U.S. Government Printing Office, 1997.

Predicting Treatment Entry among Treatment-Seeking Drug Abusers

Treatment-seeking drug abusers were recruited from two sources: a community resource center which provided treatment referrals and also from a separate descriptive study conducted at the Drug Abuse Research Center at the University of California at Los Angeles. All respondents were provided with a referral to drug treatment at the end of their first interview; a second interview was conducted approximately six months later. At the six-month follow-up, 171 (62.0%) subjects had entered treatment. Subject characteristics related to treatment entry were examined, which included severity of problem drug use, severity of other problems (e.g., alcohol use, legal, family, psychological, medical, housing), social enabling factors (legal coercion, health insurance, employment obligations, social support), and prior drug treatment experiences. Treatment-entry and non-entry subjects did not differ in demographics, type of drug use, or years of use. Treatment-entry subjects were more likely to have had a prior successful treatment experience and legal system involvement, but less severity in current drug use, psychological distress, and family problems. Prior treatment experience and legal coercion were factors promoting treatment entry. Those that had more severe problems (drug and others) seemed less likely to enter treatment indicating that psychological distress and problems with families may undermine a drug abusers motivation to follow through on treatment referral. These results suggest that while external pressure such as legal coercion may help motivate drug users to enter treatment, referral and outreach efforts need to be sensitive to the distress of drug users who are suffering from significant psychological problems. Hser, Y.I., Maglione, M.A., Polinsky, M.L., and Anglin, M.D. Journal of Substance Abuse Treatment, 14(5), pp.1-8, 1997.

Drug Addiction and Treatment Careers among Clients in DATOS

Considerable heterogeneity in patterns of addiction and treatment career histories was observed among 10,010 clients interviewed by the Drug Abuse Treatment Outcome Study (DATOS). Drug use history, mental health status, physical health status, history of criminal behavior, and social functioning data were collected between 1991 and 1993 at clients entry into treatment in 96 programs in 11 cities purposely chosen across the United States. First treatment entry was on average seven years after the initiation of use of heroin or cocaine; about one-half of the clients admitted to DATOS were entering their first treatment episode. The mean number of prior treatment episodes was 3.5 among those who had any treatment prior to DATOS admission. Regression analyses showed that prior treatment utilization was associated with more severe levels of drug dependence, HIV-risk behaviors, and criminal activities. The present findings suggest that policy efforts have encouraged drug treatment among individuals at high risk for HIV, as well as among drug users involved with the criminal justice system. Anglin, M.D., Hser, Y.I., and Grella, C.E. Drug Addiction and Treatment Careers among Clients in DATOS. Psychology of Addictive Behaviors, 11(4), 1997.

Factors Associated with Early Sexual Activity among Urban Adolescents

This study uses lifespan and ecological frameworks to investigate the factors associated with early adolescent sexual activity. Data from a longitudinal study of urban teenagers of color address three issues: (1) the prevalence and pattern of sexual activity among boys and girls ages 15 and younger, (2) the link between early sexual activity and high-risk sexual behavior, and (3) the life contexts linked with early sexual activity. Results from 803 African American and Hispanic adolescents suggest a high prevalence of early sexual activity, which is associated with higher rates of childbearing and risky sexual behavior than sexual activity initiated in later adolescence. Somewhat different factors are associated with early sexual activity for boys and girls, although family composition, parent attachment, and substance use are important for both genders. Implications for intervention are discussed. Smith, C.A. Social

Work, 42, pp. 334-346, 1997.

Interrelationships Between Adolescent Drug Use and Drug Use 5 Years Later

In 1990 (T1), African American (n=695) and Puerto Rican (n=637) youths in East Harlem schools completed questionnaires on six domains: personality attributes, family relationships, peer factors, ecological variables, acculturation measures, and stage of drug use. Five years later (T2), 459 of the African American youth and 423 of the Puerto Rican youth were re-contacted to complete a follow-up questionnaire on the same domains. At T1, there were no significant differences in self-reported drug use between the African American and Puerto Rican youths but at T2, significantly more Puerto Ricans used drugs than did African Americans. The variables within the different domains were analyzed to determine those in T1 which were related to T2 drug use. Acculturation, family, personality, and peer domains were found to be related to stage of drug use in young adulthood, with control for stage of drug use in adolescence. The study suggests that stability of drug use alone cannot explain the relationship between earlier domains and later drug use, and that specific adolescent risk factors have long-lasting effects into young adulthood. Targeting risk factors related to adolescent drug use during adolescence is likely to reduce contemporaneous and later drug use. Brook, J.S., et al. African-American and Puerto Rican Drug Use: A Longitudinal Study, J. Am. Acad. Child Adolesc. Psychiatry, 36 (9), pp. 1260-1268, 1997.

Risk Factors for Teenage Fatherhood

The study of teen parenthood has become almost synonymous with the study of teen mothers, but relatively little research attention has been devoted to the study of teen fathers. Nevertheless, because it appears that becoming a teen father has negative developmental consequences for both the teen father and his children, it is an important area of inquiry. This article uses data from the Rochester Youth Development Study, an ongoing panel study of urban youth, to identify early risk factors for the likelihood of becoming a teen father. The study is well suited to this task because the prevalence of teen fatherhood in this sample is quite high, and the project has collected extensive data in a range of developmental domains. Teen fatherhood is related to a variety of risk factors, such as social class, educational performance, precocious sexual activity, and drug use. Perhaps most important is the finding that teen fatherhood is strongly related to the cumulation of risk factors across many domains. Thornberry, T.P., Smith, C.A., and Howard, G.J. Journal of Marriage and the Family, 59, pp. 505-522, 1997.

Patterns by Gender and Ethnicity Among School Attenders and Dropouts

Differences in patterns of volatile solvent use were explored with special emphasis on use as related to school enrollment status. The sample included American Indian, Mexican-American and White American youth. Three enrollment status categories were identified: dropout, academically at-risk (enrolled), and control. A self report survey was used to assess both level and intensity of volatile solvent use. Findings indicated that a higher proportion of the dropout cohort have used volatile solvents, used volatile solvents regularly, and used volatile solvents with more intensity than either the academically at-risk group or the control group. An interaction between gender and ethnicity was also revealed; American Indian females reported higher lifetime prevalence and thirty-day prevalence than did American Indian males, whereas for both the Mexican-American and White American samples, males report higher rates than females. Findings are discussed in terms of the influence of volatile solvent abuse and school success as well as previous findings. Bates, S.C., Plemons, B.W., Jumper-Thurman, P. Beauvais, F. Patterns by Gender and Ethnicity Among School Attenders and Dropouts. Drugs and Society, 10, pp. 67-78, 1997.

The ATLAS Program: Effects During Two Seasons

The largest group of adolescents who use anabolic steroids (AS) participate in high school football. The greatest risk for initiating AS appears to occur during the football season. The effect of an educational intervention designed to prevent AS use and promote healthy behaviors was tested. ATLAS capitalized on the social influences of a team sport setting. Thirty-one football teams were separated into experimental and control schools with new subjects assessed over two successive years in a randomized trial. An interactive intervention presented by coaches, research staff and student team leaders, included weight room sessions, sports nutrition and strength training, alternatives to AS use, drug knowledge, drug refusal role play, and anti-AS media campaigns. Pre- and post-intervention questionnaires assessed risk factors, intentions and use of AS, and dietary and exercise habits. Compared to the controls, experimental subjects reported greater understanding of the effects of alcohol, marijuana and AS, greater belief in

personal harm by AS use, more negative feelings toward AS users, reduced impulsivity, improved feeling of athletic abilities and self-esteem, greater belief that coaches were anti-AS, less belief in media, and improved refusal skills. There was reduced intent to use AS and less than half the new AS users were among experimental group. In addition, beneficial changes in strength training self-efficacy and nutrition behaviors were present. Goldberg, L., Elliot D., MacKinnon, D., Moe, E., Clarke, G., Lapin, A., Green, C., Miller, D. & Greffrath, E., The ATLAS (Adolescents Training and Learning to Avoid Steroids) Intervention: Effects During 2 Seasons. Med Sci Sports Exercise (Supplement), pp. 29S:S293, 1997.

Methylphenidate Use and Dysfunctional Causal Attributions

Researchers affiliated with CEDAR investigated the effects of 0.3 mg/kg methylphenidate (MPH) and expectancy regarding medication on the performance and task persistence of 60 boys with attention deficit hyperactivity disorder (ADHD). In a balanced-placebo design, boys in 4 groups (received placebo/drug crossed with told placebo/drug) completed the task in success and failure conditions. Medication improved participants' task persistence following failure. Participants' task performance was not affected by whether they thought they had received medication or placebo. Children made internal attributions for success and made external attributions for failure, regardless of medication or expectancy. These findings confirm previous reports that it is the pharmacological activity of MPH that affects ADHD children's self-evaluations and persistence. The results contradict anecdotal reports that MPH causes dysfunctional attributions and confirm previous studies showing that medication does not produce adverse effects on the causal attributions of children with ADHD. Pelham, W.E., Hoza, B., Kipp, H.L., Gnagy, E.M., Trane, S.T. Experimental and Clinical Psychopharmacology, 5(1), pp. 3-13, 1997.

Temperament and Novelty Seeking in Adolescent Substance Use: Convergence of Dimensions of Temperament With Constructs From Cloninger's Theory

This study investigated the convergence of temperament dimensions with constructs from C. R. Cloninger's (1987) theory using data from a sample of 949 adolescents (M age = 13.6 years). Substantial convergence was found, and both types of constructs were related in predicted ways to self-regulation variables and adolescent substance use. Structural modeling procedures tested a mediational model for substance use; results showed mediation through self-control, academic competence, negative life events, and deviant peer affiliations. Interactions indicated that substance use could be predicted from a balance of systems for good control and poor control. Poor self-control was present for dimensions implicated in both externalizing and internalizing disorders. Results are discussed with reference to self-regulation models of substance use and the comorbidity of substance abuse and mental disorder. Wills, T.A., Windle, M., and Cleary, S.D. Journal of Personality and Social Psychology, 74(2), pp. 387-406, 1998.

Effect of Parental Mental Health Status on Adolescents' Dietary Behaviors

In a study by NORC, investigators examined whether adolescents of substance-abusing and depressed parents were more likely to have poor dietary behaviors that those in the health comparison families the examined 841 adolescents in families of substance-abusing parents, depressed parents, and parents without diagnosable psychiatric disorder. All adolescents were given a food frequency questionnaire. Adolescents whose parents had substance abuse disorder had lower intakes of fruits and higher intakes of high fat foods, and also ate more frequently at fast-food restaurants and purchased more snacks. Adolescents whose parents were depressed had lower intakes of all food groups. Mothers' mental health status impacted more on adolescents dietary behaviors than did the father's mental health status. This research suggests that at-risk behaviors among youth of psychiatrically impaired parents may extend to food behaviors. Su, L.J., Story, M., and Su., S.S. Journal of Adolescent Health, 20, pp. 426-433, 1997.

Concurrent Versus Simultaneous Polydrug Use: Prevalence, Correlates, Discriminant Validity, and Prospective Effects on Health Outcomes

Few studies have addressed the distinction between concurrent polydrug use (various drugs used on separate occasions) and simultaneous polydrug use (the use of more than 1 drug at the same time). The authors assessed simultaneous polydrug use in a community sample to examine the prevalence of drug combinations, whether simultaneous can be distinguished from concurrent, and the prospective effects of these styles of drug use on subsequent health service utilization, physical symptoms, and psychological distress 4 years later. Marijuana and alcohol were the most common drugs used simultaneously, followed by alcohol and cigarettes. Simultaneous and

Concurrent Polydrug Use formed 2 correlated but discriminable constructs. Neither Simultaneous nor Concurrent Polydrug use predicted subsequent Health Service Utilization, Physical Symptoms, or Psychological Distress. Data did reveal unique effects of specific drugs used simultaneously on these outcomes that were larger and more numerous than specific effects of concurrent drug use. Earleywine, M., and Newcomb, M.D. Experimental and Clinical Psychopharmacology, 5(4), pp. 353-364, 1997.

A Test of Reciprocal Causal Relationships Among Parental Supervision, Affective Ties, and Delinquency

Current family-delinquency research suggests that the relationships between parenting and delinquency should be viewed from interactional and developmental perspectives. The relationship between parent and child is thought to change over time, partly as a function of reciprocal causal influences between them. In this study, using panel data from a representative sample of 838 urban adolescents, the authors test the hypothesis that parenting and delinquency are reciprocally related. They also hypothesize that two central parenting dimensions, affective ties and supervision, are bidirectionally related. It is found that delinquency and parental supervision are reciprocally related, whereas affective ties appear to be a consequence rather than a cause of delinquency, at least by middle adolescence. In general, the interrelationships among these variables are more complex than those suggested by earlier unidirectional theories, and they underline the importance of interactional perspectives in understanding the interrelationship of adolescent behavior and parenting. Jang, S.J., and Smith, C.A. Journal of Research in Crime and Delinquency, 34(3), pp. 307-336, 1997.

Childhood, Adolescent, Familial, and Peer Antecedents of Cigarette Smoking in Young Adults

This study examined the interrelation of personality, family, and peer determinants and their effects on tobacco use by young adults. Mothers were first interviewed about their children when they were between the ages of 1 and 10 years old. Three subsequent interviews were conducted with the children when they reached adolescence and young adulthood. Results show support for the mediational model, which is derived from the family interactional theory framework to examine pathways that may lead to adolescent legal and illegal drug use and other problem behavior. There was a sequence in patterning: from parenting during early adolescence, to personality and peer factors, extending to smoking in late adolescence and culminating in smoking in adulthood. With a developmental approach, a number of psychosocial measures appear related in both younger and older children. Developmental differences also emerged, suggesting four possible targets for therapeutic or preventive intervention: the parent, the child, the adolescent, and the peer group. Brook, J.S., et al. Cigarette Smoking in Young Adults: Childhood and Adolescent Personality, Familial, and Peer Antecedents, J. Genetic Psychology, 158(2), pp. 172-188, 1997.

Implementation Issues in Drug Abuse Prevention Research

Methodological issues evaluating quality of implementation of drug use prevention programs are reviewed: definition (adherence, exposure, reinvention), measurement (self-report, other's report, behavioral observation), and parameters of influence (person, situation, environment). When implementation is defined as the interaction of person, situation, and environment, the "true" drug use prevention program effect is established as the average of effect generated from experimental assignment and program implementation. Differences between researcher and programmer standards of implementation quality are interpreted in terms of an efficacy/effectiveness continuum. Pentz, M.A. & Trebow, E. Implementation Issues in Drug Abuse Prevention Research. Substance Use and Misuse, 32, pp. 1655-1660, 1997.

Drug-User Treatment Programs in a Large Metropolitan Area

In 1993/1994 a compre- hensive survey of the Los Angeles County drug-user treatment systems was undertaken. The system contains more than 300 programs covering over 4,000 sq. miles and serves clients from a diverse population of over nine million people. Overall, 58% of the 14,860 clients being served at the time of the survey were male; about 35% were White, 34% Latino/Latina, 26% African-American, 2% Asian/Pacific Islander, 0.5% Native American and 2.5% of unknown ethnicity. Almost all programs reported a smaller number of current clients than allowed by maximum capacity, indicating that waiting lists were not necessarily related to lack of treatment slots, but more a lack of affordable (i.e., publicly-funded or insurance-covered) treatment slots. Waiting times ranged from one day to over one year. Polinsky, M.L., Hser, Y.I., Anglin, M.D., and Maglione, M.A. Subs. Use & Misuse, 33(8), pp.

1739-1765, 1998.

Consideration of Special Populations in the Drug Treatment System of a Large Metropolitan Area

Findings are based on a recent comprehensive survey of 294 drug treatment programs in Los Angeles County. Special populations were grouped by health status, ethnic background, language needs, and gender-related needs (groups are not mutually exclusive.) Survey results indicated a generally high proportion of programs capable of meeting the unique needs of a variety of special population clients and most programs have some mix of special population clients in their current caseload. About 62% of programs reported being able to serve clients who were primarily Spanish speakers. Clients using American Sign Language could be served by 11% of programs. About 40% of programs reported not being able to serve pregnant women, including almost half of the hospital inpatient programs and a quarter of the outpatient drug-free programs. Although almost 70% of programs reported being able to serve clients with mobility impairments, only 26% of the residential programs reported this capacity. Polinsky, M.L., Hser, Y.I., and Grella, C.E. Journal of Behavioral Health Services & Research, 25(1), pp. 7-21, 1998.

Substance Use among Nurses: Differences between Specialties

Valid data on factors that increase a health care worker's likelihood of substance use are integral in assuring professional standards and quality health care for consumers. This study explored the association between nursing speciality and past-year substance use. In an anonymous mailed survey, a balanced stratified sample of registered nurses (n=4438) reported their use of marijuana, cocaine, and prescription-type drugs, as well as cigarette smoking and binge drinking. Prevalence of use of all substances was 32%. Rates varied by specialty, even when sociodemographics were controlled. Compared with nurses in women's health, pediatrics, and general practice, emergency nurses were 3.5 times as likely to use marijuana or cocaine (odds ratio [OR]=3.5, 95% confidence interval [CI]=1.5, 8.2), oncology and administration nurses were twice as likely to engage in binge drinking; and psychiatric nurses were most likely to smoke (OR=2.4, 95% CI=1.6, 3.8). No specialty differences appeared for prescription-type drug use. These data suggest that certain nursing specialities were more likely than others to be associated with substance use. The differences were not explained by demographic characteristics. Inasmuch as a comparison of these results for nurses with prior work on physicians found considerable agreement by speciality, preventive initiatives should consider interdisciplinary approaches to substance use education. Trinkoff, A.M., and Storr, C.L. Amer J Pub Health, 88, pp. 1-5, 1998.

General Deviance and Psychological Distress: Impact of Family Support/Bonding over 12 Years from Adolescence to Adulthood

Comorbidity occurs within and across various domains of human pathology and may be diverse manifestations of a single, general dysfunction in early family support and bonding. Family socialization, pseudo maturity, and self-derogation theories were tested using cross-sectional and 12-year prospective data from a community sample assessed in late adolescence (age 18) and again in adulthood (age 30). All of the hypotheses and expected findings received some support in the data analyses these confirmed that: general deviance and psychological distress were significantly correlated for both men and women and therefore are overlapping and comorbid disorders; both general distress and psychological distress were significantly predicted by family support/bonding fully accounted for the cross-sectional association between general deviance and psychological distress for the women and general deviance for the men: both theories of pseudo maturity and self-derogation explained many of the prospective effects from late adolescence into adulthood: sexual involvement, although an indicator of general deviance, related negatively with indicators of psychological distress; different patterns were evident for the development periods of adolescence compared with adulthood; and many of the processes differed by sex. Newcomb, M.D. Criminal Behavior and Mental Health, 7, pp. 369-400, 1997.

Standardized Test Performance of Children with a History of Prenatal Exposure to Mutiple Drugs/Cocaine

Children with histories of prenatal polydrug exposure which included cocaine scored significantly lower on standardized test measures of language development (Receptive and Expressive subtests of the Sequenced Inventory of Communicative Development -Revised) than nonexposed children. Clinically, 45.8% of the children in the drug-

exposed group qualified for early intervention services. Significant differences between groups were also noted on the Bayley Scales of Infant Development. No differences were found on the Peabody Picture Vocabulary Test - Revised. Each group had 24 children, age 14 to 50 months, and included 13 males and 11 females. All children were living in stable, drug-free environments (foster/adoptive/natural homes). Tests were administered by a certified Speech-Language Pathologist and language samples were taken from 30 minute videotaping sessions showing the child and caregiver playing. Results indicate that, due to the cumulative effects of prenatal history, children with histories of prenatal drug exposure should be considered at-risk for language delay. Johnson, J.M., Seikel, J.A., Madison, C.M., Foose, S.M., and Rinard, K.D. Journal of Communication Disorders, 30, pp. 45-73, 1997.

Delinquency and Antisocial Behavior: A Review of Family Processes and Intervention Research

Recent longitudinal research employing complex measurement and analytic strategies has generated new, more intricate conceptualizations of the relationship between family life and delinquency, all of which have important implications for intervention with delinquents and their families. This critical review of the current research on the role of the family, its implications for family-based interventions with delinquents, and the existing treatment outcome research highlights four areas: the link between different family processes and delinquency, reciprocal relationships between parenting and delinquency, the effects of family context on parenting and delinquency, and the family as one cause of delinquency among many. Smith, C.A., and Stern, S.B. Social Service Review, 71, pp. 382-420, 1997.

Survey Finds Parenting Differences Between Narcotic Addicts and Their Parents

A 2-part survey was administered to male and female narcotic addicts receiving methadone maintenance to examine their retrospective self-reports about how they were parented and compare them with their views about their own parenting practices of their adolescent children. The sample of 313 adult addicts included 248 females (79%) and 65 males (21%). The average age was 37.6 years. There were 250 African Americans (80%) and 63 Whites (20%) in the sample. The mean age of addiction (narcotic use 4 days a week for a month or more) was 22.5 years, and the average period of continuous use was 5.4 years. Since the age of addiction, the subjects had spent an average of 10.7 months in prison. The addicts viewed their mothers as significantly more effective at parenting than their fathers, especially in terms of interaction, communication, and affection. Fathers were generally perceived as unavailable and distant. In terms of their own parent practices, the addicts reported being significantly more involved, more responsible, and more closely attached to their children than their parents were to them. They also reported that they were more active disciplinarians and utilized significantly fewer punitive behaviors with their children. Nurco, D.N.,et al., The Family Experiences of Narcotic Addicts and Their Subsequent Parenting Practices. Am. J. Drug Alcohol Abuse, 24(1), pp. 37-59, 1998.

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National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse
May, 1998

Research Findings

Intramural Research

Cellular Neurobiology Branch
Cellular Neurophysiology Section

Contributions of Neurons in the Nucleus Accumbens and the Amygdala to Drug Self- Administration

Work in the Cellular Neurophysiology Section has included continued study of the contribution of neurons in the nucleus accumbens and the amygdala to drug self-administration. These studies are conducted by recording from large groups of individual neurons of the rat brain during self-administration of addictive drugs. In association with co-workers at the Wake Forest University School of Medicine, we have found distinct groups of accumbens neurons code for different drug (cocaine, heroin, and alcohol) and non-drug (sweetened water) rewards. Woodward, Janak, and Chang, ACER, 22, pp. 3-22, 1998; Chang, Janak, and Woodward, J.Neurosci., 18, pp. 3098-3115, 1998.

Cellular Neurobiology Branch
Molecular Neuropsychiatry Section

Free Radicals and the Pathobiology of Brain Dopamine Systems

Oxygen is an essential element for normal life. However, reactive oxygen species (ROS) can also participate in deleterious reactions that can affect lipid, protein, and nucleic acid. Normal physiological function thus depends on a balance between these ROS and the scavenging systems that aerobic organisms have developed over millennia. Tilting of that balance towards a pro-oxidant state may result from both endogenous and exogenous causes. In this paper, investigators elaborate on the thesis that the neurodegenerative effects of two drugs, namely methamphetamine (METH) and methylenedioxymethamphetamine (MDMA) are due to ROS overproduction in monoaminergic systems in the brain. The authors also discuss the role of oxygen-based species in 6-hydroxydopamine-induced nigrostriatal dopaminergic degeneration and in Parkinson's disease. Studies are underway to identify specific cellular and molecular mechanisms that are regulated by oxygen species. These studies promise to further clarify the role of oxidative stress in neurodegeneration and in plastic changes that occur during the administration of addictive agents that affect the brain. Free Radicals and the Pathobiology of Brain Dopamine Systems. Cadet, J.L and Brannock, C. Neurochem. Int. 32, pp. 117-131, 1998.

Methampetamine Causes Apopotosis

Methamphetamine (METH) is an amphetamine analog that produces degeneration of the dopaminergic system in mammals. The neurotoxic effects of the drug are thought to be mediated by oxygen-based free radicals. In this study investigators used immortalized neural cells obtained from rat mesencephalon in order to further assess the role of oxidative stress in METH-induced neurotoxicity. Authors tested if the anti-death proto-oncogene, bcl-2, could protect

against METH-induced neurotoxicity. METH caused dose-dependent loss of cellular viability in control cells while bcl-2-expressing cells were protected against these deleterious effects. Using flow cytometry, immunofluorescent staining, and DNA electrophoreses, authors show that METH exposure can cause DNA strand breaks, chromatic condensation, nuclear fragmentation, and DNA laddering. All these changes were prevented by Bcl-2 expression. These observations provide further support for the involve-ment of oxidative stress in the toxic effects of amphetamine analogs and document that METH- induced cytotoxicity is secondary to apoptosis. These findings may be of relevance to the cause(s) of Parkinson's disease which involves degeneration of the nigrostriatal dopamin-ergic pathway. Methamphetamine Induces Apoptosis in Immortalized Neural Cells: Protection by the Protoncogene, bcl-2. Cadet, J.L., Ordonez, S.V. and Ordonez, J.V. Synapse, 25, pp. 176-184, 1997.

P-53 is Involved in the Toxic Effects of Methamphetamine

p53-Knockout mice provide a useful model to test the role of p53 in the neurotoxic effects of drugs in vivo. To test the involvement of p53 in methamphetamine (METH)-induced toxicity, wild-type mice, as well as heterozygous and homozygous p53-knockout male mice, were administered four injections of three different doses (2.5, 5.0, and 10.0 mg/kg) of the drug given at 2-h intervals within the space of 1 day. METH caused a marked dose-dependent loss of dopamine transporters in both the striatum and the nucleus accumbens of wild-type mice killed 2 weeks after drug adminis-tration. However, this METH-induced decrease in dopamine transporters was attenuated in both homozygous and heterozygous p53-knockout mice, with homozygous animals showing significantly greater protection. The possibility for -p53 involvement in METH-induced toxicity was also supported by the observation that METH caused marked increases in p53- knockout mice, with homozygous animals showing significantly greater protection. The possibility for p53 involvement in METH-induced toxicity was also supported by the observation that METH caused marked increases in p53-like immunostaining in the homo-zygous p53-knockout mice. Further support for p53 involvement was provided by the fact that METH treatment caused significant decreases in dopamine transporter mRNA and the number of tyrosine hydroxylase-positive cells in the substantia nigra pars compacta and the ventral tegmental area of wild-type but not homozygous p53-knockout mice killed 2 weeks after cessation of METH administration. These results provide concordant evidence for a role of the tumor suppressor, p53, in the long-term deleterious effects of a drug acting on brain dopamine system. p53-Knockout mice are protected against the long-term effects of methamphetamine on dopaminergic terminals and cell bodies. Hirata H., and Cadet J.L. J. of Neurochem, 69, pp. 780-790, 1997.

Kainic-acid Toxicity Occurs through Production of Superoxide Radicals

Peripheral administration of kainic acid (KA) can cause cell death in the hippocampus of rodents. This is thought to involve oxidative stress. In this study invesigators tested the possibility that KA-induced neuronal cell death might be attenuated in CuZn superoxide dismutase transgenic (SOD-Tg) mice. Acute administration of KA causes animal death in a dose-dependent fashion; this was attenuated in SOD-Tg mice. Similarly, KA caused dose-dependent neuronal cell death in the hippocampus of wild-type mice; this cell death was attenuated in the SOD-Tg mice, in a gene-dosage-dependent fashion, with homozygous mice showing complete protection even at the highest dose (45 mg/kg) of KA used in this study. These results provide further support for the involvement of oxygen-based radicals in the toxic effects of KA. Kainate-Induced Hippocampal DNA Damage is Attenuated in Superoxide Dismutase Transgenic Mice. Hirata H., and Cadet J.L. Molecular Brain Research, 48, pp. 145-148, 1997.

Methamphetamine (METH-induced) Serotonergic Nerve Terminals

Methamphetamine (METH) causes deleterious effects in brain monoaminergic systems. Evidence has accumulated to suggest that these effects may be mediated via the overproduction of the superoxide radicals. IRP investigators have recently shown that METH-induced dopamine (DA) depletion is attenuated in copper-zinc superoxide dismutase (CuZnSOD) transgenic (Tg) mice. In this study, autoradiographic studies of [125I]RTI-55 labeled serotonin (5-HT) uptake sites were used to evaluate the effect of a two dosing schedule (5 mg/kg over 10 mg/kg x4) of METH on striatal 5-HT uptake sites in nontransgenic (Non-Tg), heterozygous (Hetero and homozygous (Homo) SOD-Tg mice. The low dose caused no significant changes in striatal 5-HT uptake sites in any of the groups. The high dose caused marked decreases (-74%) in striatal 5-HT uptake sites in Non-Tg mice. In contrast, 5-HT uptake sites showed only a 31% decrease in homozygous SOD-Tg mice whereas heterozygous SOD-Tg mice showed 63% depletion. These results suggest that increased SOD activity can protect against METH- induced neurotoxicity in striatal serotonergic terminals. These data provide further evidence for a role of oxidative stress in the neurotoxic effects of METH. Methamphetamine- Induced Serotonin Neurotoxicity is Mediated by Superoxide Radicals. Hirata H., Ladenheim B., Rothman R.B., Epstein C., and Cadet J.L.

Hydrogen Peroxide Causes Apoptosis to Immortalized Neurons which is Abrogated by Catalase Overexpression

Hydrogen peroxide (h3O2) is a known toxicant which causes its damage via the production of hydroxyl radicals. It has been reported to cause both necrotic and apoptotic cell death. The present study was undertaken to evaluate the mode of h3O2- induced cell death and to assess if overexpression of catalase could protect against its toxicity. h3O2 causes cell death of immortalized CSM 14.1 neural cells in a dose-dependent manner. h3O2-induced death was associated wit hDNA laddering as shown by agarose gel electro- phoresis. Stable overexpression of catalase by transfection of a vector containing human cDNA into these dells markedly attenuated h3O2-induced toxic effects. Transfection of a vector containing a SOD cDNA afforded no protection. These results indicated that h3O2 can lead to the activation of endonuclease enzymes that break DNA into oligosomes. These cells which overexpress catalase or SOD will help to determine the specific role of h3O2 or O2- in the deleterious effects of a number of toxins. Overexpression of Superoxide Dismutase and Catalase in Immortalized Neuronal Cells: Toxic Effects of Hydrogen Peroxide. Mann H., McCoy M.T., Subramaniam J., Van Remmen H., and Cadet J.L. Brain Research, 770, pp. 163-168, 1997.

The Cellular Resistance Developed to the Toxic Effects of Drugs with Different Chemical Structures and Mechanisms of Action is Known as Multidrug Resistance (MDR)

The toxic effects of methamphetamine (METH) (2.5, 5.0, and 10.0 mg/kg) and methylenedioxymeth-amphetamine (MDMA) (5.0, 10.0 and 20.0 mg/kg) on dopaminergic systems were assessed in the striatum and of the nucleus accumbens in mdrla wild-type and knockout mice. METH caused significant dose-dependent decreases of dopamine (DA) DA transporters (DAT) in the striatum and the nucleus accumbens (NAc) of both wild-type and knockout mice. The lowest dose of METH (2.5 mg/kg) caused only small changes in the wild-type, but marked decreases in mdrla knockout mice. The two higher doses (5 mg/kg) caused similar changes in both strain of mice. In contrast to METH, MDMA caused a greater percentage decrease in DAT in the wild-type mice. For example, the lowest dose (5 mg/kg) caused significant decreases in DAT in the NAc of wild-type but not of mdrla knockout mice. The highest dose (20 mg/kg) cased similar changes in both the strains. These results suggest that EMTh and MDMA interact differently with P-glycoproteins. These observations document, for the first time, a role for these proteins in the entry of METH and MDMA in to the brain via the blood -brain barrier, with P-glycoprotein possibly facilitating the entry of MDMA but interfering with that of METH in the brain. Differential Toxic Effects of Methamphetamine (METH) and Methylene-dioxymethamphetamine (MDMA) in Multidrug-Resistant (Mmdrla) Knockout Mice. Mann H., Ladenheim B., Hirata H., Moran T.H., and Cadet J.L.

3,4-Methylenedioxymethamphetamine (MDMA), A Substitute Amphetamine, is Well Known as a Drug of Abuse In the United States and Europe

The drug 3,4-methylene- dioxymethamphetamine (MDMA) is a serotonergic neurotoxiant that causes hyperthermia and depletion of serotonin (5-HT) and 5-hydroxy-indole-3-acetic acid (5-HIAA) in the central nervous system. Formation of neurotoxic metabolites of MDMA, e.g., 2,4,5-tryhydroxy- methamphetamine and 2,4,5-trihydroxyamphetamine, involves hydroxyl and/or superoxide free radicals. This study was designed to determine whether the hydroxyl free-radical- trapping agent salicylate could provide protection against MDMA neurotoxicity in rats. In the acute studies, sodium salicylate (12.5-400 mg/kg, calculated as free acid) was injected inter-peritoneally (IP) 1 h before subcutaneous (SC) injections of MDMA (20 mg/kg as base). In the chronic studies, sodium salicylate (3.1-100 mg/kg) was injected IP 1 h before repeated SC injections of MDMA (10 mg/kg as base, twice daily, at 0830 and 1730 h for 4 consecutive days). Repeated MDMA administration depleted contents of 5-HT and 5-HIAA in the frontal cortex, hippocampus and striatum. Coadministration of salicylate plus MDMA did not significantly alter MDMA-induced depletion of 5-HT and 5-HIAA in these tissues. Thus, salicylate, a hydroxyl free-radical-trapping agent, does not protect against MDMA-induced hyperthermia and depletion of 5-HT and 5-HIAA. These observations suggest that MDMA- induced neurotoxicity may occur mainly through the production of superoxide or other radicals rather than hydroxyl free radicals. Salicylate actually potentiated MDMA-induced hyperthermia and lethality, findings that might be of clinical relevance. Yeh, S.Y. Effects of Salicylate on 3,4-Methylenedioxymethamphetamine (MDMA)-Induced Neurotoxicity in Rats. Pharm. Biohem. & Behav, 58, pp. 701-708, 1997.

The Intracellular Calcium Mobilizing Effect of Dantrolene - A Drug Used to Treat Malignant Hyperthermia and Neuroleptic Malignant Syndrome

Dantrolene is a hydantoin derivative with muscle relaxant properties that is used to treat both the malignant hyperthermia triggered by a volatile anesthetic such as halothane and the neuroleptic malignant syndrome (NMS) triggered by neuroleptic therapy. The exact mechanism underlying the action of dantrolene, however, is not well known. Dantrolene has also been shown to block long-term potentiation in hippocampal slices. As intracellular calcium ([Ca2+]i) is implicated in these actions affected by dantrolene, investigators examined the effects of dantrolene in this study using rat frontal cortical cultures. Micromolar concentrations of dantrolene inhibited the NMDA- and KCl-induced increase in [Ca2+]i. Dantrolene partially inhibited the caffeine-induced increase in [Ca2+]i whereas it did not affect the bradykinin-induced increase in [Ca2+]i. Blocking the Ca2+ influx into cells did not affect

these actions of dantrolene. These results indicate that dantrolene affects the ryanodine-sensitive intracellular calcium pools while not affecting the IP3 receptor-controlled [Ca2+]i. Results also suggest that dantrolene's mobilizing effect on the [Ca2+]i operates independently of the Ca2+ influx from the medium. Hayashi, T., Kagaya, A., Takebayashi, M. Oyamada, T., Inagaki, M., Tahara, Y., Yokota, N., Horiguchi, J., Su T-P. and Yamawaki, S. J. Neural Transmission, 104, pp. 811-824, 1997.

Beneficial Effect of the Sigma Selective Ligand PRE-084 and Neurosteroids on the Impairment of Learning Induced after the Central Administration of ß25-35-Amyloid Peptide

PRE-084, a sigma ligand discovered at the NIDA IRP, improves learning and memory impairment induced by ß25-35-amyloid peptide known to be related to Alzheimer's disease. As a continuing effort to demonstrate its memory-improving effects investigators examined if PRE-084 might affect the mnemonic deficit induced by the central injection of ß25- 35-amyloid peptide which is known to be related to Alzheimer's disease. PRE-084, like certain neurosteroids, dramatically improved the learning and memory impairment induced by the amyloid peptide. Another sigma receptor agonist (+)pentazocine also prevented the learning impairment induced by ß25-35-amyloid. In addition, neurosteroids such as dehydro-epiandrosterone sulfate (DHEAS) and pregnenolone sulfate (PGNS) which have been shown to react with sigma receptors also improved the memory deficit induced by ß25-35-amyloid. Interestingly, progesterone antagonized the memory-improving effects of PRE-084, (+)pentazocine, DHEAS, and PGNS. These results show a cross-beneficial effects between alkaloidal and steroidal classes of sigma receptor ligands and suggest a possibility of the clinical development of PRE-084 as a therapeutic drug for mnemonic deficit. Maurice, T., Su, T-P. and Privat, A. Neuroscience, 83, pp. 413-428, 1998.

Isolation and Partial Characterization of an Opioid-Like 88 KDa Hibernation-Related Protein

In a continual effort to characterize the protein component responsible for the induction of animal hibernation, we first partially purified protein fractions from both winter-hibernating and summer-active woodchucks and performed the differential SDS-PAGE electrophoresis. A 88 KDa protein was thus identified which is much enriched in the winter plasma when compared to the summer sample. A partially purified protein fraction containing the 88 KDa protein fraction was able to inhibit the contractions of mouse vas deferens - indicative of an opioid action in nature. Proteolytic digestion of the protein yielded several peptides whose amino acid sequences were determined. Searches of Genbank and EMBL databases showed no proteins having significant homology with the peptides from the 88 KDa protein. Pursuing the identification of the 88 KDa protein, a 590 bp fragment of the cDNA of the protein was amplified from hibernating woodchuck liver. Search through the SwissProt database of the nuclei acid sequence of the 590 bp produced a single match with an overall identity of 65.4% with a human á1B-glycoprotein. However, despite the high homology, the molecular weight of the á1B-glycoprotein is only 63 KDa. We are pursuing a full clone of the 88 KDa protein in order to determine its genuine identity and biochemical activity. Horton, N.D., Oeltgen, P.R., Kaftani, D., Bruce, D.S., Turker, M., Khattar, N., Su T.-P. and Bolling, S.F. Comparative Biochem. & Physiol., In Press.

Clinical Pharmacology Branch
Chemistry and Drug Metabolism Section

Cocaine Binds Directly to Human Hair: In Vitro Characterization

Previous studies at the IRP have shown that human hair can sequester cocaine. However, detailed binding studies examining the complex nature of binding of cocaine to human hair have never been carried out. The effect of differences between hair types on the extent of drug incorporation into hair is an important issue, because hair is currently being collected and analyzed to identify drug use by individuals in the workplace. A major concern is that hair test results may not be consistent or impartial for individuals with different hair types. Therefore, an understanding of the nature of drug binding to hair is needed in interpreting hair testing results. In this study investigators carried out the in vitro characterization of binding of radiolabeled cocaine to human hair. Results indicate that human hair can bind cocaine directly in a saturable manner with a stereoselectivity favoring the levoisomer of cocaine. Greater radioligand binding occurred in male Africoid hair than in female Africoid hair and in all Caucasoid hair types. Melanin was considered the most likely binding site for cocaine in hair. Differences in radioligand binding between hair types appeared to be due to differences in the density of binding sites formed by melanin in hair. Joseph, R.E., Tsai, W.J., Tsao, L-I, Su T-P and Cone E.J. J. Pharmacol. Exp. Ther., 282, pp. 1228-1241, 1997.

Neuroimaging Research Branch

Atrophy in the Gray Matter of the Prefrontal Cortex of Substance Abusers may Contribute to the Neuropathology of Functional Impairments Associated with Substance Abuse Disorder

Volumes of the prefrontal lobe in subjects with histories of polysubstance abuse (n=25) were measured and compared with those in normal volunteers (n=14), using high-resolution volumetric magnetic resonance imaging (MRI). The total volumes of the prefrontal lobes were significantly smaller in the substance abuse group than in controls. When the prefrontal lobe was segmented for gray and white matter, the deficit in the substance abusers was seen as significantly smaller volumes of gray but not of white matter. These results indicate that hypoplasia and/or atrophy in the prefrontal cortex accompany substance abuse and suggest that structural deficits in the prefrontal cortex may play an essential role in the neuropathological basis of functional impairments in substance abuse disorder, as demonstrated by functional brain imaging and cognitive studies. Liu, X., Matochik, J.A., Cadet, J.L., and London, E.D. Smaller Volume of Prefrontal Lobe in Polysubstance Abusers: A Magnetic Resonance Imaging Study. Neuropsychopharmacology, 18, pp. 243-252, 1998.

A Simple Radiosynthesis of a High Specific Activity Radiofluorinated Ligand for Labeling Nicotinic Acetylcholine Receptors in the Brain is Suitable for *in vivo* PET Imaging Studies

Only recently have epibatidine-related radioligands for the nicotinic acetylcholine receptor (nAChR) been synthesized that have high specific activity, high affinity for the receptor, and relatively low non-specific binding. IRP scientists have used a new chemical series of 3-pyridyl ethers synthesized by Abbott Laboratories and having subnanomolar affinity for the nAChR to develop a new fluorinated radioligand. The radiosynthesis of 2-[18-F]A-85380 has yielded a radiotracer with a high specific activity (1050 mCi/mol). It is noteworthy that the parent compound, A-85380, has a substantially wider margin of safety than epibatidine-type compounds in animal studies. Therefore, a high specific activity combined with the potential for a wider margin of safety suggest that of 2-[18-F]A-85380 that may be an excellent positron emission tomography (PET) imaging radiotracer for nAChRs. Horti, A.G., Koren, A.O., Ravert, H.T., Musachio, J.L., Mathews, W.B., London, E.D. and Dannals, R.F. Synthesis of a Radiotracer for Studying Nicotinic Acetylcholine Receptors: 2-[18F]fluoro-3-(2(S)-azetidinyl- methoxy)pyridine (2-[18F]A-85380). J. Label Compds. Radiopharm. XLI, pp. 309-318, 1998.

Preclinical Pharmacology Branch
Behavioral Pharmacology Section

Chronic Exposure to Caffeine Changes the Behavioral Effects of Psychostimulant Drugs

Epidemiological surveys in humans demonstrate that caffeine, the main psychoactive ingredient of coffee, is a positive correlate in drug abuse. To characterize the behavioral nature of caffeine interactions with other psychostimulants, we examined the effects of chronic exposure to caffeine in the drinking water on the behavioral response to nicotine, amphetamine, and cocaine in rats responding under a fixed interval (FI) schedule of food reinforcement. Chronic exposure to caffeine produced complete and insurmountable tolerance to the response-rate increasing (stimulant) effects of acute caffeine in caffeine-drinking rats but it sensitized rats to the stimulant effects of amphetamine and cocaine on schedule-controlled, food maintained- behavior. In contrast to amphetamine and cocaine, the behavioral effects of nicotine remained unaffected by chronic caffeine exposure. The results of this experiment (1) suggest that different pharmacological mechanisms precipitate the behavioral response to different psychomotor stimulant drugs, and, more generally, (2) warns against the simplistic notion of nicotine as an abused substance through its stimulatory actions on dopaminergic reinforcement process. Jaszyna, M., Gasior, M., Shoaib, M., Yasar, S. and Goldberg S.R. Behavioral Effects of Nicotine, Amphetamine and Cocaine under a Fixed-Interval Schedule of Food Reinforcement in Rats Chronically Exposed to Caffeine. Psychopharmacology, In Press.

Motivational Properties of Stimuli Associated with Cocaine

Compounding stimuli previously associated with two different appetitive reinforcers produces additive summation (an increase in responding to the compound over the elements). However, compounding stimuli associated with appetitive and aversive reinforcers produces no increases in responding. Therefore, by compounding a drug-associated stimulus with an appetitive reinforcer we can determine whether the drug reinforcer controls responding through appetitive or aversive motivational states. NIDA researchers recently showed that compounding stimuli associated with cocaine and food reinforcement produces additive summation comparable, to that seen when food and water associated stimuli are compounded. These results suggest that discriminative stimuli associated with cocaine reinforcement are appetitive in nature and that stimuli associated with non-drug appetitive reinforcers may increase the motivation to self-administer cocaine. Panlilio, L.V., Weiss, S.J., and Schindler, C.W. Motivational Effects of Compounding Discriminative Stimuli Associated with Food and Cocaine. Psychopharmacology, 136, pp. 70-74, 1998.

Butyrylcholinesterase as a Cocaine Abuse Treatment

A primary enzyme for the metabolism of cocaine is butyrylcholinesterase (BChE). To determine whether the systemic administration of BChE could increase metabolism of cocaine sufficiently to alter a behavioral effect, rats were tested in a locomotor activity chamber following 17 mg/kg cocaine IP. In rats pretreated IV with 5000 IU horse-serum derived BChE, the locomotor activating effect was significantly attenuated. The BChE pretreatment produced a peak increase of approximately 400 fold in plasma BChE levels. When added to rat plasma, this amount of BChE reduced the cocaine half-life from over 5 hours to less than 5 min. BChE altered the cocaine metabolic pattern such that the relatively non-toxic metabolite ecgonine methyl ester was produced, rather then benzoylecgonine. These results suggest that systemic administration of BChE can increase metabolism of cocaine sufficiently to alter a behavioral effect of cocaine, and thus should be investigated as a potential treatment for cocaine abuse. Carmona, G.N., Schindler, C.W., Shoaib, M., Jufer, R., Cone, E.J., Goldberg, S.R., Greig, N.H., Yu, Q.-S. and Gorelick, D.A. Attenuation of Cocaine-Induced Locomotor Activity by Butyrylcholinesterase. Exp. Clin. Psychopharmacology, In Press.

Novel Rapid Cardiovascular and Behavioral Actions of Cocaine

In collaboration with scientists at Georgetown University IRP scientists have recently reported a novel pharmacological effect of cocaine. This novel effect is rapid in onset and brief in duration and precede cocaine's prolonged dopamine-dependent pharmacological effects. This rapid effect appears to be independent of its inhibitory effects either on monoamine transporters or sodium channels. The rapid effect consisted of marked increases in blood pressure and heart rate and an intense, abrupt behavioral arousal. In humans, intravenous cocaine has been shown to produce a rapid and brief "rush" followed by a prolonged "high." There are pharmacological and time-course similarities between the "rush" reported in humans and the present novel rapid effect in animals. Further studies are underway to characterize the neuropharmacological mechanisms that precipitate these rapid onset, brief duration, cardiovascular and behavioral effects of cocaine. Tella, S.R. and Goldberg, S.R. Monoamine Transporter and Sodium Channel Mechanisms in the Rapid Pressor Response to Cocaine. Pharmacol Biochem Behav, 59, pp. 305-312, 1998.

Genotype and Previous Nicotine Exposure Are Determinants of the Reinforcing Effects of Nicotine in Rats

In the course of studying various pharmacological and genetic influences on i.v. nicotine self-administration in monkeys and rats, we have recently developed an acquisition paradigm in rats free from previous food shaping and food deprivation, which allows us to assess the initiation phase of nicotine-seeking behavior. Sprague-Dawley rats acquired nicotine self-administration over a 10-to-14 day test period, while a Long-Evans strain showed less reliable acquisition and Fisher and Lewis rats failed to show acquisition. To examine consequences of adaptation to motivational effects of nicotine, we examined the effects of chronic nicotine treatment prior to acquisition tests, using a regimen found to facilitate conditioning of nicotine-induced place preferences. Results strongly suggest that nicotine's effects as a reinforcer in rodents can be altered by previous nicotine exposure and that genotypic differences may govern sensitivity to the reinforcing properties of nicotine. Shoaib, M., Schindler, C.W. and Goldberg, S.R. Nicotine Self-administration in Rats: Strain and Nicotine Pre-exposure Effects on Acquisition. Psychopharmacology, 129, pp. 35-43, 1997; Shoaib, M., Thorndike, E., Schindler, C.W. and Goldberg, S.R. Discriminative Stimulus Effects of Nicotine and Chronic Tolerance. Pharmacology, Biochemistry and Behavior, 56, pp. 167-173, 1997.

Behavioral Effects of Selegiline Alone and in Combination with Amphetamine and Cocaine

Selegiline, an irreversible ß-type monoamine oxidase inhibitor, in clinical use for treatment of Parkinson's disease, is metabolized to *l*-methamphetamine and *l*-amphetamine which release dopamine from presynaptic nerve terminals. A series of studies have been conducted in rats, squirrel monkeys and rhesus monkeys that involve assessment of the behavioral actions of ß-PEA and the stereoisomers of amphetamine, methamphetamine and selegiline alone, and of selegiline as a pretreatment prior to assessing the behavioral actions of ß-PEA, amphetamine and methamphetamine. In i.v. self-administration studies conducted in rhesus monkeys, *l*-methylamphetamine, the major metabolite of *l*-deprenyl, was as effective and only slightly less potent a reinforcer as methamphetamine (*d*-methylamphetamine) and was as effective a reinforcer as *l*-cocaine. In contrast, selegiline failed to maintain self-admin- istration behavior above saline levels, even at high doses. Acute i.m. treatment with selegiline up to a 1.0 mg/kg dose, which was as high as we could go without signs of nonspecific toxicity such as reduction of food intake, had no effect on either *l*-methamphetamine or *l*-cocaine self- administration. There was, however, a dramatic potentiation of ß-PEA self-administration, indicating strong MAO-B inhibiting activity. In drug-discrimination studies with both rats and squirrel monkeys, selegiline had dose-dependent amphetamine- and methamphetamine-like discriminative stimulus properties but only at doses tenfold or more above the clinically relevant dose range. Results indicate that selegiline (1) has amphetamine-like discriminative stimulus effects attributable to its metabolites at very high doses, (2) does

not function as a reinforcer under conditions normally used to assess abuse liability in animals and, (3) does not appear promising as a medication for treatment of stimulant abuse, although further studies under more chronic dosing conditions are underway. Goldberg, S.R. and Yasar, S. Methamphetamine Administration and Associated Neurotoxicity: Effects of Selegiline (*l*-Deprenyl). In: Teelken, A.W. and Korf, J. (eds.) Neurochemistry: Cellular, Molecular, and Clinical Aspects, Plenum Pub. Corp., pp. 327-330, 1997.

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National Institute on Drug Abuse

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

May, 1998

Program Activities

Program Announcements/RFAs

On February 25, 1998, NIDA issued a Program Announcement to encourage research on the **Role of Limbic System and Brain Ontogeny in Drug Abuse (PA-98-032)**. This initiative is designed to support basic research into the fundamental mechanisms of development of the midbrain and basal forebrain structures that mediate the euphoric properties of drugs as well as understanding how drugs of abuse affect the cellular and molecular mechanisms underlying nervous system development.

On February 25, 1998, NIDA and a number of other NIH components including the Office of Alternative Medicine, NCI, NHLBI, NIDR, NIAMS, NINDS and the Agency for Health Care Policy and Research issued a joint Program Announcement on **Acupuncture Clinical Trial Pilot Grants (PAS-98-033)**. This PA encourages pilot studies to establish the methodological feasibilty and strengthen the scientific rationale for proceeding to full-scale randomized clinical trials on the use of acupuncture to prevent, manage, or treat various symptoms or disorders.

On February 20, 1998, NIDA issued an RFA entitled **Drug Abuse Prevention and Communications Research (DA-98-006).** This RFA, funded with dollars transferred to NIDA from the Office of National Drug Control Policy (ONDCP), will encourage scientists to submit applications to study the influences of the media on the onset and continuation of drug use, and the use of mass media and communications as a prevention intervention. The purpose of the program is to conduct research and produce results that can guide the design and development process of the national Youth Anti-Drug Media campaign over the next five years. These areas of research include: a) emotional and cognitive functioning and their relationship to message development; b) assessment of communications messages and strategies for specific youth audiences; c) relationship between knowledge about drugs and their effects, attitudes, perceptions of risk, and personal susceptibility, and drug using/refusal behaviors; and d) other areas of research on the influence of the public media--ie., television, radio, news, the internet, and entertainment, sports, films, music and fashion and how that affects drug use among youth. Grant proposals were due May 7, 1998 with eligible grants due for review by the National Advisory Council in September 1998.

Evaluation of the National Youth Anti-Drug Media Campaign

On April 1, 1998, NIDA released a Request for Proposals (RFP) for an openly competitive contract, funded by the Office of National Drug Control Policy, to assess the direct impact of the National Youth Anti-Drug Media Campaign on youth and parents. The evaluation of the Campaign, which incorporated the advice and consultation of a group of research experts in evaluation, will be designed to be able to determine the extent to which changes in drug abuse-related knowledge, attitudes, beliefs, and behaviors can be attributed to exposure to the media campaign.

The evaluation will do the following to measure major evaluation objectives:

- Analyze data from existing and ongoing national surveys to assess prevalence rates of drug abuse and drug-related beliefs and attitudes;

- Design and conduct new surveys of children aged 9-18 and parents of children aged 9-18;
- Design and conduct new longitudinal surveys of linked panels of children and parents at 4 to 6 NIDA-designated sentinel sites to assess more in-depth relationships over time between exposure to the media and behavior/attitude change;
- Monitor the media exposure of the target audiences using existing and ongoing tracking system(s) for measuring the number, placement, and type (paid/unpaid, print/electronic) of advertisements, target groups, and message content, both nationally and at sentinel sites; and
- Design and develop a system for measuring community-based drug abuse prevention and other related activities at the sentinel sites.

The contract will produce campaign evaluation reports every six months throughout the five years. NIDA plans to award the contract in late September.

Phase I Clinical Trial of Cocaine Vaccine

The cocaine vaccine product developed by the ImmuLogic Pharmaceutical Corp., partially funded by two SBIR grants and a SPIRCAP (U19) award, was first administered to humans in a Phase I clinical trial, April 1998. This marks the first clinical study of a peripheral blocker and the first time a new molecular entity developed specifically for cocaine abuse/dependence treatment has been administered to humans.

NIDA'S New/Competing Awards Since May 1997

Abel, Marc S. --- Fuhs Chicago Medical School
Cocaine-induced Behavioral Sensitization and Seizures

Agar, Michael H. --- University of Maryland--Department of Anthropology
Trend Theory in Community Context

Alvarado, Rose --- University of Utah School of Medicine
NIDA Strengthening Washington, DC Families Grant

Andrews, Judy A. --- Oregon Research Institute
Social Influences on Child Substance Use and Attitude

August, Gerald J. --- University of Minnesota
Risk-focused Prevention Drug Abuse in Aggressive Youth

Baraban, Jay M. --- Johns Hopkins University
Psychotropic Drug Responsive Transcription Factors

Batki, Steven L. --- University of California at San Francisco
Iradipine Pharmacotherapy of Methamphetamine Dependence

Bayer, Barbara M. --- Georgetown University Medical Center
Lymphocyte Activity During Stress: Effects of Morphine

Bennett, Charles L. --- Lakeside VA Medical Center
Multicity Study of Quality of Care for HIV-related PCP

Berger, S. Paul --- University of Cincinnati
Pharmacotherapy of Cue-induced Cocaine Craving

Berman, L. Yemiliya --- New York University Medical Center
Opiate Peptides and Receptors in the FAT/FAT Mice

Bernstein, Edward --- Boston University
A Randomized Trial of the Brief Negotiated Interview

Bigelow, George E. --- Johns Hopkins Bayview Campus
Human Behavioral Pharmacology of Drug Abuse

Bigelow, George E. --- Johns Hopkins Bayview Campus
Pharmacological Modulation of Cocaine Effects

Booth, Brenda M. --- University of Arkansas for Medical Sciences
Outcomes and Health Services in Drug Use Disorders

Booze, Rosemarie M. --- University of Kentucky Medical Center
Gender Differences in Cocaine Responsiveness

Bosron, William F. --- Indiana University School of Medicine
Cocaine, Heroin & Opioid Metabolism by Carboxylesterases

Boulter, James R. --- University of California at Los Angeles
Transgenic Approaches to Acetylcholine Receptor Function

Bradberry, Charles W. --- VA Medical Center
CNS Consequences of Chronic Cocaine Self-administration

Brecht, Mary-Lynn --- University of California at Los Angeles
Methamphetamine Abuse: Natural History, Treatment Effects

Butler, Stephen F. --- Innovative Training Systems
Development of an Addiction Severity Assessment Tool

Carr, Kenneth D. --- New York University Medical Center
CNS Opioid Mechanisms That Modulate Reward and Aversion

Castagnoli, Neal, Jr. --- Virginia Polytechnic Institute
Inhibition of Mao-A and Mao-B by Tobacco Alkaloids

Cheng, Li S. --- SRI International
Genetic Analysis of Smoking Behavior & Smoking Relapse

Cheng, Peter Y. --- Cornell University Medical College
ACTH Release by Dyn A: Role of NMDA Receptors

Chiauzzi, Emil --- Innovative Training Systems
Smart: An Alternative for Incarcerated Substance Abusers

Cinciripini, Paul M. --- University of Texas M.D. Anderson Cancer Center
Scheduled Smoking with Transdermal Nicotine

Cox, Brian M. --- Henry M. Jackson Foundation
Med Regulation of Opioid Systems

Crimmins, Susan M. --- National Development/Research Institute Inc.
Learning about Violence and Drugs among Adolescents

Deadwyler, Samuel A. --- Bowman Gray School of Medicine
Neurophysiological Analysis of Self-administration of Cocaine

Deadwyler, Samuel A. --- Bowman Gray School of Medicine
Hippocampus Correlates of Drug Abuse in Rats

Deren, Sherry --- National Development/Research Institute Inc.
High-risk Drug Use & HIV: Learning from the New York City Epidemic

Deutsch, Dale G. --- State University of New York
Anandamide: Chemistry and Biochemistry

Dow-Edwards, Diana L. --- State University of New York -- Health Science Center
Cocaine and Development: Neurobiological Perspectives

Dwoskin, Linda P. --- University of Kentucky
Development of Selective Nicotinic Receptor Antagonists

Engel, Jorgen A. --- Goteborg University Faculty of Medicine
Ethanol and Nicotine: Neurobiological Interactions

Ettenberg, Aaron --- University of California
Mechanisms of Opiate and Stimulant Drug Reinforcement

Falk, John L. --- Rutgers University
Cocaine, Caffeine and Nicotine: Oral Abuse and Behavior

Fiorentine, Robert --- UCLA Drug Abuse Research Center
Abuse-Distress Model of Drug Treatment Engagement

Fischman, Marian W. --- Trustees of Columbia University
IV Cocaine Abuse Treatment: A Laboratory Model

Flay, Brian R. --- University of Illinois -- Chicago
Extension of Aban Aya Youth Project

Fleckenstein, Annette E. --- University of Utah
Methamphetamine and Dopamine Transporters

Fricker, Lloyd D. --- Albert Einstein College of Medicine
Regulation of Neuropeptide-processing Enzymes

Gatley, S. John --- Associated Universities, Inc.
Estimation of Synaptic Dopamine Using PET and SPECT

Glick, Stanley D. --- Albany Medical College
Neuro-behavioral Mechanisms of Drug Addiction

Gutstein, Howard B. --- University of Michigan
The Role of ERK Signaling in Acute Opioid Tolerance

Hagan, Holly C. --- King County Department of Health
The Raven Study: Advancing HIV Prevention for IDUs

Hampson, Robert E. --- Bowman Gray School of Medicine
Cannabinoid Effects on Sensory Processing in Brain

Hansen, William B. --- Tanglewood Research, Inc.
Drug Prevention Mediating Variables Survey

Hanson, Glen R. --- University of Utah
Role of Neurotensin in Methamphetamine Effects

Hasin, Deborah S. --- Research Foundation for Mental Hygiene
Prism: Comorbidity Diagnosis for Drug Abuse Treatment

Hauser, Kurt F. --- University of Kentucky
Role of Abused Opiate Drugs in Neural Development

Henriksen, Steven J. --- Scripps Research Institute
Electrophysiological Substrates of Opioid Abuse

Hook, Vivian Y. --- University of Calif at San Diego
Biosynthesis of Enkephalin Opioid Peptides

Hops, Hyman --- Oregon Research Institute
Young Adult Substance Use-- Predictors and Consequences

Houghten, Richard A. --- Torrey Pines Institute/Molecular Studies
Small Molecule Orphanin FQ/Nociceptin Receptor Ligands

Ho, Wenzhe --- Stokes Research Institute/Childrens Hospital
Opioids, Substance P, and HIV-1 Infection of Microglia

Jackson, Denise --- Northeastern University
Neurochemical Effects of Prenatal Cocaine in Rat Striata

Jarbe, Torbjorn U. --- Allegheny University of the Health Sciences
Exogenous and Endogenous Cannabinoids: A Comparison

Jarvik, Murray E. --- University of California -- Neuropsychiatric Institute
Selective Attention to Smoking Stimuli

Javitch, Jonathan A. --- Columbia University
Dopamine Transporter: Substrate & Cocaine Binding Sites

Jones, Reese T. --- University of California
Pharmacokinetics of Drugs of Abuse in Skin and Hair

Kanarek, Robin B. --- Tufts University
Actions of Opiate Drugs: Dietary Modulation

Kantak, Kathleen M. --- Boston University
Cognitive Aspects of Addiction-related Behavior

Kelley, Ann E. --- University of Wisconsin
Neural Mechanisms in the Nucleus Accumbens and Behavior

Kendall, Carl --- Tulane University
Adherence to HIV Therapies in Drug Users in New Orleans

Kilts, Clinton D. --- Emory University School of Medicine
Functional Anatomy of Drug Craving in Cocaine Addiction

Klein, Thomas W. --- University of South Florida
Cannabinoid Receptors on Immune Cells

Kosobud, Ann E. K. --- Indiana University
Functional Properties of VTA Neurons

Kosobud, Ann E. K. --- Indiana University
Circadian Anticipation as a Determinant of Drug Craving

Kosofsky, Barry E. --- Massachusetts General Hospital
Cocaine-altered Brain Growth: Dopamine Knockout Analysis

Kreek, Mary J. --- Rockefeller University
Addictive Drugs- Pharmacology and Physiology

Kuhar, Michael J. --- Yerkes Primate Research Center
Cart: A Novel Cocaine Regulated Neurochemical

Kuhn, Cynthia M. --- Duke University Medical Center
Gender Differences in Stimulant Action

Lee, Tong H. --- Duke University Medical Center
Dopamine Presynaptic Inhibition and Cocaine Treatment

Lehman, Wayne --- Texas Christian University
Drug Use in the Workplace: A Prevention Training Program

Lemos, Jose R. --- University of Massachusetts/Department of Physiology
Mechanisms of Opioid Action on Peptide Release

Leventhal, Bennett L. --- American Academy of Child and Adolescent Psychiatrists
AACAP Physician Scientist Program in Substance Abuse

Levin, Frances R. --- Research Foundation for Mental Hygiene
Methylphenidate Treatment for Cocaine Abuse and ADHD

Levin, Frances R. --- Research Foundation for Mental Hygiene
Treatment of Adult ADHD in Methadone Patients

Liddle, Howard A. --- University of Miami
Center for Treatment Research on Adolescent Drug Abuse

Lockridge, Oksana --- University of Nebraska Medical Center
Rapid Detoxification of Cocaine by Butyrylcholinesterase

Lowy, Franklin D. --- Montefiore Medical Center
Staphylococcal Colonization and Diseases in Drug Users

Luther, Suniya S. --- APT Foundation, Inc.
Relational Parenting Therapy for Opioid Abusing Mothers

Mackie, Kenneth P. --- University of Washington
Neuronal Cannabinoid Receptor: Function & Regulation

Malcolm, Robert J. --- Medical University of South Carolina
Amlodipine Treatment for Cocaine Dependence

Mash, Deborah C. --- University of Miami
CNS Mechanisms in Cocaine Related Sudden Death

Mc Evoy, Joseph P. --- Duke University Medical Center
Smoking, Schizophrenia, and Atypical Antipsychotics

Mc Ginnis, Marilyn Y. --- Mount Sinai School of Medicine
Anabolic Androgenic Steroid Effects on Brain & Behavior

Mckay, Dennis B. --- Ohio State University
Adrenal Nicotinic Receptors and Catecholamine Secretion

Mckay, James R. --- University of Pennsylvania
Studies of Aftercare for Substance Abusers

Mendelson, Wallace B. --- University of Chicago
The Preoptic Area and Pharmacologic Sleep Induction

Metzger, David S. --- University of Pennsylvania
Effectiveness of Multi-site NEP in Preventing HIV & HBV

Milby, Jesse B. --- University of Alabama
Sustaining Abstinence in Dually Diagnosed Homeless

Miller, Bonnie C. --- University of Texas Southwestern Medical Center
Characterization of Opioid Receptors on T Cell Subsets

Miller, Leslie M. --- William Marsh Rice University
Medicinal Mysteries from History

Milner, Teresa A. --- Cornell University Medical College
Ultrastructural Interactions of Opioids in Hippocampus

Montague, P. Read --- Baylor College of Medicine
Computational Substances of Addiction and Reward

Montoya, Isaac D. --- Affiliated Systems Corporation
Employment Dynamics in Response to Welfare Reform

Nelson, Suchitra S. --- Case Western University
Iron Deficiency Anemia in Cocaine Exposed Children

O'Leary, Daniel S. --- University of Iowa Hospitals & Clinics
Acute Marijuana Effects on Regional Cerebral Blood Flow

O'Malley, Karen L. --- Washington University
Modulation of Dopamine Autoreceptor Function by Cocaine

Owens, Samuel M. --- University of Arkansas for Medical Sciences
Antibody-based Therapy for Methamphetamine Abuse

Parsons, Loren H. --- Scripps Research Institute
Cocaine Reward and 5-HT-1b Receptors: Neural Mechanisms

Pasternak, Gavril W. --- Sloan Kettering Institute for Cancer Research
Synthesis and Pharmacology of Novel Opiate Ligands

Paterlini, Maria G. --- University of Minnesota
Modeling of Chemokine Receptors with Ligands and HIV

Pechnick, Robert N. --- Louisiana State University Medical Center
Neuroendocrine Effects of Self-administered Cocaine

Peterson, Phillip K. --- Minneapolis Medical Research Foundation, Inc.
Modulation of Cell-mediated Immune Function by Opiates

Picciotto, Marina R. --- Yale University School of Medicine
A Transgenic Approach to Nicotine's Effect on Cognition

Pincus, Harold A. --- American Psychiatric Association
Drug Abuse Research Scholars Program in Psychiatry

Pineda, Jaime A. --- University of California
Neurocognitive Etiology of Addiction-related Behavior

Polich, John M. --- Scripps Research Institute
Marijuana CNS Effects in Low- and High-risk Adults

Porreca, Frank --- University of Arizona
Opioid and Non-opioid Actions of Dynorphin in Pain

Prather, Paul L. --- University of Arkansas for Medical Sciences
Opioid Control Mechanisms of Signal Transduction

Prendergast, Michael --- UCLA Drug Abuse Research Center
TC Treatment for Prisoners: Long-term Outcomes & Costs

Ramsay, Douglas S. --- University of Washington
Individual Differences and Addictive Vulnerability

Razdan, Raj K. --- Organix Inc.
Anandamide: Structure-activity Relationships

Ringwalt, Christopher --- Research Triangle Institute
School Based Drug Prevention Program

Robertson, Hugh D. --- Cornell University Medical College
Modulation of Opioid & NMDA Receptor MRNA by Ribozymes

Rohde, Paul D. --- Oregon Research Institute
Psychiatric Disorders and the Natural History of Smoking

Rothenberg, Richard B. --- Emory University School of Medicine
Validity of Drug Users' Information on Network Contacts

Schafer, William --- University of California at San Diego
Genetic Analysis of Nicotine Adaptation in C Elegans

Schensul, Jean J. --- Institute for Community Research
Pathways to High-risk Drug Abuse among Urban Youth

Segal, David S. --- University of Califonia at San Diego School of Medicine
Behavioral Pharmacology of Acute and Chronic Amphetamine

Segre, Mariangela --- University of Illinois --Veterinary Pathobiology
Is An Anti-cocaine Idiotypic Vaccine Feasible?

Semple, William E. --- Case Western Reserve
Brain and Attention in Substance Abusers with PTSD

Simon, Eric J. --- New York University Medical Center
29th Annual International Narcotic Research Conference

Smith, Robert F. --- George Mason University
An Animal Model of Adolescent Drug Progression

Soderberg, Lee S. --- University of Arkansas for Medical Sciences
Immunotoxicity of Abused Nitrite Inhalants

Sokoloff, Pierre --- Institute de La Sante et De La Recherche
Synthesis & Evaluation of D3r Ligands for Cocaine Abuse

Solbrig, Marylou V. --- University of California
CNS Viral Injury and Vulnerability to Opiate Drug Abuse

Svikis, Dace S. --- Johns Hopkins Bayview Medical Center
Brief Intervention for Drug Use in Pregnant Women

Swan, Gary E. --- SRI International
Pharmacokinetics of Nicotine in Twins

Tancer, Manuel E. --- Wayne State University School of Medicine
HT/DA System Interaction in Psychostimulant Drug Effects

Taylor, Bradley K. --- University of California at San Francisco
Pain, Opioid Analgesia and Blood Pressure Control

Taylor, Jane R. --- Yale University School of Medicine
Cognitive Dysfunction after Chronic PCP, THC and Cocaine

Taylor, Jane R. --- Yale University School of Medicine
Cocaine Sensitization and Conditioned Reinforcement

Thomas, David L. --- Johns Hopkins University
HIV, Drug Use and Hepatitis C Pathogenesis

Triffleman, Elisa G. --- Central Treatment Unit
Psychotherapy of PTSD in Substance Dependent Patient

Tyor, William R. --- Medical University of South Carolina
Cocaine Effects on HIV Encephalitis in Scid Mice

Urban, Mark O. --- University of Iowa
Supraspinal Modulation of Hyperalgesia

Uretsky, Norman J. --- Ohio State University
Pertussis Toxin and Effects of Psychostimulant Drugs

Vaccarino, Anthony L. --- University of New Orleans
Tolerance to Morphine Analgesia: Biobehavior Factors

Vijayaraghavan, Sukumar --- University of Colorado Health Sciences Center
Calcium Signaling by Hippocampal Nicotinic Receptors

Vorhees, Charles V. --- Children's Hospital Research
Developmental Methamphetamine-induced Cognitive Deficits

Wagner, John J. --- North Dakota State University
Dynorphin Opioid Peptide Actions in the Hippocampus

Wechsberg, Wendee M. --- Research Triangle Institute
Woman-focused HIV Prevention with African Americans

Werling, Linda L. --- George Washington University
Molecular Mechanisms of PCP and Sigma Drug Action

Wessinger, William D. --- University of Arkansas for Medical Sciences
Dextromethorphan: Stimulus Properties & Pharmacokinetics

West, Mark O. --- Rutgers University
Cocaine's Effects on Movement-related Striatal Firing

Whitbeck, Leslie B. --- Iowa State University
Mille Lacs Family Alcohol and Drug Prevention Project

Worley, Paul F. --- Johns Hopkins University School of Medicine
IEG Homer and Drug Addiction Effector

Wu, Ping --- Research Foundation for Mental Hygiene Inc.
Adolescent Use of Alcohol and Drug Treatment Services

Xie, Xiang-qun --- University of Connecticut
NMR/computer Modeling for Cannabinoid Ligand Design

Yeomans, David C. --- University of Illinois
Nociceptor-selective Analgesia

Zadina, James E. --- Tulane University School of Medicine
Neurobiology of Endomorphis

Zhou, Renping --- Rutgers University
EPH Molecules in Otogeny of Brain Reward Circuits

Review Activities

Career Development Scientific Review Group

The first meeting of the career development review group to assess training, career development, fellowship, and related development applications from across all NIDA scientific areas met in April. Dr. Mark Swieter served as the Scientific Review Administrator (SRA). This meeting placed the entire spectrum of NIDA supported science together in one meeting, united by the theme of career development. Feedback suggests that it was a very successful meeting. It is anticipated that this group will become a standing committee.

Staff Development

As part of its ongoing series of staff development activities, OEPR sponsored a seminar for NIDA staff on the new review criteria of Significance, Approach, Innovation, Investigator, and Environment, which were applied in this review cycle. Drs. Teresa Levitin and William Grace led a discussion of the new criteria, the steps NIDA has taken to ensure that reviewers understand and use the new criteria, and the likely impacts of the new criteria.

OEPR developed and hosted another staff development workshop on "Working with the Center for Scientific Review" to prepare NIDA and NIMH staff for likely changes resulting from the integration of the review of some scientific areas into the CSR structure. Senior management and review staff from CSR, along with a project officer from another NIH Institute, presented methods of enhancing communication and cooperation with CSR. NIDA's Receipt and Referral Officer, Dr. Rita Liu, presented on coordination of receipt and referral activities with CSR. Drs. Levitin, Liu, and Grace organized the program and led the discussion, and the success of this workshop has been noted at the NIH Review Policy Committee and the NIH Extramural Scientist Training and Development Committee, which is developing plans

to present similar training based on this workshop.

Dr. William Grace assisted the NIH Office of Extramural Programs by serving as a facilitator for case studies presentations on two occasions. He facilitated a group for the Extramural Scientist Administrator Seminar Series and then served as a facilitator and panel member for an NIH-wide Core Topics/Case Studies training session. These case studies present actual events from NIH files that address complex issues in review administration, program management, and application of extramural policy.

Updates on Review Policies and Procedures

Dr. Teresa Levitin presented an update on changes in review policies and procedures to a NIDA sponsored meeting of the African American Researchers and Scholars Group on March 6. Similar presentations were made to other groups, including representatives from Historically Black Colleges and Universities at the Drug Abuse Research Technical Assistance Project (March 9, Dr. Grace), the NIDA INVEST and Hubert H. Humphrey Drug Abuse Research Fellows (March 13, Dr. Levitin), and the Hispano/Latino Researchers and Scholars Group (March 16, Drs. Levitin and Grace).

New Policies

The NIH has informed the extramural community of a new policy requiring the appropriate inclusion of children in NIH sponsored research. The policy becomes effective for applications received after the October 1, 1998 receipt date. Plans are being made for training all extramural staff on this new policy. The policy may be found at: http://grants.nih.gov/grants/guide/notice-files/not98-024.html.

The NIH has informed the extramural community that any investigator-initiated application requesting more than $500,000 in direct costs in any year, with the exception of those submitted in response to specific announcements with specific budget guidelines, must receive prior approval from a receiving Institute or Center. This policy is effective June 1, 1998 and may be found at: http://grants.nih.gov/grants/guide/notice-files/not98-030.html.

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Congressional Affairs

FY 1999 APPROPRIATIONS

On March 19, 1998, NIDA Director Alan Leshner testified before the House Appropriations Subcommittee on Labor, Health and Human Services, and Education. Dr. Leshner told the Subcommittee members that NIDA had a "year of exceptional accomplishment", and that "NIDA-supported researchers made enormous strides toward improved understanding, prevention and treatment of one of our Nation's most serious public health problems--drug abuse and addiction." Highlighting NIDA's efforts to launch its first ever large scale multi-center clinical trial for cocaine medication, Dr. Leshner explained that NIDA is capitalizing on a body of current findings that suggest that medications consistently work better when they are used in combination with behavioral therapies. He went on to say that addiction science "has matured to the point where we can take a more systematic approach to rapidly and efficiently test the effectiveness of behavioral, psychosocial and pharmacological treatments in large-scale, multi-site clinical trials."

Dr. Leshner cited some of NIDA's major scientific accomplishments, including the use of functional magnetic resonance imaging (fMRI) to look at the dynamic changes of the brain as an individual takes a drug; research demonstrating the long-lasting neurochemical and neurotoxic effects of methamphetamine abuse; and effective drug addiction treatments such as methadone, LAAM (levo-alpha-acetyl-methadol), and nicotine-replacement therapies. In closing, he emphasized the need for a multi-disciplinary approach to unravel the remaining mysteries of addiction and noted future scientific opportunities in addiction treatment, genetics research, and drug prevention for children and adolescents. The full text of Dr. Leshner's formal statement is available on NIDA's homepage at http://www.drugabuse.gov/.

During the question and answer period, Mr. Porter expressed great interest in techniques to effectively deliver the anti-drug message to young people. Dr. Leshner described some of NIDA's collaborative efforts with the private sector and with other federal agencies and pointed out that the arm of government that has taken major leadership in this area is the Office of National Drug Control Policy (ONDCP). He indicated that NIDA works closely with ONDCP to make sure that the national media campaign is scientifically accurate. He also spoke of the phenomenal growth of anti-drug coalitions throughout the country and described the effect of the Practical Theorist series, a publication of the Community Anti-Drug Coalitions of America, supported in part by NIDA, which translates scientific findings for practical use in community settings.

Rep. Hoyer asked Dr. Leshner to comment on the appropriateness of ONDCP's long- and short-term drug prevention strategies in terms of the objectives, time frame, and probability of success. Dr. Leshner called the strategy "positive" because it embraces a rational, systematic approach that incorporates science as the core element for each goal, and explained that we do not expect quick solutions to this complex problem. He emphasized that the strategy is realistic and in line with the current knowledge base and capabilities and reminded Mr. Hoyer that ONDCP will have the opportunity to raise the bar annually, in light of scientific breakthroughs and improvements in technical capabilities. Mr. Hoyer said that General McCaffrey, Director of ONDCP, considers NIDA to be a critically important component of the national drug prevention strategy.

Responding to a question on prenatal cocaine exposure, Dr. Leshner explained that the American public has moved from hysteria over "crack babies" in the 1980s to an excess of indifference. In fact, it has been found that children exposed to cocaine prenatally experience latent and subtle effects, including the emergence of attention deficit problems at ages 5-6 and learning problems at around 10. Also, the aggregate mean IQ of this population is 3 points lower, when compared to children without prenatal cocaine exposure. Currently, 1,400 children need intervention due to prenatal cocaine exposure.

When asked to comment on the existence of best practices in drug-free workplace policy, Dr. Leshner remarked on the importance of research on workplace drug prevention, noting that approximately 70% of addicts are employed. Research has shown that the most successful employee assistance programs are the ones that successfully match the most appropriate treatment modality with the individual employee.

Rep. Lowey expressed an interest in NIDA's Genetics of Addiction Initiative, saying that research will help clarify whether addiction has a biological or socioeconomic basis. Dr. Leshner responded that addiction is a result of interaction between genetics and environmental influences, adding that about 50-70% of an individual's vulnerabilities can be attributed to genetics, but not everyone who carries a genetic load will become addicted.

FY 1999 Funding Request:

For NIDA, the President's budget request for FY 1999, including the AIDS allocation, is $576.3 million, a 9.3 percent increase over FY 1998. The President's request of $14.798 billion for the NIH in FY 1999 is an increase of $1.15 billion (or 8.4%) over the FY 98 appropriations, and is part of a plan to increase the NIH budget to $20 billion by 2003, a 46 percent increase in NIH funding over the next five years.

SENATE APPROVED BUDGET PLAN

Before leaving for Spring recess, the Senate passed its FY 1999 budget resolution, S.Con.Res. 86, which outlines Congressional spending and revenue priorities for the $1.73 trillion federal budget. The Committee Report accompanying the budget resolution states the plan, as approved by the Senate Budget Committee, assumes an 11 percent increase in NIH funding for FY 1999.

- The Senate agreed by voice vote to a "sense of the Senate" amendment offered by Senator Connie Mack (R-FL) that the NIH budget should be increased by $2 billion in FY 99 and doubled over the next 5 years.
- The Senate rejected an amendment by Senator Specter, Chair of the Senate Appropriations Subcommittee with jurisdiction over NIH, to add $2 billion to the health portion of the budget to ensure his subcommittee would have adequate funds to provide the increase for NIH.
- Passed by voice vote was an amendment to prohibit the use of marijuana for medicinal purposes. The language was offered by Sen. Smith (R-OR) and was intended to specifically exempt "federally sponsored research." According to Senate staff, an error by the clerk resulted in omission of the research exemption, but subsequent efforts corrected the error.
- The Senate also agreed by voice vote to a "sense of the Senate" resolution that the next budget submission by the President and next Congressional budget resolution should reclassify all civilian research and development activities, including the NIH, within the "General Science, Space, and Technology" portion of the budget, also known as budget function 250. Currently NIH is in the budget function 550 (health).

DR. LESHNER TESTIFIES BEFORE THE SENATE

Nicotine Addiction

On February 10, 1998, at the request of the Senate Committee on Labor and Human Resources, Dr. Leshner testified on the topic of nicotine addiction.

Acknowledging that "just as with other drugs, ultimately our best treatment is prevention," Dr. Leshner emphasized that "Never before has the momentum for addressing this public health crisis been greater. There are tremendous scientific opportunities, based on at least two decades of scientific accomplishments."

Describing how emerging basic research is reinforcing what earlier studies indicated about the highly addictive nature

of nicotine, he explained that recently scientists have been able to prove that some of nicotine's most important effects are exerted through the very same brain circuits as those of other drugs of abuse, supporting the convergence of data pointing toward at least one major commonality among all drugs of abuse: they all elevate levels of the neurotransmitter dopamine. This change in dopamine is believed to be a fundamental root of all addictions.

NIDA researchers are unraveling the mysteries of not only smoking as an addiction, but the findings give new insights that may be relevant to other addictions as well. Through NIDA's leadership, there are a variety of effective pharmacological and behavioral treatments to select from to help people conquer their smoking addiction, but we need more. Addiction researchers have developed a number of new pharmacological weapons to combat nicotine addiction and researchers are working on a number of non-nicotine replacement therapies as well. The preeminent compound in this line is Buproprion, trade name Zyban ®, which is showing promising results in treating nicotine addiction. In conclusion, Dr. Leshner pointed out that, as with all other disorders, it is research on addiction that provides hope for even more effective prevention and treatment approaches.

Addiction and Recovery

On a panel that included such celebrities as Bill Moyers and Carroll O'Connor, Dr. Alan Leshner testified before the Senate Appropriations Committee on March 24, 1998 to talk about what the science shows about drug addiction and recovery. Dr. Leshner delivered an optimistic message, saying that although drug addiction is a difficult disease to treat, drug abuse treatment does work --in fact, just as well as other established medical treatments. He said the most effective treatment approaches must attend to all of the addiction's biological and behavioral components. After describing NIDA's research and research dissemination efforts, Dr. Leshner reaffirmed NIDA's commitment to continuing to take the science to those who need it --the American public.

SELECTED BILLS OF INTEREST

Tobacco Legislation

S. 1415 -On November 11, 1997, Senator McCain (R-AZ) introduced the "Universal Tobacco Settlement Act." This bipartisan bill, approved by the Senate Commerce Committee during markup April 1, includes research funds for NIH and would establish an NIH Office of Tobacco Related Research. The bill, renamed ATobacco Products Control Act of 1998," would give NIH $2.5 billion annually from FY 1999 to 2008. This bill is expected to go to the Senate floor in May.

Among other provisions, the bill would authorize the NIH Director, in consultation with the National Tobacco Task Force, to use tobacco revenue to "conduct or support epidemiological, behavioral, biomedical, and social science research (including the training of researchers) related to the prevention and treatment of tobacco addiction and the prevention and treatment of diseases associated with tobacco use." According to the proposal, an NIH "tobacco-related research initiative" should be established by the Director of NIH in consultation with a National Tobacco Task Force. The task force would include the NIH Director, the Surgeon General, Administrator of AHCPR, public health officials and advocates, and would be chaired by a CDC representative. The task force would coordinate tobacco-related research activities in accordance with a research agenda that would be developed by IOM.

S. 1492 -On November 8, 1997, Mr. Kennedy (for himself, Mr. Lautenberg, Mr. Durbin, Mr. Reed and Mr. Kerry) introduced "Health and Smoke Free Children Act." The bill was referred to the Committee on Labor and Human Resources.

S. 1530 -On November 13, 1997, Senator Hatch (R-UT) introduced, "Placing Restraints on Tobacco's Endangerment of Children & Teens Act." Committee hearings were held in February and March by the Senate Judiciary Committee.

S. 1638 -On December 12, 1997, Senator Conrad (D-ND) introduced the "Healthy Kids Act." The bill was referred to the Committee on Finance.

S. 1648 -On Feb. 12, 1998, Senator Jeffords (R-VT) introduced the "Preventing Addiction to Smoking among Teens Act" or the "PAST Act." The bill would provide $2.5 billion annually to NIH for research funding for FY 99 -2008. The bill has two co-sponsors, Senators Susan Collins (R-ME) and Mike Enzi (R-WY), and was referred to the Committee on Labor and Human Resources.

S. 1889 --On March 31, 1998, Senator Tom Harkin (D-IA) introduced the "Kids Deserve Freedom From Tobacco Act of 1998," The bill would allocate yearly to NIH a certain percentage of a trust fund financed by taxes and penalties on tobacco manufacturers. Within NIH, funds would be allocated to the Institutes and Centers in the same proportion as they are otherwise appropriated. The director of each center would be required to appropriately prioritize the use of

funds made available from the Fund for tobacco-related diseases and conditions, including those affecting women and minorities.

Medical Privacy

S. 1921 --On April 2, 1998, Senator James Jeffords (R-VT) introduced the "Health Care Personal Information Nondisclosure Act of 1998." The purpose of the bill is to establish strong and effective mechanisms to protect against the unauthorized and inappropriate use of protected health information, to promote the efficiency and security of the health information infrastructure, and to create incentives to turn personal health information into nonidentifiable health information for oversight, health research, public health, law enforcement, judicial, and administrative purposes. The bill has a number of provisions that would have an impact on health researchers: it delineates (1) the types of researchers who can gain access to protected health information, (2) the conditions under which researchers may obtain information, (3) access of research participants to their own health information and (4) the extent to which researchers may share information with others.

Federal Reports Elimination

S. 1364 --On March 10, 1998, the Senate Committee on Governmental Affairs marked-up and ordered favorably reported S. 1364, the Federal Reports Elimination Act of 1997, which seeks to eliminate "unnecessary and wasteful Federal reports." Included in the list of DHHS reports to be eliminated are the following: the biennial report of the NIH Director; the NIH annual report on administrative expenses; the annual report of the National Kidney and Urologic Diseases Interagency Coordinating Committee; the annual reports of the National Diabetes Advisory Board, the National Digestive Diseases Advisory Board, and the National Kidney and Urologic Diseases Advisory Board; the annual reports of the Arthritis and Musculoskeletal and Skin Diseases Interagency Coordinating Committee and Advisory Board; **the report on health services research; the triennial report on drug abuse**; the family planning and population research report; the sudden infant death syndrome research report; report of the Task Force on Aging Research; chronic fatigue syndrome research report; and the report on end-stage renal disease.

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International Activities

On March 5, 1998, Dr. Patricia Needle, International Program, OSPC, presented a report on recent NIDA collaborative activities in the area of drug abuse and HIV prevention research with Russia at the 7th Gore-Chernomyrdin Health Committee Meeting held in Washington at the Department of State. Dr. Needle reported on the outcomes of the October U.S.-Russia Bilateral Workshop **Prevention of HIV and Other Infectious Diseases Among Drug Abusers** held in St. Petersburg. Four workgroups prepared recommendations in the areas of: Epidemiologic strategies for monitoring infectious disease epidemics; research issues in the clinical management of infectious diseases; drug abuse treatment - research and intervention strategies to prevent infectious diseases; and community strategies - research and intervention strategies to prevent infectious diseases. Copies of the report are available from the NIDA International Program office.

NIDA researchers Drs. Sherry Deren, Robert Heimer, Walter Ling, Patricia Marshall, Clyde McCoy, Mangai Natarajan, and Robert Trotter, and M. Patricia Needle, NIDA, joined 25 Indian colleagues for the **Indo-U.S. Workshop on HIV Prevention Research Methodology** held February 24-27, 1998 in Chennai (formerly Madras). The workshop was cosponsored by YRG Care and Research Foundation, Chennai, and the Indian National AIDS Control Organization, with support from NIDA and the U.S. Embassy in New Delhi. Indian participants brought draft proposals and concept papers for collaborative research that served as the basis for workshop discussions. This meeting was an extension of two earlier workshops held in India in 1994 and 1996, which have so far led to the funding of a collaborative project by the U.S.-India Fund.

On February 13, 1998, the review committee for the NIDA Hubert H. Humphrey Drug Abuse Research Fellowship met to select Fellows for the 1998-1999 academic year. Three prospective Fellows and one alternate - Drs. Amani El Mougy of Egypt, Gained Novistky of Russia, Gabor Kelemen of Hungary, and Leonardo Estacio of the Philippines (alternate) - were selected to participate in the program at The Johns Hopkins University. This NIDA-supported portion of the Humphrey Fellows Program includes a six-week or longer professional affiliation with a NIDA grantee to design a research proposal for implementation in the Fellow's home country.

NIDA staff Drs. Donald Vereen, Special Assistant to the Director for Medical Affairs, Dr. Zili Sloboda, Director, DEPR, and M. Patricia Needle, International Program, participated in the first **U.S.-Mexico Demand Reduction Conference** held in El Paso, Texas, on March 18-20, 1998. More than 200 attendees at the conference explored ways to reduce the demand for illegal drugs in both countries during general sessions and work group meetings that addressed a range of topics, including community participation, drug-related violence, evaluation of treatment and prevention programs, HIV/AIDS, and drug abuse research. NIDA cofacilitated the working group on research cooperation and exchange of technical information, which produced a set of recommendations for the continued development of research cooperation between Mexico and the U.S.

NIDA's International Program, since February 1998 has arranged Institute overviews and meetings with Institute staff for 11 groups of international visitors. These include 3 groups representing 15 countries sponsored by the United States Information Agency; groups from Turkey, India, Germany, Russia, and Japan; an official delegation from The Netherlands; and an orientation visit for NIDA INVEST Research Fellows.

Mr. Nicholas J. Kozel, DEPR, participated in the **South African Community Epidemiology Network on Drug Abuse (SACENDU)** in Cape Town, South Africa on March 24-26, 1998. SACENDU is sponsored by the Medical Research Council of South Africa and World Health Organization (WHO). Its mission is to develop a multi-city drug abuse surveillance program in the country based on epidemiologic and ethnographic data. Historically, the most serious substance abuse problem in the country has involved alcohol, cannabis and Mandrax (methaqualone). Recently, new drugs, especially crack cocaine, have appeared as well as heroin, LSD and ecstasy. The program is in the initial stages of attempting to expand program participation to several other Southern African Developing Countries (SADC), including Namibia, Zimbabwe, Botswana, Zambia, Mozambique and Swaziland, with the prospect of establishing a regional epidemiologic surveillance program.

Moira O'Brien, Epidemiology Research Branch, DEPR, conducted a workshop, **Building International Frameworks for NIH Grants on Drug Abuse**, for the International Training Institute of the Annual Meeting of the Society for Applied Anthropology which was held in San Juan, Puerto Rico, April 21-22, 1998.

Drs. Elizabeth Robertson and Larry Seitz of DEPR's Prevention Research Branch met with NIDA Humphrey Fellow Victor V. Chtenguelov, M.D., Ph.D. on February 12, 1998. Dr. Chtenguelov is the Science Director, Ukrainian Research Institute of Social and Forensic Psychiatry, Kiev, Ukraine. Discussions focused on prevention including its theory, principles, and current research literature. Dr. Chtenguelov also met with staff of the Community Research Branch, DEPR, and the Office of Science Policy and Communications.

Nicholas Kozel and Larry Seitz of the Division of Epidemiology and Prevention Research met with Mr. Yukihisa Kitamura, Deputy Director General, Physical Education and Sports Bureau, Ministry of Education, Science, Sports and Culture, Mr. Noriyuki Matsukawa, First Secretary of the Embassy of Japan, and Professor Shingo Katsuno, Hyogo University of Teacher Education from Japan on March 12, 1998. Considerable time was spent discussing prevention including types of prevention, prevention principles, and examples of good prevention intervention programs.

Dr. Robert Battjes, DCSR, attended a meeting of the instrument development task force of the WHO/NIH Joint Project on the Assessment and Classification of Disablements, March 9-12, 1998, in Geneva, Switzerland.

Dr. Roman Stefanski, IRP Preclinical Pharmacology Laboratory, presented a talk entitled, "Neuroadaptations to Long-Term Methamphetamine Self-Administration in Rats," at the Pharmacology, Biochemistry and Behavior Meeting in Morzine, France, January 3-11, 1998.

A grant was awarded by the Civilian Research and Development Foundation for the Independent States of the FSU (CRDF) for collaborative research to the State Research Institute of Addictions, Moscow, Russia, and NIDA's Intramural Preclinical Pharmacology Laboratory. Sergey Sudakov, M.D., Ph.D. and Dr. Steven Goldberg and colleagues will cooperate on the research project entitled, "Finding of New Compounds for Treatment of Opiate Addiction on the Basis of Study of Non-Opiate Peptide Systems." Dr. Sudakov visited the Intramural Program during April to initiate work on the project.

In a collaborative research project between Marjolein Beekman and Durk Dijkstra, Department of Medicine Chemistry, University Centre of Pharmacy, Groningen, The Netherlands, and Dr. Jeffrey Witkin, Behavioral Neuroscience Branch, IRP, a potential neural trigger for schizophrenia and a new atypical antipsychotic drug have been discovered. Work also continues on the role of neuroactive steroids in drug dependence and drug-abuse related toxicities.

In a collaborative research project with N. Savtchenko and M. Mashkovsky, Center of Chemistry of Drugs, Russian Ministry of Public Health, Moscow, and Dr. Jeffrey Witkin, the preclinical pharmacology of a novel stimulant, sydnocarb, has recently been characterized for possible use as a treatment agent for psychomotor stimulant abuse.

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Meetings/Conferences

Receptor Internalization: Implications on Receptor Function and Regulation This workshop, organized by Dr. Rita Liu of OEPR and Dr. David Thomas of DBR, was held on February 9, 1998. Speakers were members of the NIDA-B Review Subcommittee and included Drs. Chris J. Evans of the University of California, Los Angeles; Robert P. Elde of the University of Minnesota; Susan R. George of the University of Toronto; Kenneth P. Mackie of the University of Washington; and Bryan Roth of Case Western Reserve University Medical School. The workshop was filled to capacity, and attendees included members of the NIDA Neuroscience Consortium and NIH intramural and extramural scientists.

Women and HIV Investigators Group (WHIG) Meeting The WHIG, composed of women researchers who have grants that are sponsored by the Community Research Branch under the NIDA Program Announcement, "Women's HIV Risk and Protective Behaviors" (#95-083), held its second meeting in Washington, D.C. February 27-28, 1998. The meeting covered several key issues, including the role of power and its impact on women's HIV risk behaviors; high risk behaviors and other serious infections (e.g., other STDs, such as chlamydia, syphilis, gonorrhea, viral hepatitis, and others); the effects of welfare reform changes on women at risk for HIV; interventions for partners and couples; and strategies for addressing research challenges in the field, such as behavior measurement, recruitment, outreach, and ethical decision making. NIDA staff involved in the initiation of WHIG included Susan Coyle, Ph.D. and Richard H. Needle, Ph.D., M.P.H., Chief, CRB.

NIDA's African American Researchers and Scholars Group met with NIDA staff in Bethesda, Maryland on March 5-6, 1998. Topics of discussion included Institute minority program activities, changes in NIDA and NIH peer review, collaborative activities with professional organizations, and recruitment and retention of African American and other minority researchers.

NIDA's Hispano/Latino Researchers and Scholars Group met March 16-17, 1998 in Rockville, Maryland. Participants heard research updates from NIDA program staff, overviews of Hispanic activities at other Public Health Service (PHS) agencies, and summaries of research and other activities related to US/Mexico border issues.

Understanding Drug Abuse and Addiction: Myths Vs. Reality NIDA organized this **"Town Meeting"** which was held in Boston, Massachusetts on April 7, 1998. NIDA Director, Dr. Alan I. Leshner and NIDA researchers discussed ways that state policy makers, organizations, schools and communities can utilize the latest scientific research to assess state and local drug problems and develop programs to meet their needs.

Meeting on Gender and Pain Drs. David Thomas and Robert Caudle of the Division of Basic Research helped plan and arrange for NIDA sponsorship of the meeting entitled "Gender and Pain: A Focus on How Pain Impacts Women Differently Than Men." This multi-institute sponsored meeting was held in Bethesda MD, April 7-8, 1998.

National Conference on Drug Addiction Treatment: From Research to Practice This NIDA-sponsored conference was held in Washington, DC on April 8-9, 1998. The conference was called to order by Dr. Alan I. Leshner followed by the keynote address presented by General Barry R. McCaffrey, USA (Ret.), Director of the White House Office of National Drug Control Policy. With the emphasis on informing leaders of national drug abuse and other professional organizations, treatment practitioners, the media, and the public, the conference highlighted over two decades of drug addiction treatment research. More than thirty conference speakers and discussants summarized the

current state of scientific knowledge on a variety of topics, including health, social and economic benefits of treating drug addiction, the roles of behavioral and medication treatment, and the barriers impeding the delivery of and access to drug addiction treatment. The conference was organized through the combined efforts of NIDA staff in the Division of Clinical and Services Research and Office of Science Policy and Communications.

Stress, the CRF System, and Drugs of Abuse This NIDA sponsored workshop was held on April 14, 1998 in Bethesda, MD. Presenting participants included Dr. Paul Plotsky, Dr. Errol De Souza, Dr. Barbara Sorg, Dr. Friedbert Weiss, Dr. Jane Stewart, Dr. Franco Vaccarino, Dr. Stanley Watson, Dr. David Schultz, Dr. Donald Gehlert, and Dr. Rajita Sinha. Although the merits of various medication development targets (e.g., CRF and CCK receptor antagonists) was a primary focus of the meeting, implications for prevention and treatment research were also discussed.

NIDA/ASAM Symposium -- Treating Adolescent Drug Abuse and Addiction This Symposium was held at the American Society of Addiction Medicine's 29th Annual Medical-Scientific Conference, April 18, 1998 in New Orleans , LA, and presented scientific information on: adolescent drug abuse and co-occurring behavioral problems; psychopathology and risk of drug abuse; assessment and treatment of drug abusing adolescents with substance use disorders and comorbid mental disorders; pharmacotherapy for drug abusing adolescents; brief behavioral interventions appropriate for primary care settings; and family-focussed therapy, sensitive to drug abusing adolescents from different cultural backgrounds. The meeting was cochaired by Stephen Zukin, M.D., Director of NIDA's Division of Clinical and Services Research, and Marie Armentano, M.D., Chair of ASAM's Committee on Children and Youth. Drs. Dorynne Czechowicz, Elizabeth Rahdert, and Vincent Smeriglio, all of NIDA's Division of Clinical and Services Research, organized this meeting in collaboration with ASAM.

Developmental Follow-Up of Prenatal Drug Exposure: School-Age Children This meeting, sponsored by NIDA's Child and Adolescent Research Workgroup, was held on April 21-22, 1998. Overall purposes of the meeting were: to assess the status of the search for developmental sequelae of prenatal drug exposure, to examine the state of the science as to possible biological and environmental mechanisms underlying sequelae, and to address new and ongoing methodological challenges in studying cohorts of children when they reach school age. The meeting emphasized problem-solving and direction-setting discussions among investigators who are currently immersed in the issues.

Peripheral Blockers as Treatments for Substance Abuse and Dependence: Using Antibodies and Enzymes to keep Cocaine and Other Drugs of Abuse Out of the Central Nervous System This NIDA sponsored scientific meeting was held on April 27-28, 1998 to review the progress of research and development of vaccines, catalytic antibodies and enzyme enhancements that will block, or slow, the entry of cocaine or other abused substances into the brain. Presentations by 19 NIDA grantees, NIDA staff, and other scientists focussed on the biochemical and immunological aspects of peripheral blockers and on their behavioral effects in rodents challenged with drugs of abuse. Five postdoctoral fellows and graduate students were invited to present posters on related topics. The meeting was organized and conducted by Steven Sparenborg, Ph.D. with the assistance of Medications Development Division and Office of Science Policy and Communications staff members.

The Glutamate Cascade: Common Pathways of Central Nervous System Disease States was held on May 3-5, 1998 at the NIH Masur Auditorium to explore the evidence that the "glutamate cascade" appears to be associated with several seemingly diverse disease processes of the CNS. The related excitotoxic cascade has been demonstrated in some of these processes: addiction, stroke, epilepsy, degenerative disorders, brain trauma, neuropathic pain, schizophrenia, anxiety, and depression. The goal of the symposium was to stimulate a cross-fertilization of ideas in basic brain mechanisms and preclinical and clinical medications development of direct or indirect glutamatergic antagonists in diverse medical disciplines which focus on these disorders. This multi-Institute NIH symposium was organized by Barbara Herman, Ph.D., Medications Development Division.

The Second Annual PRISM Awards, co-sponsored by NIDA and the Entertainment Industry Council and honoring accurate depiction of drug, alcohol and tobacco use in film and television, took place on May 5, 1998, in Beverly Hills, California. Awards, commendations, and certificates of merit were presented for feature films and five TV categories -- comedy series, drama series, children's series, movies or dramatic specials, and reality series or specials. An award was also given for community service.

On February 5-6, 1998, NIDA convened two groups of technical experts in program evaluation design and measurement to advise NIDA and the Office of National Drug Control Policy (ONDCP) on the most potentially effective research plan and structure to evaluate the impact of ONDCP's **National Youth Anti-Drug Media Campaign**. Leading experts in statistical sampling, design, and measurement, and prevention and communications research met together to consider these issues needing to be addressed in the overall campaign evaluation. Briefings were provided about the campaign audiences and objectives, and the initial phases of evaluation undertaken by ONDCP by

senior ONDCP staff, including Dr. Hoover Adger, Deputy Director, ONDCP, and Dr. John Carnevale, Director of the Office of Programs, Budget, Research and Evaluation. The session, co-chaired by Dr. Zili Sloboda, Director of DEPR, addressed general structural questions about the research design and domains of interest and then considered the specific design questions and the measurements and instrumentation that can be applied to the overall campaign evaluation program. The report of the experts' meeting assisted NIDA staff in the development of the contract, and also provided guidance to the ONDCP staff in the design of questionnaires being employed in earlier phases of the evaluation being conducted outside of NIDA.

NIDA staff from the Division of Clinical and Services Research (DCSR) and the Division of Epidemiology and Prevention Research (DEPR) convened a meeting with extramural health services researchers to plan a health services research agenda for drug abuse prevention and treatment, in Rockville, March 5, 1998, on the Organization and Management of Drug Abuse Prevention and Treatment.

NIDA staff from DCSR and DEPR convened a meeting with extramural health services researchers to plan a health services research agenda for drug abuse prevention and treatment, in Rockville, March 19, 1998, on the Effectiveness and Outcomes of Drug Abuse Treatment.

NIDA staff from DCSR and DEPR convened a meeting with extramural health services researchers to plan a health services research agenda for drug abuse prevention and treatment, in Rockville, April 7, 1998, on the Economics of Drug Treatment and Prevention.

NIDA staff from DCSR and DEPR convened a meeting with extramural health services researchers to plan a health services research agenda for drug abuse prevention and treatment, in Rockville, MD, April 28, 1998, on the Prevention of Drug Abuse.

On February 13, 1998, NIDA Deputy Director Richard A. Millstein met with Peter Pennekamp, Netherlands Under Secretary of Health, Welfare and Sport on international drug research policy and issues, Rockville, MD.

On February 26, 1998, NIDA Deputy Director Richard A. Millstein met with Harry Montoya, Eduardo Hernandez and Paul Cardenas of the Hispano/Latino National Network to plan NIDA outreach and education efforts to Hispanics and Latinos in the west and southwest, Rockville, MD.

On March 5, 1998, NIDA Deputy Director Richard A. Millstein presented to the African-American Researchers and Scholars Group on NIDA minority program activities and plans, Bethesda, MD.

On March 16, 1998, NIDA Deputy Director Richard A. Millstein presented to the Hispano/Latino Researchers and Scholars Group on minority program activities and plans, Rockville, MD.

On March 25, 1998, NIDA Director Alan I. Leshner and Deputy Director Richard A. Millstein met with Judge Jeffrey Tauber, Director, National Association of Drug Court Professionals on drug courts research and education, Washington, D.C.

On April 2, 1998, NIDA Deputy Director Richard A. Millstein presented on public awareness of and education on drug addiction as a disease to the Interagency Demand Reduction Working Group of the White House Office of National Drug Control Policy, Washington, D.C.

On April 2, 1998, NIDA Deputy Director Richard A. Millstein presented to the National Academy of Sciences Institute of Medicine on NIDA's research priority setting process, Washington, D.C.

On April 7, 1998, NIDA Deputy Director Richard A. Millstein represented NIDA at the press conference at the NIH Conference on Gender and Pain, Bethesda, Maryland.

On May 4-5, 1998, NIDA Deputy Director Richard A. Millstein represented NIDA Director, Dr. Alan I. Leshner at the first meeting of the Attorney General's Methamphetamine Task Force Federal Advisory Committee. Mr. Millstein presented an overview of NIDA's research activities relating to methamphetamine (May 4) and made a presentation on the demographics and epidemiology of methamphetamine use (May 5). On May 5, Dr. Andrea Baruchin, Chief, OSPC Science Policy Branch presented on methamphetamine pharmacology and Dr. Frank Vocci, Director, MDD, presented on methamphetamine treatment.

Dr. Timothy Condon, NIDA's Associate Director for Science Policy, gave a presentation on the state of the science in drug abuse and addiction treatment and prevention at the American Society of Addiction Medicine Annual Medical-Scientific Conference on April 17, 1998 in New Orleans, LA.

Dr. Andrea Baruchin, Chief, OSPC Science Policy Branch made a presentation on February 24, 1998 to the National

Research Council Committee on National Needs for Biomedical and Behavioral Science about NIDA's efforts to train behavioral scientists and the future needs for behavioral scientists.

Beverly Wyckoff Jackson, Chief, PIB, represented NIDA at meetings of the Secretary's Initiative on Substance Abuse and the Deglamorization Subcomittee of the Secretary's Initiative on Tobacco Use.

Dr. Jaylan Turkkan, DBR represented NIDA at the Summit of Psychological Science Societies in May 1998. Summit attendees were asked how they can capitalize on the base of knowledge in behavioral research, and to project into the future new theories, methods and applications for public health benefit. The Summit was supported by several NIH Institutes, Offices, and private foundations, and featured NIDA Director, Dr. Alan I. Leshner, as the keynote speaker.

Mr. Joel Egertson of MDD represented NIDA on the workshop committee of the American Methadone Treatment Association, at a meeting held in New York City on February 27-28, 1998. The workshop was held to consider and approve applications for presentation at the AMTA National Conference to be held in New York, September 26-19, 1998. The workshop group filled all 30 time slots from a list of 87 applications.

Peter Cohen, M.D., J.D. of MDD presented a discussion of "Treatment of Substance Dependent Professionals: Physicians' Health Programs" at the 29th Annual Medical-Scientific Conference of the American Society of Addiction Medicine, New Orleans, April 17, 1998.

Peter Cohen, M.D., J.D., presented a lecture entitled "A Physician's Guide to Legal Thinking", at an FDA Center for Scientific Review Seminar, March 26, 1998.

Lula Beatty presented a session on "HBCUs in Drug Abuse Research: Opportunities and Challenges" at the HBCU Alliance meeting held April 14, 1998 in Washington, DC.

On March 27-28, 1998, Lula Beatty attended a research meeting on HIV/AIDS Prevention in Native American populations in Tucson, AZ.

On March 9-10, 1998, an HBCU technical assistance meeting was held in Rockville. This is part of NIDA's HBCU Initiative. Lula Beatty presented a session on funding mechanisms.

On March 9, 1998, Lula Beatty attended a meeting of program directors participating in NIGMS supported minority programs where she provided information on NIDA programs to attendees.

On April 20, 1998, Lula Beatty and Ana Anders presented an overview of NIDA and the Special Populations Office to participants in the Okura Mental Health Leadership Foundation.

On March 20-22, 1998, Lula Beatty, liaison for the Division of Women, attended the meeting of the Committee on Women, Consolidated Meeting of the American Psychological Association.

On April 23, 1998, Lula Beatty presented a class lecture on drug abuse in African American communities and a brown bag seminar on research opportunities at NIDA at Virginia Commonwealth University in Richmond.

In March, 1998, Lula Beatty served as a field reviewer for the 12th Annual Child Abuse and Neglect Conference to be held in November, 1998.

On April 3, 1998, Lula Beatty attended, as the NIDA representative, the first Advisory Board meeting of the Office of Research on Minority Health, NIH.

On February 16-18, 1998, Ana Anders attended the National Asian Pacific American Families Against Substance Abuse (NAPAFASA) meeting in Los Angeles, CA. At the meeting, which was attended by Gen. Mc. Caffrey, she discussed NIDA's plans to develop an Asian and Pacific Islanders Initiative.

On March 4, 1998, Ana Anders, as the NIDA representative, attended the first meeting of the SAMHSA/CSAP Editorial and Advisory Board on Media Campaign Issues for the Hispanic/ Latino population.

On March 18-20, 1998, Ana Anders, as the NIDA representative, attended the ONDCP/ SAMSHA planning meeting of a U.S./Mexico Binational Conference on Substance Abuse in El Paso, TX.

As a part of NIDA's HBCU Initiative, the Center for Drug Abuse Research at Howard University sponsored a Conference on Epidemiology and Prevention of ATOD in South Africa and the United States. At this conference, Lula Beatty gave a presentation on drug use and the African-American population.

Arnold Mills, CRB/DEPR participated in a HIV Prevention and Treatment Adherence Meeting held in Albuquerque, NM on March 2-3, 1998, hosted by the Indian Health Service to discuss HIV/AIDS intervention strategies in Native American Communities.

Katherine Davenny, CMB/DCSR, gave a presentation on Hepatitis C infection, and co-infection with HIV, in drug users to the New York State AIDS Institute, Substance Abuse Section, in New York City, April 21, 1998.

Drs. Robert Battjes and Bennett Fletcher, DCSR, participated in NIMH's National Advisory Mental Health Council's Clinical Treatment and Services Research Workgroup, April 5-6, 1998 in Arlington, VA. The workgroup's goal is to bridge the gap between mental health research and the informational needs of consumers, practitioners, administrators, and payers.

Dr. William Cartwright, SRB/DCSR, presented a lecture entitled, "Cost-Benefit Analysis in Health and Medicine," at the George Washington University on March 25, 1998.

Dr. Teresa Levitin was an invited speaker at the Society for Research on Adolescence in February, 1998. She discussed the application and grant review process with specific reference to research on adolescent behavior and health.

On February 7, 1998, Dr. Elizabeth Robertson represented NIDA at the first graduation ceremony of participants in Washington, D.C. FAST (Families and Schools Together) prevention intervention. This project is jointly funded by NIDA, the Office on National Drug Control Policy and the Department of Education.

Drs. Elizabeth Robertson and Teri Levitin presented at an invited symposium on March 1, 1998 at the biennial Society for Research on Adolescence meeting in San Diego. The title of the presentation was " NIH Research Priorities and Funding Opportunities."

Dr. Elizabeth Robertson presented a paper on Family-based Prevention Interventions at the Clean Focus Coalition annual meeting in Winchester, Virginia on April 1, 1998.

Dr. Naimah Weinberg, DEPR, presented a poster on child psychopathology risk factors for drug abuse at the annual meeting of the American Psychopathology Assocation in New York City, March 1998.

Peter Hartsock, Dr. P.H., CRB, represented NIDA at the world-wide EREIDs briefing, held at the U.S. State Department in Washington, D.C. on March 25, 1998. The purpose of the briefing was to consider the status of infectious diseases around the world and what can be done to lessen their effects.

On March 9-10, 1998 Arnold Mills, Community Research Branch, DEPR, represented the Institute at a NIDA sponsored two-day technical assistance Workshop for faculty and staff from Historically Black Colleges and Universities (HBCU). The workshop was designed to encourage HBCU faculty to pursue drug abuse research careers. Representatives from eight HBCUs attended the meeting.

Dr. Katherine Bonson, IRP, presented a lecture entitled "Neuropharmacology of Drugs of Abuse" at Widener University, Philadelphia, PA, February 3, 1998.

Dr. Edythe D. London, IRP, presented "Effects of Nicotine on Cerebral Glucose Metabolism" at the Society for Research on Nicotine and Tobacco Symposium entitled "Brain Imaging of Nicotine and Tobacco Smoking", New Orleans, LA, March 27-29, 1998.

Dr. Monique Ernst, IRP, presented "Effects of Nicotine on Cognitive Performance in Smokers and Nonsmokers" at the Society for Research on Nicotine and Tobacco, New Orleans, LA, March 27-29, 1998.

Dr. John Matochik, IRP, presented "Using Magnetic Resonance Imaging to Study Drug Abuse" at the Neuroscience Seminar Series, Lehigh University, Bethlehem, PA on April 2, 1998.

Dr. Edythe D. London presented "Brain Imaging Studies of Substance Abusers" at Duke University Medical Center and Health System, Durham, NC, April 7, 1998.

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Media and Education Activities

MIND OVER MATTER SERIES RECEIVES AWARD

NIDA's new *Mind Over Matter* series has recently received a Silver Certificate in the Astrid Awards given by MerComm, Inc. MerComm, Inc. was founded with the principal purpose of advancing the arts and sciences of communications in an international arena. Their awards programs are in their 12th year with over 3000 entries coming from all over the world. The *Mind Over Matter* series was developed by NIDA to teach middle school students about how drugs of abuse act in the brain. The series consists of six full-color glossy magazines that unfold into posters, and a teacher's guide that provides additional information on the brain and the effects of drugs. The series includes magazines on marijuana, opiates, stimulants, hallucinogens, inhalants, and steroids.

Press Releases

January 26, 1998 - One Step Closer to Unraveling Nicotine's Addictive Properties. An important discovery about the mechanisms of nicotine addiction brings researchers even closer to the development of an effective treatment for one of the Nation's deadliest and most costly health problems--nicotine addiction. Building on a series of recent scientific findings suggesting that, independent of a drug's initial site of action, every drug of abuse--be it nicotine, alcohol, heroin, cocaine, or amphetamine--appears to increase the levels of the neurotransmitter dopamine in a particular brain pathway, scientists may now have found a molecular link between nicotine addiction and this common reward or pleasure producing pathway.

February 3, 1998 - Study Identifies Mechanism for Cocaine-Induced Stroke and Other Brain Damage. Scientists at McLean Hospital and Harvard Medical School have identified a likely mechanism by which cocaine use can cause brain damage and decreased cognitive function. Using advanced brain imaging techniques, scientists have clearly demonstrated for the first time that cocaine use temporarily narrows blood vessels in the human brain. The study also shows that repeated cocaine use has a cumulative effect, where the more an individual uses the drug, the more it causes blood vessel narrowing. The study was to appear in the February 4, 1998, issue of the *Journal of the American Medical Association*.

March 24, 1998 - Science and Public *Join Together* to Confront Local Drug Abuse and Addiction Issues at Boston Town Meeting. This announced the April 2 Boston Town Meeting, sponsored by NIDA and *Join Together*/Boston University School of Public Health. NIDA staff and local grantees highlighted some new research findings to help individuals, families, and communities gain more insight into preventing and treating the illness of drug addiction. Attendees included scientists, civic leaders, policy makers, public officials, and drug abuse prevention and treatment professionals. The meeting also served as a forum for local participants to advise NIDA on the kinds of research-based information needed at their particular State and local levels.

March 31, 1998 - Troubled Teens Risk Rapid Dependence on Marijuana. Marijuana use by teenagers who have

prior serious antisocial problems can quickly lead to dependence on the drug, according to a study by researchers at the Addiction Research and Treatment Service, University of Colorado School of Medicine. The study also found that, for troubled teens using tobacco, alcohol, and marijuana, the progression from first use of marijuana to regular use was more rapid than the progression to regular use for alcohol and about the same for nicotine.

April 2, 1998 - New Help Available For Communities to Assess Local Drug Problems. Dr. Alan I. Leshner, NIDA Director, announces release of a new guide to help communities determine the nature of their local drug problems. The science-based guide, **Assessing Drug Abuse Within and Across Communities**, provides strategies to assess local drug abuse patterns and trends, and especially emerging problems, allowing communities to do a better job of focusing their efforts at preventing and reducing drug use in their local environment.

April 7, 1998 - New Addiction Treatments To Be Focus of National Conference in Washington. On April 8-9, NIDA's **National Conference on Drug Addiction Treatment: From Research to Practice** allowed researchers and service providers to exchange findings about what treatments work, what aspects of individual programs can be tailored for specific populations. General Barry McCaffrey, Director of the White House Office of National Drug Control Policy, delivered the keynote address. At the conference, NIDA Director Dr. Alan I. Leshner released the first two in a series of treatment delivery manuals developed to help drug treatment practitioners provide the best possible care that science has to offer.

Other Press Activities

Broadcast Media

March 29, 30, and 31, 1998 - Bill Moyers' PBS Special on Addiction: Close to Home - Amid considerable publicity, this series premiered 1 year after Bill Moyers interviewed Dr. Leshner and filmed his science-based question/answer session with middle school children. The 5-part PBS series aired nationwide, covering the science of addiction as well as prevention and treatment issues. Moyers also interviewed and featured the work of several NIDA grantees throughout the special. NIDA staff also worked with the production staff to develop viewers' guides and student guides to accompany a variety of community-oriented activities planned to coincide with the broadcast. One activity was a satellite "forum" broadcast on February 26, featuring Dr. Leshner and other experts in addiction and treatment.

April 8 and 9, 1998 - NIDA National Treatment Research Conference, Washington, D.C. This conference generated much media interest. More than 20 reporters and writers attended throughout the conference. A wire story from Reuters was carried in several papers nationwide. In addition, Dr. Leshner conducted radio interviews with NPR, ABC, NBC, and Talk America. Dr. Zukin conducted an interview with CBS radio.

April 2, 1998 - NIDA's Boston Town Meeting - Considerable media attention ensured that this was the best-attended town meeting to date. NIDA's media partner was WGBH, Boston's PBS station. The public relations staff of ***Join Together***, which cosponsored the conference, also garnered considerable publicity, including an editorial board meeting of Dr. Leshner with The Boston Globe, which resulted in two articles.

March 18, 1998 - ABC Nightline - Dr. Leshner was interviewed and appeared in a segment on the effectiveness of treatment for drug addiction.

March 27, 1998 - CBS Evening News - Dr. Leshner was interviewed and appeared in a segment on congressional hearings on addiction that focused on the upcoming Bill Moyers' PBS Special on addiction.

Planned Meetings

Cognition and Emotion Meeting at APS An all-day miniconference entitled "Cognition and Emotion: Applications to Drug Abuse", which will be held on May 21, 1998, is being co-sponsored by NIDA's Behavioral Science Working Group and the American Psychological Society. The conference, which will be conducted at the Washington Hilton Hotel, is the second in a series of conferences highlighting NIDA's interest in cognitive sciences. Leading researchers in cognition, decision making, expectancy and emotional processes will participate in symposia on topics such as smoking motivation, the role of prefrontal functions in decision making, and problem solving approaches. Links to etiology, prevention and treatment of drug abuse and high-risk behaviors will be emphasized, and active interchange

between speakers and attenders will be encouraged.

Council's Craving Consensus Workshop The purpose of this workshop to be held May 26-27, 1998 is to define craving from a human perspective.

Drug Addiction: A Treatable Disease, a special research-based program track of the American Psychiatric Association 151st Annual Meeting, will take place May 30 - June 4, 1998 in Toronto, Canada. This meeting is the culmination of a collaborative effort of NIDA and the APA with the goal of disseminating state-of-the-at research findings in drug addiction treatment and prevention to pyschiatrists in the field.

Forging the Link: Health Services Research on Drug Abuse Prevention and Treatment. A NIDA sponsored symposium will be held on Saturday, June 20, from 1:00 - 5:00 pm at the Washington Hilton. This meeting will present an overview of progress in health services research on drug abuse prevention and treatment, and focus on an agenda for health services research to help achieve significant advances in access to, quality, and outcomes of drug abuse treatment and prevention.

Frontiers in Neuroscience Series: Wired for Addiction will be held June 22, 1998. Speakers will discuss the anatomical, mechanistic, and functional aspects of interconnecting neural circuits, from the evaluation of the salience of a stimulus, like cocaine, to its translation into an action such as taking a drug.

National Nicotine Conference NIDA and the Robert Wood Johnson Foundation, in conjunction with the National Cancer Institute and Centers for Disease Control and Prevention (Office of Smoking and Health), are co-sponsoring a national conference entitled "Addicted to Nicotine: A National Research Forum" on July 27-28, 1998. This two-day conference, which will be held on the NIH campus (Natcher Auditorium), will focus on the latest research findings about behavioral, cognitive and neurobiological factors contributing to nicotine addiction, as well as feature presentations on the latest science-based smoking prevention and treatment strategies.

NIDA/American Psychological Association (APA) Sponsored Symposium A symposium entitled "Expectancies: A Cognitive Science Approach to Substance Abuse," will be held at the APA meeting on August 14, 1998 at the Moscone Conference Center in San Francisco, CA. The symposium will bring together basic and clinical researchers to discuss and summarize the major finding of expectancy research and the role of this cognitive process in the etiology, treatment, and prevention of drug abuse.

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Publications

Research Monographs

Laboratory Behavioral Studies of Vulnerability to Drug Abuse--Research Monograph 169, NIH Pub. 98-4122.
This monograph provides comprehensive information on methodological and paradigmatic issues, as well as recommendations for future research directions in the field of behavioral laboratory research on vulnerability to drug abuse.

The Problems of Drug Dependence, 1997: Proceedings from the 59th Annual Meeting of The College on Problems of Drug Dependence--Research Monograph 178, NIH Pub. 98-4305.
This monograph contains the results from an annual meeting and is comprised of comprehensive, up-to-date reviews of research in progress from many disciplines in drug abuse and drug dependence. It is fully indexed by subject and author, and offers the state-of-the-art on many areas encompassing many disciplines in drug abuse research.

Other Publications

Epidemiologic Trends in Drug Abuse: Community Epidemiology Work Group--June 1997 Volume II: Proceedings, NIH Pub. 98-4208A.
This publication provides an in-depth analysis of epidemiologic trends and special reports as described at the annual meeting of the Community Epidemiology Work Group.

International Epidemiology Work Group on Drug Abuse--June 1997: Volume II: Proceedings, NIH Pub. 98-4208B.
This report provides a forum for representatives of different nations and regions of the world to exchange information about current drug abuse patterns and trends; emerging drugs of abuse; risk factors; vulnerable populations; consequences of use; sources of data/information; and methods of collecting, analyzing and reporting data/information.

Assessing Drug Abuse Within and Across Communities, NIH Pub. 98-3614.
This publication serves as a guide for the development of community based networks which could provide ongoing assessment of the epidemiology of drug abuse in local areas in the United States with the purpose of keeping both public and private sector policy makers and researchers informed with current and accurate data.

Drug Abuse Research and the Health of Women (Executive Summary), NIH Pub. 98-4290.
This publication contains condensed versions of presentations and discussion sessions from the 1994 NIDA sponsored conference, "Drug Addiction Research and the Health of Women."

This conference brought together leading researchers to present state-of-the-science findings, discuss research issues and challenges confronting the field, and lay the framework for NIDA's research agenda in this important area.

Drug Abuse Research and the Health of Women, NIH Pub. 98-4289.
This publication builds on presentations from the 1994 NIDA sponsored conference, "Drug Addiction Research and the Health of Women." The chapters in this volume contain in-depth, state-of-the-science reviews that highlight much of what is known about the epidemiology, etiology, health, social, and behavioral consequences of drug abuse and addiction. Biological mechanisms underlying these processes and legal, prevention, and treatment issues surrounding drug abuse and addiction are also discussed. The material presented in this publication clearly illustrates the breadth and complexity of drug abuse-related issues that affect women's health.

Perspectives on Rural Substance Abuse: Summary of the National Institute on Drug Abuse Symposium on Rural Drug Abuse - Administrative Report, February, 1998.
This publication provides an executive summary of the meeting and an agenda for epidemiologic, etiologic and intervention research in rural areas.

Spotlight on Depiction of Health and Social Issues: A Resource Encyclopedia for the Entertainment Community.
NIDA collaborated with the Entertainment Industries Council for the printing and distribution of 5,000 Depiction Notebooks for distribution to the entertainment industry for use in preparing movies, TV shows and cable programming, and to assure accurate depiction of drugs, alcohol and tobacco.

Arthur MacNeill Horton, Jr., Ed.D., published a paper on the "Comorbidity of Drug Abuse Treatment" in the Journal of Psychopathology and Behavioral Assessment, 19(2), pp. 79-90, 1997.

Weinberg, N.Z., Rahdert, E., Colliver, J.C., Glantz, M.D. Adolescent Substance Abuse: A Review of the Past 10 Years. Journal of the American Academy of Child and Adolescent Psychiatry, 37, pp. 252-261, 1998. This widely circulated article reviews and synthesizes the research literature on adolescent drug abuse published in the last decade.

Therapy Manuals for Drug Addiction Series A Community Reinforcement Plus Vouchers Approach: Treating Cocaine Addiction, NIH Pub. 98-4309.
This publication recommends that four life problem areas in addiction to drug craving be addressed in counseling sessions with all patients, although the number and duration of time spent on each area may vary depending upon negative drug urine test results. Tests are incrementally scheduled in order to promote increased periods of abstinence.

A Cognitive-Behavioral Approach: Treating Cocaine Addiction, NIH Pub. 98-4308.
This publication discusses a variety of implementation and administrative issues. Topics include possible modifications to the format and duration of the treatment model without reducing its clinical integrity, and appropriateness of patients with certain symptoms for the treatment approach.

Research Report Series

Methamphetamine: Abuse and Addiction, NIH Pub. 98-4210.
This Research Report provides scientific information on methamphetamine abuse. It describes methamphetamine and related drug analogues (e.g., MDMA); how it enters the body; current epidemiological data regarding its abuse; and the short-term and long-term effects of abuse with an emphasis on how it affects the brain.

NIDA NOTES

September/October 1997 - NCADI NN0025.
This issue features results from NIDA's Drug Abuse Treatment Outcome Study. The issue also reports findings that morphine shrinks nerve cells in the brain. NIDA's cooperative work with Latin American countries to advance drug abuse research is also reported. Another article describes drug abuse education materials for middle school students.

November/December 1997 - NCADI NN0027.
The lead article in this issue reports on NIDA's Heroin Conference in Washington, D.C. Other articles discuss the conclusions of two panels: one on effective medical treatment of heroin addiction, and the other on the need for

research on medical potential of marijuana. Another feature article looks at recent progress in research on pain relief.

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Staff Highlights

Honors and Awards

Dr. Charles Sharp, Special Assistant to the Director of the Division of Basic Research, recently received the Blue Cross/Blue Shield Distinguished Federal Employees Award in recognition of his service in promoting the public's health. Dr. Sharp was recognized for his significant contribution to the National Institute on Drug Abuse's (NIDA) program development. Dr. Sharp developed and continues to be involved in NIDA's training and fellowship program which supports the development of pre- and post-doctoral fellows in scientific areas related to drug abuse and addiction. Dr. Sharp initiated NIDA's participation in the annual Society of Neuroscience meeting exhibit booth where information describing NIDA's programs is distributed to interested neuroscientists. Dr. Sharp began and continues NIDA's inhalant program, one outcome of which has been the important discovery that toluene exposure results in auditory nerve damage. As an offshoot of the inhalant program, Dr. Sharp began the HIV/AIDS research program at NIDA and, importantly, organized seminars to teach NIDA staff about current concepts in immunology and neuropsychoimmunology. As a recipient of this award, Dr. Sharp was given a Certificate of Appreciation and a gift and his name and picture were displayed at the Blue Cross/Blue Shield exhibit during Public Service Recognition Week on the National Mall. Public Service Recognition Week is sponsored by the Public Employees Roundtable and the President's Council on Management Improvement.

Staff Changes

Dr. Susan Coyle, DEPR/Community Research Branch, has joined the Office of Extramural Program Review, in the position of Chief of the Clinical, Epidemiological, and Applied Sciences Research Branch.

Ms. Kimberly Crown has accepted a position as a Program Assistant in OEPR and will assist in the coordination of extramural policy implementation, staff training, and policy development.

Ms. Flair Lindsey became a Program Assistant in NIDA's Special Populations Office in March 1998.

Dr. Minda Lynch joined the staff of the Behavioral Sciences Research Branch, Division of Basic Research as a Health Scientist Administrator in March 1998. Dr. Lynch moved to NIDA from an Intramural Program at the Department of Veterans Affairs in Syracuse, New York, where she ran a laboratory research program in neuropsychopharmacology for the past 13 years.

Ms. Deborah Musumeci has recently joined NIDA as a Secretary in the Basic Neurobiology and Biological Systems Research Branch of the Division of Basic Research.

Dr. Amrat Patel, formerly with the Food and Drug Administration (FDA), joined NIDA's Medications Development Division as a Health Scientist Administrator on April 12, 1998.

Dr. Herbert Weingartner, former Chief of the Cognitive Neuroscience Branch (Intramural) at the NIAAA, has assumed a detail, effective April 26, 1998, to work with NIDA's Behavioral Sciences Research Branch, DBR to aid in building an extramural research program in cognitive sciences.

Grantee Honors

Dr. Thomas J. Dishion of the Oregon Social Learning Center was the recipient of a NIDA MERIT Award. Dr. Dishion was recognized for his study titled "Understanding and Preventing Adolescent Drug Abuse". This includes (1) a follow-up of a sample of high-risk youth at ages 18-20 who participated in the Adolescent Transitions Program (ATP) to determine consequences of substance abuse on development during adulthood and (2) conducting prevention trials with families to test the impact of ATP in improving parenting skills and reducing drug use.

Dr. Marian Fischman of Columbia University is the recipient of the 1998 Solvay Award. The award is given by Solvay Pharmaceuticals and administered by Division 28 of the American Psychological Association.

Dr. Peter Schiller of the Clinical Research Institute of Montreal was a co-recipient of the 1998 Vincent du Vigneaud award. Dr. Schiller has made significant contributions to the design of biologically active peptide hormones and neurotransmitters. Dr. Schiller and colleagues developed several novel approaches to peptide and peptidomimetic design, and discovered several peptide analogs with unique biological properties. Some of his contributions include his work on the use of conformational constraints to improve biological potency and selectivity, development of TIPP-related peptides and the development of opioids with mixed opioid receptor agonist- opioid receptor antagonist activities that have potential to be useful analgesics. Dr. Schiller was presented the award at the Gordon Research Conference, held February 15-19, 1998, in Ventura, CA.

Dr. Richard L. Spoth of Iowa State University's Department of Sociology and Anthropology received a NIDA MERIT Award. Dr. Spoth's "Rural Youth and Family Competencies Building Project" will conduct a longitudinal, controlled study of a theory-based, comprehensive intervention targeting rural youth and families. The intervention will be implemented via the cooperative extension service when students are in 7th grade. Family- and peer-related risk and protective factors will be evaluated.

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