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

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****February, 1998**

Research Findings

Basic Research

Studies on Sensitization to Morphine

Drugs of abuse such as cocaine, amphetamine, and morphine produce long-term changes in the nervous system that are reflected by increases in locomotor behavior and by increases in the rewarding properties of these drugs. Work by Dr. Eric Nestler and his colleagues published in *Science* suggest that these changes in brain function can be related in part to increases in expression of a single gene encoding an AMPA glutamate receptor subunit called GluR1. Glutamate, a neurotransmitter, is released from neurons onto dopamine neurons located in the midbrain. Glutamate activates a glutamate receptor, containing the GluR1 subunit, located on the surface of these dopamine neurons, causing the dopamine neurons to fire. The subsequent release of dopamine produces the sensation of reward and elicits locomotor activity. Repeated administration of morphine had previously been shown to be associated with increased expression of the GluR1 subunit on dopamine neurons. Since other changes in brain chemistry occur with repeated administration of morphine, it is not possible to infer from this previous work that increases in locomotor activity and the rewarding properties are due to the increases in the GluR1 receptors on dopamine neurons that might make dopamine neurons more sensitive to the excitatory effects of glutamate. To test directly the theory that the increased rewarding properties and increased locomotor activity produced by repeated morphine administration result from increased expression of GluR1 receptors, Dr. Nestler and his colleagues genetically engineered a herpes simplex virus to express the GluR1 receptors when neurons are infected with the virus. They then injected the virus in the vicinity of the dopamine neurons of rats that had not been exposed to morphine. The dopamine neurons of these naive rats became infected with the virus and expressed the GluR1 subunit. Following infection of the dopamine neurons with the genetically engineered virus, the naive rats when injected with morphine mimicked the response of rats who had been repeatedly injected with morphine. They showed increases in locomotor activity and the reinforcing effects of morphine were also increased. Rats whose dopamine neurons were injected with virus that had not been engineered or engineered to express a slightly different protein than the GluR1 receptors did not show the sensitized response to morphine. Since this experiment was done under controlled conditions, it suggests that the main mechanism by which morphine produces its enhanced responses is due to an increase in the expression of GluR1 in dopamine neurons that accompany the changes following chronic administration of morphine. These experiments might also lead scientists to test whether other abused drugs such as marijuana and alcohol increase the expression of the GluR1 subunit and increase the rewarding properties of drugs such as cocaine, morphine, and amphetamine when given repeatedly. Furthermore, the experiments by Nestler and colleagues suggest the possibility of gene therapy for addiction and other brain diseases using genetically engineered viruses. Carlezon, W.A. Jr., Boundy, V.A., Haile, C.N., Lane, S.B., Kalb, R.G., Neve, R.L., Nestler, E.J. Sensitization to Morphine Induced by Viral-Mediated Gene Transfer. *Science*. 277(5327), pp. 812-814, August 8, 1997.

Cocaine and fosB Mutant Mice

Chronic exposure to psychomotor stimulants such as cocaine and amphetamine produce long lasting changes in behavior that are accompanied by increases in transcription factors in a region of the brain called the striatum that includes the nucleus accumbens and the caudate putamen. These structures lie between the cortex and the midbrain. Some transcription factors activated by chronic cocaine exposure are the chronic fos related proteins. The chronic fos related proteins are derived from processing of the FosB gene. Transcription factors such as the chronic fos related proteins instruct the cellular machinery in neurons to reduce or increase the synthesis of proteins required for a particular cellular function. To test the role of the chronic fos related antigens in mediating the long lasting behavioral changes produced by cocaine, Nestler and colleagues used *fosB* mutant mice. Dr. Nestler in the September 16, 1997 issue of the Proceedings of the National Academy of Sciences reports that *fosB* mutant mice completely lack basal levels of the fos related antigens in the striatum and repeated administration of cocaine fails to produce any increase in fos related proteins. No change in striatal cytoarchitecture was observed in the mutant mice. The absence of the chronic fos related proteins was associated with increased behavioral responses to cocaine. The *fosB* mutant mice showed increased locomotor responses as compared to normal mice administered the same initial dose of cocaine. In addition, the mice lacking the fos related proteins showed robust conditioned place preference to a lower dose of cocaine than controls. These results suggest that the induction of the chronic fos related proteins represent a compensatory adaptation in striatal neurons that oppose the action of cocaine. Hiroi, N., Brown, J.R., Haile, C.N., Ye, H., Greenberg, M.E., and Nestler, E.J. FosB Mutant Mice: Loss of Chronic Cocaine Induction of Fos-Related Proteins and Heightened Sensitivity to Cocaine's Psychomotor and Rewarding Effects PNAS, 94, pp. 10397-10402, 1997.

Causes of Nerve-Injury Related Pain

Dr. Allan I. Basbaum of the University of California has recently made some important discoveries reported in *Science*, Oct. 10, 1997 related to the causes of nerve-injury related pain. People with this "neuropathic" pain often suffer greatly, because neuropathic pain typically lasts for years and is resistant to known pain treatments. Basbaum found that in mice where the protein kinase C-gamma (PKC-g) gene was knocked out, behavioral signs of chronic pain were not present following nerve injury. However, these same mice still had normal pain responses to noxious heat stimuli. Thus, PKC-g appears to be specifically involved in the occurrence of neuropathic pain. PKC-g may be a target for new drugs to treat neuropathic pain.

Mechanism of Action of Morphine Metabolite

A recent study has suggested that there may be a different receptor for the metabolite morphine-6-glucuronide (M6G), based on non-linear ("two-site") Scatchard results on brain membrane preparations with tritiated M6G. A "biphasic" competition curve was obtained from the studies in brain tissue. Most of the binding was attributable to a lower affinity site resembling the mu receptor, with a smaller fraction attributable to a higher affinity site. The antagonist 3-methoxynaltrexone was useful in differentiating these sites, since it competes for tritiated M6G more strongly than it competes for tritiated morphine. The distribution of this potential M6G site was highest in striatum and frontal cortex. Brown, G.P., Yang, K.E., Ouerfelli, Q., Standifer, K., Byrd, D., and Pasternak, G. Journal of Pharmacology and Experimental Therapeutics, 282, pp. 1291-1297, 1997.

Biphalin Crosses Blood Brain Barrier

Biphalin, an analog of enkephalin, is a lipophilic peptide more potent than morphine as an analgesic when administered intrathecally in animals. A recent study using ¹²⁵I-labeled biphalin has shown that this compound accumulates in the nucleus accumbens, pituitary, choroid plexus, cerebral spinal fluid (CSF) and lumbar region, following I.V. injection; the extent of uptake was inhibited by pretreatment with the antagonist naloxone. Secondly, the uptake of labeled biphalin was shown to be saturable, i.e., inhibited by unlabeled biphalin, across the blood brain barrier, but non-saturable into the CSF. While the transport has not been fully explained, it is possibly based on a neutral amino acid carrier, and not on a carrier of enkephalin, or via a calcium channel. The maximum concentration of biphalin obtained in brain and CSF occurred approximately 20 minutes following injection, with 80% of the radioactivity due to intact biphalin. Abbruscato, T., Thomas, S., Hruba, V., Davis, T. Journal of Neurochemistry, 69, pp. 1236-1245, 1997.

DALDA and Obstetric Analgesia

Dr. Hazel Szeto and colleagues have recently investigated the usefulness of a peptide drug, DALDA (Tyr-D-Arg-Phe-Lys-NH₂), for obstetric analgesia. DALDA is a potent and highly selective μ -agonist. In this study, Szeto et al. determined the pharmacokinetics and placental transfer of DALDA after systemic administration in sheep. DALDA was administered to pregnant and nonpregnant sheep. A one-compartment model provided an excellent fit for pregnant and nonpregnant plasma data. This data revealed that the volume of distribution of DALDA is restricted to plasma volume and that its disposition is not altered in pregnancy. DALDA was not detected in any of the plasma samples. The highly restricted placental distribution of DALDA suggests that DALDA may be a promising opioid drug for obstetrical use. Szeto, H.H., Clapp, J.F., Desiderio, D.M., Schiller, P.W., Grigoriants, O.O., Soong, Y., Wu, D., Olariu, N., Tseng, J-L and Becklin, R. In Press.

Females and Anabolic Steroid Use

Research findings, soon to be published, report that three commonly used anabolic-androgenic steroid (AAS), stanozolol, oxymetholone, or testosterone cypionate, produce alterations in the reproductive behavior and physiology of female rats. Dr. Ann Clark and her associates found AAS-induced disruptions in the cyclical display of vaginal estrus following acute or 14 days paradigm; however, their effects on sexual receptivity were different. Studies in ovariectomized rats also showed a time course variation with respect to sexual receptivity. For example, methyltestosterone, methandrostenolone and stanozolol interfered with the display of sexual receptivity on Day 14, whereas oxymetholone and testosterone cypionate had no effect. These findings illustrate that short-term administration of AAS compounds do elicit measurable and distinct effects on the estrous cycle as well as on female sexual behavior. Blasberg, M.E., Langan, C.J. & Clark, A.S. Physiology & Behavior, In Press; Clark, A.S., et al. Hormone & Behavior, In Press.

Adolescence and Anabolic-Androgenic Steroid

Dr. Richard Melloni and his group have reported recently that administration of high doses of multiple anabolic-androgenic steroids (AAS) during the adolescence period in male hamsters induced aggressive behavior as well as significant increases in arginine vasopressin (AVP) in the regions of the anterior hypothalamus (AH) implicated in the stimulation of offensive aggression. The doses of synthetic AAS selected for these experiments were similar to those heavy use self-administration regimens used by athletes. From these findings, the researchers suggest a possible role of AH-AVP in AAS-stimulated aggression. Studies are currently underway to compare the genetic and biochemical control of AVP production in the brains of AAS-exposed and control hamsters. Melloni, R.H. et al. Physiology & Behavior, 61, pp. 359-364, 1997.

Pulmonary Consequences and Marijuana/Cocaine

Recent findings published by Dr. Donald Tashkin and his group demonstrate that habitual smoking of either marijuana or cocaine significantly impairs the antibacterial and tumoricidal activities of human alveolar macrophages (AMs). In the case of marijuana, there were additional effects on the pulmonary function such as a reduction in AMs ability to produce inflammatory cytokines and a suppression of phagocytosis. While *in vitro* studies and animal models have long predicted some of these results, Dr. Tashkin's study provides conclusive evidence as to the immunosuppressive consequences of these drugs. These findings are important from a health perspective as the habitual smoking of these substances may enhance the susceptibility to infectious diseases, cancer, and AIDS. Baldwin, G.C., Tashkin, D.P. et al. AM J Respir Crit Care Med, 156, pp. 1606-1613, 1997.

Mice Lacking Dopamine D4 Receptors are Supersensitive to Ethanol, Cocaine and Methamphetamine

To clarify the role of Dopamine D4 receptor (D4R), NIDA Grantee David K. Grandy and his colleagues produced and analyzed mutant mice (D4R^{-/-}) lacking this human protein. The mutant mice displayed locomotor supersensitivity to ethanol, cocaine and methamphetamine. Although less active in open field tests, the mutant mice outperformed wild-type mice on the rotorod test. Dopamine synthesis and its conversion to DOPAC were elevated in the dorsal striatum from the mutant mice. Clozapine has a high affinity for the Dopamine D4 receptor *in vitro* and was shown to block apomorphine-induced locomotion in rodents. Clozapine attenuated the locomotor activity of wild-type mice, but had no effect on the mutant mice. The Dopamine D4 receptor-deficient mice provide a new and useful model system to

explore the *in vivo* role of Dopamine D4 receptor in normal and drug-induced behaviors. Rubinstein, M., Phillips, T.J., Bunzow, J.R., Falzone, T.L., Dziewczapolski, G., Zhang, G., Fang, Y., Larson, J.L., McDougall, J.A., Chester, J.A., Saez, C., Pugsley, T.A., Gershanik, O., Low, M.L., and Grandy, D.K. *Cell*, 90, p. 991, 1997.

Cocaine Binding Site on the Serotonin Transporter

NIDA grantee Dr. Gary Rudnick and his colleagues at Yale University have identified part of the cocaine binding site on the serotonin transporter. The Yale group replaced 20 amino acids of the transporter of the third transmembrane domain, which were deep in the interior of the protein, one at a time, with cysteine. Two of these amino acids, I172 and Y176, were close to, or in the cocaine binding site, since cocaine could protect them from reacting with a cysteine probe, MTSET. Serotonin also inhibited the labeling of both I172 and Y176 with MTSET. When MTSET was attached to either of these amino acids, it prevented the cocaine analogue (beta-CIT) from binding to the transporter. The same amino acids in the transporter involved with the binding sites for serotonin and cocaine raises the possibility that the two sites overlap considerably. The finding that serotonin and cocaine bind to the same part of the serotonin transporter suggests that the same will be true for dopamine and cocaine in the dopamine transporter and for norepinephrine and cocaine at the norepinephrine transporter. The prospect has important implications for designing drugs to combat cocaine abuse. Because cocaine itself acts by inhibiting neurotransmitter transport, any inhibitor that prevents cocaine binding may itself block transport. Chen, J.G., Sachpatzidis, A. and Rudnick, G. *Journal of Biological Chemistry*, 272, pp. 28321-28327, 1997.

Genetically Deficient CYP2D6 Metabolism Provides Protection Against Oral Opiate Dependence

Oral opiates (e.g. codeine, oxycodone, and hydrocodone) are metabolized by cytochrome CYP2D6 to metabolites of increased activity (e.g. morphine, oxymorphone and hydro-morphine). CYP2D6 is genetically polymorphic. Four to ten percent of Caucasians lack CYP2D6 activity (poor metabolizers) due to inheritance of two non-functional alleles. Dr. Edward Sellers of Addiction Research Foundation of Ontario, Canada, a NIDA grantee, and his colleagues tested whether the failure to activate oral opiates was a protection factor in opiate dependence by genotyping (CYP2D6*3 and CYP2D6*4 defective mutant alleles) Caucasians who met or didn't meet DSM criteria for oral opiate dependence. In opiate dependent subjects they found no poor metabolizers. In contrast, the poor metabolizer frequency in never-dependent control and multi-drug dependent comparison groups was 4% and 6.5%, respectively. This under-representation of poor metabolizers in people dependent on oral opiates suggests that the CYP2D6 defective genotype is a pharmacogenetic protection factor for oral opiate dependence. This is the first investigation and demonstration of differences in genetically determined P450 metabolism influencing risk for substance dependence. Tyndale, R.E., Droll, K.P., and Sellers, E.M. *Genetically Deficient CYP2D6 Metabolism Provides Protection Against Oral Opiate Dependence. Pharmacogenetics*, 7, pp. 375-379, 1997.

Pharmacological Characterization of Orphanin FQ/Nociceptin and its Fragments

The cloning of a fourth member of the opioid receptor family has led to the discovery of a new neuropeptide termed orphanin FQ or nociceptin (OFQ/N). Dr. Gavrill W. Pasternak and his research team of the Memorial Sloan-Kettering Cancer Center studied OFQ/N in CD-1 mice confirming the ability of OFQ/N to rapidly induce hyperalgesia within 15 min which is insensitive to opioid antagonists. This is followed in the next 30 min by loss of hyperalgesia and the appearance of analgesia in the tailflick assay which is readily reversed by opioid antagonists. However, the very poor affinity of OFQ/N for all the traditional opioid receptors and the insensitivity of OFQ/N analgesia to antisense oligodeoxynucleotides active against MOR-1, DOR-1 or KOR-1 sequences that selectively block mu, delta or kappa₁ analgesia, respectively, make it unlikely that OFQ/N analgesia is mediated through typical opioid receptors. Blockade of the antiopioid F system by haloperidol enhances the analgesic potency of OFQ/N of more than 100-fold. This effect is pronounced in BALB-C and Swiss-Webster mice. Although OFQ/N alone has little analgesic activity in these mice, the blockade of sigma systems with haloperidol uncovers a robust analgesic response in both strains. Two shorter OFQ/N fragments, OFQ/N(1-7) and OFQ/N(1-11), also are analgesic in CD-1 mice and their actions are reversed by the opioid antagonist diprenorphine despite very poor affinities of both peptides against [¹²⁵I]OFQ/N binding and all the opioid receptors. In antisense studies, a probe targeting the first coding exon of KOR-3 eliminates OFQ/N hyperalgesia, but not OFQ/N analgesia. Conversely, antisense probes based on the second and third coding exons are inactive against OFQ/N hyperalgesia but readily reverse μ_3 opioid analgesia. These results suggest that OFQ/N elicits both analgesia and hyperalgesia through pharmacologically distinct receptors that do not correspond to traditional opioid receptors. Rossi, G.C., Leventhal, L., Bolan, E., and Pasternak, G.W. *Pharmacological Characterization of*

Orphanin FQ/Nociceptin and its Fragments. JPET 282(2), pp. 858-865, 1997.

Chronic Morphine Exposure and the Immune System

Groups of rats were differentially pre-exposed to morphine in a drinking solution (0.2, 0.4 or 0.6 mg/ml) or to tap water 20 days prior to an acute injection of morphine (15 mg/kg) administered 1 hour prior to sacrifice. For the control group, a single acute dose of morphine resulted in significant suppression in natural killer (NK) activity, mitogen-stimulated splenic T- and B-cell proliferation, and gamma-interferon production. In the morphine pre-exposure groups, although mitogen stimulated T- and B-cell proliferation and gamma-interferon production was suppressed, NK activity was not suppressed in rats that drank the two highest concentrations of morphine. These results suggest that tolerance develops to morphine's suppressive effect on NK activity but not on other measures of immune status following a chronic regimen of morphine administration that produces tolerance to morphine's antinociceptive effects and physical dependence. West, J.P., Lysle, D.T., & Dykstra, L. Tolerance Development to Morphine-Induced Alterations of Immune Status. Drug and Alcohol Dependence, 46, pp. 147-157, 1997.

GDNF Prevents the Neurotoxic Effects of Methamphetamine on Dopamine Systems

GDNF is Glial cell line-Derived Neurotrophic Factor, a recently identified and cloned polypeptide that has striking effects on dopamine (DA) neurons. GDNF has previously shown long-lasting neurotrophic effects on DA cells in culture and on adult DA cells *in vivo*. In addition, Dr. Barry Hoffer, Intramural Research Program Director at NIDA, as well as several other investigators, have shown that GDNF inhibits the neurotoxicity, and promotes recovery from the neurotoxic effects, of 6-OHDA and MPTP. Wayne A. Cass, Ph.D. from the University of Kentucky College of Medicine administered GDNF unilaterally into the striatum of rats one day before they received a neurotoxic regimen of methamphetamine (METH). This METH regimen normally results in long-lasting decreases in striatal DA and serotonin function and levels in rats. It is possible that similar neurotoxic effects could occur in METH abusers. Using *in vivo* electrochemistry, he found that GDNF prevented the METH-induced reductions in potassium-evoked release of DA on the GDNF-treated side of the brain, a week after the METH treatment. GDNF also prevented the reduction in tissue levels of DA normally observed following this METH treatment. The ability of METH to reduce brain serotonin levels was not affected by GDNF (J. Neurosci. 16, pp. 8132-8139, 1996), emphasizing the selectivity of GDNF for DA systems. Recent studies also indicate that GDNF appears to up-regulate DA functioning in normal rats within 24 hours of administration. Soc. Neurosci. Abstr. 23, p. 56, 1997.

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Research Findings

Behavioral Research

CB1 Receptors May Mediate Marijuana's Effects on Learning

Researchers at Louisiana State University Medical Center recently reported that many of the behavioral and learning deficits induced by the active compound in marijuana, delta-9 THC and other cannabinoid ligands are mediated through the brain receptor CB1. Rats pre-administered delta-9 THC or the cannabinoid agonist R-methandamide increased errors on a learning and memory task. The selective CB1 cannabinoid antagonist (SR141716A) administered concurrent with the cannabinoids resulted in fewer errors. These data suggest that cannabinoids disrupt learning processes as a result of direct stimulation of the CB1 receptor. Brodtkin, J. & Moerschbaecher, J.M. *The Journal of Pharmacology and Experimental Therapeutics*, 282, pp. 1526-1532, 1997.

Does Smoking Increase Your Desire to Smoke?

Researchers at University of Pittsburgh recently explored whether limited prior smoke exposure primes smokers to continue smoking. Following overnight smoking abstinence, smokers were given the opportunity to take between 0-12 puffs, or to smoke an entire cigarette. Following this, they reported their desire to continue smoking, and then chose between earning money vs taking more cigarette puffs. Smokers reported less desire for smoking as prior smoke exposure (number of puffs) increased. However, responding for puffs on the computer task was only modestly reduced by prior smoke exposure and was only significantly reduced following the smoking of an entire cigarette. These results suggest that smoking following a relatively brief abstinence period reduces the stated desire to smoke, but does not result in a priming effect (i.e., an increase in responding for cigarette puffs). Perkins, K. A., Grobe, P., & Fonte, C. *Experimental and Clinical Psychopharmacology*, 5, pp. 277-285, 1997.

Kappa Agonists and Cocaine Self-Administration

Two kappa opioid agonists, the benzomorphan ethylketocyclazocine (EKC) and the arylacetamide U50,488 were examined for their effects on cocaine self-administration in rhesus monkeys. Monkeys responded for 0.032 mg/kg/injection cocaine (i.v.) and food pellets during alternating daily sessions of cocaine and food availability. Chronic treatment for 10 consecutive days with EKC (0.0032-0.032 mg/kg/hr) or U50,488 (0.032-0.1 mg/kg/hr) dose-dependently decreased self-administration of cocaine, often sustained throughout the 10 days of treatment. Note however that food-maintained responding was reduced as well. In addition, EKC and U50,488 often produced emesis and sedation during the first few days of treatment, although tolerance appeared to develop rapidly to these effects. The kappa antagonist norbinaltorphimine (3.2 mg/kg) did not affect responding maintained by cocaine or food. However, both norbinaltorphimine (3.2 mg/kg) and the opioid antagonist naloxone (1.0 mg/kg/hr) blocked the effects of EKC and U50,488. While chronic administration of EKC and U50,488 produced dose-dependent, kappa

receptor-mediated and often sustained decreases in cocaine self-administration, they also produced undesirable behavioral effects that may complicate their use as treatments for cocaine dependence. Negus, S.S., Mello, N.K., Portoghese, P.S., Lin, C.E., Effects of Kappa Opioids on Cocaine Self-Administration by Rhesus Monkeys. *J Pharmacol Exp Ther*, 282, pp. 44-55, 1997.

Abuse Liability of New Nicotine Delivery Systems

Overnight-deprived adult smokers received between 0-16 active puffs from nicotine-containing cigarettes (0.1 mg per puff); between 0-4 nasal sprays (0.5 mg nicotine per spray), and between 0-120 vapor inhalations (estimated 0.013 mg nicotine per inhalation) in a within-S single blinded design. While smokers clearly liked cigarette puffs, they liked nasal spray or vapor inhaler less well, with only modest elevations on a "good drug effects" scale. The spray and inhaler products produced unpleasant effects of burning throat and nose, watery eyes, runny nose, coughing and sneezing that might be expected to limit abuse liability. Nicotine plasma level and heart rate increases were dose-related for cigarettes and nasal spray but not for vapor inhaler, indicating limited nicotine delivery with inhalers. Nicotine nasal spray and vapor inhaler appear to have substantially lower abuse liability than cigarettes in experienced cigarette smokers initially exposed to these products. Schuh, K.I., Schuh, L.M., Henningfield, J.E., and Stitzer, M.L. Nicotine Nasal Spray and Vapor Inhaler: Abuse Liability Assessment. *Psychopharmacology*. 130, pp. 352-361, 1997.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****February, 1998**

Research Findings

Clinical and Services Research

Psychosocial Predictors of Drug Abuse Among Drug Clinic-Referred Youths

In a study that examined 2582 adolescents referred to drug treatment facilities nationwide and in Ontario, Canada, who met criteria for DSM-III-Revised drug abuse or dependence of at least one psychoactive substance, Winters, Latimer and Stinchfield found the strongest predictors of drug use severity at the time of referral, as measured by the Personal Experience Inventory, to be use of illicit drugs by peers and by siblings. Less predictive were psychological distress (emotional disturbance; social isolation), declaration of nonconventional values (e.g., rejecting conventional values; absence of goals; spiritual isolation), and family distress (e.g., parent drug use; parent dysfunction; family estrangement). Results were similar for all racial/ethnic, gender, and age subgroups represented in the study sample. *Journal of Pediatric Psychology*. In Press.

DSM-IV Criteria for Adolescent Alcohol and Cannabis Use Disorders

In a study comparing DSM-III-Revised and DSM-IV criteria for alcohol and cannabis use disorders among 772 teenagers (63% boys; 77% white) referred to adolescent outpatient drug treatment programs in the Minneapolis, MN area, Winters, Latimer and Stinchfield found that compared to the use of the DSM-III-R criteria, the application of DSM-IV criteria for alcohol and cannabis use resulted in more "abuse" assignments and fewer "dependence" assignments. Study results indicated that the shift in diagnostic assignments when using DSM-IV compared to DSM-III-R was due to a lowering of the abuse threshold rather than a tightening of the dependence criteria. *Journal of Studies on Alcohol*. In Press.

Marijuana Use and Treatment Outcome Among Opioid-Dependent Patients

Dr. Alan Budney and colleagues at the University of Vermont assessed marijuana use in 107 persons enrolled in treatment for opioid dependence. The relationship between marijuana use and treatment outcome was explored in a subset of this sample who received treatment that included buprenorphine detoxification and behavior therapy (N=79). Sixty-six percent of participants were current marijuana users and almost all (94%) continued to use during treatment. Only a few markers of increased psychosocial impairment or adverse consequences associated with marijuana use were observed. Users were less likely to be married than nonusers, and more likely to report financial difficulties, be involved in drug dealing and engage in sharing of needles ($p < .05$). A unique effect of marijuana use on drug dealing and sharing needles was retained after statistically controlling for the influence of heroin and alcohol use and other sociodemographic variables. No significant adverse relations were observed between marijuana use and treatment outcome. These outcome findings are consistent with previous studies examining marijuana use in opioid-

dependent and cocaine-dependent patients. This suggests that progress in treatment for opioid dependence can be made without mandating that patients abstain from marijuana use. *Addiction*, In Press.

Persistence and Clinical Significance of Hepatitis G Virus (HGV) Infections in Injecting Drug Users

To determine the prevalence of HGV infection and its association with liver disease, HGV RNA was assessed in the most recent serum sample for 246 long-term IDUs and in prior specimens for those found HGV-RNA positive. HGV RNA was detected at the most recent visit in 15%. Of those found positive, 82% also had HGV-RNA positive serum samples at all prior visits occurring a median of 6.1 years earlier. HGV-positive IDUs were younger and had fewer years duration of drug use, suggesting that HGV RNA had previously been cleared. Serial samples from 29 short-term IDUs detected HGV RNA in 9 (31%) and in 56% of those HGV infection cleared. No differences were detected in serum levels of liver-related enzymes among HGV RNA-positive vs. HGV RNA-negative IDUs ($p > .20$). These data indicate that HGV infection is not associated with hepatic inflammation, and that HGV clearance occurs after many acute infections but uncommonly in persons who remain RNA-positive years after exposure. Thomas, D.L., Nakatsuji, Y., Shih, J.W. et al., *J Infect Dis*, 176, pp. 586-592, 1997.

Cannabis Dependence, Withdrawal, and Reinforcing Effects Among Adolescents with Conduct Symptoms and Substance Use Disorders

Crowley and his colleagues from the University of Colorado assessed 209 adolescents (165 males, 64 female; 13-19 year old), who were referred for substance and conduct problems, to determine if cannabis produced dependence and withdrawal. The subjects were diagnosed with substance dependence, 100%; current conduct disorder, 82.1%; major depression, 17.5%; and attention-deficit/hyperactivity disorder, 14.8%. Most patients claimed serious problems from cannabis, and 78.6% met standard adult criteria for cannabis dependence. Two-thirds of cannabis-dependent patients reported withdrawal. Progression from first to regular cannabis use was as rapid as tobacco progression, and more rapid than that of alcohol, suggesting that cannabis is a potent reinforcer. Data indicate that for adolescents with conduct problems cannabis is not benign, and that the drug potently reinforces cannabis-taking, producing both dependence and withdrawal. However, the authors suggested that findings from this severely affected clinical population should not be generalized broadly to all other adolescents. Crowley, T.J., MacDonald, M.J., Whitmore, E.A., and Mukulich, S.K. *Drug and Alcohol Dependence*, In Press.

Influences on Adolescent Substance Dependence: Conduct Disorder, Depression, Attention Deficit Hyperactivity Disorder, and Gender

Whitmore and his colleagues from the University of Colorado conducted a study to determine if prevalence and severity of conduct disorder (CD), major depression and ADHD would differ by gender, and that these conditions would associate differentially with severity of substance disorder (SD) in males and females. The subjects were 285 male and 82 female adolescents referred for treatment for comorbid CD and SD. The investigators found that males and females did not differ significantly in severity of substance involvement, major depression, or ADHD, but males had more severe CD. Major depression was the only variable significantly associated with SD severity for females, while for males, severity of CD combined with major depression and ADHD was significantly associated with SD severity. The authors concluded that among referred adolescents, CD, major depression, and ADHD may all be important concomitants of SD in males, while in females, depression may be the primary variable related to SD. Whitmore, E.A., Mikulich, S.K., Thompson, L.L., Riggs, P.D., Aarons, G.A., and Crowley, T.J., *Drug and Alcohol Dependence*, 47, pp. 87-97, 1997.

Fluoxetine in Drug-Dependent Delinquents with Major Depression: An Open Trial

Riggs et al. treated, in an open trial for > 7 weeks with a fixed dose of 20 mg of fluoxetine, a group of adolescents, who had been referred to residential treatment for substance use disorder. A >50% improvement was observed in mean scores on the 10-point depression scale. Of the 8 adolescents, 7 showed marked improvement and wished to continue fluoxetine after trial. Side effects were mild and transient. No subject required dosage reduction or discontinuation of medication because of side effects. Fluoxetine appeared useful in treating substance-dependent delinquents whose major depressions persisted or emerged after 4 weeks of abstinence. These preliminary findings justify a controlled trial in such youths. Riggs, P.D., Mikulich, S.K., Coffman, L.M., Crowley, T.J. *J. Child and*

Adolescent Psychopharmacol, 7(2), pp. 87-95, 1997.

Risk Factors for Disruption of Primary Caregiving of Substance-Abusing Mothers

Researchers at the University of Maryland School of Medicine have identified perinatal factors (i.e., postpartum hospital stay and 2-week visit) that are predictive of disruption of primary infant caregiving among high-risk, substance-abusing mothers. Disruption of primary caregiving was defined as the infant receiving substitute care during the first 18 months of life because of the mother's inability to care for her infant due to neglect/abuse, incarceration, continued drug abuse, or homelessness (includes voluntary placement with a relative as well as protective service referral). All women in the study were at high risk for disruption based on histories of drug abuse, poverty, limited education, and other social problems. All had a history of heroin and/or cocaine use during pregnancy. Analyses were based on 152 mother-infant dyads from a larger, ongoing longitudinal study. Forty-three percent of the sample had disruption in primary caregiving. Bivariate analyses compared the disruptive care group with the non-disruptive care group on maternal and neonatal factors. Results of a multiple logistic regression showed that younger maternal age, two or more other children, positive heroin tox at delivery, and reported depressive symptoms were significantly associated with disruption of caregiving. The investigators discuss possible processes underlying these relationships, and implications of the findings for screening and service delivery. Nair, P., Black, M.M., Schuler, M., et al. *Child Abuse & Neglect*, 21, pp. 1039-1051, 1997.

Demographic, Drug Use, and Psychosocial Characteristics of Rural Pregnant Cocaine Users

Data from a University of Florida project following the development of children exposed to cocaine in utero provide important new information on the demographics, drug use patterns, and psychosocial factors of a sample of women rarely characterized in the scientific literature, i.e., women from a generally rural population with minimal access to drug treatment, and with varying amounts of crack cocaine use during pregnancy, but with little other illicit drug use during pregnancy. The study involved 154 women in the cocaine use group, and 154 in the non-cocaine comparison group, matched on race, parity, socioeconomic status, and level of prenatal risk. Based on information collected at the time of study enrollment (i.e., the earliest contact possible after the first trimester of pregnancy) for the demographic and drug use factors, and at the time of delivery for the psychosocial variables, cocaine users were found more likely to be older, to use other drugs, to begin their drug use at an earlier age, to have more depressive symptoms, to have an external locus of control, to have lower self-esteem, to have a more simplistic understanding of child development, and to have higher positive life event impact scores. There were also similarities between the two groups, such as level of education completed (average of 11th grade for both groups) and marital status (69% never married in each group). Both groups exhibited a very low level of reading skills, a finding that led to reading the interviews and measures to each participant, and that has implications for healthcare and drug treatment programs. Behnke, M., Eyler, F.D., Woods, N.S., et al. *Journal of Drug Issues*, 27, pp. 501-524, 1997.

MDMA Neurotoxicity - Occurrence and Consequences

George A. Ricaurte, M.D., Ph.D. and colleagues at the Johns Hopkins School of Medicine have been studying MDMA ("Ecstasy") in a large cohort of MDMA-exposed humans. They have found that cerebrospinal fluid (CSF) measures of monoamine metabolites indicate that MDMA users have selective decreases in CSF 5-HIAA, the major metabolite of serotonin and a valid indicator of brain serotonin neurotoxicity in nonhuman primates. Also, MDMA users have been found to be more impulsive, less harm-avoidant, and more sensation seeking than control subjects. As recreational use of MDMA is increasing, it is essential to understand the possible long-term deleterious effects of MDMA on serotonin neurons in the human brain. This research delineates public health risks of recreational MDMA use and elucidates the role of brain serotonin in humans. (These findings were presented at the September 24, 1997 NIH Clinical Staff Conference and a manuscript summarizing the findings was invited by *Annals of Internal Medicine*).

Marijuana Intoxication and Brain Activation

Roy J. Mathew, M.D. and colleagues at the Duke University Medical Center have studied brain activation in marijuana smokers with regional cerebral blood flow (rCBF) measured with positron emission tomography (PET). He found that THC increased rCBF especially in the frontal regions bilaterally, insula and cingulate gyrus and subcortical regions with somewhat greater effects in the right hemisphere. Self ratings of THC intoxication showed significant effects and

regression analysis indicated intoxication correlated most markedly with the right frontal region. Behavioral manifestations of marijuana intoxication may be associated with increased functional activity of the brain especially the frontal cortex, insula and cingulate gyrus. Mathew, R.J. et al., *Life Sciences*, 60 (23), 1997.

Serotonin and Aggression in Cocaine Dependence

Frederick G. Moeller, M.D. and colleagues at the University of Texas Health Sciences Center at Houston have found a significant correlation between the presence of antisocial personality disorder (ASPD) and frequency of aggressive responding. When ASPD was statistically controlled, no significant relationship was found between aggressive responding and cocaine craving, withdrawal symptoms, amount of cocaine used, or length of time since use. These preliminary results suggest that in cocaine-dependent persons seeking treatment, current aggression is most dependent upon the individual's previous history of aggressive behavior. Knowledge of the precise relationships among the variables of aggression, cocaine dependence, cocaine withdrawal, brain functioning and serotonin will enable researchers to have a firm basis upon which to construct more effective diagnostic and treatment strategies for cocaine dependent users with and without a history of violence and aggressive behavior. Moeller, F.G. et al., *Drug Alcohol Depend*, 44(2-3), 1997.

Concordance for ADHD Greater for Monozygotic than Dizygotic Twin Pairs

Twin concordance was assessed in a community-based sample of 194 monozygotic and 94 dizygotic male twins, aged 11-12 and with DSM-III diagnoses of ADHD from structured interviews of teachers and of mothers. Concordance rates for ADHD diagnoses were greater for monozygotic twin pairs compared to dizygotic, especially for diagnoses based on mothers' ratings; concordance rates were more similar for teachers' ratings. Thus, the magnitude of the genetic component seems to depend, in part, on the informant (of phenotype). Nevertheless, model-fitting analyses indicated strong additive genetic components, smaller non-shared environmental components and no shared environment components. These data are important because ADHD is recognized as a risk factor for development of substance abuse. Sherman, D.K., Iacono, W.G., & McGue, M.K., *J Am Acad Child Adolesc Psychiatry*, 36(6), 1997; Sherman, D.K., McGue, M.K., & Iacono, W.G., *Am J Psychiatry*, 154(4), 1997.

DATOS

A special issue of the *Psychology of Addictive Behaviors* (December 1997) is devoted to findings from NIDA's Drug Abuse Treatment Outcome Study (DATOS). This issue is introduced by Dr. Alan Leshner and features 7 articles by cooperative study participants. The articles include an overview of DATOS and treatment evaluation research in the United States by Fletcher et al.; the methodology and research design of DATOS by Flynn et al.; an overview of 1-year follow-up outcomes in DATOS by Hubbard et al.; treatment retention and follow-up outcomes by Simpson et al.; DATOS treatment structure and program services by Etheridge et al.; the relationship of program diversity and retention by Simpson et al.; and a paper on the drug addiction and treatment careers of patients in DATOS by Anglin et al. DATOS is featured in an upcoming issue of *NIDA NOTES*.

Effectiveness of Node-Link Mapping Enhanced Counseling for Opiate Addicts: A 12- Month Posttreatment Follow-Up

A series of experimental studies at Texas Christian University has shown that a relatively low-cost visual enhancement to drug abuse counseling, called node-link mapping, leads to better during treatment outcomes than counseling-as-usual for patients in outpatient methadone treatment. "Mapping" is associated with greater patient commitment to treatment in terms of session attendance, improved relationships with the counselor, and fewer urine samples positive for opioid and cocaine metabolites. Findings show enhanced communication with patients having attention problems, minorities, and cocaine-using opioid addicts. A new posttreatment follow-up study (n=180) shows patients assigned randomly to mapping counseling reported less criminal activity and exposure to HIV risks due to the reduced use of contaminated needles in the 12 months after treatment than did patients in the standard counseling condition. It was also found that among patients staying less than 6 months in treatment, those in the mapping group had fewer urines that tested positive for opiates at follow-up and were also significantly lower in dirty needle risks than standard counseling patients. Thus, mapping-enhanced counseling may be especially beneficial for patients who leave treatment prematurely. The cumulative evidence from this and previous studies indicates that mapping represents a tool that has promise for improving the effectiveness and efficiency of drug abuse counseling

programs. Joe, G.W., Dansereau, D. F., Pitre, U. and Simpson, D.D. *Journal of Nervous and Mental Disease*, 185, pp. 306-313, 1997.

Influences of Family and Friends on Client Progress During Drug Abuse Treatment

Relationships with family and friends reported by 439 heroin addicts during the first 3 months of drug abuse treatment were examined in relation to behavioral improvements of clients. Family conflict and peer deviance were significant predictors of injection frequency and illegal activity during treatment, and reductions in family conflict were associated with lower drug use, injection frequency, and illegal activity during treatment. These results support treatment emphasis on helping clients reduce conflict among family member and on replacing deviant friendships with others that encourage treatment participation and conformance to social norms. Knight, D.K., & Simpson, D.D. *Journal of Substance Abuse Treatment*, 8(4), pp. 417-429, 1996.

Managed Care of Substance Abuse Disorders

Definitive characterizations of managed care with regard to substance abuse issues are difficult given the rapidly changing landscape of both private and public health plan programs. The dynamic nature of Managed Care Organizations (MCOs) creates both problems and opportunities for generalist physicians who see substance-abusing patients. Problems include fiscal incentives that may run counter to the physician role, and more fragmented communication between physicians and other addiction providers when psychiatrists, mental health nonphysicians clinicians, and other specialty programs are carved out into separate delivery systems. Opportunities include the potential for psychiatric consultation liaison, for expanded physician intervention and case management roles, for more health plan resources focused on prevention and treatment, and profiling to achieve overall improvements in service delivery. MCOs may rely more heavily on generalist physician involvement with substance-abusing patients if potential benefits of linking substance abuse treatment and primary care can be realized. Larson, M.J., Samet, J.H., and McCarty, D. *Medical Clinics of North America*, 81(4), pp.1053-1069, 1997.

Estimating the Economic Cost of Substance Abuse Treatment

Few studies have estimated the economic cost and benefits of substance abuse treatment services. French and McGeary have developed a data collection instrument and method for estimating the economic cost of substance abuse treatment programs. The Drug Abuse Treatment Cost Analysis Program (DATCAP) is based on standard economic principles and the method has been tested in two drug abuse intervention studies. Findings from case studies at three treatment programs are presented to demonstrate the feasibility and reliability of the instrument. The estimation methods and results can be used by treatment programs for self-evaluation purposes and by researchers who are interested in performing cost-effectiveness or benefit-cost analyses of substance abuse services. French, M.T. and McGeary, K.A., *Health Economics*, Vol 5, pp. 539-544, 1997.

A Structured Instrument for Estimating the Economic Cost of Drug Abuse Treatment, the Drug Abuse Treatment Cost Analysis Program (DATCAP)

Drug abuse treatment programs need to know the cost of the services they provide since public and private funding is now being linked to cost and performance measures, and since programs can use financial data to improve efficiency. However, most program staff lack the knowledge to perform a cost analysis, and little user-friendly assistance is available. Furthermore, not all cost methods are consistent, which can lead to noncomparable estimates that are difficult to use for policy or planning purposes. This study reports on a cost methodology developed to provide treatment programs with a needed technical assistance tool. The Drug Abuse Treatment Cost Analysis Program (DATCAP), a structured and scientifically-based instrument for estimating the economic cost of treatment services, is discussed, as is a companion instrument to analyze treatment financing: the Drug Abuse Treatment Financing Analysis Program (DATFin). The DATCAP User's Manual, which will enable individual programs to begin collecting the necessary data and estimating economic costs at their own clinics, is described. French, M.T. Dunlap, L.J., Zarkin, G.A., McGeary, K.A., McLellan, A.T. *Journal of Substance Abuse Treatment*, 14(4), pp. 1-11, 1997.

Modeling Missing Data

In a paper presented at the American Society of Criminology, in November, 1997, Strauss and Falkin discussed early findings of a new methodological approach to examine non-ignorable nonresponse in a sample of (approx. 330) women offenders in drug treatment in New York City. In their sample, about 17 percent self-reported HIV infection. An analysis taking missing data into account increased the upper bound estimate of seroprevalence to 35 percent. Strauss, S. & Falkin, G. Modeling the Missing Data Mechanism: An Exploration into the Unknown, Presented at the Annual Meeting of the American Society of Criminology, San Diego, November 1997.

A Bi-Costal Comparison of Criminal Activity and Drug Use

In November 1997, Falkin and Strauss presented findings from Project WORTH (Women's Options for Recovery Treatment and Health), a large scale evaluation of treatment programs that serve women mandated into treatment in New York City and Portland, Oregon. They found that three-quarters of the women in New York City used crack, while methamphetamine was the most commonly used drug in the Portland sample (reported by over 50% of women). Over three quarters of the women in both cities reported use of stimulants, including cocaine, crack, methamphetamine, and other amphetamines. Injection drug use was more prevalent in the Portland sample. Falkin, G. & Strauss, S., East Coast Meets West Coast: A Comparison of Criminal Activity and Drug Use Among Women in New York City and Portland, Oregon. Presented at the Annual Meeting of the American Society of Criminology, San Diego, November 1997.

Health Needs of Women in Drug Treatment

In a study of 500 women who entered drug treatment programs through the criminal justice system in New York, Falkin and Strauss found that nearly half rated their health as only fair or poor. This is an unfavorable comparison with women in the general population. The most frequently cited health problems were lung problems, gynecological problems, excessive undesired weight loss, night sweats, and HIV/AIDS. Almost one third of the women perceived no connection between their drug use and physical health, and only 20% recognized a close connection between their drug use and health. Health status was poorest among long-time drug users. Falkin, G. and Strauss, S., Emotional and Physical Health Problems and Needs of Women in Drug Treatment, paper presented at the American Public Health Association, Indianapolis, November 1997.

Potential for Child Abuse

Falkin and Strauss found average scores on the Child Abuse Potential Inventory (CAP) among women substance-abusing offenders with minor children (N=300) were in the same range as scores for individuals convicted of child abuse. These scores were significantly higher for women with psychological problems and those who had experienced physical abuse as children. The children of these women may be at high risk for abuse if the women do not receive appropriate interventions after treatment. Falkin, G. and Strauss, S., The Potential for Child Abuse Among Women Offenders Who Abuse Substances, paper presented at the 7th International Conference on Family Violence, Durham, New Hampshire, June 1997.

Predicting Treatment Outcomes for Felony Drug Offenders

In a study of 150 treatment admissions to the Drug Treatment Alternative Program (DTAP), Belenko examined factors that predict length of treatment and treatment outcomes for felony drug offenders diverted into residential treatment. He found that 70 percent of the DTAP clients were still in treatment after one year. Those that did drop out tended to have more extensive involvement in drug dealing and earned more from dealing than those that stayed in treatment. Dropouts were also younger, scored higher on various measures of risk-taking, had higher psychological impairment scores, greater involvement with marijuana and less alcohol involvement, had a lower perceived level of legal pressure to remain in treatment, and perceived prison as less aversive than those who remained in treatment. Belenko, S., Sufian, M, and Young, D. Predictors of Treatment Outcomes for Felony Drug Offenders: Individual Risk Factors and Legal Pressures. Presented at the Annual Conference of the American Society of Criminology, San Diego, November 1997.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****February, 1998**

Research Findings

AIDS Research

The Influence of Drug Use Patterns on the Rate of CD4+ Lymphocyte Decline Among HIV Infected IDUs

An analysis to assess the relationship between injecting drug use patterns (e.g., frequency, duration, continuous vs. intermittent) and the rate of CD4+ lymphocyte decline (change in CD4 count per month as compared with previous CD4 count) was performed in a cohort of active IDUs. Among 605 IDUs, the median initial CD4 count was 513 and the mean change in CD4 count was -3.2 cells $\times 10(6)/l$ per month. The rate of CD4 decline was higher in those with a higher level of CD4 ($p < .01$) and greater with length of drug use ($p < .01$), but did not vary by injection frequency or injection intensity by drug type, or by pattern of administration (intermittent vs. continuous). Although animal studies have suggested that the pattern of drug administration and episodes of withdrawal or overdose might have an impact on the rate of CD4 decline, injection patterns by self-report were not associated with the rate of CD4 decline in this study of active injectors. Lyles, C.M., Margolick, J.B., Astemborski, J. et al., *AIDS*, 11: pp. 1255-1262, 1997.

HIV Seroprevalence Rates Among Homicide Victims in New York City: 1991-1993

Tardiff and his team (Cornell) assessed HIV seroprevalence in homicide victims killed in New York City in 1991-1993, using data from the Office of Chief Medical Examiner. Among 5,852 homicide victims, there were 344 (5.9%) victims who were HIV+. Females were just as likely as males to be HIV+. For females, the rates were 11.7% and 12.6% in the 25-34 and 35-44 year age group, respectively. The highest rates of HIV infection for homicide victims were among those using both opiates and cocaine (males: 23.0%; females: 27.3%). The rate of HIV infection among women using cocaine was 18.4%. In comparison, the victims not using these drugs had rates of HIV infection around 2%. According to the investigators, the high risk of HIV among homicide victims may be due to the use of cocaine and associated risky use of needles and risky sex practices. Tardiff, K., Marzuk, P.M., Leon, A.C., Hirsch, C.S., Stajic, M., Portera, L., Hartwell, N. *J Forensic Sci.*, 42(6), pp. 1070-1073, 1997.

HIV Seroprevalence Among Suicide Victims in New York City, 1991-1993

Marzuk, Tardiff and others (Cornell) determined the HIV seroprevalence among suicide victims in New York City for the period of 1991 through 1993, using the data from the Office of Chief Medical Examiner. HIV-seropositive suicide victims were assessed for pathological findings suggestive of HIV-related illnesses. Over 90% of all HIV+ suicide victims were aged 25-54 years, and almost 90% were men. Among black and Hispanic men aged 35-54 years who committed suicide, the proportion who were HIV seropositive was 0.252, the highest seropositive rate of any

demographic group. More than 66% of HIV+ suicide victims had no HIV-related pathology or AIDS-indicator conditions at autopsy. The authors concluded that the demographically adjusted proportion of suicide victims who were HIV+ (approx. 0.038 to 0.059), contrasted with the HIV seroprevalence estimates for the New York City general population (approx. 0.014 to 0.032), the absence of HIV-related pathology among suicide victims, and the likelihood that many HIV+ individuals had other risk factors for suicide, such as substance abuse, suggests that a positive HIV serostatus is associated, at most, with a modest elevation in suicide risk. Marzuk, P.M., Tardiff, K., Leon, A.C., Hirsch, C.S., Hartwell, N., Portera, L., and Iqbal, M.I. *Am J Psychiatry*, 154, pp. 1720-1725, 1997.

HIV Infection Among Victims of Accidental Fatal Drug Overdoses in New York City

Tardiff and his colleagues at Cornell determined the factors associated with HIV seroprevalence rates for victims (n=2,159; over 15 years of age) of drug overdoses in New York City (population 7,322,564) in 1991-1993, using data from the Office of Chief Medical Examiner. There were 646 (29.9%) victims who were HIV positive. Women (37.5%) were more likely than men (27.9%) to be HIV+. African-Americans (39.4%) had a higher rate of HIV infection than Latinos (27.5%), whites (19.2%) or Asians (8.3%). The rates of HIV positive seroprevalence were 38.8%, 33.7% and 20.4% among victims aged 35-44, 45-54, and 25-34, respectively. Dying from opiates overdose was associated with a 24 times increase in the likelihood of being HIV positive. Women who died of drug overdoses were more likely than men to be HIV positive. The authors stated that this may be related to risky sex practices as well as sharing needles (Inciardi et al. 1993 and Beveer et al. 1995). They suggest that harm reduction programs should address risky sex as well as needle programs. Tardiff, K., Marzuk, P.M., Leon, A.C., Hirsch, C.S., Portera, L., Hartwell, N. *Addiction*, 92(8), pp. 1017-1022, 1997.

Hepatitis A (HAV) among Homosexual Men and Injection Drug Users: More Evidence for Vaccination

Serum samples from 292 IDUs, 294 homosexual men, and 300 blood donors were tested for the presence of total antibody to Hepatitis A virus (anti-HAV). Anti-HAV was detected in 66% of IDUs, 32% of homosexual men, and 14% of blood donors. The prevalence of anti-HAV among IDUs was not associated with any specific drug use practice, including the duration of injection drug use, the frequency of injection, needle sharing, or injection in a shooting gallery ($p > .10$). Exposure to HAV was not correlated with serologic evidence of hepatitis B or C, syphilis, or HIV infection ($p > .05$), nor did the presence of anti-HAV correlate with reported number of sexual partners or a history of a sexually transmitted disease ($p > .10$). Anti-HAV was more prevalent among IDUs with annual incomes $< \$5000$ ($p < .02$). The data indicate that IDUs are at increased risk for HAV infection but that factors related to low socioeconomic status, such as poor hygiene or overcrowding, contribute more to the occurrence of HAV infection than does injection drug use. Further study is needed to clarify routes of HAV transmission among IDUs. The high prevalence of anti-HAV among IDUs in this study suggests that IDUs are an important reservoir of HAV infection, and indicates the need for HAV vaccination of IDUs and persons at risk for injection drug use. Villano, S.A., Nelson, K.E., Vlahov, D. et al., *Clin Infect Dis*, 25, pp. 726-728, 1997.

Impact of AIDS Prevention Intervention on Risky Behaviors and Drug Use

This study examined the impact on specific risky behaviors of two randomly assigned cognitive-behavioral community-based AIDS interventions for high-risk impoverished African-American (N = 353) and Latina (N = 31) women residing in homeless shelters or drug treatment facilities. The study participants were contrasted with untreated, newly recruited controls. An in-depth Specialized program provided AIDS information, and psychosocial and behavioral skill enhancement; a shorter Traditional program provided basic AIDS information. Both treatment groups received information about community resources. At follow-up, women exposed to either program reported significant decreases from their baseline scores in unprotected sexual activity, illegal activities (providing sex for drugs or money), cocaine use, heroin use, and high risk drug-related behaviors such as sex with injection drug users and needle-sharing. After controlling for pre-existing differences between the groups and whether they were in drug treatment, the Specialized group reported less cocaine use and fewer illegal activities. Further comparisons with the untreated newly-recruited control group supported findings of improvement across the two years for both treatment groups. Community-based AIDS health education efforts are discussed. Stein, J.A., Nyamathi, A., and Kington, R. *Journal of Community Psychology*, 25, pp. 519-533, 1997.

Adolescent Conduct Disorder Predictive of HIV Risk Taking Behaviors

A study was conducted to assess the prevalence of conduct disorder among runaway and homeless adolescents and to investigate associations between conduct disorder and HIV risk behaviors. The Diagnostic Interview Schedule for Children and a standardized HIV risk assessment questionnaire were administered to 219 runaway and homeless adolescents recruited from a drop-in center serving high risk youth. One half of the males and 60% of the females were diagnosed with conduct disorder. In multivariate analyses, conduct disorder was the strongest predictor of lifetime use of heroin and/or cocaine and exchanging sex for money, drugs, food or shelter, as well as the number of drugs used and the number of sex partners in the last 3 months. The high rate of conduct disorder in this population, and the association between conduct disorder and both drug and sex-related HIV risk behaviors, indicate a need for interventions that consider the influence of psychiatric diagnosis on high risk behaviors. Booth, R.E. and Zhang, Y. Conduct Disorder and HIV Risk Behaviors among Runaway and Homeless Adolescents. *Drug and Alcohol Dependence*, 48: pp. 69-76, 1997.

High HIV Seroprevalence in Street-Recruited IDUs and Crack Users in 16 U.S. Cities

Researchers conducted an analytical assessment of the national database from NIDA's Cooperative Agreement program to determine the seroprevalence of HIV and the risk factors for HIV among street-recruited IDUs and crack cocaine smokers. The analysis examined data on HIV serologies and self-reported risk behaviors of 6,402 IDUs and 3,383 crack smokers from 16 U.S. municipalities, collected in 1992 and 1993. Among the IDUs, HIV seroprevalence was 12.7%, and among crack smokers, HIV seroprevalence was 7.5%. The highest seroprevalence municipalities were along the eastern seaboard of the U.S. The key predictors of HIV among injectors were having injected cocaine, having injected speedball, and unsafe sex; among crack smokers, sexual risk behaviors were most predictive of HIV seropositivity. This study provides a national-level assessment of HIV seroprevalence among IDUs and crack smokers. All of the study participants were recruited from street settings (i.e., community-based), and not-in-drug treatment, suggesting that the risks for HIV continue at very high levels for IDUs and crack users in community, street, and nonclinical locations. Kral, A.H., Bluthenthal, R.N., Booth, R.E., Watters, J.K., et al. HIV Seroprevalence among Street-Recruited IDUs and Crack Cocaine Users in 16 U.S. Municipalities. *Amer. J. Public Health*, In Press.

Psychosocial Risk Factors for HIV Transmission in Female Drug Abusers

This cross-sectional study examined the influences of domains of psychosocial risk factors on needle-sharing with familiar people and with strangers in a cohort of female injecting drug users (IDUs). Subjects were 119 female IDUs, 46% of whom were HIV+. Subjects were given individually administered questionnaire interviews. Using Pearson correlation coefficients and multiple hierarchical regression analyses, personality, family, and peer attributes related to needle-sharing in women were similar to those found in men, with certain exceptions. Specifically, in males, the family was more distal in its effect on needle-sharing behavior. The role of the family, particularly the significant other, was more important and proximal in its effect on needle-sharing behavior in women than in men. The data suggest that women's resilience and resistance to self-destructive behavior are closely related to ties with others. There was a main effect as well as mediating effects of protective family factors in women, buffering the risk factors leading to needle-sharing. Brook, D.W., Brook, J.S., Whiteman, M., Win, P.T., Gordon-Maloul, C., Roberto, J., Amundsen, F., Masci, J.R., de Catalogne, J. Psychosocial Risk Factors for HIV Transmission in Female Drug Abusers. *The American Journal on Addictions*, 6 (2), pp. 1-12, 1997.

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 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., Flakerud, J., and Leake, B. *Nursing Research*, 46 (3), pp. 133-137, 1997.

Coping with AIDS: A Longitudinal Study

The three goals of this longitudinal, prospective study were: (1) to examine coping strategies of HIV positive and HIV negative IDUs; (2) to study the relationship of earlier social support to later coping in HIV positive men; and (3) to examine the effects of earlier coping strategies on later psychosocial functioning. The authors studied 287 HIV positive and negative men who were patients in an AIDS or a methadone maintenance clinic in an urban hospital. Subjects were given a structured questionnaire at two points in time by ethnically matched interviewers. HIV positive subjects scored higher than HIV negative subjects on measures of AIDS-related adaptive coping (social support) and AIDS-related maladaptive coping (aggression), but not on general coping. General coping was not specifically AIDS-related, but was correlated positively with adaptive coping and negatively with maladaptive coping. These results suggest that earlier general coping is related to the later avoidance of maladaptive coping, with specific implications for teaching preventive strategies. AIDS-related adaptive or maladaptive coping techniques may be used simultaneously, and coping behavior may change over time. Earlier social support is related positively to aspects of later coping in HIV positive men. Thus, social support should enhance later coping in HIV positive men and should be included in intervention programs. Brook, J.S., Brook, D.W., Win, P.T., Whiteman, M., Masci, J.R., de Catalogne, J., Roberto, J., Amundsen, F. Coping with AIDS: A Longitudinal Study. *The American Journal on Addictions*, 6 (1), pp. 11-20, 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 after traditional or specialized AIDS education were assessed 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 two 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. Also, when compared with the traditional group at two 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 are discussed. Nyamathi, A.M. and Stein, J.A. *AIDS Education and Prevention*, 9, pp. 253-273, 1997.

Participant Observation Fieldwork Provides Contextual Understandings of Individual HIV Risks

Extensive field observations of homeless heroin injectors in San Francisco underscore the importance of context in understanding individual behaviors and the transmission of HIV. Relationships between and among individuals and their personal, demographic, sexual, social, political, economic, and geographic environments shape risky behaviors. For example, substance use and HIV risk behaviors are influenced by addicts' income-generating strategies as well as by hierarchies of respect and identity. Individual risks for HIV transmission increase when addicts who have no money engage in sex-for-drug or money exchanges, pool resources to buy drugs and/or to obtain drug injection equipment, or when there is a need to win personal respect (e.g., by acting on a dare or by aggression). Recognizing the power and dynamics of relationships and the contexts in which they occur provides for a full understanding of the who, why, how, and where of HIV infection. Bourgois, P., Lettiere, M., and Quesada, J. *Social Misery and the Sanctions of Substance Abuse: Confronting HIV Risk Among Homeless Heroin Addicts in San Francisco*. *Social Problems*, 44(2): pp. 155-173, 1997.

Factors which Introduce HIV into Drug Injector Networks in Low Seroprevalence Cities

Although many are knowledgeable about how HIV is transmitted, IDUs today continue to be at high risk for infection, particularly those who reside in cities where HIV seroprevalence levels are low. This study examined factors which facilitate the introduction of HIV into networks of IDUs in low HIV seroprevalence cities by analyzing data from a large (n=9492) multi-site sample of IDUs recruited in 9 low seroprevalence cities between June 1988 and June 1991 as

part of NIDA's National AIDS Demonstration Research (NADR) project. The results of univariate and multivariate analyses indicate that, after male-to-male sexual contact, having sex at least twice in an AIDS epicenter was the strongest predictor of HIV infection. Higher odds of HIV seropositivity were also associated with the African American and Puerto Rican racial/ethnic groups, daily drug injection, and injecting drugs in an AIDS epicenter. Traveling to an AIDS epicenter and having sex or injecting drugs play a large role in the introduction of HIV into drug injector networks in low seroprevalence cities. Williams, M.L., et al. Introduction of HIV into Drug Injector Networks Outside AIDS Epicenters. *International J. STDs & AIDS*, 8: pp. 629-635, 1997.

Behavioral Change in HIV+ Adolescents

This study examined whether HIV+ adolescents (N=102) linked to care then change risk and health-related behaviors subsequent to learning their HIV serostatus, and to document the stability of their current behavior patterns over a 6-month period. Over their lifetime, youths engaged in unprotected sexual acts with multiple partners (M=284; median=44; consistent condom protection, 5%) and substance use (21% injecting drug use; 68% hard drugs). When current risk behaviors were assessed twice over two consecutive 3-month periods, almost one third had been sexually abstinent. Among youths who were currently sexually active, most had multiple sexual partners (M=5.7, time 1; 4.9, time 2) and used condoms (72-77% sexual acts protected); most of the youths (63-64%) always used condoms. Use of alcohol (63%), marijuana (41%), hard drugs (36%), and injecting drugs (12%) was substantial. There were gender difference among sexual behavior (females had fewer sexual partners) and substance use behavior (fewer females injected drugs or shared needles). Youths were relatively healthy (M T cells=521.4; 14% T cells < 200; 1.9 diseases and 3.7 physical symptoms in the previous 3 months). There was an exceptionally high rate of adherence, about 66% for appointment over 3-6 months. Rotheram-Borus M.J., Murphy D.A., Coleman C.L., Kennedy M., Reid H.M., Cline T.R., Birnbaum J.M., Futterman D., Levin L., Schneir A., Chabon B., O'Keefe Z., & Kipke M. Risk Acts, Health Care, and Medical Adherence among HIV+ Youths in Care Over Time. *AIDS and Behavior*, 1, pp. 43-51, 1997.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****February, 1998**

Research Findings

Epidemiology, Etiology and Prevention Research

Monitoring the Future Study

Results from the 1997 Monitoring the Future Study were released on December 20, 1997 (Lloyd Johnston, et al.). Following are the most significant findings:

Use of marijuana, cocaine, opiates other than heroin, and alcohol in the lifetime increased from 1996 to 1997 among high school seniors, and lifetime marijuana use increased among 10th graders. More recent use (past year and past month) remained stable with few exceptions. Results for 8th graders provided a glimmer of hope, with no increases, and decreases in a few categories. Attitudes toward substance use were mostly stable between 1996 and 1997. Perceived risk of harm was mostly stable for students in all three grades. Encouraging results were found for 8th graders, with disapproval increasing for selected marijuana, cocaine, alcohol, and cigarette use indicators. All changes presented below are statistically significant.

Illicit Drug Use

- Lifetime use of marijuana/hashish increased from 1996 to 1997 among 12th and 10th graders. Seniors' rate of lifetime marijuana use is higher than any year since 1987 but well below the peak seen in 1979. Past year and past month rates for marijuana remained unchanged for 10th and 12th graders. However, daily marijuana use in the past month increased among seniors but decreased among 8th graders.
- Driven in large part by the rise in marijuana, lifetime use of any illicit drug increased among 12th graders. Past month use of any illicit drug decreased among 8th graders; past year aggregate drug use remained stable for each grade.
- Lifetime use of cocaine, both as crack and powder, increased among 12th graders to reach its highest level since 1990 (highest since 1989 for crack). No changes in cocaine use were found for other recency periods or other grades.
- Past month use of LSD increased among 12th graders between 1996 and 1997.
- Heroin use in the past year decreased from 1996 to 1997 among 8th graders.
- Other opiate use in the lifetime and the past year increased among seniors.
- Stimulant use in the past month increased among 12th graders, but use of these drugs in the past year and in the past month decreased among 8th graders.
- Past month use of tranquilizers increased among 10th graders but decreased among 8th graders.

- Use of inhalants, hallucinogens other than LSD, MDMA, ice, and barbiturates remained stable for each grade level and recency-of-use category.

Perceived Harmfulness, Disapproval, and Perceived Availability

- The percentage of 8th graders reporting "great risk" in trying marijuana once or twice decreased. Perceived harmfulness of trying heroin once or twice and taking barbiturates regularly decreased among seniors.
- Disapproval of smoking marijuana occasionally or regularly increased among 8th graders.
- Disapproval of taking cocaine powder occasionally increased among 8th graders.
- Perceived availability of LSD and barbiturates decreased among 10th graders, and perceived availability of amphetamines decreased for 8th and 10th graders.

Alcohol Use

- Alcohol continues to be used at unacceptably high levels. Lifetime and past-year alcohol use increased for 12th graders. However, having "been drunk" in the past month decreased among 8th graders.
- The percentage of 8th graders reporting "great risk" in having five or more drinks once or twice each weekend increased for 8th graders and decreased for 12th graders.

Use of Cigarettes and Smokeless Tobacco

- Between 1996 and 1997, seniors' use of cigarettes in the past month along with daily smoking in the past month increased. Daily cigarette use among seniors is at its highest level since 1979.
- Among 8th graders, daily smoking in the past month decreased, and smoking a half-pack or more cigarettes per day decreased.
- Disapproval of smoking one or more packs of cigarettes per day increased among 8th and 10th graders.
- Lifetime use and past month use of smokeless tobacco decreased among 8th graders.

Community Epidemiology Work Group (CEWG)

The 43rd biannual meeting of the CEWG was held in Phoenix, Arizona on December 9-12, 1997. The CEWG is composed of researchers from 21 metropolitan areas of the United States who meet semiannually to report on patterns and trends of drug abuse in their respective areas; emerging drugs of abuse; vulnerable populations and factors that may place people at risk of drug use and abuse; and, negative health and social consequences. Reports are based on drug abuse indicator data, such as morbidity and mortality information, treatment data, and local and State law enforcement data. Additional sources of information include criminal justice, correctional, medical and community health data, local and State survey information, and research findings from ethnographic studies. The following are highlights from the meetings:

- **Cocaine:** Crack cocaine continues to dominate as the Nation's primary illicit drug problem, but indicator data show a leveling off in many urban areas: cocaine-related deaths were stable or up slightly in 6 of the 8 areas where such information was reported; emergency department (ED) mentions increased* in only 3 of the 20 CEWG cities in the Drug Abuse Warning Network (DAWN); the percentage of treatment admissions for primary cocaine problems declined slightly or remained stable in 13 of the 15 areas where data were available; and prices remained stable or declined slightly in most areas. Supplies remain abundant in nearly every city. Cocaine continues to be frequently used in combination with other drugs in some cities, including heroin and marijuana in Atlanta and Philadelphia, and methamphetamine in Denver. Demographic data continue to show most cocaine users as older, inner-city crack addicts; only in Miami were any new using populations reported this period. [* DAWN comparisons are for 1994 versus 1996; they are included only when they are reliable at $p < 0.05$.]
- **Heroin:** Heroin overshadows cocaine in some indicators: it was the top-ranking ED mention in three cities, and it was the most common primary drug of abuse among treatment admissions in six areas. The rate of ED mentions per 100,000 increased significantly* in eight cities. Mortality, treatment, arrestee urinalysis, and price/purity figures were mixed, with increases in some cities, declines in others, and stable trends in others. In six CEWG cities, noteworthy percentages (@10 percent) of arrestees, both male and female, tested heroin-positive in the

Alcohol and Drug Abuse Monitoring (ADAM) program.

Injecting remains the most common route of heroin administration—particularly in the West, but also in some eastern and midwestern cities. However, it is declining sharply in some cities. Snorting predominates in several eastern and midwestern cities. Smoking is increasing among treatment admissions in Hawaii, San Diego, San Francisco, Atlanta, and Denver. Younger heroin users tend to snort or smoke the drug. Overall, heroin users tend to be males, older than 35, but in some cities, qualitative and quantitative data—including mortality figures in Miami—indicate increases among those age 18–25. Those age 17 and younger still account for relatively few ED mentions or treatment admissions, but even the low numbers, in areas such as Dallas, Minneapolis/St. Paul, San Francisco, and Texas, are a cause for serious concern.

- **Marijuana:** Continuing the upward trend in many cities since 1992, marijuana ED rates increased significantly* in 9 CEWG cities and primary marijuana abuse as a percentage of treatment admissions increased slightly to moderately in at least 10 reporting areas since the previous reporting period. Marijuana is now the top-ranking primary drug in at least four areas, and it accounts for substantial proportions (>20 percent) of nonalcohol admissions in at least three others. Among adult male arrestees, marijuana now exceeds cocaine as the most frequently detected drug in eight of the CEWG cities in ADAM; moreover, in each of the seven CEWG cities where ADAM tests juvenile males, the percentage of positive urinalyses is much higher for juveniles than for adults. Treatment demographics have similarly become increasingly youth dominated: the <17 age group now accounts for the largest percentages of marijuana admissions in at least eight areas. That age group also accounted for 20 percent or more of marijuana ED mentions in seven of the CEWG cities in 1996. All age groups, however, are substantially represented in all indicators, both qualitative and quantitative. Youth often consume marijuana with malt liquor. In some cities, joints or blunts are also dipped in PCP, codeine cough syrup, or embalming fluid; sometimes they contain crack or cocaine HCl, or they are laced with heroin.
- **Stimulants:** Except for ED mentions, methamphetamine indicators—mortality, treatment, and arrestee urinalysis—and ethnographic research show increases in the West, where the problem has been historically centered. Recent ADAM data show increases** in all the western CEWG cities. San Diego mortality figures also show increases, as do treatment figures in Denver, Los Angeles, and San Francisco. Methamphetamine is the most common primary drug among treatment admissions in San Diego and Hawaii, and it equals heroin as the number-one drug in Arizona. By contrast, ED rates declined significantly by 30-40 percent* throughout the West. They also declined* in Philadelphia, but the numbers are much lower there. The only city with a significant increase* was Minneapolis/St. Paul, but, again, the numbers are sharply lower than in the West. Smoking has recently overtaken inhalation as the primary route of administration in San Diego and Los Angeles. "Ice" smoking also predominates in Hawaii, and it is increasing in Denver and San Francisco. Injecting, however, still predominates in Denver, San Francisco, and Texas. In San Francisco, methamphetamine remains widespread among the gay and club scenes. Denver drug dealers sometimes cut crack or heroin with methamphetamine. Elsewhere in the country, methamphetamine appears in indicators in Minneapolis/St. Paul and in the rural areas surrounding St. Louis; availability is reported in Atlanta and New Orleans; and it is associated with the club or rave scenes in Boston, Baltimore, Miami, and New York City. [*ADAM comparisons are for first half of 1996 versus first half of 1997.]

Methylenedioxymethamphetamine (MDMA or "ecstasy") availability is reported in 12 CEWG areas, primarily as a club drug at raves and dance parties. Increases are reported in Boston and Miami. Ephedrine-based products remain a major concern, with products such as "herbal ecstasy" widely available at convenience stores and truck stops in many CEWG areas, including Minneapolis/St. Paul and Arizona. Methylphenidate (Ritalin) abuse is reported among school-aged adolescents in Boston and Washington, DC, and it is the drug of choice for some stimulant users in Chicago. Seizures of khat, a flowering evergreen shrub also known as "qat" or "Somali tea," continue in Minneapolis/St. Paul.

- **Depressants:** Gamma-hydroxybutyrate (GHB) has been involved in poison control cases in Boston, Miami, and Texas, and is suspected in deaths in Miami; it is also part of the club scene (but not reported as a significant problem) in Baltimore, Honolulu, New York City, and areas of New Jersey; in Atlanta, it has become common as a synthetic steroid. Another club drug, ketamine ("Special K" or "Vitamin K"), is available in Boston (where youth both smoke and inject it), Honolulu, Miami, Minneapolis/St. Paul (where adolescents and young adults snort it and sometimes sprinkle it on tobacco or marijuana), New York City (where recent legislation has classified it as a controlled substance), and Washington, DC. Flunetrazepam (Rohypnol) availability has been sharply curtailed in Miami since State and Federal legislative measures were enacted. In Texas, however, it continues to be reported by treatment admissions, especially youth, in border areas. It continues to be reported in "date rape" incidents in Atlanta, Minnesota (where large quantities have been seized), and the Washington, DC, area; and it is used as a club drug in Atlanta and Honolulu. It has received media attention in some cities, such as San Diego and Seattle, but is not a widespread problem there. Clonazepam (marketed as Klonopin in the United States and Rivotril in Mexico), is sold and abused as flunetrazepam in Miami; on the Texas-Mexico border, juveniles widely use it in

combination with beer, just as they had used flunetrazepam before the import ban. Opiate addicts use it to enhance the effects of methadone in Atlanta, Boston, and Minneapolis/St. Paul (where availability has declined).

- **Hallucinogens:** Lysergic acid diethylamide (LSD) is reportedly available in many CEWG cities and prices have become somewhat lower. However, indicators are declining in most areas. Rates of LSD-related ED mentions declined* in every CEWG area with the exception of San Diego and New Orleans. Similarly, phencyclidine (PCP)-related ED mentions declined* in six CEWG cities, but rose slightly in three. Primary hallucinogen users generally continue to constitute small percentages of total treatment admissions. Most hallucinogen users are young, suburban and middle class. In numerous areas, such as Chicago, Philadelphia, St. Louis and Texas, PCP is frequently used in combination with other drugs, primarily marijuana. In Boston and Seattle, LSD and other hallucinogens are often regarded as club drugs and used in the rave scene.

Behavioral Self-Regulation and Liability to Substance Abuse

Researchers at the Center for Education and Drug Abuse Research (CEDAR) investigated behavioral self-regulation (BSR) as a salient component of substance abuse liability. Three dimensions of childhood behavior were used to create a dimensional model of BSR: inattention, impulsivity/ hyperactivity and aggressivity. Multiple measures and multiple informants were used to develop indices of the three traits in a sample of 10-12 year old sons of substance abusing fathers (high risk (HR); n = 180) and normal controls (low average risk (LAR); n = 200). Informants included mothers, boys and their teachers. The results confirmed the presence of a first-order latent trait of BSR. HR boys had significantly poorer scores on BSR than LAR boys. Concurrent validity of the BSR trait scores was supported by significant associations with measures of family dysfunction, deviant peer affiliations and poor school performance. These latter problems are commonly prodromal to substance abuse. Predictive validity of the (poor) BSR trait baseline scores (age 10-12 years) was supported at 2 year follow-up by significant associations of poor BSR scores with magnitude of deviant peer affiliations; trends toward significance were found for family dysfunction and poor school performance. Taken together, these results confirm and extend previous findings which indicate that poor BSR is prodromal to substance abuse. Dawes, M.A., Tarter, R.E., and Kirisci, L. Behavioral Self-Regulation: Correlates and Two Year Follow-ups for Boys at Risk for Substance Abuse. *Drug and Alcohol Dependence*, 45(3), pp. 165-76, 1997.

The Emergence of Narcotic Addict Types and Prediction of Addiction Career Outcomes

Based on the retrospective self-reports about activities, perceptions, and experiences in early adolescence (12-14 years), researchers classified 255 narcotic addicts into four distinct groups using risk factor information from five descriptive domains: family, peer deviance, personal deviance, psychological status, and protective factors. The four groups (Marginal Deviants, Socially Damaged, Early Drug Abusers, and Behavioral Deviants) were differentiated primarily by the extent of early drug use, other behavioral deviance, and family dysfunction. The predictive utility of the typology was examined in terms of outcome over the first 10 years of the addiction career, including age at first narcotic addiction, amount of time incarcerated, and percentage of time addicted while in the community. Nine of 10 risk factors were statistically significant in differentiating addicts from nonaddicts. Narcotic addicts, as adolescents, were more likely to be characterized by greater family, peer, personal, and emotional difficulties and to be less protected from negative influences in their lives than were never-addicted individuals from the same neighborhood. The extent of preaddiction deviance during adolescence was the key dimension in differentiating types in relation to outcome. And, although family dysfunction was a prominent feature in classifying individuals who were comparatively low in deviance, this characteristic added little in the way of predictive relevance to the outcome measures examined. Nurco, D. N., et al. The Early Emergence of Narcotic Addict Types. *Am. J. Drug Alcohol Abuse*, 23(4), pp. 523-542, 1997.

High Prevalence of Sexual and Drug Use Risks Found in Drug-Using Women Who Have Sex With Women

Researchers analyzed the HIV-related risks of women IDUs and crack cocaine users who have sex with women. Between 1992-1994, 3,856 women were recruited from street settings in 19 U.S. cities participating as sites in NIDA's Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program. This analysis focused on data from 231 women who reported female sex partners in the 30 days before interview. In the 30 days before interview, 53% of the women had shared syringes and 66% had shared injection supplies. Only 11 women (6%) always used barrier protection while giving oral sex to women and 5 (3%) while receiving oral sex from women in the 30 days before interview. Fifty percent of the women reported sex with men as well as women in the previous

30 days, but only 26%-30% of the women who had sex with men used barrier methods to protect themselves from acquiring or transmitting HIV or other STDs. Having sex with men was predicted by commercial sex work, but not by self-identifying as a "lesbian." Differences in risk perception were significant between women who reported varying sexual risks, but not significant between women who reported varying injection-related risks. There is a high prevalence of risky sex and drug behaviors among drug using women who have sex with women, indicating a need to increase prevention efforts aimed toward this risk group. Kral, A.H., Lorvick, J., Bluthenthal, R., and Watters, J. HIV Risk Profile of Drug-Using Women Who Have Sex With Women in 19 U.S. Cities. *J. AIDS*, 16: pp. 211-217, 1997.

Precursors and Consequences of Gang Membership and Delinquency

Social scientific knowledge about youth gangs and how their members differ from nongang youths is limited and controversial. Knowledge of the etiology of gangs and the temporal relationship between gang membership and criminal behavior is especially limited. This study examines the relationship between gang membership and delinquency using self-report data from a survey of youths. This model-based study was conducted to explain gang membership in a population of 11,000 secondary school students in Colorado. Three models that can account for gang membership were tested: selection, social facilitation, or enhancement. Lower self-esteem, lower perceived academic ability, lower psychosocial health, and weaker bonds with institutions preceded gang membership which supports a selection model. Furthermore, greater drug use, greater delinquency, greater fear of harm, and being armed were both precursors and consequences of gang membership (facilitation and selection models). "Wannabes" were positioned half way between nonmembers and members and had the lowest level of self-esteem of any group. Being in a gang actually seemed to improve the self-esteem of the members, at least initially. Findings were consistent with theories that gang membership results from a lack of social integration. Dukes, R.L., Martinez, R.O., and Stein, J.A. *Youth & Society*, 29, pp. 139-165, 1997.

Alcohol Expectancies as Potential Mediators of Parent Alcoholism Effects on the Development of Adolescent Heavy Drinking

Children of Alcoholics (COAs) are at heightened risk for early onset of alcohol use, for heavy drinking, and for alcohol-related impairment. However, little is known about the mediating mechanisms that account for this risk. In a study of adolescents' expectancies about alcohol effects as potential mediators of their growth over time in heavy drinking, participants (n=428) were from an ongoing longitudinal study of parent alcoholism and data were collected in three annual in-person interviews with adolescents and their parents. Latent growth curve modeling analyses showed that COAs started the study at higher levels of heavy drinking and increased their heavy drinking at a steeper rate than did non-COAs over the course of the study. However, expectancies about alcohol effects could not explain these parent alcoholism effects. Although expectancies were related to adolescents' initial drinking levels, they did not prospectively predict growth over time in adolescent alcohol use. Thus, other mediating mechanisms (e.g., personality, parent and peer socialization) are necessary to explain parent alcoholism risk for escalation in heavy drinking during adolescence. Colder, C.R., Chassin, L., Stice, E., and Curran, P. *Journal of Research on Adolescence*, 7, pp. 359-374, 1997.

Sequence of Drug Use among Serious Drug Users: Typical vs Atypical Progression

The "typical" sequence of drug use onset identified in previous studies (alcohol, then marijuana, followed by other illicit drugs) was found to be much less prevalent among serious drug users than in samples of high school students. Sequence of drug use was examined in a secondary analysis of two samples of serious drug users: one of 152 men and one of 133 women. The data were collected in ethnographic studies of adult drug users and distributors in New York City between 1984 and 1987. The proportions of drug users following specified patterns of drug use onset were compared to proportions obtained in previous research in samples of high school youth, and serious drug users. Only 33% of the serious drug users followed the typical sequence, compared to 75-93% of subjects in previous studies of high school students. The serious drug users were more likely to have used marijuana before using alcohol, and more likely to have used other illicit drugs before using marijuana. In addition, atypical sequencing was associated with earlier initiation of the use of illicit drugs other than marijuana and greater lifetime drug involvement. These findings suggest that for a large number of serious drug users, marijuana does not play the role of a gateway drug. Prevention efforts that focus on alcohol and marijuana may be of limited effectiveness for youth who are at risk for serious drug abuse. Mackesy-Amiti, M.E., Fendrich, M., and Goldstein, P.J. *Drug and Alcohol Dependence*, 45, pp. 185-196, 1997.

Violence, Suicidality, and Alcohol/Drug Use Involvement in Adolescent Females with a Psychoactive Substance Use Disorder and Controls

This study had three aims: (1) to determine the relationship between behavioral dysregulation, negative affectivity, and familial impairment with violence and suicidality (i.e., severity of ideation and attempts) in a sample of adolescent females with a psychoactive substance use disorder and controls; (2) to determine whether these relations are mediated by internalizing (depression/anxiety) and externalizing (nonviolent antisocial behavior) symptomatology; and (3) to determine whether severity of alcohol/drug use involvement moderates the relations between the mediating variables with violence and suicidality. Multiple behavioral, psychiatric interview, and self-report measures were used to index behavioral dysregulation, negative affectivity, familial impairment, internalizing and externalizing symptomatology, and violence and suicidality in 161 14- to 18- year old adolescent females with a psychoactive substance use disorder and in 80 controls. Structural equation modeling was used to determine the proposed relations. Results indicated that behavioral dysregulation, negative affectivity, and familial impairment were related to violence, whereas only familial impairment was related to suicidality. Internalizing symptomatology mediated the relation between familial impairment and suicidality, and was related to violence, where as externalizing symptomatology mediated the relations between behavioral dysregulation, negative affectivity, and familial impairment with violence. Severity of alcohol/drug use involvement did not moderate the relations between internalizing or externalizing symptomatology with suicidality or violence. Nevertheless, the relation between internalizing symptomatology and suicidality was stronger in females with a greater degree of alcohol/drug use involvement, compared with those with a milder degree of involvement. Therefore, from a prevention standpoint, behavioral dysregulation, negative affectivity, familial impairment, as well as internalizing and externalizing symptoms, may serve as clinical "points of intervention" for altering the development of violence and suicidality in high risk and substance abusing youth. Mezzich, A.C., Giancola, P.R., Tarter, R.E., Lu, S., Parks, S.M., and Barrett, C.M. *Alcoholism Clinical and Experimental Research*, 21 (7), pp. 1300-1307, 1997.

Associations Between Attention Deficit Hyperactivity Disorder (ADHD) and Psychoactive Substance Use Disorders (PSUD)

In a sample of siblings of ADHD and non-ADHD probands, ADHD, conduct disorder, anxiety disorders, and male gender in the sibling were associated with higher rates of PSUD. There was also a statistical interaction between ADHD and conduct disorder in which nearly all siblings with both disorders had PSUD and a particularly early onset of that disorder. Using DSM-III-R structured diagnostic interviews and blind raters, a four-year follow-up of siblings from ADHD (N=152) and control families (N=117) was conducted. The mean age of the siblings was 17.3 (range 9 to 41) and roughly half were males. Information on PSUD was obtained in a standardized manner blind to the proband's clinical status. Cox proportional hazards models evaluated baseline diagnoses of ADHD and other psychiatric disorders (conduct, anxiety, and mood) as potential predictors of PSUD. These Cox analyses simultaneously controlled for confounding variables such as age, gender, intactness of family, and SES. These findings linking ADHD and PSUD could have significant public health significance. 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 illicit drug use. Considering that the earliest age at onset of PSUD in our sample was 12 years and that the latest age at onset of ADHD is 7 years, there may be a window of several years where prevention and early intervention efforts could be targeted. Milberger, S., Biederman, J., Faraone, S.V., Wilens, T., and Chu, M.P. *American Journal on Addictions*, 6, pp. 318-329, 1997.

A Test of Socioeconomic Status As A Predictor of Initial Marijuana Use

The current study examined the effects of socioeconomic status (SES) on adolescent marijuana use using data from a national longitudinal survey of subjects aged 11 to 17 (N = 1,725). Both direct and indirect measures of SES (e.g., Hollingshead's measure of SES, urbanicity, neighborhood problems) were used to determine the extent to which SES predicts marijuana use among adolescents. For males, this study found a nonlinear relationship between the Hollingshead measure and marijuana use that had not been identified in previous research. For females, the Hollingshead measure was insignificant when alcohol use and having friends who use marijuana were added to the model. This finding suggests that the effects of SES on marijuana use are mediated by alcohol use and friends' use of marijuana. Weekly alcohol users were much more likely than nonusers to initiate marijuana use for both males and females. Other significant variables for both sexes included having a job, having friends who use marijuana, and having used some alcohol in the past year. For males, grade point average (GPA), commitment to friends, urbanicity, time spent with friends, and peer strain were also significant predictors of initial marijuana use. For females, prior

victimization and low school aspirations were significant. In sum, these findings suggest that psychosocial risk factors for marijuana use are substantially different for males than for females and that future researchers need to test for nonlinear relationships between SES and adolescent substance use. Miller, D.S., and Miller, T.Q. *Addictive Behaviors*, 22 (4), pp. 479-489.

Risk and Protective Factors as Predictors of Adolescent Alcohol Involvement and Transitions in Alcohol Use: A Prospective Analysis

Determinants of initial alcohol use may differ from predictors of accelerated or problematic consumption. Social influences may be strong predictors of initial drinking; however, later stages of problem drinking may be linked developmentally to intrapersonal deficits. This study prospectively examined the influence of chronic and changing risk and protective status in predicting adolescent alcohol involvement and transitions in alcohol use. Data were obtained from a three-wave cohort (N=823) of 8th- 10th grade nonintervention students participating in a school-based drug abuse prevention trial. Cognitive, attitudinal and social influence measures were dichotomized using empirical cut-offs to designate risk or protective status. Using a conceptually based assignment scheme, additive risk indices were created assessing chronic (averaging across time) and changing features of competence, psychological and interpersonal functioning, cognitive-affective and social influences. Three chronic and change protective indices were created tapping competence, psychological, and interpersonal functioning. Controlling for initial drinking and gender, chronic risk for social influence and psychological functioning and increased risk for social influences and competency predicted subsequent drinking behavior. Chronic psychological protection attenuated subsequent drinking. Using categorical measures of drinking behavior to designate nonuse, experimental or moderate-heavy use, chronic social influence and competency risk were associated with an increased likelihood of accelerated drinking, whereas improved psychological functioning diminished the likelihood of increased drinking behavior. Findings underscore the need for implementing prevention strategies that reinforce developmentally appropriate skills and enhance personal competence and psychological functioning as effective barriers against initial and more problematic alcohol use. The unique contribution of protective forces also underscores that risk reduction and protection enhancement are complementary processes and are both required to offset social influences for alcohol consumption. Scheier, L.M., Botvin, G.J., and Baker, E. *Journal of Studies Alcohol*, 58, pp. 652-667, 1997.

High Prevalence of Hepatitis C Found in Alaskan Drug Users

To identify the prevalence of and predictors for hepatitis C virus (HCV) among not-in-treatment drug users in Anchorage, Alaska, researchers recruited 500 men (71%) and women (29%) from nonclinical settings to participate in structured interviews (i.e., NIDA's Risk Behavior Assessment) and to be tested for HIV and HCV. The mean age of the sample was 35 years; 48% were White, 29% African American, and 17% American Indian/Alaskan Native. Ninety-two percent reported smoking cocaine in the past 30 days, and 42% reported injecting drugs in the past 30 days (with a mean number of times injected in the last month of 18.6). There was a significant bivariate association between HCV positivity and injection drug use status; positivity among those reporting only injection drug use was very high, at 81%. Risk factors for HCV were drug injection in the past 30 days, ever having injected cocaine, ever having used speedball, ever having used heroin, number of days in jail, and number of sex partners in the last 30 days. The researchers note that although Anchorage is a small city in a rural state, the prevalence of HCV there is as high as it is in major U.S. metropolitan areas, suggesting that geographic location may not define differences in risk. In addition, recent reports indicate a high potential diffusion of blood-borne pathogens into rural American Indian/Alaskan Native populations in association with regular migration between rural and urban areas. This study demonstrates that, with the prevalence of HCV among drug injectors in Anchorage being so high, early interventions are critical to prevent persons at risk from acquiring and spreading the infection. Fisher, D.G., et al. *Hepatitis C Virus Infection among Alaskan Drug Users*. *Amer. J. Public Health*, 87(10): pp. 1722-1723, 1997 (letter).

Predicting Dropping Out of High-School Based on Data from a 19-Year Longitudinal Study of Family Lifestyles

In this study, nested latent-variable causal models were contrasted to compare the direct and indirect relationships of distal family and child and proximal adolescent factors to dropping out of high school. The sample included 194 conventional and nonconventional families that have been participating in a 19-year longitudinal study, the Family Lifestyles Project. The findings showed that dropping out of high school is a multiply-determined process, with early influences beginning in childhood, that involves family as well as child and adolescent factors. Among the hypothesized predictors of dropping out were early child drug exposure and adolescent drug use. Early child drug

exposure by adult models directly predicted later adolescent drug use which in turn predicted more high school dropout. The indirect effect of early drug exposure on later dropping out was also significant. Early family nonconventionality when combined with a higher commitment to lifestyle values was associated with a lower probability of dropping out. Garnier, H.E., Stein, J.A., and Jacobs, J. *American Educational Research Journal*, 34, pp. 395-419, 1997.

Drug Treatment Careers: A Conceptual Framework and Existing Research Findings

A treatment careers perspective applies a longitudinal dynamic approach to identify and understand key factors influencing the development of, and transition in the course of, drug dependence and its treatment. This paper reviews and discusses relevant research issues and findings on 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 drug users, late development of treatment careers relative to addiction and criminal careers, short duration of most treatment episodes, cumulative and facilitative effects of treatment experiences, and beneficial effects of matching clients to treatment. Overall, longer periods of treatment are associated with larger and longer periods of prosocial functioning following treatment. In conclusion, treatment has been shown to be far less costly to society than incarceration or the drug-related antisocial activities of untreated dependent users. Hser, Y.I., Anglin, M.D., Grella, C.E., Longshore, D., and Prendergast, M. *Drug Treatment Careers: A Conceptual Framework and Existing Research Findings*. *Journal of Substance Abuse Treatment*, 14 (3), pp. 1-16, 1997.

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

Children with histories of prenatal polydrug exposure that 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.

Intra-Family Substance Use

Analyses that specifically model the within-level and between-level covariance matrices are used to examine family levels of substance use and predictors of family substance use. Data from 1135 participants and 430 families (430 target adolescents, 137 siblings, and 568 parents) were included in the analyses, with family cluster sizes ranging from two to five. Adolescents had a mean age of 16.15 years. Between-level variation in substance use scores represented approximately 38% of the total variation in substance use scores, illustrating the importance of a common environment, such as the family, in accounting for levels of substance use. Contextual variables, or family-level predictors included marital status, SES, and biological relatedness. Intra-class correlation coefficients for biologically related families were higher for alcohol, cigarettes, marijuana, and illicit drugs, than they were for non-biologically related families with all three family-level variables significantly predicting the between-level substance use variance. In general, those families characterized as more economically disadvantaged, of a single parent nature, and non-biologically related, had higher family-levels of substance use. Duncan, T.E., Duncan, S.C., Hops, H., and Alpert, A. *Drug and Alcohol Dependence*, 46, pp. 167-180, 1997.

Latent Variable Modeling of Longitudinal and Multilevel Substance Use Data

Multilevel Latent Growth Modeling (MLGM) was used to analyze longitudinal and multilevel data for adolescent and parent substance use measured at four annual time points. An associative LGM model was tested for alcohol, cigarette and marijuana use with a sample of 435 families (435 target adolescents, 203 siblings, and 566 parents).

Adolescents (targets and siblings) had a mean age at T1 of 13.69 years. Sufficient homogeneity in substance use within families was found, with the proportion of between variation, or intraclass correlation, for the four repeated measures, ranging from .26 to .30 for alcohol, .26 to .29 for cigarettes, and .28 to .33 for marijuana. Results revealed a significant upward trend in the development of alcohol, cigarette and marijuana use among families. The shapes of the family-level developmental curves for each substance were also strongly related. Younger family members had higher initial levels of use and developed in their use of substances at a faster rate than older family members. Males had higher levels of alcohol use than females. Single and step-parent families had higher family-levels of substance use, whereas families characterized as less educated and more economically disadvantaged had higher levels of cigarette use and developed in their use of marijuana at a greater rate. Duncan, T.E., Duncan, S.C., Alpert, A., Hops, H., Stoolmiller, M., and Muth, N. B. Latent Variable Modeling of Longitudinal and Multilevel Substance Use Data. *Multivariate Behavioral Research*, 32, pp. 275-318, 1997.

Effects of Community Intervention on Drug Use among High Risk Adolescents

In a study of the second site for the Midwestern prevention project (Indianapolis), 3 years effects of a multi-component community-based drug abuse prevention program were evaluated on a panel sample of 3400 students from 57 junior high schools who were randomly assigned to a program or control condition. The study, which has already shown sustained effects on delaying drug use onset and decreasing population-based use prevalence, evaluated effects on decreasing drug use among baseline users, a high risk sample. Results showed significant effects by decreasing drug use among users for tobacco, alcohol, and marijuana. The study counters a commonly held belief that primary prevention works only with non-users or occasional users. Chou, C.P., Montgomery, S.B., Pentz, M.A., Rohrbach, L.A., Johnson, C.A., Flay, B.R., & Mackinnon, D. Effects of a Community-Based Prevention Program on Decreasing Drug Use in High Risk Adolescents. *American Journal of Public Health*, In Press.

Assessing Drug Use in the Workplace

A study intending to provide information on the accuracy and validity of different forms of drug use prevalence assessment in the workplace, and to suggest ways in which the methods of workplace drug use prevalence assessment could be improved, was conducted. A comparison of self-report, urinalysis, and hair analysis was made on 928 steel plant workers and the findings indicated that combining data from self-reports and bioassays resulted in a drug use prevalence rate that was approximately 50% higher than the prevalence rate produced by self-report alone. Among four different forms of self-report -- individual interview in the workplace, telephone interview, group-administered questionnaire in the workplace and individual interview off the worksite -- all produced very similar prevalence rates, except for the group condition, which resulted in rates that were roughly half of those of the other self-report methods. Cook, R.F., Bernstein, A.D., and Andrews, C.M. Assessing Drug Use in the Workplace: A Comparison of Self-Report, Urinalysis, and Hair Analysis. In Harrison & Hughes (Eds.) *NIDA Research Monograph #167, The Validity of Self-Reported Drug Use: Improving the Accuracy of Survey Estimates*. Rockville: NIDA, 1997.

Latent Transition Analysis Shows Caffeine Use is Correlated to Initiation of Drug Use

This chapter introduces a relatively new methodology, latent transition analysis (LTA) and demonstrates its usefulness in substance abuse prevention research. LTA can be used to evaluate various aspects of stage-sequential models. It can help the user to assess whether a hypothesized set of stages is a realistic representation of a data set, and can be used to compare different models of the stage transition process. LTA is a latent variable model for longitudinal panel data.. It was measured in 7th grade and again in 8th grade students. Using a cross-validation procedure developed for LTA, the model accepted was an 8-stage model: "no use", "alcohol only", "tobacco only", "alcohol + tobacco", "alcohol + drunk", "alcohol, drunk, advanced", "alcohol, tobacco, advanced", and "alcohol, tobacco, drunk, advanced". In this study, caffeine risk was defined as low through high use. Results showed that those in the "high risk" group based on caffeine use at 7th grade, by any definition of caffeine risk, were 1.5 to 2.5 times less likely than those in the "low-risk" group to be in the "no use" stage in 7th grade. Those in the "high risk" group were also 2.4 to 3.9 times more likely than those in the "low risk" group to be in the highest drug use stage at 7th grade. Finally, those in the "high risk" group were 1.2 to 1.9 times more likely than those in the "low risk" group to transition out of the "no use" drug stage between 7th and 8th grades. The results of this study suggest that high use of caffeine is associated with an increased probability that an individual will initiate the onset process. Collins, L.M., Graham, J.W., Rousculp, S.S., & Hansen, W.B. Heavy Caffeine Use and the Beginning of the Substance Use Onset Process: An Illustration of Latent Transition Analysis. In K. Bryant, M. Windle, and S. G. West (Eds.) *The Science of Prevention: Methodological Advances from Alcohol and Substance Abuse Research*. pp. 79-99. Washington,

D.C.: American Psychological Association, 1997.

Role of Acculturation in Substance Use among Latino Adolescents

In a study of at-risk multi-ethnic middle school students, 448 Latino adolescents ranging in age from 11 to 14 completed measures of social influence variables (attitudes, subjective norms, and perceived behavioral control), intentions toward substance use, and acculturation. Language use/exposure was not significantly related to the social influence variables nor intentions to use alcohol, cigarettes, and marijuana. However, increased interaction with non-Latino peers was positively related to attitudes and perceived peer norms against substance use. In addition, for those of high acculturation, perceived normative expectations against substance use by referent others appeared to play a key role in future substance use. For those of low acculturation, attitudes against substance use appeared to have a stronger impact on avoidance of future substance use. The findings of this study are relevant to increasing the effectiveness of substance use prevention programs targeting Latino adolescents. Interventions that address risk and protective factors of substance use in Latino adolescents may consider measuring various components of acculturation. Carvajal, S.C., Photiades, J.R., Evans, R.I., & Nash, S.G. Relating a Social Influence Model to the Role of Acculturation in Substance Use among Latino Adolescents. *Journal of Applied Social Psychology*, pp. 1617-1628, 1997.

Consequences of Sexual Assault

Data were obtained from a nonclinical sample of 1,121 Mexican American and White non-Hispanic adolescent females. The three hundred and three participants who reported being sexually assaulted were compared to the 793 who reported no history of sexual assault on a number of psychosocial characteristics. Although rates of sexual assault differed across ethnicity, ethnicity did not influence the relationship between sexual assault and psychosocial characteristics of victims. Results indicated that sexual assault victims reported more emotional distress, more social isolation and more deviant behaviors than non-victims. Sexual assault victims also reported poorer school adjustment, were more like to affiliate with deviant peers, and were more likely to come from homes in which there was parental substance use and family conflict. Arellano, C.M., Kuhn, J.A., & Chavez, E.L. Psychosocial Correlates of Sexual Assault Among Mexican American and White Non-Hispanic Adolescent Females. *Hispanic Journal of Behavioral Sciences*, 19 (4), pp. 446-460, 1997.

Effects of a Family-Based Prevention Intervention

A number of family-related factors have been identified that contribute to the risk for or protection against initiation of substance use and other problem behaviors as children move from childhood into early adolescence. This article reports results from an experimental test of the effects of Preparing for the Drug Free Years (PDFY) on targeted parental behaviors. PDFY is based on the social development model; it seeks to reduce risks and enhance protection against early substance abuse initiation by improving patterns of parental behavior and family interaction. The sample consisted of economically stressed, rural Midwestern families. Consistent with hypotheses, the program increased proactive communications between parents and children. Specifically, following the program, intervention group mothers exhibited more proactive communications in general and in problem solving tasks and less negative interactions with their children than did the control group mothers. Intervention group fathers exhibited significantly more proactive communications with children in problem solving situations than did the control group fathers. Kosterman, R., Hawkins, J. D., Spoth, R., Haggerty, K.P., & Zhu, K. Effects of 'Preparing for the Drug Free Years' on Parenting Behavior and Family Interactions. *Journal of Community Psychology*, 25(4), pp. 337-352, 1997.

Program Evaluation Approaches for Prevention Data

Recent literature underscores the need for studies of family-based preventive interventions oriented toward public health. This article illustrates a program evaluation approach that is especially suitable to the study of family intervention outcomes in general populations. Thirty-three rural schools were randomly assigned to one of three conditions: the Preparing for the Drug Free Years Program (PDFY), the Iowa Strengthening Families Program (ISFP), and a minimal contact control group. Self-report and observational data collected for 523 families were used to develop measurement models of the three latent parenting constructs that included measurement methods effects. Analyses were conducted (a) to assure initial and attrition-related group equivalencies and (b) to assess school level effects. Structural equation models of the hypothesized sequence of direct and indirect effects for both PDFY and ISFP

were then fitted to the data. All hypothesized effects were significant for both interventions. The discussion addresses the potential public health benefits of evaluation research on universal prevention interventions. Spoth, R., Redmond, C., and Shin, C. Direct and Indirect Latent Variable Parenting Outcome of Two Universal Family-Focused Prevention Interventions: Extending a Public Health-Oriented Research Base. *Journal of Consulting and Clinical Psychology*, In Press.

Young Adults' Drug Use: A 17 Year Longitudinal Inquiry of Antecedents

This longitudinal study examined the interrelation of personality and peer factors on young adults' drug use. This research also examined the influence of the interaction of personality and peer factors on drug use. The samples of 756 males and females was interviewed four times between the mean ages of 6 and 22. Personality attributes in childhood were related to peer factors in early adolescence which, in turn, were related to personality traits in later adolescence. These traits were linked with the selection of peers and, ultimately, drug use in young adulthood. Additionally, the adolescent and young adult domains had direct effects on young adults' drug use. Significant interactions indicated that a few protective childhood personality traits buffered the risk factor of the adverse effects of deviant peers in adolescence on young adults' drug use. The presence of protective characteristics from one domain in childhood enhanced the preventive effect of later protective traits from the other domain in young adulthood on drug use. Brook, J.S., Balka, E.B., Gursen, M., Brook, D.W., Shapiro, J., Cohen, P. *Psychological Reports*, 1997.

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

Prior research has demonstrated a complex interplay of a number of distinct psychosocial risk factors as they relate to cigarette smoking in young adults. In addressing the risk factors associated with tobacco use by young adults, this study examined: (1) the identification of the specific childhood and adolescent risk factors; (2) the interrelation of personality, family, and peer factors and (3) the extent to which the behaviors related to tobacco use vary by developmental stage. Three models (independent, mediational, and interdependent) were hypothesized to examine the interrelation of these variables and their effects on young adult cigarette smoking. At initial data collection, mothers were interviewed about their children when they were between the ages of 1 and 10. Three subsequent interviews were conducted with the children when they reached adolescence and young adulthood. Results show support for the mediational model and are in accord with the family interactional framework conceptions, developed to examine the pathways that 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 late adolescent smoking, and culminating in adult smoking. More specifically, difficulty in the parent-child relationship was related to tobacco-prone personality characteristics. Using a developmental approach, a number of psychosocial measures were found to be related in both younger and older children. Nevertheless, some interesting developmental differences emerged. The findings suggest at least four possible targets for therapeutic or preventive intervention: the parent, the child, the adolescent, and the peer group. Brook, J.S., Whiteman, M., Czeisler, L.J., Shapiro, J., Cohen, P. *The Journal of Genetic Psychology*, 158 (2), pp. 172-188, 1997.

Assessing the Impact of the D.A.R.E. Program after Six Years

The long-term effectiveness of D.A.R.E. was assessed by contrasting drug use and other D.A.R.E.-related attitudinal latent variables among 356 12th-grade students who had received the program in the 6th grade with 264 others who did not receive it. A prior study of these subjects when they were in 9th grade had shown no significant differences. A follow-up survey in 12th grade assessed central D.A.R.E. concepts such as self-esteem, police bonds, delay of experimentation with drugs, and various forms of drug use. Although no relationship between prior D.A.R.E. participation and later alcohol use, cigarette smoking, or marijuana use in 12th-grade was found, there was a significant relationship between earlier D.A.R.E. participation and less use of illegal, more deviant drugs (e.g., inhalants, cocaine, LSD) in a development sample although not in a validation sample. Further analyses indicated that this effect was significant for the males and nonsignificant for the females. Findings from the two studies suggest a possible " sleeper effect " for D.A.R.E. in reference to use of harder drugs, especially among teenage males. Dukes, R., Stein, J.A., and Ullman, J.B. *Evaluation Review*, 21, pp. 483-500, 1997.

Factors which Moderate the Relationship between Parenting Practices and Children's Symptoms

A normative sample of 64 fourth and fifth grade boys, was used to assess the moderating effects of children's activity level and fear on relations between parenting practices and aggressive and depressive symptoms. Findings from multiple regression analyses showed that (a) poorly monitored active boys, and (b) fearful boys who were exposed to harsh discipline exhibited high levels of aggression. In addition, boys characterized by high fear who were exposed to harsh discipline or whose parents were extremely overinvolved showed elevated levels of depressive symptoms. These findings suggest that integrating children's individual differences with parenting models enhances our understanding of the etiology of childhood risk markers for later substance use. The results indicate that certain deficient parenting practices are likely to be associated with children's behavioral problems primarily when the children have certain temperaments high activity and high fear. Thus, intervention could more heavily emphasize altering these parenting practices (harsh discipline, poor monitoring) when specific children are high on these temperament features. Colder, C.R., Lochman, J.E., & Wells, K.C. The Moderating Effects of Children's Fear and Activity Level on Relations between Parenting Practices and Childhood Symptomatology. *Journal of Abnormal Child Psychology*, 25, pp. 251-263, 1997.

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National Institute on Drug Abuse
**Director's Report to the National Advisory Council on Drug Abuse
February, 1998**

Research Findings

Intramural Research

Cellular Neurobiology Branch
Research in Neurodegenerative Processes

Ongoing work in the laboratory of DIR Director, Dr. Barry J. Hoffer has focused on neurodegenerative processes. Dr. Hoffer and colleagues have found that several trophic factors in the TGF-superfamily reduce the size of cerebral infarcts induced by middle cerebral artery occlusion. Interestingly, intracerebral grafts of fetal kidney, which contain large amounts of such factors, also reduce infarct size.

Investigators in this laboratory have also been collaborating with scientists in the intramural program of NICHD to study GDNF null mutated mice. GDNF is a trophic factor for midbrain dopamine neurons. Mice in which the GDNF gene is knocked out show little or no changes in midbrain DA neurons at birth. Postnatal changes cannot be studied in situ since the mice die 24-48 hours after birth. However, by using transplantation protocols, we can show profound decreases in DA neuron number and size in postnatal ventral mesencephalon in these null mutated animals.

Neuroscience Research Branch
Molecular Neuropsychiatry Section
Differential Regulation of Dopamine Transporter Following Chronic Self-administration of Bupropion and Nomifensine

Inhibition of dopamine (DA) transporter function is thought to be the principal mechanisms underlying cocaine's addictive effects. In contrast to cocaine, several other inhibitors of DA transporter function are not considered to possess abuse liability. These data provide evidence for heterogeneity among DA reuptake inhibitors, with some of these drugs being able to up-regulate DA transporters after their self-administration, whereas others lack this neuroadaptive response. Tella S., Ladenheim B. and Cadet J.L. JPET, 281, pp. 508-513, 1997.

Neurophysiological Signs in Cocaine Dependence: Increased EEG Beta During Withdrawal

The percent of EEG beta in frontal and central areas of the cocaine-dependent individuals was correlated with the frequency of cocaine use during the last 30 days. High levels of EEG beta may be a neurophysiological withdrawal sign in cocaine-dependent men. Herning R.I., Guo X., Better W.E., Weinhold L.L., Lange W.R., Cadet J.L., and Gorelick, D.A. Biol Psychiatry, 41, pp. 1087-1094, 1997.

p53-Knockout Mice are Protected against the Long-term Effects of Methamphetamine on Dopaminergic Terminals and Cell Bodies

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 systems. Hirata, H. and Cadet, J.L. *J. Neurochem.*, 69, pp. 780-790, 1997.

Methamphetamine-Induced Serotonin Neurotoxicity is Attenuated in p53 Knockout Mice

These results suggest that the tumor suppressor, p53, plays an important role in METH-induced serotonergic neurotoxicity in mouse brain. These data provide further evidence for a role of p53 in the neurotoxic effects of METH. Hirata, H., and Cadet, J.L. *Brain Research*, 768, pp. 345-348, 1997.

Kainate-induced Hippocampal DNA Damage is Attenuated in Superoxide Dismutase Transgenic Mice

Peripheral administration of kainic acid (KA) can cause cell death in the hippocampus of rodents. This is thought to involve oxidative stress. These results provide further support for the involvement of oxygen-based radicals in the toxic effects of KA. Hirata H., and Cadet J.L. *Molecular Brain Research*, 48, pp. 145-148, 1997.

Differential Toxic Effects of Methamphetamine (METH) and Methylenedioxymethamphetamine (mdr1a) Knockout Mice

These observations document, for the first time, a role for these proteins in the entry of METH and MDMA into the brain via the blood-brain barrier, with P-glycoprotein possibly facilitating the entry of MDMA but interfering with that of METH into the brain. Mann, H., Ladenheim, B., Hirata, H., Moran, H.T., and Cadet, J.L. *Brain Research*, 769, pp. 340-346, 1997.

Overexpression of Superoxide Dismutase and Catalase in Immortalized Neural Cells: Toxic Effects of Hydrogen Peroxide

These results indicate that H_2O_2 can lead to the activation of endonuclease enzyme that breaks DNA into oligosomes. These which overexpress catalase or SOD will help to determine the specific role of H_2O_2 or O_2^- in the deleterious effects of a number of toxins. Mann, H., McCoy, M.T., Subramaniam, J., Van Remmen, H., and Cadet, J.L. *Brain Research*, 770, pp. 163-168, 1997.

Delta Opioid Peptide DADLE Protects Myocardium Against Ischemic Insult

A brief exposure of isolated rabbit hearts to opioid peptide DADLE (2 mM for 15 min) before a global ischemic insult dramatically improved the functional recovery of myocardium. The protection provided by DADLE was far superior to the standard cardioplegic procedure (80% versus 30% functional recovery respectively). DADLE might be a useful agent in reducing myocardial damage and facilitating cardiac transplantation. Bolling, S.F., Su, T-P, Childs, K.F., Ning, X.H., Horton, N., Kilgore, K., and Oeltgen, P.R. *The Use of Hibernation Induction Triggers for Cardiac Transplant Preservation. Transplantation*, 63, pp. 326-329, 1997.

Bear Winter Plasma Protects Myocardium Against Ischemic Insult

Plasma obtained from winter hibernating bear was shown to protect isolated rabbit hearts against global ischemia. However, unlike the effect seen with an opioid peptide DADLE, the plasma had to be administered in vivo to the rabbit before the heart was excised. Bolling, S.F., Tramontini, N.L., Kilgore, K., Su, T-P, Oeltgen, P.R., and Harlow, H.H. *The Use of "Natural" Hibernation Induction Triggers for Myocardial Protection. Ann. Thoracic Surg.*, 64, pp. 623-627, 1997.

An Opioid/Sigma Receptor?

In an attempt to purify non-opioid sigma receptors, we have instead purified a protein which resembles the opioid/sigma receptors originally proposed by Martin and coworkers. It binds benzomorphans, naloxone, morphine, and haloperidol with high affinities. The protein showed three bands in SDS/PAGE. Tsao, L-I and Su, T-P. *A Naloxone-Sensitive, Haloperidol-Sensitive, [3H](+)SKF-10047-Binding Protein Partially Purified from Rat Liver and Rat Brain Membranes: An Opioid/Sigma Receptor? Synapse*, 25, pp. 117-124, 1997.

Beneficial Effect of the Sigma Selective Ligand PRE-084 and Neurosteroids on the Impairment of Learning Induced after the Central Administration of β 25-35-Amyloid Peptide

PRE-084, a sigma ligand discovered at the NIDA IRP, improves learning and memory impairment induced by β -amyloid peptide known to be related to Alzheimer's disease. As a continuing effort to demonstrate the memory-improving effect of a selective sigma receptor ligand PRE-084, discovered at the NIDA IRP, we examined if PRE-084 might affect the mnemonic deficit induced by the central injection of β 25-35- amyloid peptide which is known to be related to the Alzheimer's disease. PRE-084, like certain neurosteroids, dramatically improved the learning and

memory impairment induced by the amyloid peptide. Maurice, T, Su, T-P, and Privat, A. Neuroscience, In Press.

Brain Imaging Section

Sex Difference in Up-regulation of Nicotinic Acetylcholine Receptors in Rat Brain

Male and female rats exhibit different neurochemical and pharmacologic responses to chronic nicotine. Recent declines in tobacco smoking have been less pronounced in women than in men and prompted an evaluation of sex differences in the effects of chronic nicotine administration and withdrawal on nicotinic acetylcholine receptor (nAChR) binding in the rat. Rats received nicotine or saline once a day for 15 days, and were killed either 1 or 20 days after discontinuing the chronic treatment. Male but not female rats receiving chronic nicotine had higher receptor densities than corresponding control groups; up-regulation of nAChRs was not seen 20 days after withdrawal. Further, in groups showing no up-regulation (controls and rats withdrawn for 20 days), nAChR densities were higher in female rats than males. The findings underscore the importance of sex differences in pharmacological responses as well as in basal neurochemical parameters. Koylu, E., Demirgoren, S., London, E.D., and Pogun, S. Life Sci., 61, pp. 185-190, 1997.

A New Detection Method for Measuring Binding to Central Nicotinic Acetylcholine Receptors in Living Animals Using a Simple Probe System

Central nicotinic acetylcholine receptors (nAChRs) are fundamental to brain function, and are affected by several neuropathological processes. Expensive imaging technologies that have been applied to the in vivo study of neurotransmitter receptors, such as nAChRs, in human subjects are not available to many investigators, but simpler radiation detector devices, called "probes", could be an alternative in vivo imaging method. NIDA researchers have now successfully used a simple probe procedure for labeling and monitoring nAChRs in the mouse brain using a radioiodinated analogue of the high affinity nicotinic agonist epibatidine, [125I]IPH. Intravenously administered [125I]IPH was taken up rapidly by nAChRs in the brain as verified by dissection experiments. Radioactivity had dissipated within 24 hours indicating no accumulation within the brain indicating that repeated studies can be performed with this radioligand on successive days. Liu, X., Musachio, J.L., Wagner, H.N. Jr., Mochizuki, T., Dannals, R.F., and London, E.D. External Monitoring of Cerebral Nicotinic Acetylcholine Receptors in Living Mice. Synapse, 24, pp. 378-380, 1997.

Exploitation of PET and SPECT Imaging Technology to Assess Specific Neurotransmitter Systems Holds Promise in Elucidating the Mechanisms Involved in Substance Abuse Disorders

An understanding of the neurobiological substrates of the maladaptive behaviors associated with substance abuse is essential for the development of effective treatments for this disorder. Noninvasive brain imaging provides a powerful approach to obtain the relevant information. It permits the in vivo assessment of brain structure and function, under different conditions that characterize various stages of an addictive cycle. Ernst, M., and London, E.D. Brain Imaging Studies of Drug Abuse: Therapeutic Implications. Semin. Neurosci., 9, pp. 120-130, 1997.

Comparison of LAAM, Morphine and Methadone in Suppression of the Opioid Withdrawal Syndrome

The effectiveness of LAAM treatment for opiate addiction is likely due to its own rapid onset of action and efficacy as well as to the equivalent efficacies and higher potencies of its nor and dinor metabolites. nor-LAAM and dinor-LAAM are active metabolites of the opiate l-alpha acetylmethadol, more commonly known as LAAM, and they are thought to primarily contribute to the prolonged actions of the parent compound. nor-LAAM, dinor-LAAM and LAAM were given intravenously to dogs to determine acute, single dose effects and their ability to suppress withdrawal. LAAM as well as its metabolites produced dose-dependent antinociception, decreases in body temperature, and pupillary constriction with dinor-LAAM being 1.5 - 3 times and nor-LAAM 6 - 12 times as potent as LAAM. Five hours after administering LAAM or either metabolite, a naltrexone injection produced withdrawal indicating the presence of acute physical dependence. In dogs physically dependent on morphine, nor-LAAM was 9 times as potent as either LAAM or dinor-LAAM in suppressing spontaneous withdrawal. The efficacies of LAAM and its demethylated metabolites in the dog for producing acute opiate effects were comparable to those of morphine and methadone. There was a trend, however, for LAAM to suppress the expression of abstinence more fully than either metabolite. Of additional interest was the finding that LAAM had a rapid onset of action in the dog, which did not differ from its active metabolites, demonstrating that the parent compound was pharmacologically active. Vaupel, D.B., and Jasinski, D.R. l-a-acetylmethadol, l-a-acetyl-N-normethadol and l-a-acetyl-N,N-dinormethadol: Comparisons with Morphine and Methadone in Suppression of the Opioid Withdrawal Syndrome. J. Pharmacol. Exp. Therap., 283, pp. 833-842, 1997.

Imaging Nicotinic Acetylcholine Receptors with Fluorine-18-FPH, An Epibatidine Analog

Successful imaging of nicotinic acetylcholine receptors (nAChRs) in the baboon brain suggests the radiotracer [18F]-FPH has the potential for imaging these receptors in the human brain. In vivo studies in mice with [3H]epibatidine, a high affinity nicotinic ligand, previously demonstrated a high brain uptake of the tracer, a regional distribution consistent with that of nAChRs, a slow clearance from brain and low nonspecific binding. This study characterized the in vivo distribution and kinetics of [18F]FPH, a fluorinated epibatidine radiotracer, binding to nAChRs in the baboon brain using positron emission tomography. Radioactivity was in the thalamus and hypothalamus/midbrain, intermediate in the neocortex and hippocampus and lowest in the cerebellum and this regional binding pattern was highly correlated with the known densities of nAChRs measured in vitro in human and rat brain. [18F]FPH appears to be a suitable tracer to study nAChRs in the human brain. Villemagne, V.L., Horti, A., Scheffel, U., Ravert, H.T., Finley, P., Clough, D., London, E.D., Wagner, H.N. Jr., and Dannals, R.F. *J. Nucl. Med.*, 38, pp. 1737-1741, 1997.

Importance of the Prefrontal Dopamine Pathway Emerges from Study of Autistic Children

Using positron emission tomography, the accumulation of [18F]Fluorodopa was measured in the head of the caudate nucleus, putamen, ventral tegmental complex, and prefrontal and occipital cortices of 14 autistic (13.1 ± 2.4 years; 8 males/6 females) and 10 healthy children (14.9 ± 2.0 years; 7 males/3 females). Autistic children showed abnormally low dopaminergic activity only in the anterior medial prefrontal cortex, a region involved in cognitive and emotional processes. This finding stresses the importance of studies that address the development and maintenance of the medial prefrontal dopamine pathway and its role in cognitive tasks known to be altered in autism and mediated by the prefrontal cortex. Ernst, M., Zametkin, A.J., Matochik, J.A., Pascualvaca, D., and Cohen, D.M. *Low Medial Prefrontal Dopaminergic Activity in Autistic Children. The Lancet*, 350, p. 638, 1997.

Functional Interactions Between Sex and Brain Development May Contribute to Attention-Deficit /Hyperactivity Disorder (ADHD) Pathophysiology

Using positron emission tomography and [18F]fluorodeoxyglucose (FDG), glucose cerebral metabolic rates (CMR_{glc}) were compared between 10 Attention-Deficit/Hyperactivity Disorder (ADHD) (14.10 ± 1.91 years) and 11 normal girls (14.3 ± 1.70 years). Lateralization of normalized CMR_{glc} differed significantly between ADHD and control girls in parietal and subcortical regions. The sylvian area of the parietal region and the anterior putamen of the subcortical region were the main contributors to this effect. Normalized CMR_{glc} of the hippocampus was higher in ADHD than in control girls. Sexual maturation correlated negatively with global CMR_{glc}. This study suggested that (1) functional interactions between sex and brain development may contribute to ADHD pathophysiology, and that (2) sexual maturation should be controlled in future CMR_{glc} studies of adolescent girls. Ernst, M., Cohen, R.M., Liebenauer, L.L., Jons, P.H., and Zametkin, A.J. *Cerebral Glucose Metabolism In Adolescent Girls With Attention-Deficit/Hyperactivity Disorder. Journal of the American Academy of Child and Adolescent Psychiatry*, 36, pp. 1399-1406, 1997.

Dextroamphetamine Facilitates Activation of Task-Related Regional Glucose Metabolism in the Brain and Reduces Activation of Glucose Metabolism Activated by Irrelevant Stimuli

The effects of intravenous dextroamphetamine on cerebral glucose metabolism were assayed by positron emission tomography (PET) and [18F]fluorodeoxy-glucose (FDG) in 13 healthy adults during the performance of a continuous visual attention task. Subcortical, limbic, frontal and cerebellar regional cerebral metabolic rates for glucose metabolism (rCMR_{glc}) were significantly increased after dextroamphetamine, while rCMR_{glc} of the temporal cortex significantly decreased. These rCMR_{glc} changes reflect both the direct pharmacological effect of dextroamphetamine on monoaminergic neurotransmitter systems as well as enhancement of the activation of the neural network mediating the performance of the continuous attention task. Ernst, M.E., Zametkin, A.J., Matochik, J., Schmidt, M., Jons, P.H., Liebenauer, L.L., Hardy, K.K., and Cohen, R.M. *Intravenous Dextroamphetamine and Brain Glucose Metabolism. Neuropsychopharmacology*, 17, pp. 391-401, 1997.

Newly Synthesized Radiotracer [18F]FPH Labels Nicotinic Acetylcholine Receptors in the Central Nervous System will Benefit the Localization and Quantitation in Pathological States

Visualization of central nicotinic acetylcholine receptors (nAChRs) using modern imaging techniques has been hampered by the lack of a radioligand with suitable in vivo binding properties. This has led to the synthesis of a highly potent 18F labeled analog of epibatidine ([18F]FPH) and the assessment of its in vivo binding, kinetics and pharmacology in mouse brain. The rapid association of the tracer to nAChRs in receptor-rich areas and rapid egress from receptor-poor areas yielded high ratios of specific-to-nonspecific binding. [18F]FPH and PET should prove useful for the localization and quantitation of nicotinic AChRs in normal physiological conditions and pathological states. Horti, A., Scheffel, U., Stathis, M., Finley, P., Ravert, H.T., London, E.D., and Dannals, R.F. *Fluorine-18-FPH for PET Imaging of Nicotinic Acetylcholine Receptors. J Nuc Med*, 38, pp. 1260-1265, 1997.

Preclinical Pharmacology Branch *Psychobiology Section*

A Novel Photoaffinity Label for the Dopamine Transporter Based on N-Substituted-4', 4''-Difluoro-3a-(diphenylmethoxy)tropane

DIR scientists have recently synthesized a novel photoaffinity label based on an N-butylphenyl- 4,4-difluorobenzotropine analog that demonstrates high affinity and selectivity for the dopamine transporter. This compound combines structural features of both cocaine and GBR 12909 and was radiolabeled with 125I. In collaboration with Roxanne Vaughan, using immuno-precipitation techniques it was discovered that this compound photolabels the dopamine transporter and is currently being used in DAT topologic characterization studies. A rapid communication on this finding was recently published. Agoston, G.E., Vaughan, R., Lever, J.R., Izenwasser, S., Terry, P.D. and Newman, A.H. Bioorg. Med. Chem. Lett. 7, pp. 3027-3032, 1997.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****February, 1998**

Program Activities

Program Announcements/RFAs

On October 24, 1997, NIDA issued a Program Announcement entitled "**Exploratory/ Developmental Grant Applications**" (PA-98-004). The objective of the exploratory/ developmental mechanism (R21) is to encourage applications from individuals who are interested in testing innovative or conceptually creative ideas that are scientifically sound and may advance our understanding of drug abuse and addiction. Another objective is to encourage necessary initial development to provide a basis for important future research in a particular field.

In November, 1997, a new Program Announcement titled the "**Minority Institutions' Drug Abuse Research Program (MIDARP)**" was released. This announcement replaces the old MIRDP announcement and will be administered by the Special Populations Office.

On December 19, 1997, NIDA issued an RFA entitled "**Neurobiological Effects of Drug Addiction Therapies**" (DA-98-004). This research program is intended to support individual research project grants, mentored career development awards, and competitive supplements on the clinical, neurobiological effects of specific treatments for drug use disorders. The principal goal of the research to be supported through this initiative is to identify how structure and/or function of neuronal systems are affected by specific treatments for drug abuse disorders. Toward this goal, NIDA is particularly interested in proposals that will utilize brain imaging and/or other state-of-the-art approaches for assessment of alterations in human brain function and structure during and following behavioral and/or pharmacological therapy for drug disorders. The Letter of Intent Receipt date for this RFA is February 26, 1998 and the Application Receipt date is March 26, 1998.

Other Program Activities

IND Filed for Anti-Cocaine Vaccine

The ImmuLogic Corporation, has filed an IND and received permission to conduct a Phase I clinical trial of an anti-cocaine vaccine. ImmuLogic has received support for this research via a SPIRCAP grant from NIDA's Medications Development Division.

Review of Phase II Trial of Seligelene

The Medications Development Division convened an outside consultant group to review data from a Phase II trial of seligelene for the treatment of cocaine dependence. Based on their review of the data, and an overview of statistical methods currently acceptable to the FDA, the group recommended that a larger and more definitive trial be

undertaken.

NIDA'S New/Competing Awards Since May 1997

Abrams, Donald I. --- Community Consortium
Short-Term Effects of Cannabinoids in HIV Patients

Adams, Jill U. --- NYU Medical Center - VA Medical Center - Psychiatry Dept.
Conditioned Effects of Cocaine in Rats

Anthony, James C. --- Johns Hopkins University/Dept. of Mental Hygiene
Cross-National Studies on Clusters of Drug Use

Baird, John C. --- Applied Behavioral Research
HIV Risk Reduction Questionnaire and Interview

Baker, Lisa E. --- Western Michigan University
Dopamine D3 Receptors in Psychostimulant Discrimination

Bardo, Michael T. --- University of Kentucky - Dept. of Psychology
Taste Cues in Morphine Conditioning

Barrett, Randy S. --- Vanderbilt University/Dept. of Psychiatry
Identifying Drugs for the Treatment of Bz Withdrawal

Baum, Marianna K. --- University of Miami
Selenium Therapy to Slow HIV Disease Progression in IDUs

Belenko, Steven --- Nat. Center for Addiction and Substance Abuse
HIV Service Needs & Access in High Risk Criminal Justice Populations

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

Berrettini, Wade H. --- University of Pennsylvania-Dept. of Psychiatry
A Genetic Study of Opioid Addiction

Blechman, Elaine A. --- University of Colorado/Dept. of Psychology
Drug Abuse Prevention, Expert Coping, & Ethnicity

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

Brauer, Lisa H. --- Duke VA Medical Center
Dopaminergic Mechanisms in Nicotine Addiction

Breslow, Ronald C. --- Columbia University/Dept. of Chemistry
Catalysts for the Hydrolysis of Cocaine

Brigham, Janet --- Western Psychiatric Institute
Nicotine in Adults' Use of Smokeless Tobacco

Britton, Brandy M. --- University of Maryland/Dept. of Sociology
The Impact of Violence on Women's Drug Use and AIDS Risk

Butler, Stephen F. --- Innovative Training Systems
The ASI: A Multimedia Interactive Version

Cashman, John R. --- Seattle Biomedical Research Institute
Combinatorial Pharmacotherapies for Cocaine Dependence

Chang, Kwen-Jen --- Duke University Medical Center
Molecular Basis of Multiple Opioid Receptors

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

Cherek, Don R. --- University of Texas Medical School/Dept. of Psychiatry
Behavioral Mechanism in High Risk Populations

Cohen, Jonathan D. --- Western Psychiatric Institute
Advanced Methods for Neuroimaging Data Analysis

Costello, Elizabeth J. --- Duke University Medical Center
Vulnerability to Drug Abuse: A Test of Competing Models

Crawford, Stephanie Y. --- University of Illinois/Dept. of Pharmacy
Rx Monitoring: Physician Attitudes and Patterns

Devane, William A. --- University of Wisconsin/Dept. of Pharmaceutical Sciences
Anandamide Pharmacology & Endogenous Cannabinoid Ligands

Eissenberg, Thomas E. --- VCU/Center for Drug & Alcohol Studies
Drug Craving: Pharmacologic and Associative Influences

Ellis, Alicja I. --- Essex Consulting, Inc.
Information System for Substance Abuse Practitioners

Elmer, Gregory I. --- Maryland Psychiatric Research Center
Neurobiological Factors in Vulnerability to Opioid Abuse

Evans, Christopher J. --- University of California at Los Angeles
Center for Study of Opioid Receptors and Drugs of Abuse

Falkin, Gregory P. --- National Development & Research Institute
Social Support & HIV Risk: Women Offenders in Recovery

Farrelly, Matthew C. --- Research Triangle Institute
An Analysis of Joint Demand/Alcohol, Tobacco, and Marijuana

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

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

Friedman, Herman --- University of South Florida
Training in Psychoneuroimmunology, AIDS & Drugs of Abuse

Friedman, Herman --- University of South Florida
Marijuana Effects on Immunity: Nature and Mechanisms

George, Frank R. --- Amethyst Technologies, Inc.
Science Education: Neurobiology for Practitioners

Graybiel, Ann M. --- Massachusetts Institute of Technology
Neurobiology of Drugs of Abuse

Gray, Brenda M. --- CSR Inc.
Developing Case Management Crisis Prevention Software

Greenblatt, David J. --- Tufts University
Chronic Benzodiazepines: Behavior and Neurochemistry

Grissom, Grant R. --- Field Diagnostic Services, Inc.
Development of Substance Abuse Relapse Reduction System

Gross, Robert A. --- University of Rochester
Opioid Signaling Pathways and Tolerant State

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

Hamid, Ansley --- John Jay College of Criminal Justice
International Drug Markets Convergence

Hansen, William B. --- Tanglewood Research, Inc.
Drug Abuse Prevention Tool Kit for Community Groups

Hansen, William B. --- Tanglewood Research, Inc.
Drug Education Through Concept Training for Teachers

Harris, Kristen, M. --- Children's Hospital Corp.
Three Dimensional Structure & Function of Synapse in Brain

Harris, Ruth M. --- University of Maryland/Dept. of Nursing Education
AIDS and Drug Use Prevention for Women in Prison

Havassy, Barbara E. --- University of California at San Francisco
Consequences of Comorbid Drug Abuse & Mental Disorders

Hawkins, J. David --- University of Washington-Social Development Group
Diffusion of State Risk/Protective-Focused Prevention

Hecht, Michael L. --- Pennsylvania State University
Drug Resistance Strategies Minority Project

Hinton, Sean C. --- Duke University/Dept. of Experimental Psychology
Dopaminergic Mechanisms of Interval Timing: fMRI Views

Hoffman, Jeffrey A. --- Danya International Inc.
Vocational Rehabilitation Job Opportunity Enhancer

Hoffman, Jeffrey A. --- Danya International, Inc.
Phases of Treatment

Horgan, Constance M. --- Brandeis University
Drug Abuse Treatment under Managed Care: Role of PPOs

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

Inturrisi, Charles E. --- Cornell University Medical College/Dept. of Pharmacology
Pharmacology and Neuroscience of Drug Abuse

Jaffe, Adam J. --- Yale University School of Medicine
Expectancy-Based Coping Skills Therapy

Jerome, Albert --- Personal Improvement Computer System
Computerized Scheduling of Nicotine Gum

Johnston, Lloyd D. --- University of Michigan/Survey Research Center
Drug Use and Lifestyle of American Youth

Justice, Joseph B. --- Emory University/Dept. of Chemistry
Neurochemistry of Drug Abuse

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

Kleber, Herbert D. --- New York State Psychiatric Institute
Opiate Dependence: Combined Naltrexone/behavior Therapy

Kleinman, Paula H. --- Nat. Center for Addiction and Substance Abuse
Promoting Entry to Treatment: A Services Enhancement

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

Kozikowski, Alan P. --- Georgetown University Medical Center
Biological Studies of Piperidine Analogs of Cocaine

Kreek, Mary J. --- Rockefeller University
Treatment of Addictions--Biological Correlates

Kuhn, Donald M. ---Wayne State University
Neurotoxic Amphetamines Radicals & 5HT Neurons

Langenbucher, James --- Rutgers/State University of New Jersey
Nosology of Drug Abuse: Emergent vs Classical Models

Lescrenier, Margaret G. --- Gammex Inc.
Medical Physics System for Testing Resolution of Ultrasound Scanners

Leventhal, Bennett L. --- AACAP
AACAP Physician Scientist Program in Substance Abuse

Lewis, John W. --- University of Bristol-School of Chemistry
Discovery of New Treatments for Drug Abuse

Lewis, Michael --- New Jersey Medical School/Robert W. Johnson Medical School
Developmental Effects of Prenatal Cocaine Exposure

Longshore, Doug Y. --- RAND
Testing-Sustaining Social Influence Model Rural School

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

Macenski, Mitchell J. --- University of Texas Health Sciences Center
Mechanisms of Increased Cocaine Self-Administration

Madras, Bertha K. --- Harvard Medical School
Evaluation of Novel Cocaine Medications

Mahata, Sushil K. --- University of California
Chromogranin A: Nicotinic Signaling and Desensitization

Malan, Thomas P., Jr. --- University of Arizona College of Medicine
GABA and Neuropathic Pain

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

Matt, Georg E. --- San Diego State University/Dept. of Psychology
Improving Self-Reports of Drug Use: A Cognitive Set Model

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

Mckay, James R. --- University of Pennsylvania/ Dept. of Psychiatry
Aftercare for Cocaine Patients: Effectiveness and Costs

Melega, William P. --- Univ. Of California/Lab of Struct. Bio & Mol Med
Brain and Behavior Alterations after Methamphetamine

Meltzer, Peter C. --- Organix Inc.
Discovery of Novel Pharmacotherapies: Cocaine Dependence

Michelson, Stephen A. --- Cyclotec Medical Industries Inc.
Electro-Therapeutic Pain Blocking Splints and Bandages

Mogil, Jeffrey S. --- University of Illinois/Dept. of Psychology
The Genetic Basis of Pain Sensitivity in Mice

Morrison, Diane M. --- University of Washington-School of Social Work
Teen Mothers into Adulthood and the Next Generation

Murphy, E. Hazel --- Allegheny University of the Health Sciences
Prenatal Cocaine Exposure and the GABAergic System

O'Brien, Charles P. --- University of Pennsylvania/Dept. of Psychiatry
Research on Treatment and Prevention of IV Drug Abuse

Oliveto, Alison H. --- Connecticut Mental Health Center/Dept. of Psychiatry
Opioid Antagonist Discrimination: A Model of Withdrawal

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

Pandina, Robert J. --- Rutgers University
Trajectories of Drug Use: Predictors and Adult Outcomes

Paronis, Carol A. --- McLean Hospital/Dept. of Psychiatry
GABAergic Drugs: Behavioral and Abuse-Related Effects

Paulus, Martin P. --- University of California/Dept. of Psychiatry
Effects of Drugs of Abuse on Behavioral Organization

Pettit, Hugh O. --- Delta Pharmaceuticals, Inc.
Clinical Applications of Delta Opiate Receptor Ligands

Pitt, Jane --- Columbia University/Dept. of Pediatrics
Women and Infants Transmission Study (WITS III)

Posnett, David N. --- Cornell University Medical Center
HIV-1 Associated Superantigen

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

Pyle, Sally J. --- University of North Dakota
Cocaine, G-proteins and Cytoskeleton in Neurite Growth

Quock, Raymond M. --- University of Illinois/Dept. of Biomedical Sciences
Genetic Control of Responsiveness to N20 Antioiception

Rachlin, Howard --- State University of New York
Tests of a Behavioral Theory of Drug Addiction

Rogers, Thomas J. --- Temple University School of Medicine
Opioids and T-Cell Differentiation

Rudnick, Gary --- Yale University School of Medicine/Dept. of Pharmacology
Neurotransmitter Transport

Schoenbaum, Ellie E. --- Montefiore Medical Center
Natural History of HIV Infection in IVDUs

Scura, William C. --- Problem Solving Technologies
Work/Social Skills Training for Drug-Abusing Offenders

Seeman, Philip --- University of Toronto
Receptors Mediating Drug Dependence

Segre, Mariangela --- University of Illinois/Dept. of Veterinary Pathobiology
Is An Anti-Cocaine Idiotypic Vaccine Feasible?

Seiden, Lewis S. --- University of Chicago
Neuropsychopharmacology Training for Drug Abuse Research

Sellers, Edward M. --- University of Toronto/Dept. of Pharmacology
Pharmacogenetic Risk Factors in Drug Abuse: Cyp Variants

Sholomskas, Diane E. --- Applied Behavioral Research
Evaluating Manual-Guided Training in Clinical Settings

Shoptaw, Steven --- LAATRC
Behavioral Therapy for Gay Male Methamphetamine Abusers

Slusher, Barbara S. --- Guilford Pharmaceuticals Inc.
Highthroughput Screening to Identify Cocaine Antagonists

Sorensen, James L. --- San Francisco General Hospital
Medication Management of HIV-Positive Drug Abusers

Spoth, Richard L. --- Social & Behavioral Research
Rural Youth and Family Competencies Building Project

Steely, Donald G. --- Oregon Center for Applied Sciences
Teaching Scientific Decision-making with Drug Abuse Cont

Strakowski, Stephen M. --- University of Cincinnati/Dept. of Psychiatry
Behavioral Sensitization in Humans

Sucholeiki, Irving --- Solid Phase Sciences Corp.
Synthesis of Peptide and Non-peptide Opioid Analogs

Sussman, Steven Y. --- USC Dept. of Preventative Medicine
Drug Use Prevention Programming in Continuation Schools

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

Toll, Lawrence R. --- SRI International
Biochemical Studies of Opiate Efficacies

Trnovsky, Jan --- One Cell Systems Inc.
Generation of Catalytic Antibodies to Neutralize Cocaine

Trudell, Mark L. --- University of New Orleans/Dept. of Chemistry
Synthesis of Potential Cocaine Abuse Therapeutics

Trujillo, Keith A. --- SCU San Marcos Foundation of California State University
NMDA Receptors & Opiate-Induced Behavioral Plasticity

Vezina, Paul --- University of Chicago/Dept. of Psychiatry
Dopamine Neurotransmission and Amphetamine Sensitization

Vlahov, David --- Johns Hopkins University/Epidemiology Dept.
Baltimore Needle Exchange Program Evaluation

Volkow, Nora D. --- Associated Universities Inc.
PET Studies of Brain Dopamine in Cocaine Abusers

Wakschlag, Lauren S. --- University of Chicago/Dept. of Psychiatry
Prenatal Smoking and Preschool Behavior Problems

Walsh, J. Michael --- Walsh Group, PA
New Training in Detection of Illicit Drugs in Drivers

Wang, Shaomeng --- Georgetown University/Dept. of Neurology
Cocaine Antagonists Through 3D Pharmacophore Searching

Watson, Stanley J. --- University of Michigan
Postdoctoral Training in the Biology of Drug Abuse

Wei, Li-Na --- University of Minnesota/Dept. of Pharmacology
Studies of the Mouse Kappa Opioid Receptor Gene

Wilens, Timothy E. --- Massachusetts General Hospital
Drug Abuse and ADHD in Adults and Their High Risk Offspring

Williams, John T. --- Oregon Health Sciences University
Chronic Morphine: Regulation of Ion Conductances

Wong, Dean F. --- Johns Hopkins University School of Medicine/Dept. of Radiology
Imaging Dopamine-Serotonin Mechanisms in Cocaine Craving

Woolverton, William L. --- University of Mississippi Medical Center
Behavioral Pharmacology of Drug Self-Administration

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

Yu, Lei --- University of Cincinnati
In Vivo Genetic Analysis of Mu Receptor Functions

Review Activities

New Guidelines for Review of Research Grant Applications

OEPR has prepared new guidelines for the review of unsolicited research grant applications, in conformance with the new guidelines released by NIH, effective for submissions on or after October 1, 1997. The guidelines have been provided to Scientific Review Groups (SRGs) and discussed at recent SRG meetings. Training on implementation of the new guidelines was held for NIDA SRAs on January 6, 1998, and the new guidelines will be implemented in the February/March reviews.

Neurosciences Integration Activity

The neurosciences integration activity is nearly completed. Twenty one new study sections have been created, and these have been grouped into three Initial Review Groups (IRGs). Three SRAs, Drs. Mary Custer, Jim Debbas and Syed Husain, and two GTAs, Ms. Sandy Camman and Ms. Sharon Dyson, from NIDA have been reassigned to the Center for Scientific Review (CSR). Reviewers are now being selected and the first review of applications by these new committees will take place in June of 1998 for applications submitted in February/March 1998. More information can be found on the CSR home page (<http://www.csr.nih.gov>).

Training/Q & A Sessions

Dr. Rita Liu organized an information and "question and answer" session on the integration of neuroscience application reviews for the Society for Neuroscience 1997 Annual Meeting in New Orleans.

Dr. Gamil Debbas presented two lectures on extramural procedures and the review of grant applications to the Division of Intramural Research in Baltimore. These lectures were provided to train post doctoral fellows on extramural issues that are often not addressed in NIH intramural programs so that they will be aware of the basics of extramural grants when they leave NIH.

OEPR sponsored a training seminar to update NIDA staff on the ending of the R29 (FIRST award) mechanism and the reasons for that change. Changes in procedures for review of R13 (Conference) applications were also discussed.

NIDA's Conference Grant (R13) Committee

The NIDA-wide committee formed to develop and implement procedures for the review of R13 (Conference Grant) applications continued to meet and define procedures. The first "in house" review of R13 applications was conducted on January 8th. The committee is chaired by Dr. William Grace (OEPR) and is coordinated by Ms. Jackie Porter (OEPR). Members are Drs. Cindy Miner (OSPC), Charles Sharp (DBR), Dorynne Czechowicz (DCSR), Jacques Normand (DEPR), and Jamie Biswas (MDD), as well as Mr. Noble Jones (OoA), and Ms. Catherine Mills (GMB).

New Study Sections

Planning continues for the creation of two new study sections, one for medications development applications and one for career development applications. The career development group will review training, career development, and fellowship applications from across all NIDA scientific areas and will begin operation with the February 1, 1998 application receipt date. Dr. Mark Swieter will be the SRA for that committee. The medications development committee will review applications for the development of new pharmacotherapies for drug abuse. Dr. Khursheed Asghar will be the SRA.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****February, 1998**

Congressional Affairs

(Prepared January 9, 1998)

FY 98 Labor/HHS Education Appropriations Act

On November 13, 1997, the President signed into law H.R. 2264 (P.L. 105-78), the Departments of Labor, Health and Human Services, Education and Related Agencies Appropriations Act, 1998. The bill increases funds for NIH by 7.1% over FY 97. NIDA received a 7.6 % increase over FY 97, for a FY 98 figure of \$527,175,000.

Selected Provisions of Interest

Distribution of Sterile Needles

(Language from the Conference Report to accompany HR 2264, House Report 105-390, pg. 114)

"The conference agreement ... includes bill language limiting the use of federal funds for sterile needle and syringe exchange projects until March 31, 1998. After that date such projects may proceed if (1) the Secretary of Health and Human Services determines that exchange projects are effective in preventing the spread of HIV and do not encourage the use of illegal drugs; and (2) the project is operated in accordance with criteria established by the Secretary for preventing the spread of HIV and for ensuring that the project does not encourage the use of illegal drugs. This provision is consistent with the goal of allowing the Secretary maximum authority to protect public health while not increasing the overall number of needles and syringes in communities."

Parkinson's Disease Research

In the Appropriations Act amending the PHS Act there is language included to authorize \$100 million to enhance Parkinson's research programs at NIH. Specifically, the amendment calls for research and training, inter-institute coordination, up to 10 Morris K. Udall Centers, a data system and information clearinghouse, Morris K. Udall Awards for Excellence in Parkinson's Disease Research, and a National Parkinson's Disease Education Program.

AIDS

The Committee maintained the FY 1997 approach of providing funds for AIDS research directly to the NIH Institutes and Centers, contrary to the President's budget request for a single consolidated AIDS appropriation to OAR. The bill language also continues the authority for the NIH and OAR Directors to reallocate up to 3 percent of the funds designated for AIDS research among the Institutes and Centers. The committee requests that the NIH Director report on the FY 1998 allocation plans within 60 days of enactment and provide notification to the Committee in the event the two directors exercise their 3-percent transfer authority. (The conference FY 1998 budget estimate for AIDS funding is \$1,595,453,000.) Report language states that the committee understands that the total could be modified

depending on changing scientific opportunities and recommendations of various advisory bodies. The AIDS transfer authority jointly held by the NIH and OAR Directors is retained for FY 1998.

Controlled Substances

There is continuation of prohibition on the use of funds for any activity that promotes the legalization of controlled substances, except this does not apply where there is medical evidence of therapeutic value or federally sponsored clinical trials are being conducted to determine such value.

FY 99 Funding Outlook For NIH

President Clinton has agreed to a \$1 billion increase for NIH in FY 99, and Members of Congress from both parties say they are virtually certain to approve an even bigger increase. Congress believes that NIH can exploit promising scientific opportunities and that investments in research will be popular with voters in this election year.

Both Rep. Porter (R-IL) and Sen. Specter (R-PA), Chairmen of the Appropriations subcommittees responsible for health spending, support major increases for NIH. Mr. Porter said he discussed the question at length with Mr. Gingrich (R-GA), Speaker of the House, who has expressed support for doubling of the NIH budget in five years "within the context of a balanced budget."

Tobacco Legislation

Under a settlement reached in June 1997 by the tobacco industry and a group of state attorneys general, the industry agreed to pay \$368.5 billion over 25 years to cover smokers' health care costs and anti-smoking programs in exchange for immunity from certain lawsuits. Much of the settlement needs to be enacted into law in order to be implemented, and a major congressional debate is expected to begin when Congress reconvenes on January 27, 1998.

Before the end of the first session, a flurry of legislation relating to the settlement had been introduced, including several major bills designed to stimulate discussion. These included bills introduced by Senators Hatch (R-OR) [S1530] and Kennedy (D-MA) [S1492], who were unable to reach agreement on a bipartisan bill. While different in many respects, both proposals would create revenues for health programs.

Biomedical Research Trust Funds

For the past several years, a number of Members of Congress considered various mechanisms to ensure continued support for biomedical research in the face of stringent budget resolutions and pressure for a balanced budget. One of these mechanisms included the establishment of a trust fund to provide a continuing source of large amounts of money for NIH, independent of the appropriations process, and with stipulations that the trust funds are not to be used if there are not increases for NIH in the regular appropriations process. The concept of establishing trust funds for NIH continued into the 105th Congress. Key bills include:

- S. 441, introduced by Sen. Harkin (D-IA), would require health plans to set aside 1 percent of all health care premiums for the National Fund for Health Research. The Secretary of HHS would phase in the 1 percent over a 4-year period.
 - S. 1411, introduced by Sen. Mack (R-FL), would disallow Federal income tax deductions for any tobacco litigation or settlement. The revenue from disallowing the deductions would be used to establish the NIH Trust Fund for Health Research.
 - H.R. 1257, introduced by Rep. Forbes (R-NY), would amend the Internal Revenue Code so that a check-off for the Biomedical Research Fund would allow individuals to designate \$5 on their tax returns for research on a disease of their choice.
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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****February, 1998**

International Activities

On October 6-8, 1997, NIDA and the Pavlov Medical University, St. Petersburg, Russia, cosponsored a **U.S.-Russia Bilateral Workshop** entitled "**Prevention of HIV and Other Infectious Diseases Among Drug Abusers**," held in St. Petersburg. Russia is faced with a rapidly expanding drug abuse epidemic and emerging epidemics of HIV and other infectious diseases associated with drug use. The meeting was designed to share information regarding HIV and other infectious diseases among drug users in the U.S. and Russia, to identify public health responses to these epidemics, to explore research initiatives and public health interventions with practical application to preventing the spread of these diseases, and to develop an action plan for future collaboration. Drs. Robert Battjes and Patricia Needle led the delegation, which also included Drs. Skip Francis and Richard Needle of NIDA, Dr. Paul Gaist of the NIH Office of AIDS Research, and Drs. Philippe Bourgois, San Francisco State University, Sherry Deren, NDRI, Marc Gourevitch, Montefiore Medical Center, David Vlahov, John Hopkins University, and George Woody, University of Pennsylvania. Following the workshop, U.S. delegation members made visits to prevention and treatment facilities in St. Petersburg. Dr. Francis reviewed clinical infectious diseases cases at the regional infectious hospital and collaborated with the hospital's medical staff in developing a research consensus for targeting specific infectious diseases for clinical prevention efforts. Drs. Battjes, Bourgois, Woody, Needle and Gaist observed HIV prevention intervention activities at the Drug Abuse Prevention Center and mobile van providing prevention and outreach services for risk reduction operated by Mediciens du Monde in St. Petersburg.

The **3rd Regional Meeting of US/Central European Countries on Drug Dependence**, titled "**Mechanisms in Drug Abuse and Addiction: Translation to Treatment**," took place in Brno, Czech Republic from November 4-8, 1997. With support from the U.S. Department of State, a delegation of 8 Americans traveled to Brno to meet with East European counterparts from Austria, Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Poland, Romania, Russia, and Slovakia. Participants from the U.S. included Drs. Frank Vocci and Patricia Needle, NIDA, Drs. Martin Adler and Toby Eisenstein, Temple University; and Drs. Huda Akil, University of Michigan, Mary Jeanne Kreek, The Rockefeller University, Charles O'Brien, University of Pennsylvania, Phillip Peterson, University of Minnesota, and Friedbert Weiss, The Scripps Research Institute. European and American scientists made presentations, which were followed by discussion on the application of the basic biomedical scientific information to drug abuse treatment. It is expected that, as a result of this meeting, new collaborations between U.S. and East European scientists will be initiated.

NIDA co-sponsored and participated in the "**First MERCOSUR Regional Congress on Alcohol and Other Drug Abuse**" in Asuncion, Paraguay, August 28-30, 1997. With support from the Department of State, Dr. Kenzie Preston, IRP, presented results of treatment research studies conducted at the NIDA IRP. Dr. Patricia Needle, International Program presented "**NIDA's Role in International Cooperation for Drug Abuse Research and Education**" via live television hookup through the conference through World Net. The conference organizers reported that there were almost 700 participants at the meeting from the MERCOSUR region (Argentina, Bolivia, Brazil, Chile, Paraguay, and Uruguay), Europe, (France, Spain, United Kingdom), and the U.S.

NIDA welcomed the **1997-1998 Hubert H. Humphrey Drug Abuse Research Fellows** with an orientation program on November 21, 1997. This annual event is designed to give the Fellows an introduction to NIDA research programs and how they are administered. The four NIDA-supported Humphrey Fellows are Drs. Jozsef Lango of

Hungary, M. Maher Hussain of India, Rahmaan Lawal of Nigeria, and Victor Chtenguelov of Ukraine. Following their course of study at The Johns Hopkins University, each Fellow will complete a six-week professional affiliation with a NIDA-funded researcher.

Dr. Skip Francis, DCSR, moderated a NIDA-sponsored symposium titled "**Drug Use and Sexually Transmitted Diseases**" at the **International Congress of Sexually Transmitted Diseases** in Seville, Spain, October 19-22, 1997. The symposium speakers and Dr. Francis presented data on the epidemiology and the definition of drug use and addiction, and on behavioral, STD and health access issues in drug abuse research.

Dr. Robert Battjes, DCSR, attended a steering committee of the **WHO/NIH Joint Project on the Assessment and Classification of Disablements**, September 23-24, 1997 in Luxembourg, and also attended a meeting of the assessment instrument development task force on September 25-27.

On January 9, 1998, Dr. Peter Cohen, MDD, presented a lecture at the **Fourth International Stapleford Conference of Addiction Management**, London, England. The lecture was entitled "**The FDA, New Drug Approval, and Off-Label Use.**"

Dr. Zili Sloboda, Director, DEPR, represented NIDA at the **European Epidemiology Experts meeting** in Strasbourg, France on December 8-9, 1997.

Dr. Zili Sloboda, DEPR, participated with Dr. Patricia Needle in a meeting in Mexico City on September 18-19, 1997, hosted by **CONADIC, Mexico's National Council on the Addictions**, to discuss issues related to drug abuse, sexual risk behaviors for HIV and other infectious diseases and to determine activities of mutual interest for cross-national studies.

Ann Blanken, DEPR, made a presentation entitled "**The Epidemiology and Prevention Strategies of Drug Abuse in the U.S.A.**" at the **International Symposium on Drug Abuse: A Memorial Event for the 50th Anniversary of the Founding of Kangwon National University** on October 10, 1997 at the Sejong cultural Center in Seoul, Korea.

Mr. Nicholas Kozel, DEPR, cochaired a joint meeting of the **East and South Asian Multi-City Epidemiology Work Group** meeting held in Penang, Malaysia on November 17-20, 1997. The East and South Asian Work Group meeting was composed of researchers from Kuala Lumpur, Manila, Bangkok, Beijing, Hanoi, Taipei, Vientiane, Dhaka, Colombo, Islamabad, and Madras. This is one of a series of regional programs being developed to provide assessment and surveillance of drug abuse with the objective of integrating these regional data into a global perspective. A meeting proceedings is produced annually describing the current status of drug abuse in the major cities of the region and emerging drugs of abuse. The project is jointly funded by the U.S. Department of State and the Association of Southeast Asian Nations and is coordinated by staff of NIDA and the Universiti Sains Malaysia.

Moirra O'Brien, DEPR, participated in the **United Nations International Drug Control Programme**, An Expert Group Meeting on Methods of Information Support to International Drug Programmes, held in Vienna, Austria, October 20-22, 1997, and gave a presentation on NIDA's Epidemiology International Research Program.

Peter Hartsock, Dr.P.H., CRB/DEPR, represented NIDA at the plenary meeting of the **European Union Concerted Action on AIDS** held in Bilthoven, the Netherlands on October 1-4, 1997. Dr. Hartsock provided information on NIDA's AIDS epidemiologic, prevention, and cost effectiveness modeling efforts and possibilities for cooperation with EU efforts. He also discussed NIDA's activities in emerging and reemerging infectious diseases (EREIDs).

On January 9, 1998, Dr. Peter Cohen, Medications Development Division, presented a lecture at the **Fourth International Stapleford Conference of Addiction Management**, London, England. The lecture was entitled "**The FDA, New Drug Approval, and Off-Label Use.**"

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National Institute on Drug Abuse

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

February, 1998

Meetings/Conferences

NIDA organized a **"Town Meeting"** in Philadelphia, Pennsylvania entitled **"Understanding Drug Abuse and Addiction: Myths Vs. Reality"** on October 20, 1997. 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 these needs.

NIDA hosted its **Fourth Annual Constituent Conference** on December 2-3, 1997 at the Lansdowne Conference Center in Lansdowne, Virginia. NIDA Director, Dr. Alan Leshner presented the "NIDA Report Card," highlighting specific action taken by the Institute in response to constituent group recommendations, and presented NIDA products and discussed with constituent organizations how they can utilize and help disseminate them. Paul Samuels, President of the Legal Action Center, and Gloria Danziger, Staff Director of the American Bar Association's Standing Committee on Substance Abuse, addressed the participants on the subject of coalition building.

A consensus panel convened by the National Institutes of Health (NIH) in November strongly recommended broader access to methadone maintenance treatment programs for people who are addicted to heroin or other opiate drugs and that the Federal and State regulations and other barriers impeding this access be eliminated. The panel issued their consensus statement following an extensive review of the existing medical literature and a series of presentations by heroin addiction research experts at a 3-day **NIH Consensus Development Conference on Effective Medical Treatment of Heroin Addiction**. This conference was sponsored by the National Institute on Drug Abuse and the NIH Office of Medical Applications of Research and was cosponsored by the NIH Office of Research on Women's Health. The full consensus statement containing specific findings and recommendations made by the panel is available by calling 1-888-NIH-CONSENSUS (1-888-644-2667) or by visiting the NIH Consensus Development Program Web site at <http://consensus.nih.gov>.

On December 9, 1997, the Services Research Branch held a meeting entitled **"Developing an Agenda for Health Services Research on Drug Abuse Treatment and Prevention."** This is the first of 4-5 planning meetings that will be held to develop the program for the NIDA-Sponsored Symposium Forging the Link, to be held next June prior to the Annual Meeting of the Association of Health Services Research. Dr. Bennett Fletcher, Chief of NIDA's Services Research Branch, chaired the meeting attended by eight drug abuse prevention and treatment and health services researchers and NIDA staff from the Division of Clinical and Services Research, the Division of Epidemiology and Prevention Research, and the Office of Science Policy and Communications.

Dr. Betty Tai, MDD, co-chaired (with Drs. Blaine, Preston, and Cohen) the NIDA Treatment Workgroup workshop entitled **"Current and Future Status of Naltrexone"**, November 12-13, 1997. The objective of this workshop was to examine the wealth of information available on the use of naltrexone to treat opioid addiction, and to discuss the potential for improvement and expansion of its use as a clinical resource.

On November 4, 1997, the NIDA Resiliency and Risk Workgroup in collaboration with the NIDA Treatment Workgroup sponsored and organized a meeting on **"The Application of Resiliency and Risk Research to the Further Development of Drug Abuse Treatment Interventions."** The meeting addressed a critical issue. Longitudinal research has produced significant information about the etiology of drug abuse and some of the resiliency and risk factors which influence an individual's drug involvement. While some of this information has been used in the

development of treatment programming, this "brain-storming" meeting explored how the further application of available research based data can advance drug abuse treatment effectiveness beyond current levels. A report of the meeting and its recommendations is being prepared.

On December 15-16, 1997, the institute-wide NIDA Resiliency and Risk Workgroup sponsored a meeting entitled "**Drug Abuse Multi-disciplinary Integration Meeting.**" The goal was for the participants to bring a multi-disciplinary perspective to further our understanding of three largely unexplained, significant, observed phenomena which are unresolved major problems for drug abuse research and intervention. The three phenomena which were explored were: Early Onset, Co-occurrence, and Relapse of Drug Abuse. A premise of this meeting was that some aspects of drug abuse may have a multiply determined nature and might only be understood and resolved through multidisciplinary approaches. The meeting generated a range of exciting ideas and possibilities for further exploration. A report of the meeting and its recommendations is being prepared.

NIDA's Community Research Branch and Division of Epidemiology and Prevention Research held an inter-agency meeting with CDC October 31 on "**The Epidemiology and Prevention of Viral Hepatitis Among Injection Drug Users.**" The objectives of the meeting were to (1) review the epidemiology and prevention of viral hepatitis among IDUs from both the CDC and the NIDA perspectives and (2) to develop an action plan for collaborative research efforts between the two agencies. The rapid spread and high seroprevalence rates of hepatitis B and hepatitis C in this population underscore the need for a concerted public health effort to intervene early, before noninjectors initiate drug injection. In addition, strategies are needed to encourage IDUs who are seronegative to protect themselves from becoming infected, including accepting and completing the HBV vaccine regiment, following up on referrals for testing, entering and completing drug treatment, and practicing behaviors which reduce and prevent the risks of spreading these infections.

On September 18-19, 1997, NIDA's Special Populations Office sponsored a two-day **Minority Supplements Assessment meeting** in Bethesda, Maryland, where approximately 50 past and present minority supplement recipients and faculty sponsors convened to assess their research and mentoring experiences under NIDA's minority supplements program, and to discuss strategies for strengthening the program.

On November 13-14, 1997, NIDA's Special Populations Office reconvened a group of ten minority supplement recipients (investigators and postdoctoral fellows) for a second two-day research development seminar in Bethesda, Maryland. The workshop provided an orientation to the NIH review process, a mock review, and individual mentoring.

On October 28, 1997, NIDA's Special Populations Office helped support the forum for minority students held in New Orleans at the annual meeting of the Society for Neuroscience. The forum was co-hosted by NIDA's Minority Institutions Research and Development Program (MIRDP) at Xavier University.

From November 6-9, 1997, NIDA's Special Populations Office co-sponsored the **Drug Abuse Prevention, Treatment and Next Steps program** at the annual Black Psychiatrists of America conference in St. Thomas, U.S. Virgin Islands. NIDA-supported presenters included Dr. Kathy Sanders-Phillips, Dr. Ronald Braithwaite, Dr. Flavia Walton, and Dr. Jean Oyemade Bailey.

Dr. Cora Lee Wetherington, NIDA's Women's Health Coordinator, served as a co-chair of a workshop entitled "Alcohol and Other Drug Use, Disorders and Consequences" conducted at the meeting "Beyond Hunt Valley: Research on Women's Health for the 21st Century," held by the NIH Office of Research on Women's Health, Bethesda, MD, November 18-19, 1997.

Dr. Nancy Pilotte, DBR, organized a satellite symposium entitled, "Cocaine and a Changing Brain," at the annual meeting of the Society for Neuroscience where speakers described novel pharmacologies directed at the dopamine transporter that might lead to novel medications in cocaine-dependent people, identified new binding sites (probably not dopaminergic) in the brain for cocaine, and discussed the functional alteration of dopamine clearance in the nucleus accumbens after withdrawal of cocaine. Other speakers described the influence of specific cortical inputs onto striatal neurons and the long-term changes that occur in the brains of humans and animals after withdrawal of cocaine. Adaptations in the adenosine system, the serotonin system, and within a recently-described peptide system, were discussed. The discovery of a new cocaine-regulated gene in the nucleus accumbens was also described.

Dr. Timothy Condon, NIDA's Associate Director for Science Policy and Director, OSPC, was keynote speaker at the Florida Summit on Behavioral Health Care held in Tallahassee, Florida, on September 10, 1997.

Dr. Timothy Condon, OSPC, convened a NIDA Grant Writing Workshop at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, held in Toronto, Canada, on October 16, 1997 to highlight for members the grant opportunities available at NIDA in the area of child and adolescent substance abuse.

Dr. Timothy Condon, OSPC, held a symposium entitled "Training Programs for Underrepresented Minorities in Neuroscience and Drugs of Abuse" on October 28 at the Society for Neuroscience Annual Meeting in New Orleans, Louisiana.

Dr. Timothy Condon, OSPC, attended the meeting "Discussion of Public Education Campaigns on the Biomedical Causes of Drug Addiction", convened by the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia on January 15, 1998, and delivered an address on the "Great Disconnect."

On November 5, 1997, Dr. Andrea Baruchin, OSPC, presented a talk, entitled "Methamphetamine: Effects on the Brain and Body," at the North Dakota Methamphetamine Summit sponsored by the Office of the Attorney General of North Dakota.

Susan Azeka, OSPC, represented NIDA at the NIH Conference on Research Involving Individuals with Questionable Capacity to Consent: Ethical Issues and Practical Considerations for IRBs. The conference, co-sponsored by NIDA, was held December 2-3, 1997, in Rockville, MD.

Dr. Peter J. Delany, Deputy Chief of NIDA's Services Research Branch, chaired a panel entitled, "Drug Abuse Treatment as Prevention for HIV/AIDS", at the 125th Annual Meeting of the American Public Health Association in Indianapolis in November 1997. This panel presented information on treatment applications and service needs aimed at enhancing the impact of drug abuse treatment on HIV risk behaviors. Dr. Delany presented work on "HIV Risk Behaviors and Access to Services: Findings from DATOS", Dr. Lana Harrison from the University of Delaware presented on "Integrating HIV Prevention Strategies in a TC Work Release Program for Criminal Offenders", Dr. Jesse Milby from the University of Alabama presented on "Integrating Drug Abuse Treatment and Abstinence Contingent Employment for Homeless, Dually Diagnosed Cocaine Abusers", Dr. David Metzger from the University of Pennsylvania presented on "A Prospective Longitudinal Study of HIV Infection and Risk Behaviors Among In- and Out-of-Treatment Drug Users", and Dr. Steve Shoptaw of the Matrix Institute presented on "Cocaine Abuse Counseling as HIV Prevention".

Dr. Robert Battjes, DCSR, attended a steering committee of the WHO/NIH Joint Project on the Assessment and Classification of Disablements, September 23-24 in Luxembourg and also attended a meeting of the assessment instrument development task force on September 25-27, 1997.

Dr. Skip Francis, CMB/DCSR, attended the Infectious Disease Society meeting in San Francisco, California, September 13-16, 1997. Dr. Francis met with the conference organizers to arrange for an Infectious disease and drug use symposium in the next meeting. Based on those discussions, CMB/NIDA will present a Symposium titled, "Drug Use as an Emerging Disease" in the September, 1998 meeting in Denver, Colorado.

Dr. Skip Francis, CMB/DCSR, moderated a panel titled, "Health Consequences of Heroin Addiction" at the NIDA sponsored conference titled, "Heroin Use and Addiction: A National Conference on Prevention, Treatment and Research Program", September 28-30, 1997, Washington, D.C. Dr. Francis and the other speakers, Ellie Schoenbaum, M.D., Karol Kaltenbach, Ph.D. and David Thomas, M.D. presented research achievements and goals for health consequences research in drug users, drug using maternal populations, drug exposed fetal populations and the interaction between Hepatitis C & HIV/AIDS.

Dr. Arthur MacNeill Horton, Jr., ECNB/DCSR presented a lecture entitled "Comorbidity of Anxiety and Adult ADHD & Substance Abuse Populations" at the Fifth Annual Conference on Behavior, Neurobiology, Substance Abuse, and Culture on October 16, 1997, in Los Angeles, California.

On November 11, 1997 Elizabeth Rahdert, Ph.D., Treatment Research Branch, DCSR, presented a poster entitled "Risk Profiles by Age and Sex of Adolescents Referred for Drug Assessment" at the 125th Annual Meeting of the American Public Health Association, in Indianapolis, Indiana.

Dr. Jack Blaine, TRB/DCSR, participated in the workshop on "Treatment and Alcohol Craving" sponsored by the National Institute on Alcohol Abuse and Alcoholism, held at the Convention Center, Washington, D.C., October 8-9, 1997.

Dr. Teresa Levitin, OEPR, chaired the Society for the Psychological Study of Social Issues 1997 Robert Chin Memorial Award Committee. Each year, this committee awards a prize for a scholarly paper that best uses research findings to address the serious problem of child abuse.

Dr. Teresa Levitin, OEPR, served on the Evaluation Committee for the 57th Westinghouse Science Talent Search in December. The Westinghouse Science Talent Search aims to further the career development of outstanding high school students with an interest in and aptitude for science, and the evaluation committee judges original

submissions of projects in a variety of basic and applied scientific areas.

Drs. Frank Vocci and Betty Tai, Medications Development Division, co-chaired and presented a workshop, along with Drs. Walter Ling, John Mendelson, and Eric Strain: "Buprenorphine: an Alternate Treatment for Opioid Dependence", at a meeting of the American Society of Addiction Medicine Conference on Models and Measures of Early Recovery; Washington D.C., October 23, 1997.

Dr. Frank Vocci, MDD, presented "Translation of Preclinical Research into Clinical Studies", at the NIDA Intramural Research Program, Baltimore, Maryland, October 21, 1997.

Dr. Frank Vocci, MDD, presented "How NIDA Developed Naltrexone", to the NIDA Treatment Working Group, November 12-13, 1997.

Dr. Frank Vocci, MDD, presented "Approaches to the Development of Medications for the Treatment of Cocaine Dependence", Psychiatry Grand Rounds, Temple University School of Medicine, January 16, 1988.

Dr. Peter Cohen, MDD, organized and participated in a Mock Trial Workshop at the annual meeting of the American Society of Anesthesiologists, October 20, 1997.

Dr. Peter Cohen, MDD, presented a talk, "Treatment of Substance Dependent Professionals: The Physicians' Health Program," at the NIDA Treatment Workgroup Workshop on Current and Future Status of Naltrexone (November 12-13, 1997).

Dr. Peter Cohen, MDD, presented two lectures at the 1998 Biennial Congress of the Pan-Pacific Surgical Association, January 26, 1998: (1) "Molecules, Mind, Myths and Addiction: Disease, Misconduct, or What?" (2) "The First Thing We Do, Let's Kill All the Lawyers": A Physician's Guide to Legal Thinking".

On November 17, 1997, Lula Beatty attended the final meeting of Beyond Hunt Valley: Research on Women's Health for the 21st Century sponsored by the Office of Research on Women's Health, NIH.

The Special Populations Office was invited to attend a conference on Historically Black Colleges and Universities (HBCU) Initiatives sponsored by the Department of Defense. Arnold Mills attended this meeting held in Bethesda on December 18-19, 1997.

Lula Beatty was a luncheon speaker for the Women of Color National Networking and Leadership Workshop held November 19-20, 1997, at Georgetown University, Washington, DC. She spoke on Mental Health and Substance Abuse in Women of Color.

On September 15, 1997, Lula Beatty presented a session on NIDA's Hispanic Initiative as part of NIH's Hispanic Heritage Program.

On January 8, 1998, Lula Beatty presented a session on research opportunities at NIDA for the NIH Extramural Associates program.

In November, 1997, Lula Beatty served as a field reviewer for Head Start's 4th National Research Conference titled Children and Families in an Era of Rapid Change - Creating a Shared Agenda for Researchers, Practitioners and Policy Makers.

On October 28, 1997, Dr. Zili Sloboda, Director of DEPR, was the keynote speaker at a meeting of a consortium of administrators and faculty from New York State on Drug Abuse Among College Students.

Dr. Zili Sloboda, DEPR, presented a paper on the Epidemiology of Crack-Cocaine at a meeting cosponsored by the National Institute on Justice and NIDA held November 4, 1997.

Dr. Zili Sloboda, DEPR, participated with Jaylan Turkkan, Steve Zukin and Tim Condon in a meeting of NIH Offices and Institutes coordinated by the Robert Wood Johnson Foundation to discuss priorities for tobacco prevention research held on October 8, 1997.

Dr. Zili Sloboda, DEPR, served as an advisor to the Porter Novelli on design issues relative to the ONDCP National Youth Anti-Drug Campaign along with NIDA researchers: Gil Botvin, Mary Ann Pentz, Lloyd Johnston, Phil Palmgreen, and Tony Biglan on October 20, 1997.

On November 12, 1997, Dr. Zili Sloboda, DEPR, participated in and cochaired a joint meeting with ONDCP on modelling drug use over time. NIDA grantees in attendance were: Jim Anthony, Lloyd Johnston, Patrick O'Malley, and Denise Kandel.

Ann Blanken, DEPR, participated in the Join Together training seminar for Fighting Back Information Specialists which was held at Brandeis University on September 23-26, 1997. A major goal of the Fighting Back program for the next five years is to have drug and alcohol abuse decline in a measurable way in each community. Ms. Blanken spoke about NIDA's Community Epidemiology Work Group as a model for the Join Together effort, the importance of community-level assessment, monitoring approaches and potential data sources.

Richard H. Needle, Ph.D., M.P.H., Chief, Community Research Branch, DEPR, gave a presentation on "Drug Abuse and HIV Research in the Next Century: What Anthropology Has to Contribute" at the annual meeting of the American Anthropological Association, November 20, 1997 in Washington, D.C.

On November 10, 1997, Andrea Kopstein of DEPR/ERB, presented a paper at the American Public Health Association Meeting titled: "Trends for Self-Reported Incidents While Driving After Drinking Alcohol for High School Seniors."

Mr. Nicholas Kozel, DEPR, chaired the 43rd biannual meeting of the Community Epidemiology Work Group (CEWG) which was held in Phoenix, Arizona on December 9-12, 1997.

Elizabeth Robertson, Ph.D., DEPR, represented NIDA at the Center for Substance Abuse Prevention, National Center for the Application of Prevention site visits in Minneapolis, MN, Springfield, IL, Reno, NV, and Portland, OR, on September 25-29, 1997.

Dr. Elizabeth Robertson, DEPR, participated in a Work Group meeting of the Positive Youth Development Group of the HHS Secretary's Initiative on Youth Substance Abuse Prevention on September 10, 1997.

The Workgroup on Preventing Substance Abuse and Mental Health Problems in Managed Health Care Settings co-sponsored by the National Mental Health Association and CSAP is preparing a publication for dissemination to practitioners. The group last met on December 4-5, 1997. Dr. Elizabeth Robertson attended the meeting and serves on the writing team.

Dr. Elizabeth Robertson chaired a workgroup meeting on the topic of Drug Abuse Prevention Through Family-Focused Health Care, at the Double Tree Hotel in Rockville, on September 11, 1997.

Peter Hartsock, Dr.P.H., CRB/DEPR gave a presentation on "Drug-Related AIDS in the Commonwealth of Independent States," at the June 1997 meeting of the Community Epidemiology Work Group, in Washington, D.C.

Susan Coyle, Ph.D., DEPR/Community Research Branch, participated in a workshop on "Drug Abuse and HIV Infection: Behavioral and Neurologic Aspects" at the NIH Research Festival, October 6-10, 1997, in Bethesda, MD. Dr. Coyle gave a presentation on the use of effects of outreach-based HIV interventions for drug users.

Elizabeth Lambert, M.Sc., CRB/DEPR, in collaboration with Fe Caces, Ph.D. and Tracy Gordon, M.P.S. of CSR, Inc., and Richard H. Needle, Ph.D., M.P.H. and Helen Cesari, M.S., of CRB/DEPR developed and presented a poster on "Pregnant Drug Users in an AIDS Outreach/Intervention Research Program: Profiles of HIV Risk," at the 1997 annual meeting of the American Public Health Association in Indianapolis.

Dr. Monique Ernst, IRP, presented "The Dopaminergic Hypothesis of Attention-Deficit/ Hyperactivity Disorder" at Grand Rounds, Brookhaven National Laboratory, Brookhaven, NY on August 20, 1997.

Dr. Monique Ernst, IRP, presented "Neuroimaging in Attention-Deficit/Hyperactivity Disorder" at the National CHADD Meeting held in Towson, MD on October 4, 1997.

Dr. Edythe D. London, IRP, presented "Neuroimaging: Assessing Sites of Action and Their Implications" at the ASAM Conference entitled "State of the Art in Addiction Medicine-- Models & Measures of Early Recovery: Implications for New Treatment Strategies" held in Washington, D.C., October 24-25, 1997.

Dr. James A. Bell, IRP, presented "Long-term Agonist Effects of Amphiphile Congeners of Etorphine Suggest Interfacial Location of m-opioid Receptor Recognition Site" at the 27th Annual Meeting of the Society for Neuroscience held in New Orleans, LA, October 25-30, 1997.

Dr. Monique Ernst, IRP, presented "Cognitive Activation in Nicotine Withdrawal" at the 27th Annual Meeting of the Society for Neuroscience held in New Orleans, LA, October 25-30, 1997.

Dr. Steven Grant, IRP, presented "Drug Abusers Show Impaired Performance on a Test of Orbitofrontal Function" at the 27th Annual Meeting of the Society for Neuroscience held in New Orleans, LA, October 25-30, 1997.

Ms. Geraldine R. Hill, IRP, presented "[N,N-dimethylamino)methyl]-2- (3,4-dichlorophenyl-acetamide)-1,2,3,4-

tetrahydroisoquinoline binding to k opioid receptor subtypes" at the 27th Annual Meeting of the Society for Neuroscience held in New Orleans, LA, October 25-30, 1997.

Dr. Andrew G. Horti, IRP, presented "[18F]-2-Fluoro-5-(2(s)-azetidylmethoxy)pyridine, a radioligand for in vivo imaging of central nicotinic acetylcholine receptors (nAChRs)" at the 27th Annual Meeting of the Society for Neuroscience held in New Orleans, LA, October 25-30, 1997.

Dr. Edythe D. London, IRP, presented "Cerebral Metabolism During Cue-Elicited Cocaine Craving" at the 36th Annual Meeting the American College of Neuropsychopharmacology held in Kamuela, Hawaii, Dec. 8-12, 1997.

Dr. Evan D. Morris, IRP, presented "Can PET Accurately Measure Receptor Binding Potential in the Rhesus Monkey Striatum? Computer Simulations Can Help" at the 27th Annual Meeting of the Society for Neuroscience held in New Orleans, LA, October 25-30, 1997.

Dr. D. Bruce Vaupel, IRP, presented "Effect of Cocaine-related Environmental Stimulation on the Spontaneous Electroencephalogram in Polydrug Abusers" at the 27th Annual Meeting of the Society for Neuroscience held in New Orleans, LA, October 25-30, 1997.

Dr. Monique Ernst, IRP, presented a seminar at NIH PET Meeting entitled "Neurochemical Substrates of Nicotine Withdrawal" held in Bethesda, MD on November 14, 1997.

Dr. Amy H. Newman, IRP, was invited to present a lecture entitled: "Novel 3a-(Diphenylmethoxy) tropane Analogs as Probes for the Dopamine Transporter" at the Department of Chemistry, University of Bristol, Bristol, England, U.K. in October, 1997.

Dr. Amy H. Newman, IRP, was invited to present a lecture entitled "Novel 3a-(Diphenylmethoxy) tropane Analogs as Probes for the Dopamine Transporter" at the Department of Organic and Medicinal Chemistry, Research Triangle Institute, Research Triangle, North Carolina in December, 1997.

Dr. Jonathan L. Katz, IRP, was invited to present a lecture entitled "Behavioral Pharmacology and Drug Abuse" at the Department of Pharmacology, George Washington University, Washington, D.C. in January, 1998.

Cadet J.L. Regulation of Cell Death-related Genes by Methamphetamine in Immortalized Neural Cells. Presented at the Intl. Soc. Neurochemistry/American Society for Neurochemistry held in Hamilton, Bermuda on July 16-18, 1997.

Subramaniam, J.S., Ladenheim, B., and Cadet, J.L. METH-induced Changes in Antioxidant Enzymes and Lipid Peroxidation in Copper/Zinc Superoxide Dismutase Transgenic Mice. Presented at the Society for Neuroscience annual meeting held in New Orleans, LA, October 25-30, 1997.

Asunama, A., Hirata, H., and Cadet, J.L. Attenuation of 5-hydroxydopamine-induced Dopaminergic Nigrostriatal Lesions in Superoxide Dismutase Transgenic Mice. Presented at the Society for Neuroscience annual meeting held in New Orleans, LA, October 25-30, 1997.

Herning, R. EEG Differences in HIV+ and HIV- Cocaine Abusers. Presented at The American Medical Electroencephalographic Association (AMEEGA) meeting held in Baltimore, MD, November 7-8, 1997.

McCoy, M., Mann, H. and Cadet J.L. HFGF-b and rhTGF-a Protects Against Methamphetamine-induced Cell Death in the Neuroglioma Cell Line, H4. Presented at the Society for Neuroscience annual meeting held in New Orleans, LA, October 25-30, 1997.

Hayashi, T., Su, T.-P, Kagaya, A., Oyamada, T., and Yamawaki, S. Enhancement of N-methyl-d-aspartate-induced [CA2+]I Response by Sulpiride: Involvement of Protein Kinase and Modulation by Sigma Ligands. Presented at the Society for Neuroscience annual meeting held in New Orleans, LA, October 25-30, 1997.

Tsao L.I., Ladenheim B.N., Cadet J.L., and Su, T.-P. The Delta Opioid Peptide DADLE Blocked and Reversed METH-induced Dopamine Transporter Loss in Mouse Brain without Any Apparent Effect on Dopamine Level. Presented at the Society for Neuroscience annual meeting held in New Orleans, LA, October 25-30, 1997.

Yeh, S.Y. Chloropheniramine (CPA) Protects Against 3,4-methylene-doxymeth-amphetamine (MDMA)-induced Depletion of Indoles in Rats. Presented at the Society for Neuroscience annual meeting held in New Orleans, LA, October 25-30, 1997.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****February, 1998**

Media and Education Activities

Press Releases

December 20, 1997 -Drug Use Survey Shows Mixed Results for Nation's Youth -Use Among Younger Adolescents Appears to be Slowing. HHS/NIDA released the results of the 23rd annual Monitoring the Future Survey showing that after years of dramatic increases, illicit drug use among eighth graders remained stable for most drugs and decreased slightly for marijuana, cigarettes, and certain other substances. The survey found general stability among the proportion of high school seniors and 10th graders using most illicit drugs although there were some increases, generally, in lifetime use. *(The Monitoring the Future study was released by President Clinton during his December 20 radio address. On December 19, Dr. Leshner joined General McCaffrey, Secretary Shalala for a press briefing on the study findings.)*

December 15, 1997 -New Research Documents Success of Drug Abuse Treatments. At least four major types of drug abuse treatment can be extremely effective in reducing drug use, producing decreases in illegal acts and increases in full-time work. These and other findings from the Drug Abuse Treatment Outcome Study (DATOS) were published in the December volume of *Psychology of Addictive Behaviors*.

December 4, 1997 -NIDA Infobox, Science-based Facts on Drug Abuse and Addiction. NIDA Infobox, a new information resource of science-based facts about drug abuse and addiction was announced at NIDA's Fourth Annual Constituent Conference. Infobox offers fact sheets via fax-on-demand, mail or TTY; access 24 hours a day in English, Spanish or TTY; and brief audio messages on drugs of abuse and other topics.

November 19, 1997 -NIH Consensus Panel Recommends Expanding Access to and Improving Methadone Treatment Programs for Heroin Addiction. The NIH consensus panel strongly recommended broader access to methadone maintenance treatment programs for people who are addicted to heroin or other opiate drugs and that the Federal and State regulations and other barriers impeding this access be eliminated.

October 8, 1997 -New Science-Based Drug Education Materials Available for Students and Teachers. Dr. Alan I. Leshner, NIDA Director announces the availability of Mind Over Matter, a new series of drug education materials for students in grades five through nine. Six colorful, oversized, glossy magazines that unfold into posters explore the effects drugs have on the brain and also help encourage student interest in science.

September 29, 1997 -Preventing and Treating Heroin Use is Focus of National Research Conference. HHS Secretary Donna Shalala, General Barry McCaffrey, and Dr. Alan Leshner issued a challenge to over 500 attendees representing national drug abuse organizations, prevention and treatment practitioners, the media, criminal justice and law enforcement personnel, and policy makers, to use available research to respond to the changing problem of heroin use in the U.S. Secretary Shalala and General McCaffrey delivered keynote addresses at the first national research-based conference on heroin use and addiction, sponsored by NIDA and held at the Sheraton Washington Hotel in Washington, D.C., September 29 and 30, 1997.

September 25, 1997 -New Imaging Techniques Provide Brain Map of Cocaine-Induced Euphoria and Craving. Using advanced brain imaging techniques, researchers from Harvard Medical School and Massachusetts General Hospital have identified the brain circuits activated during the distinct experiences which follow cocaine use. Their research shows that different regions of the brain are activated during a cocaine "rush", cocaine "high", and cocaine craving. The results of this study were published in the September 25 issue of Neuron.

August 8, 1997 -NIH Releases Panel's Report on the Possible Medical Uses of Marijuana. NIH has made available the report of the group of experts it convened February 19-20, 1997, to review the scientific data concerning the potential therapeutic uses for marijuana and the need for, and feasibility of, additional research.

Other Press Activities

Print Media

January 4, 1998 -Associated Press Wire Story -Human Experiments Use MRI ; Doctors Map Cocaine's Effects on the Brain. Dr. Leshner was interviewed by AP Science Editor, Daniel Haney for this story that was disseminated to newspapers nationwide.

December 1997 -Ft. Lauderdale Sun Sentinel Features NIDA staff and research in editorial series. Drs. Leshner and Sloboda were interviewed by Sun Sentinel editorial writer, Jim Driscoll, for a five-part series of editorials on aspects of drug abuse and addiction. The series featured Dr. Leshner's discussion of the nature of addiction and the needs of those who are addicted. Dr. Sloboda spoke at length about prevention research findings and how they can be applied in a variety of communities. The Sun Sentinel has the second largest circulation in Florida.

October 20, 1997 -Editorial Board Meeting, Philadelphia Daily News Dr. Leshner met with editors of the Philadelphia Daily News while in Philadelphia for the NIDA Town Meeting. Dr. Leshner was also interviewed by the Philadelphia Inquirer, the Jewish Exponent, and the New Scientist while in Philadelphia.

October 20, 1997 -Straight Talk Magazine Reprint Straight Talk is a health-oriented magazine distributed to high school seniors nationwide. A special reprint of an issue featuring a student interview with Dr. Leshner was produced and distributed at the Philadelphia Town Meeting as well as at NIDA exhibits and Science Education seminars.

September 29-30, 1997 -NIDA's National Heroin Conference NIDA maintained a press room and support for press attending and covering the Heroin Conference. Over 20 journalists registered and attended the conference. Numerous print articles appeared in papers nationwide, including an article in the New York Times on the conference and research presented during the conference.

November 1997 -Washingtonian Magazine Dr. Leshner was interviewed for a feature article by Harry Jaffe entitled "Not in This House", a story of drug use in the Washington metropolitan area.

Broadcast Media

October 8, 1997 -Dr. Leshner was interviewed by Minnesota Public Radio, the largest broadcast radio station in the Midwest, at their studios in St. Paul. Dr. Leshner spoke on understanding drug abuse and addiction, new findings on prevention and treatment, and NIDA's new science education materials.

November 16, 1997 -Dr. Leshner appeared on WRC TV "Viewpoint" a local weekly public affairs program. He participated on a panel to discuss teen drug use, particularly in the Washington metropolitan area and ways to prevent drug use.

Special Projects

December 2-3 -Launch of NIDA Infobox

NIDA's newest information dissemination system was introduced at the Fourth Annual Constituent Conference in Lansdowne, Virginia. By calling a 24-hour toll-free number (1-888-NIH-NIDA or -644-6432), any individual can access research-based fact sheets on 40 topics, in English or Spanish. Callers have the option of receiving fact sheets by either fax or mail, and may also listen to brief audio messages on each topic. The system accommodates the hearing-impaired at 1-888-TTY-NIDA or -889-6432. NIDA Infifax is the first network-based system of its kind at NIH and the third in the Federal government.

September 1997 -The Essence of Drug Addiction

Dr. Leshner's article on addiction was distributed to newspapers nationwide. To date, 200 newspapers in 12 different states with a readership of 8.2 million have run the article.

Science Education

Launch of "Mind of Matter" Educational Series, October 8, 1997.

Dr. Alan Leshner launched NIDA's latest science education materials, Mind Over Matter at the Annual Conference of the National Association of Biology Teachers in Minneapolis, Minnesota. Developed as part of NIDA's Science Education Program, Mind Over Matter is a six part magazine series that uses a brightly colored format to explore the brain's response to drugs. It prompts students to think about the effects of drugs on their brains and seeks to discourage drug use by children. In addition, this series contains an underlying message that neuroscience is a challenging and exciting field and anyone, regardless of race or sex, can become a scientist. The six magazines focus on marijuana, opiates, inhalants, steroids, stimulants, and hallucinogens. On the reverse of the unfolded magazines is an artistic photograph of a brain image with a quotation that inspires curiosity about science. The series includes a comprehensive teacher's guide that provides additional information about each of the drugs, as well as classroom activities that can be used to reinforce the concepts in the magazine.

Slide Teaching Packet Now Available on the NIDA Website.

In response to the overwhelming number of requests for NIDA's Slide teaching Packet for Scientists: The Brain and the Actions of Cocaine, Opiates, and Marijuana, the packet is now available on NIDA's home page. Detailed instructions are provided for those wishing to make either slides or overheads. Although developed for neuroscientists to use when speaking to high school students, the teaching packet has become popular with both high school and college teachers.

Planned Meetings

National Conference on Drug Abuse Treatment: From Research to Practice will be held on April 8-9, 1998 at the Sheraton Washington Hotel in Washington D.C. Among the highlights at this major NIDA conference will be an update on models of effective drug abuse treatment; a discussion of effective behavioral and pharmacological drug abuse treatments; and an overview of the state of current research on special populations.

Cognition and Emotion: Applications to Drug Abuse, a miniconvention sponsored by NIDA's Behavioral Science Working Group with the American Psychological Society will occur on the day preceding the 10th anniversary meeting of the APS, on Thursday May 21, 1998 at the Washington (D.C.) Hilton. This followup to last year's Cognitive Science meeting will focus on emotion, mood, and arousal as important modulators of decision making and judgment, and by extension to risky and impulsive behavior surrounding drug initiation and relapse. Leading researchers in cognition, decision theory and emotional factors will be featured at the miniconvention, including Alan Marlatt, George Loewenstein, Antoine Bechara, Alice Isen and Damaris Rohsenow, among others.

Addicted to Nicotine: Recent Research on Causes, Prevention and Treatment will be held on July 27-28, 1998 in the Natcher Auditorium (NIH Campus, Bethesda, MD). This 2-day national conference will present the latest research findings on the behavioral, cognitive and neurobiological sources of nicotine addiction, prevention of tobacco product use and dependence, and state-of-the art treatment strategies. The conference will be comprised of several multidisciplinary symposia and keynote speakers.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****February, 1998**

Publications

Research Monographs

Beyond Therapeutic Alliance: Keeping The Drug-Dependent Individual in Treatment--Research Monograph 165, NIH Pub. 97-4142.

This monograph reviews current treatment research on the best ways to retain patients in drug dependence treatment and to guide clinicians and clinical researchers on how to deal with this issue. This monograph addresses the issue of keeping addicted individuals in treatment long enough for the treatment to have a positive effect.

The Validity of Self-Reported Drug Use: Improving the Accuracy of Survey Estimates-- Research Monograph 167, NIH Pub. 97-4147.

This monograph examines recent research on validity using internal or external criteria and examines methodological advances that can contribute to improved estimates of drug use in a survey environment.

Rural Substance Abuse: State of Knowledge and Issues--Research Monograph 168, NIH Pub. 97-4177.

This monograph provides significant information about the special nature and context of rural communities, particularly relative to urban settings, that might impact patterns of alcohol and drug consumption and the delivery of services to prevent and treat alcohol and drug abuse.

Meta-Analysis of Drug Abuse Prevention Program--Research Monograph 170, NIH Pub. 97-4146.

The purpose of this monograph is to inform the drug abuse prevention research and practitioner community of the latest advances in research integration methods and scientific findings in the area of drug abuse prevention programs.

Treatment of Drug-Dependent Individuals with Comorbid Mental Disorders--Research Monograph 172, NIH Pub. 97-4172.

The purpose of this monograph is to promote the effective treatment of individuals with comorbid mental and addictive disorders by reporting state-of-the-art science treatment research on individuals with comorbid mental and addictive disorders.

Pharmacokinetics, Metabolism and Pharmaceutics of Drug Abuse--Research Monograph 173, NIH Pub. 97-4141.

This monograph provides the current status of research on metabolism, pharmacokinetics and pharmacodynamics of drugs of abuse. It also addresses the ability of the drugs to effectively cross the various membrane barriers and to reach receptors depending upon the nature of the drug moiety.

The Problems of Drug Dependence 1996: Proceedings of the 58th Annual Scientific Meeting of the College on Problems of Drug Dependence--Research Monograph 174, NIH Pub. 97-4236.

This publication updates and provides the most current information regarding the findings of preclinical and clinical researchers. The contents are written by the participants at the annual scientific meeting.

Medications Development for the Treatment of Cocaine Dependence: Issues in Clinical Efficacy Trials-- Research Monograph 175, NIH Pub. 97-4125.

This monograph is intended to be used as a state-of-the-art handbook by clinical investigators, pharmaceutical scientists and treatment researchers to effectively conduct clinical trials to evaluate the safety and efficacy of potential treatment medications for cocaine addiction.

Other Publications

Epidemiologic Trends in Drug Abuse: Community and Epidemiology Work Group-- December 1996 - Advance Report, NIH Pub. 97-4203.

The Advance Report is biannual and provides descriptive information on the most recent significant trends, emerging problems and populations at risk.

Epidemiologic Trends in Drug Abuse: Community and Epidemiology Work Group-- December 1996 Volume I: Highlights and Executive Summary, NIH Pub. 97-4204.

This publication provides a detailed and quantitatively driven overview of current drug abuse patterns and trends. The report provides program administrators and officials with specific indicators and ethnographic information on current patterns and trends as well as emerging problems.

Epidemiologic Trends in Drug Abuse: Community and Epidemiology Work Group-- December 1996 Volume II: Proceedings, NIH Pub. 97-4205.

This publication provides an in-depth analysis of epidemiologic trends and special reports as reported at the annual meeting of the Community Epidemiology Work Group.

Epidemiologic Trends in Drug Abuse: Community and Epidemiology Work Group--June 1997 -Advance Report.

The Advance Report is biannual and provides descriptive information on the most recent trends, emerging problems and populations at risk.

Epidemiologic Trends in Drug Abuse: Community and Epidemiology Work Group--June 1997 Volume I: Highlights and Executive Summary.

Volume I provides a detailed and quantitatively driven overview of current drug abuse patterns and trends. The report provides program administrators and officials with specific indicators and ethnographic information on current patterns and trends as well as emerging problems.

La Marijuana: Lo Que Los Padres Deben Saber (Marijuana: What Parents Should Know) Spanish Version, NIH Pub. 95-4036.

Presents answers to some of the most frequently asked questions of parents about marijuana, the latest scientific information, suggestions about how to talk to teens about marijuana use.

La Marijuana: Informacions Para Los Jovenes (Marijuana: Facts for Teens) Spanish Version, NIH Pub. 95-4037.

Presents answers to some of the most frequently asked questions of teens about marijuana, the latest scientific information and the words of teenage users and non-users who communicate their own reactions to marijuana use.

National Survey Results on Drug Use From The Monitoring The Future, 1975-1995, Volume I -Secondary School Students, NIH Pub. 96-4139.

This two-volume publication reports the results of the 21st national survey of drug use and related attitudes among American high school seniors, the 16th such survey of American college students, and the fifth such survey of eighth and tenth grade students. Volume I contains the results from the secondary school samples of eighth, tenth, and twelfth graders. The results from college students and young adults are reported in Volume II.

National Survey Results on Drug Use From The Monitoring The Future, 1975-1995, Volume II: College Students and Young Adults, NIH Pub. 96-4140.

This is the second volume in a two-volume set reporting the results of all surveys through 1995 from the Monitoring the Future study of American secondary school students, college students, and young adults. This volume provides the results of follow-up surveys of the graduating high school classes of 1976 through 1994 as these respondents have progressed through young adulthood.

Preventing Drug Abuse Among Children and Adolescents, NIH Pub. 97-4212 -(Also reprinted in 1997 with

minor revisions).

This guide is designed to provide important research-based concepts and information to further efforts to develop and carry out effective drug abuse prevention programs. The answers were developed in consultation with prevention scientists. This guide presents an overview of the research on the origins and pathways of drug abuse, the basic principles derived from effective drug abuse prevention research, and the application of research results to the prevention of drug use among young people.

Research Report Series

Heroin: Abuse and Addiction, NIH Pub. 97-4165.

This publication provides information on the prevalence of heroin abuse, methods of use, short-and long-term effects of heroin abuse, and the medical complications of chronic abuse. Describes effective treatment for heroin addiction. Lists resources to learn more about heroin abuse.

Research Dissemination Package

Drug Abuse Prevention Package: Brochure -NIH Pub. 97-4109.

Drug Abuse Prevention: What Works -NIH Pub. 97-4110.

Drug Abuse Prevention: Community Readiness for Drug Abuse Prevention: Issues, Tips, and Tools -NIH Pub. 97-4111.

Drug Abuse Prevention and Community Readiness: Training Facilitator's Manual -NIH Pub. 97-4112.

This package provides drug abuse prevention practitioners with information they can use to prepare their communities for drug abuse prevention programming and to select prevention strategies that effectively address the needs of their local communities. It discusses factors associated with community readiness and ways to assess and increase such readiness. The materials provide an overview of three prevention strategies, the research which has shown these models to be effective and program descriptions which illustrate each prevention approach.

Stand Alone

Drug Abuse Prevention for the General Population -NIH Pub. 97-4113.

This publication discusses the history and key features of universal prevention programs. Project START--a community-wide program to teach adolescents skills to counteract psychosocial influences that can lead to drug abuse--is described as an illustration.

Drug Abuse Prevention for At-Risk Groups -NIH Pub. 97-4114.

This publication discusses the history and key features of selective prevention programs. The Strengthening Families Program--a family-focused program targeted children ages 6 to 10 whose parents are substance abusers--is described as an illustration.

Drug Abuse Prevention for At-Risk Individuals -NIH Pub. 97-4115.

This publication discusses the history and key features of indicated prevention programs. The Reconnecting Youth Program--a school-based program targeting 9th-through 12th-grade students who are at risk for substance abuse, school failure, social problems, delinquency or antisocial behaviors or psychological problems--is described as an illustration.

NIDA NOTES

July/August 1997 -NCADI NN0023.

This issue highlights drug abuse treatment for the homeless, describing one in New York City and one in Birmingham, Alabama. The issue announces the launching of a NIDA drug abuse treatment initiative, and the Director's Column discusses that initiative. A special report on understanding the genetic roots of addiction is included. Two other stories look at a steroid abuse prevention program and how gender affects drug abuse and psychiatric disorders.

May/June 1997 -NCADI NN0022.

The lead articles in this issue make up a special section, "Children on the Brink: Youths at Risk of Drug Abuse." The three articles in the section describe two prevention programs that work with families, two prevention programs that work in high schools, and an epidemiologic study of drug abuse among runaway and homeless youths. The Director's Column highlights advances in drug abuse prevention research. Other articles look at compounds that show strong promise for treating cocaine addiction and gender differences in nicotine addiction. The tear-off guides researchers to sources of information on applying for grants.

Science Education Materials

Mind Over Matter: The Brain's Response to Steroids -NIH Pub. 97-3860.

Mind Over Matter: The Brain's Response to Hallucinogens -NIH Pub. 97-3858.

Mind Over Matter: The Brain's Response to Stimulants -NIH Pub. 97-3857.

Mind Over Matter: The Brain's Response to Opiates -NIH Pub. 96-3856.

Mind Over Matter: The Brain's Response to Inhalants -NIH Pub. 96-4038.

Mind Over Matter: The Brain's Response to Marijuana -NIH Pub. 96-3859.

This eye-catching series encourages teens in grades 5 through 9 to reject drug use by teaching them about the effects of drugs on the brain. In each magazine, "Sara Bellum" takes students on a scientific journey to learn about the brain's complex responses to specific drugs. A brightly colored poster appears on the back of each magazine.

Mind Over Matter: The Brain's Response to Drugs: Teacher's Guide, NIH Pub. 98-4248.

It includes chapters on stimulants, hallucinogens, inhalants, marijuana, opiates, and steroids; each of which describes the effects of specific drugs or drug types on the anatomy and physiology of the brain and the body. Each chapter also contains activities that can be used in the classroom. The background information and lesson plans contained in this guide, when used in combination with the magazines in the series, will promote an understanding of the physical reality of drug use, as well as curiosity about neuroscience.

Cohen, P.J. Immunization for Prevention and Treatment of Cocaine Abuse: Legal and Ethical Implications. *Drug and Alcohol Dependence*, 48, pp. 167-174, 1997.

Cohen, P.J. The Placebo is not Dead: Three Historical Vignettes, IRB, In Press.

Glowa, J., LeSage, M., Stafford, D., and Vocci, F. Novel Pharmacotherapies for Cocaine Abuse-1995 to Present. *Expert Opinion in Therapeutic Patents*, 7(12), pp. 1459-1476, 1997.

Sparenborg, S., Vocci, F., and Zukin, S. Peripheral Cocaine-Blocking Agents: New Medications for Cocaine Dependence: An Introduction to Immunological and Enzymatic Approaches to Treating Cocaine Dependence reported by Fox, Gorelick, and Cohen in the immediately succeeding articles, (see pages 153-174). *Drug and Alcohol Dependence*, 48, pp. 149-151, 1997.

Hamawy, M.M., Swieter, M., Mergenhagen, S.E. and Siraganian, R.P. Reconstitution of High Affinity IgE Receptor-Mediated Secretion by Transfecting Protein Tyrosine Kinase pp125FAK. *J Biol Chem* 272: pp. 30498-30503, 1997. This work showed that secretion from mast cells initiated by aggregating cell surface receptors for IgE requires focal adhesion kinase. It also showed that neither the ATP binding site nor the autophosphorylation site on FAK were needed to subserve this function.

Sagawa, K., Kimura, T., Swieter, M. and Siraganian, R.P. The Protein-Tyrosine Phosphatase SHP-2 Associates with Tyrosine-Phosphorylated Adhesion Molecule PECAM-1 (CD31). *J Biol Chem* 272: pp. 31086-31091, 1997. This work showed that specific physical and functional interactions of a cytoplasmic protein tyrosine phosphatase and a transmembrane cellular adhesion molecule were dramatically influenced by the secretory process in mast cells.

Pilotte, N.S., *Neurochemistry of Cocaine Withdrawal. Current Opinions in Neurology*, 10, pp. 534-538, 1997.

Robertson, E.B. and Donnermeyer, J.F. Illegal Drug Use among Rural Adults: Mental Health Consequences and Treatment Utilization. *American Journal of Drug and Alcohol Abuse*, 23(3): pp. 467-484, 1997.

Gfroerer, J., Wright, D., and Kopstein, A. Prevalence of Youth Substance Use: The Impact of Methodological Differences between Two National Surveys. *Drug and Alcohol Dependence*, 47(1): pp. 19-30, July 25, 1997.

Yesalis, C.E., Barsukiewicz, C.K., Kopstein, A.N., and Bahrke, M.S. Trends in Anabolic-Androgenic Steroid Use Among

Adolescents. Archives of Pediatric & Adolescent Medicine, 151: pp. 1197-1206, December 1997.

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National Institute on Drug Abuse

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Staff Highlights

Honors and Awards

The following individuals/groups received the **NIDA Director's Award** in October 1997:

Pamela Goodlow, SPO/OD

Gary Fleming, GMB/OPRM

Gloria Lester, PFMB/OPRM

Tina McDonald-Bennett, IRMB/OPRM

Catherine Mills, GMB/OPRM

Maryann Postorino, MASB/OPRM

Grants Management Branch, OPRM:

- Debra Battle-Dudley
- Debra Carle
- David Fenimore
- Gary Fleming
- Diana Haikalis
- Christine Kidd
- Mark Lombardi
- Jack Manischewitz
- Catherine Mills
- Le-Hong Nguyen
- Daisey Parker
- Deborah Wertz

Robin Mackar, SPB, OSPC

Mary Mayhew, SPB, OSPC

DBR Secretaries Roundtable:

- Anner Grantham
- Anne Hannessian
- Doug Janes
- Shelly Simmons

Chris Ann Davis, TRB/DCSR

Joseph Frascella, ECNB/DCSR
Lisa Simon Onken, TRB/DCSR
Elizabeth Rahdert, TRB/DCSR
Susan Coyle, CRB/DEPR
Arnold Mills, CRB/DEPR
Naimah Weinberg, ERB/DEPR
Janice Carico, MAB/DIR
Mary Abreu, PTB/MDD
Nora Chiang, CPB/MDD
Joanne Grant, RAB/MDD
Steven Sparenborg, PTB/MDD
Robert Walsh, RAB/MDD

The following individual received a **Commissioned Corp Award** in October 1997:

Steven Sparenborg -- PHS Achievement Medal

The following individuals/groups received an **EEO Award** in October 1997:

Rita Liu, BSRB/OEPR
Dorothea Moon, TRB/DIR
NIDA Special Populations Office/OD:

- Lula Beatty
 - Mario DeLaRosa
 - Pamela Goodlow
 - Flair Lindsey
-

The following individuals received awards recognizing **30 Years of Federal Service** in October 1997:

Gerald Brodsky, MASB/OPRM
David Fenimore, GMB/OPRM
Joanne Grant, RAB/MDD
Laura Rosenthal, OD/OPRM

Dr. Hari Singh received the Federal Asian Pacific American Council (FAPAC) outstanding service Award in September 1997 in recognition of his outstanding contribution to the FAPAC. He serves as the Chairperson of the FAPAC Constitution & Bylaws committee, and FAPAC Chapter Committee on the National level. Dr. Singh also represents the NIH Asian Pacific Islander Organization at the Council.

Peter Hartsock, Dr. P.H., CRB/DEPR, has been inducted into the St. Petersburg, Russia Society of Scientists and Scholars, in recognition of his 20 years of work helping to build strong research collaborations and partnerships with Russia and the former Soviet Union.

Staff Changes

Ana Anders, formerly of SAMHSA joined NIDA's Special Populations Office on December 7, 1997.

Regina Berthold joined NIDA on December 21, 1997 as a Secretary in the Office of the Director. Ms. Berthold was formerly with the National Cancer Institute.

In November, 1997, **Dr. Robert Caudle** joined the Behavioral Neurobiology Research Branch in the Division of Basic Research. Dr. Caudle is a neurophysiologist and his program will include neuroadaptive mechanisms. He comes to NIDA from the National Institute of Dental Research where he studied the neurophysiology and pharmacology of opiate receptor mechanisms.

Frank Feustel, formerly with Orkland Corporation joined OPRM's Information Resources Management Branch as a Computer Specialist on October 26, 1997.

Robert "Paul" Freund joined NIDA's Executive Secretariat as an Office Automation Clerk on December 21, 1997.

Jessica Grantling, formerly with the Department of Agriculture, joined NIDA on September 12, 1997 as a Secretary in OSPC's Science Policy Branch.

Penny Holland joined the Public Information Branch of OSPC in December as a writer/editor. Previously, she was a public affairs specialist at SAMHSA's Center for Mental Health Services (CMHS) and FDA's Office of Public Affairs. Her experience includes acting as media officer, writing speeches for the CMHS Director, producing media advisories, organizing exhibit plans, and coordinating publications production. As a part of the publications/marketing team at NIDA, she will be working on expanding marketing efforts for publications and the web site.

Dr. David Shurtleff was selected to serve as Acting Deputy Director in the Division of Basic Research, NIDA.

Dr. Rita Liu has been appointed as the Receipt and Referral Officer for NIDA. In this capacity, she coordinates committee assignments and program referrals within the Institute, and she serves as NIDA's liaison with the Center for Scientific Review.

Monglan "Lana" Le moved from NIDA's Executive Secretariat to the Office of Extramural Program Review in late August where she serves as a Grants Technical Assistant.

Grantee Honors

Edward Kaplan, Ph.D., of the Yale University School of Organization and Management, is the recent recipient of the prestigious Ira V. Hiscock Award, from the Connecticut Public Health Association. Dr. Kaplan was recognized for "his dedication to the linking of innovative research with the application of measures to improve health within the community and to honor his contribution to advancing the scope of public health practice in the interest of improving community and individual health status."

Thomas Wills, Ph.D. was promoted to Professor in the Ferkauf Graduate School of Psychology (of Yeshiva University). Dr. Wills was also appointed to the editorial board for Personality and Social Psychology Bulletin, the publication of Division 8 of the American Psychological Association.

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