National Institute on Drug Abuse

Director's Report

to the

National Advisory Council on Drug Abuse

September, 1998

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Research Findings

Basic Research

Mouse Model for Cannabinoid Withdrawal Described

In addition to published reports by various research groups demonstrating cannabinoid dependence in monkeys and rats, Dr. Billy Martin and colleagues (Medical College of Virginia) have provided evidence of dependence in a mouse model. The work was based on behavioral observations made following administration of the cannabinoid antagonist SR141716A, used to precipitate withdrawal in mice previously given delta-9-THC. The manifestations of withdrawal in mice (e.g., tremors, disorganized movement) paralleled those found in the rat, and were found to be dependent both on the dose of chronically administered delta-9-THC (two, three, seven, and 14 days), and on the dose of SR 141716A. Cook, S.A., Lowe, J.A., Martin, B.R. *J. Pharm. Exp. Therapeutics* 285, pp. 1150-1156, 1998.

Structure-Activity Relationships in Hallucinogen Analogs

Dr. David Nichols and coworkers at Purdue University have prepared a series of tetrahydronaphtho-furans designed to incorporate chemical features of hallucinogenic phenethylamines. The compounds were expected to bind to the serotonin receptor subtype 5-HT2A based on hydrogen binding possibilities with the receptor, and on other stereochemical information. They also contain an alkylamine side chain coplanar with the phenyl ring of the phenylethylamine. The results of the study indicate that, although one of the compounds binds to the human cloned 5-HT2A and 5-HT2C receptors, they all lack LSD-like behavioral effects in drug discrimination studies, and instead, several of the compounds are potent ligands for binding to the muscarinic receptor. It was concluded that the binding site(s) of the serotonin receptor fit LSD and phenethylamines differently, possibly involving different receptor amino acid residues. Monte, A.P., Marona-Lewicka, D., Lewis, M.M., Mailman, R.B., Wainscott, D.B., Nelson, D.L., Nichols, D.E. *J. Med. Chem*. 41, pp. 2134-2145, 1998.

MDMA Administration Induces Expression of HSP70 in the Rat Brain

Heat stress or heat shock proteins were induced after a variety of neuronal injuries and pathological conditions. The inducible 70-kDA heat shock protein (HSP70) has been shown to protect against glutamate neurotoxicity and may play a similar role in ischemic tolerance. Previous studies have shown that HSP70 expression is also induced in the rat by administration of amphetamine or methamphetamine at doses of 10 mg/kg. Dr. Seiden at the University of Chicago and his research team investigated the effect of a neurotoxic dose of MDMA (40 mg/kg), a substituted amphetamine, on HSP70 synthesis in the rat at 30°C ambient temperature, using 30°C and 42°C ambient temperatures as control temperatures for the saline-treated rats. These results show that rats treated with MDMA (average core temperature 39.3°C; maximum core temperature 40.3°C) at an ambient temperature of 30°C had core

temperatures comparable to those observed in saline-treated rats exposed to an ambient temperature of 42°C (average 39.6°C; maximum 40.6°C) and higher than saline-treated rats exposed to 30°C environment (average 37.7°C). Moreover, the MDMA-treated rats also expressed HSP70 levels similar to those observed in saline-treated rats exposed to a 42°C environment. The HSP70 levels expressed by MDMA-treated rats were higher than those observed in saline-treated rats exposed to an ambient temperature of 30°C. Since HSP70's are neuroprotective in other types of toxicity, this finding suggests that HSP70's may play a role in reducing damage induced by amphetamine derivatives such as MDMA. Malberg, J.E. and Seiden, L.S., Poster, 1997. Society for Neuroscience Annual Meeting, New Orleans, LA, October 25-30, 1997.

Nitrous Oxide, the Inhalational General Anesthetic and Drug of Abuse, Is an NMDA Antagonist

Nitrous oxide (N_2O) is a general inhalational anesthetic, used widely in medicine and dentistry, but also widely abused. Its mechanism of action was unknown. Unlike other general anesthetics such as barbiturates and halothane, it does not increase inhibitory neurotransmission through GABAA receptors. An important recent discovery by John W. Olney, MD and Vesna Jevtovic-Todorovic, MD, Ph.D., of the departments of Psychiatry and Anesthesiology, Washington University, St. Louis, is that N_2O is a *N*-methyl-D-aspartate (NMDA) receptor antagonist; i.e. it decreases glutamate excitatory transmission by blocking NMDA glutamate receptors at relevant concentrations. Thus, N_2O resembles the intravenous dissociative anesthetics and drugs of abuse, ketamine and phencyclidine (PCP). Like these and other NMDA antagonists, N_2O inhibits excitotoxic neurodegeneration mediated through NMDA receptors, but unlike them produces a distinctive vacuolar injury to specific pyramidal neurons of the posterior cingulate and retrosplenial cortices (the "Olney lesion"). The Olney lesion can be prevented by drugs that enhance GABAergic inhibition. The neurotoxic properties of N_2O have the same age dependency that Olney's group had previously shown for other NMDA antagonists. One reason N_2O's mechanism was unknown was the inability of researchers to achieve appropriate concentrations in lab animals while maintaining an adequate oxygen supply. Olney's group overcame this problem with a hyperbaric chamber. Jevtovic- Todorovic, Todorovic, Mennerick, Powell, Dikranian, Benshoff, Zorumski and Olney, *Nature Medicine* 4(4), pp. 460-463, April 1998.

Receptor Mechanisms of Opioid Tolerance and Dependence by Agonists of Varying Efficacies

Dr. Fedor Medzihradsky of the University of Michigan Medical School and his team have been investigating the molecular mechanisms involved in the development of tolerance by agonists of varying efficacies. Prolonged exposure to agonists induced desensitization of the receptor as estimated by a reduction in the maximal stimulation of $[^{35}S]GTP_{\gamma}S$ binding by DAMGO. In C6 glioma cells stably expressing the mu opioid receptor, treatment with maximally efficacious concentrations of partial and full agonists reduced DAMGO-stimulated $[^{35}S]GTP_{\gamma}S$ binding. The reduction correlated with agonist efficacy where the more efficacious agonists reduced DAMGO stimulated $[^{35}S]GTP_{\gamma}S$ binding to a greater extent. Guanine nucleotide regulation of agonist binding was lower in membranes from tolerant cells. The potency of DAMGO to inhibit cAMP accumulation was lower in morphine and DAMGO tolerant cells. Pertussis toxin treatment of the cells prior to agonist treatment did not prevent the down-regulation by full agonists such as DAMGO while the ability of partial agonists was greatly impaired showing that down-regulation by full agonists proceeds almost completely in the absence of a functional G protein. These results indicate important differences in the inactivation pathways of receptors triggered by full and partial agonists. Yabaluri, N. and Medzihradsky, F. *Molecular Pharmacology*, 52, pp. 896-902, 1997.

Sigma Receptors & Abused Drugs

In papers published recently, Dr. Vadivel Ganapathy and his colleagues report isolating and cloning sigma receptors from mouse cDNA and from rat brain. They are the first group to observe that an identical sigma receptor is present in the liver, placenta, and brain of the rat. The structural information generated on this gene, especially in the mouse, has potential utility in the development of transgenic and knock-out models. Such models would be useful for studying the physiological significance of sigma receptor function and for understanding the pathologial consequences of sigma receptor dysfunction. In a parallel study, Dr. Vadivel Ganapathy and his colleagues report the structure and organization of human gene coding for the type 1 sigma receptor. Kekuda, R., et al., Biochem. Biophysical Res. Commun. 229, pp. 553-55, 1996. Seth, P., Leibach, F.H. and Ganapathy, V. *Biochem. Biophysical Res. Commun*. 241, pp. 535-540, 1997.

Lung Cancer Risk and Habitual Smokers of Marijuana, Cocaine and/or Tobacco

More frequent alterations in molecular markers and histopathologic parameters were found in the bronchial epithelium of habitual marijuana and/or cocaine smokers, who may or may not also smoke tobacco, than in non-smokers. These findings suggest that smoking marijuana and/or cocaine, like tobacco smoking, exerts field cancerization effects on bronchial epithelium which may place smokers of these substances at increased risk for the subsequent development of lung cancer. An accompanying editorial appeared with this paper. Barsky, S.H., Roth, M.D., Kleerup, E.C., Simmons, M. and Tashkin, D.P., *Journal of the National Cancer Institute*, 90(16), pp. 1198-1205, August 19, 1998.

Presynaptic Recording of Quanta from Midbrain Dopamine Neurons and Modulation of the Quantal Size

Neurons communicate with each other by releasing chemical substances from nerve terminals at specialized junctions called synapses. More than thirty years ago it was shown by Sir Bernard Katz that neurotransmitters are secreted from synaptic vesicles. The amount released from a synaptic vesicle is known as quanta because the amount of excitation produced by the release of transmitter released from a single vesicle is the same. As more vesicles are released, the amount of excitation increases in step wise or quantal fashion. The strength of the signal between two neurons can be increased by either increasing the amount of neurotransmitter stored in a single vesicle, increasing the number of vesicles that release their contents, or by increasing the sensitivity of the neighboring neurons to the neurotransmitter being released. Thus, analysis of quantal events and how synaptic transmission is regulated is key to understanding how neurons communicate with each other. The mechanisms of quantal transmission are well studied at synapses where the neurotransmitter has a rapid onset and offset. However, for a transmitter such as dopamine, a neurotransmitter implicated in mediating addiction, the mechanisms of quantal release are not well characterized because the action of dopamine has a slow onset. To overcome this problem, Dr. Sulzer and his colleagues used a technique called amperometry. Released neurotransmitter is rapidly detected as a change in current by an electrode connected to an amperometer. Dr. Sulzer and his colleagues report that dopamine is released in quantal fashion that is likely to originate from small vesicles instead of large dense core vesicles because the amount released is smaller than the amount seen in neuroendocrine cells. In addition, they observed that L-Dopa, the precursor for dopamine and glia derived growth neurotrophic factor (GDNF), a survival factor for dopamine neurons, increases the amount of neurotransmitter packaged in a single vesicle. The work by Dr. Sulzer and his colleagues lays the foundation for elucidating the modulatory actions of growth factors and neurotransmitters on dopamine transmission in the brain. By understanding how dopamine release is modulated, new therapies can be devised for the treatment of addiction, Parkinson's Disease, and schizophrenia because the neurotransmitter dopamine has been implicated in the etiologies of these diseases. Pothos, E.N., Davila, V., and Sulzer, D. *The Journal of Neuroscience*, 18(11), pp. 4106-4118, June 1, 1998.

Increased Vulnerability to Cocaine in Mice Lacking the Serotonin 1B Receptor

NIDA grantee Dr. Rene Hen and his coworkers at Columbia University, demonstrated that knockout mice lacking one serotonin receptor subtype (serotonin 1B), are more sensitive to both the motor and rewarding effects of cocaine. As a result, these knockout mice lacking the serotonin 1B subtype are more motivated to self-administer cocaine than wild-type mice. Dr. Hen and his coworkers have characterized the biochemical changes which occurred in these knockout mice which they believe relate to their preference for cocaine. These changes include an increase in the immediate early protein FosB that has been shown to be upregulated following chronic cocaine exposure. Dr. Hen and his colleagues used a large panel of techniques, such as intra-venous self-administration of cocaine and in vivo microdialysis in freely moving mice, that until recently had not been applied to transgenic mice. They demonstrated that changes in the dopaminergic system took place in these knockout mice and that these changes are likely to explain their increased responsiveness to cocaine and psychostimulants. Dr. Hen and his coworkers are in the process of generating and characterizing several lines of tissue-specific and inducible knockout mice of the 5-HT1B receptor. In conclusion, this is the first example of a gene that might be related to the large individual differences in vulnerability to cocaine that are found in rodents and humans. The identification of a candidate gene that, when mutated, is responsible for increased vulnerability to psychostimulants, has considerable implications for the understanding of the genetics of drug abuse in humans. Rene Hen, et.al. *Nature*, 393, pp. 175, June 18, 1998.

Dopamine Neurons Make Glutamatergic Synapses In Vitro

Dopamine is a neurotransmitter synthesized by neurons located in the substantia nigra and ventral tegmental areas of the midbrain. Dopamine plays a key role in the initiation of movement. Degeneration of dopamine neurons in the substantia nigra lead to the development of Parkinson's disease. Furthermore, all drugs of abuse and pleasurable stimuli appear to cause increased release of dopamine. Thus, most of the work on how dopamine neurons communicate with neighboring neurons, known as synaptic transmission, has focused on the synthesis and release of dopamine as well as the effect of dopamine on neighboring neurons. The onset of the actions of dopamine on neighboring neurons is slow and does not explain the reason that stimulating dopamine neurons also produces rapid effects on neighboring neurons. One possibility is that dopamine neurons release, in addition to dopamine, another neurotransmitter such as glutamate that has a rapid action on a neighboring neuron. To test the possibility that dopamine and glutamate are co-localized in the same neurons, Dr. David Sulzer and his colleagues at Columbia University used anatomical and electrophysiological techniques. They report that the enzyme glutaminase needed for the synthesis of glutamate, and the enzyme tyrosine hydroxylase needed for the synthesis of dopamine, are colocalized in neurons of the substantia nigra and ventral tegmental region in both rat and monkey. Excitatory actions were blocked by a glutamate antagonist suggesting that glutamate is released onto the dopamine neuron being stimulated. Application of dopamine onto the neuron prior to stimulation blocked or reduced the amount of excitation, suggesting that dopamine acts to inhibit the release of glutamate. These results suggest that neurons of the substantia nigra and ventral tegmental area exert their rapid actions via glutamate and their slower and modulatory actions via dopamine. Sulzer, D., Joyce, M.P., Lin, L., Geldwert, D., Haber, S.N., Hattori, T., and Rayport, S. Dopamine Neurons Make Glutamatergic Synapses In Vitro. *The Journal of Neuroscience*, 18(12), pp. 4588-4602, June 15, 1998.

Morphine Induces Sepsis in Mice

A recent publication has identified an action whereby morphine causes dissemination of bacteria from the gut into areas causing an immune response, inflammation and hyperemia. The end result can be toxic shock which can result in the death of the animal. Although these studies were conducted in mice, a similar result may occur in some humans as gram-negative sepsis and subsequent endotoxic shock remain major health problems in the United States. The present study examined the role of morphine in inducing sepsis. Mice who were administered morphine by the subcutaneous implantation of a slow-release pellet developed colonization of the liver, spleen, and peritoneal cavity with gram-negative and other enteric bacteria. In addition, the mice became hypersusceptible to sublethal endotoxin challenge. The effects were blocked by the simultaneous implantation of a pellet containing the opioid antagonist naltrexone. These findings show that morphine pellet implantation in mice results in the escape of gram-negative organisms from the gastrointestinal tract, leading to the hypothesis that morphine used postoperatively or chronically for analgesia may serve as a cofactor in the precipitation of sepsis and shock. In addition, morphine-induced sepsis may provide a physiologically relevant model of gram-negative sepsis and endotoxic shock. Hilburger, M.E., Adler, M.W., Truant, A.L., Meissler, J.J., Jr., Satishchandran, V., Rogers, T.J., and Eisenstein, T.K. Morphine Induces Sepsis in Mice, *Journal of Infectious Diseases*. 176, pp. 183-188, 1997. (Text taken largely from article abstract).

Reduced Delayed Hypersensitivity: Skin Reactions in Opiate Addicted Patients (OAP)

Despite the in vitro and animal evidence that opiates impair cell-mediated immunity (CMI), it is unknown whether human opiate dependence is associated with significant suppression of CMI manifested by delayed hypersensitivity skin reaction (DHR) response. Seventy-four OAP enrolled in a methadone clinic and 86 healthy volunteers (HV), were skin tested intradermally using five standardized antigens: tetanus (neat); mumps(neat); candida albicans (1:100); trichophyton mentagrophytes (1:100); and tuberculin (5 T.U.). Subjects were excluded if they had a significant illness, were on immunosuppressive medications, were HIV (+), or had known tuberculin DHR (+). Mean induration diameter (forearm long axis + perpendicular/2) were measured by "ball point pen" method using an electronic digital caliper. Demographics showed no significant age differences between OAP and HV, but significantly more males ($p = <.001$) and non-Caucasians ($p<.001$) were in the addict group. Analysis of DHR prevalence showed no significant differences between OAP & HV for tetanus ($p=.55$), candida ($p=.77$), tuberculin ($p=.85$), trichophyton ($p=.24$); borderline significance for mumps ($p=.05$); and no significant differences for individuals showing any of five reactions ($p=.53$). However, highly significant decreases in size (mm) of DHR were seen in the OAP for tetanus 32.2 percent smaller. ($P=<.001$) and mumps 30.4 percent smaller ($p=<.001$), and the other groups were too small to analyze. In the OAP, no significant differences were seen either in the prevalence or degree of DHR reactivity for any antigen between male or female or Caucasian and non-Caucasian subgroups. One group of OAP demonstrated highly

significant hypoergy rather than anergy to DHR antigens. Since tuberculin skin testing is the standard public health method for identifying infected individuals, this study suggests that criteria for positivity of DHR in OAP needs to be adjusted downward. Steinberg, P., McFadden, R.,Carlson, G.A., Bullock, M.L., Pheley, A.M., O'Hara, C.M. and Peterson, P.K. Reduced Delayed Hypersensitivity: Skin Reactions in Opiate Addicted Patients (OAP). *Journal of Allergy and Clinical Immunology*, 1(1, Part 2), S55, 1998. (Text taken largely from article abstract).

Opioid Receptors in Immune Function

This publication describes the expression and relation of opioid receptors in immune cells and their possible role in combating disease, especially in relation to humans. Delta opioid receptor (DOR) transcripts and binding sites are expressed by lymphocytes and lymphoid cell lines from several species. Direct modulation of lymphocyte function through DORs affects T cell proliferation, interleukin-2 production, chemotaxis, and intracellular signaling. Moreover, in human DOR-transfected T cells (DOR-Ju.1), delta opioids have been shown previously to mobilize intracellular calcium rapidly, to inhibit forskolin- stimulated cyclic AMP production, and to activate the mitogen-activated protein kinases ERKs 1 and 2. These observations led us to consider whether delta agonists modify T cell functions, thus affecting the expression of human immunodeficiency virus-1 (HIV-1) by CD4+ T cells. To test this hypothesis, DOR-Ju.1 cells, derived from Jurkat cells (a modified human cell line) stably transfected with a cDNA encoding the neuronal DOR, were stimulated with deltorphin or benzamide,4-[[2,5-dimethyl-4- (2-propenyl)-1-piperazinyl] (3-methoxyphenyl)methyl]-N,-, [2S-[1(S*),2a,5b]]-(9Cl) (SNC-80) prior to the addition of HIV-1. Both deltorphin and SNC-80 concentration dependently inhibited the production of p24 antigen, an index of HIV-1 expression. Inhibition was maximal with 10^{-13} to 10^{-9} M SNC- 80 (>60% reduction) or 10^{-15} to 10^{-11} M deltorphin (> 50% reduction). At higher concentrations, less inhibition of p24 antigen production was found. Naltrindole (NTI, 10^{-11} M), a selective DOR antagonist, abolished the inhibitory effects of 10^{-9} M SNC-80, whereas 10^{-13} M NTI partially reversed the effect of SNC-80. Thus activation of DORS expressed by CD4+ T cells significantly reduced the expression of HIV-1 by these cells. These findings suggest that opioid immunomodulation directed at host T cells may be adjunctive to standard anti-viral approaches to HIV-1 infection. Sharp, B., Gekker, G., Li, M.D., Chao, C.C., Peterson, P. Delta Opioid Suppression of Human Immunodeficiency Virus-1 Expression in T Cells, *Biochemical Pharmacology*, August 1998. (Text taken largely from article abstract).

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Research Findings

Behavioral Research

Food Deprivation Enhances Drug Cues

It is known that food deprivation in animal models increases the self-administration of a variety of drugs that have high abuse liability in man. Some food deprivation conditions may actually enhance a relapse or "reinstatement" of drug self-administration following a priming dose of a drug. But can deprivation enhance the motivational and reinforcing properties of exteroceptive cues such as locations in which drugs are received? Dr. Richard Meisch and colleagues at the University of Texas Houston Health Science Center report in *Psychopharmacology* (131, pp. 1-8, 1997) that rats maintained at 80 percent free-feeding body weights preferred locations previously associated with intraperitoneal cocaine when given a choice between cocaine versus saline paired locations. The food deprivation condition also enhanced psychostimulant-induced locomotor activity and sensitization to this behavioral activation. Dr. Meisch suggests that the deprivation state may enhance HPA-axis activation of the central dopaminergic substrate for cocaine reinforcement, implicating neurobiological substrates for stress having an important role.

Circadian Shifts After Nicotine

Dr. Bruce O'Hara at Stanford University has found that nicotine is capable of causing phase shifts in the circadian rhythms of rodents, an effect that supports a role for cholinergic influences on the circadian system mediated by nicotinic acetylcholine receptors. Dr. O'Hara has previously found a dramatic sensitivity of the perinatal suprachiasmatic nucleus of the hypothalamus to nicotine. He postulates that such effects on the SCN may contribute to alterations caused by nicotine in other physiological systems, and may also contribute to nicotine's addictive properties through influences on arousal. O'Hara, Edgar, Cao, Wiler, Heller et al. Nicotine and Nicotinic Receptors in the Circadian System. *Psychoneuroendocrinology*, 23, pp. 161-173, 1998.

Cues Can Enhance Drug Taking

External stimuli paired with drugs may have more than one function: they may signal drug availability, and may also act as secondary reinforcers capable of strengthening behavior. Dr. Stanley Weiss at the American University in Washington, D.C. has been studying the effects of combining external stimuli, each of which has been paired with different reinforcing (e.g., food or cocaine) outcomes. A recent paper (Panlilio et al., *Psychopharmacology*, 135, pp. 70-74, 1998) found that animals' self-administration of single doses of cocaine (0.66mg/kg) doubled in the presence of two combined external stimuli that had each been paired with cocaine or food. Although administering primary reinforcers can attenuate drug selection behavior, as shown in other literature, it appears that cues which are associated with primary rewards can in fact enhance drug taking responses.

Assessing Effects of Drugs on Complex Motor Behavior

Measures of motor behavior in rodents are commonly used behavioral tools to assess the effects of a variety of experimental manipulations from the effects of drug challenges to evaluating differences in genetically altered mice (e.g., knock out mice). These methods are widely used because a variety of behaviors comprising motor behavior can be assessed with automated equipment and results are rapidly obtained. However, quantifying, and accurately characterizing what often appears to be random behavior is difficult. Researchers at the University of California at San Diego have addressed this problem and developed a mathematical technique to quantify motor behavior. The approach, which was derived from theoretical physics, takes into account the sequence, or pattern of movements, and the amount of motor activity displayed by the animal. Using this new mathematical approach, the researchers are able to uncover and quantify how drugs of abuse affect various aspects of motor behavior and can begin to determine how drugs of abuse act on various neurotransmitter systems to produce these effects. The mathematical tools developed by these researchers will allow for comprehensive studies of the effects of drugs of abuse on behavior. The ultimate goal is to predict behavioral changes and to identify the associated underlying neurochemical changes produced by drugs of abuse. Krebs-Thomson et al. Modulation of Phencyclidine (PCP)- induced Changes in Locomotor Activity and Patterns in Rats by Serotonin, *European Journal of Pharmacology*, 343, pp. 135-143, 1998.

High Rate of Passive Exposure to Crack/Cocaine in Infants

Researchers at the Yale Child Study Center prospectively obtained 124 urine samples from 122 children less than one year old for routine clinical indications from the Emergency Department at Yale-New Haven Hospital. Samples were analyzed by radioimmunoassay (RIA) for cocaine, with cross-reactivity for its major metabolite, benzoylecgogine (BE), using a threshold for detection of cocaine and BE that is lower than the current DHHS standard. The presence of cocaine or BE was presumed to indicate passive exposure to crack/cocaine. Of the 124 samples, 36.3 percent were positive (greater than or equal to 50ng/mL BE equivalents) for cocaine and/or BE. The positive samples were highly correlated with lower and upper respiratory symptoms and with seeking medical care more often. Lustbader, A.S., Mayes, L.C., McGee, B.A., Jatlow, P., and Roberts, W.L. Incidence of Passive Exposure to Crack/Cocaine and Clinical Findings in Infants Seen in an Outpatient Service, *Pediatrics*, (1 Part 1), E5, July 1998.

Pergolide Effects on Cocaine Craving and Self-Administration

Based on clinical evidence that pergolide, a D1/D2 dopamine receptor agonist, may be useful in maintaining cocaine abstinence, its effects were investigated in twelve inpatient volunteers who reported spending an average of $170 per week on cocaine. Subjects received pergolide (0.05mg BID) for eight days and placebo for eight days, with drug order balanced across subjects. Self-administration sessions occurred on the last four days of maintenance on each medication. A modified 7-trial progressive ratio choice procedure (0, 8, 16, 32 mg/70 kg cocaine vs. $5) was utilized with sessions consisting of: two sample trials wherein subjects responded to receive the dose and tokens available that day; and five choice trials wherein subjects chose between the available dose and tokens. Following each trial, the response requirement for the chosen option increased by 400. Maintenance on pergolide: decreased cocaine-induced increases in ratings of "High," "Stimulated," cocaine "Potency;" decreased estimates of street value; decreased heart rates; increased ratings of craving, i.e., "I want cocaine;" and had no effect on cocaine self-administration. According to the authors, the increased desire to use cocaine during pergolide maintenance suggests that it has limited treatment utility at this dose. However, given the finding of an attenuation of cocaine's subjective and cardiovascular effects, an investigation of a wide range of pergolide doses on cocaine self-administration and subjective effects may be warranted. Another finding of this research was that women reported lower ratings of "Stimulated" and dose quality, and had relatively smaller increases in systolic pressure following cocaine administration. Haney, M., Foltin, R.W., and Fischman, M.W. Effects of Pergolide on Intravenous Cocaine Self-Administration in Men and Women, *Psychopharmacology*, 137, pp. 15-24, 1998.

New Method for Studying Drug Reinforcement

Dr. Richard Meisch reports development of a new method for studying drug reinforcement using an alternative to intravenous (I.V.) self-administration and to oral self-administration. This procedure involves the animal, in this case the rat, responding under a long fixed-interval schedule. The reinforcer is delivery of a drug, in this case etonitazene, administered intraperitoneally (I.P.) by the experimenter. This procedure offers a number of practical advantages over the conventional I.V. route and the oral route of self-administration. Ahlgren-Beckendorf, J.A., Steward, R.B., Gomez, T.H., Silverman, P.B., and Meisch, R.A. Lever-press Responding Maintained by Contingent Intraperitoneal

Administration of Etonitazene in Long Evans Hooded Rats, *Journal of Neuroscience Methods*, 80, pp. 149-154, 1998.

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Research Findings

Clinical and Services Research

Matching Coping Styles and Treatment Strategies

Dr. Edward Gottheil at Thomas Jefferson University in Philadelphia is conducting a study designed to estimate the relative contributions of treatment, client and counselor factors in determining the response of polysubstance abusers to brief individual counseling. The two counseling styles being employed are 1) high-structure, behaviorally-oriented individual counseling (HSB); and 2) low-structure, facilitative style (LSF). Treatment outcomes are being compared for clients whose coping styles are matched to treatments with those whose styles are mismatched. In a sample of 60, there were no differences in treatment benefit for the LSF and HSB clients. However, clients with more severe pretreatment drug problems did better in HSB counseling, while those with less severe problems fared better in LSF treatment. These findings provide some support for the notion that treatment benefit for substance abuse patients can be improved through appropriate patient-treatment matching on the basis of addiction severity. Thornton C.C., Gottheil E., Weinstein, S.P. Kerachsky, R.S. Patient-Treatment Matching in Substance Abuse: Drug Addiction Severity. *Journal of Substance Abuse Treatment*, 15(2), pp. 1-7, 1998.

Modeling and Modifying Motivation for Change

Dr. William Miller at the University of New Mexico is testing the efficacy of a promising therapeutic procedure, Motivation Enhancement Therapy (MET), for enhancing motivation for change in heroin and cocaine addicts. Preliminary findings support the effectiveness of motivation interviewing as an additive adjunct to treatment for drug dependence. Data from 85 subjects show a significant difference in the rate of urine drug screens (UDS) positive for cocaine or opiates, between intake and the first follow-up at 3 months. Clients entering treatment for drug problems without having received motivational interviewing showed a 15.8% decrease in the frequency of UDS positive for these illicit drugs, which were the primary problem drugs precipitating treatment. Clients who first received a motivation interview and then proceeded into the same treatment programs showed a 42.2% decrease in UDS positives, a highly significant difference. Yahne, C.E., Miller, W.R., & Harris, R.J. Motivational Interviewing in Drug Abuse Services: Preliminary Results on a Self-Report Measure and a Laboratory Measure. Poster presented at the Eighth International Conference on Treatment of Addictive Behaviors, Santa Fe, New Mexico, January, 1998.

Stop Smoking Treatment for Drug/Alcohol Abuse Inpatients

Dr. Thomas Burling at the American Institutes for Research in California has completed a large scale, controlled, clinical trial examining the impact of smoking cessation treatments on substance dependent inpatients. Two smoking treatments specifically designed for newly recovering substance abusers were compared. One treatment used

multiple, intensive, stop-smoking procedures to address the high-level of nicotine dependence found in this population. The second treatment used the same procedures, but promoted generalization of cessation and relapse prevention skills from cigarettes to drugs and alcohol. Both treatments were expected to be equally successful in terms of smoking outcomes, however the "generalization" treatment was expected to produce better drug and alcohol outcomes. Analyses examined both smoking and drug/alcohol outcomes with respect to abstinence and relapse rates. Findings suggest that subjects who receive the "smoking-focused" treatment had better smoking outcomes (not significant) and better drug and alcohol outcomes (significant) than those who received the "generalization" treatment. The results indicate that providing a focused smoking treatment concurrent with drug/alcohol treatment can be effective and better in terms of drug/alcohol outcomes than a combined smoking and drug/alcohol treatment. Burling, T.A., Seidner, A.L. (Presenter), & Ramsey, T.G. A Controlled Clincal Trial of Stop-Smoking Treatment for Drug/Alcohol Dependent Inpatients. Paper presented at the Society of Behavioral Medicine Annual Convention, April, 1997.

A Comparison of Daily and 3-Day Buprenorphine/Naloxone Dosing Schedules

Dr. Leslie Amass an MDD sponsored grantee, compared the clinical efficacy of the combination tablet of buprenorphine and naloxone administered daily with that of two different 3-day dosing schedules. Under one 3-day schedule (3-day clinic), clients ingested 16, 16, and 24 mg of the combination tablet at the clinic each Monday, Wednesday and Friday, respectively. On the other 3-day schedule (3-day take-home), clients received an 8 mg tablet every Monday, Wednesday and Friday and 8 mg tablets to take at home on days between clinic visits. The data showed that there were no significant differences across conditions in rates of illicit drug use. Subjects "liked" both 3-day schedules significantly more than the daily schedule ($p=.002$), and ratings of "good" were significantly higher for the 3-day take-home as opposed to 3-day clinic condition ($p=.04$). The data suggest that reducing clinic attendance improves medication compliance and increases client satisfaction without impacting illicit drug use.

Predictive Validity of Cocaine, Sedative, and Alcohol Dependence Diagnoses

Dr. Kidorf and colleagues at the Johns Hopkins University School of Medicine examined the predictive validity of the Structured Clinical Interview for DSM-III-Revised-based substance dependence diagnoses (e.g, cocaine; sedative; alcohol) for 518 opioid-dependent outpatients entering a methadone maintenance program that included daily methadone substitution, individual and group counseling, and random urine screens 1-4 times per month. Patients were followed for over one year of treatment. Unlike a co-occurring diagnosis of sedative and/or alcohol dependence, results of the study indicate that a comorbid diagnosis of cocaine dependence at intake predicted an early dropout from the program. Kidorf, M., Brooner, R.K., King, V.L., Stoller, K.B., and Wertz, J. *Journal of Consulting and Clinical Psychology*, 66(1), pp. 168-173, 1998.

Prenatal Cocaine Exposure and Stimulus-Seeking Behaviors in Infants

Robert L. Freedland, Ph.D. and colleagues at the New York State Institute for Basic Research, Staten Island, NY, have investigated orientation sensitivity to complex perceptual patterns in groups of normal, brain-injured and cocaine-exposed infants. Previous studies with newborns revealed that normal neonates were able to modulate attention to stimulation depending on their arousal pattern, but brain-injured and cocaine-exposed neonates demonstrated poorer attention modulation. Brain-injured newborns preferred less stimulation even when more aroused (stimulus avoiding) and cocaine-exposed newborns preferred more stimulation even when more aroused (stimulus seeking). Current studies evaluated these differences in older infants (at four and seven months of age), using age-appropriate, complex visual perceptual tasks. These cocaine-exposed infants appear to be most sensitive to oblique orientations presented in a complex, herringbone visual pattern. The inference is that these older cocaine-exposed infants were responding to complex stimuli differently than non-cocaine-exposed, age-matched infants. Novelty responses of cocaine-exposed infants seem to be driven by the orientation of the stimulation-rich elements within the complex visual pattern, which may demonstrate a further instance of arousal-based "stimulation-seeking" behavior. Stimulus-seeking behavior in these older cocaine-exposed infants appeared to continue in development with the more advanced perceptual tasks. These findings are helpful in establishing a basis for the effects of cocaine exposure on infants and for determining if the effects persist. Further, the results suggest differential effects on the development of early sensory organization in cocaine-exposed infants after the first six months of life. The differences in responses to more advanced stimuli with respect to perceptual organization suggest an enduring drug-mediated effect in the sensory encoding of visual information in cocaine pre-exposed infants. Freedland, R.L., Karmel, B.Z., Gardner, J. M., & Lewkowicz, D.J. Prenatal Cocaine Exposure and Stimulus-seeking Behaviors during the First Year of Life. Annals of

the New York Academy of Sciences, 846, pp. 386-390, 1998.

Activation of Specific Brain Areas with Cue-induced Craving in Cocaine Addicts

Dr. Scott Lukas and colleagues at McLean Hospital in Belmont, Massachusetts demonstrated cerebral activation in the anterior cingulate and left dorsolateral prefrontal cortex after audiovisual stimuli in cocaine-using patients. The activation was specific to cues related to cocaine and not to neutral cues. The method used was blood-oxygenation-level-dependent (BOLD) functional activation. The results of this study demonstrate that this form of functional MRI can be useful to study the neurobiological basis of cue-induced craving. Maas, L.C., Lukas, S.E., Kaufman, M.J., Weiss, R.D., Daniels, D.L., Rogers, V.W., Kukes, T.J., and Renshaw, P.F. Functional Magnetic Resonance Imaging of Human Brain Activation During Cue-induced Cocaine Craving. *Am. J. Psychiatry*, 155(1), pp. 124-126, 1998.

Sex Differences in fMRI with Primary Visual Stimulation

Dr. Jonathan M. Levin and colleagues at the Brain Imaging Center at McLean Hospital in Belmont, Massachusetts conducted a study to determine the effect of sex on a non-cognitive, primary sensory activation task using the well-characterized, blood-oxygenation-level-dependent (BOLD) functional MRI response. BOLD signal response was measured in the primary visual cortex in response to binocular photic stimulation. It was found that women had a significantly lower (about 38%) mean BOLD signal response than men, and the influence of hemisphere revealed that women were more symmetrical than men in their response. This finding might reflect sex-based differences in the anatomy of the visual cortex, differences in visual processing, differences in regional oxygen utilization with activation, differences in vascular response to activation, or differences in baseline physiological measures related to BOLD contrast (e.g., hemoglobin level). In addition to functional implications, these results demonstrate the importance that the effect of sex might have when considering both the design and interpretation of functional MRI studies. Levin, J.M., Ross, M. H., Mendolson, J.H., Mello, N.K., Cohen, B.M., and Renshaw, P.F. Sex Differences in Blood-oxygenation-level-dependent Functional MRI with Primary Visual Stimulation. *Am. J. Psychiatry*, 155(3), pp. 434-436, 1998.

Neurochemical Alterations in Asymptomatic Abstinent Cocaine Users

Using proton magnetic resonance spectroscopy, Dr. Linda Chang and colleagues at the Harbor-UCLA Medical Center in Torrance, California investigated the effects of cocaine on brain neurochemistry in abstinent cocaine users using proton magnetic resonance spectroscopy. They found that the brain metabolites, creatinine and myo-inositol, were both elevated in the (temporoparietal) white matter, with a strong trend toward elevated creatinine in the gray matter. Further, there was a significant and positive correlation between creatinine, as well as myo-inositol, and the frequency and duration of cocaine use in the white matter, with a similar trend in the gray matter. Glutamine and glutamate levels were moderately elevated in the gray matter of cocaine users, with a significant correlation between level and duration of cocaine use. This finding suggests a perturbation of the glutaminergic system. N-acetyl-containing compounds (of which n-acetyl-aspartate, a marker of neuronal damage or loss, mostly comprises) were not different between cocaine abusers and controls in the areas assessed, thus revealing no differences in neuronal damage or cell loss. Overall, these findings demonstrate neurochemical abnormalities in the nonneuronal cells of subcortical brain regions in asymptomatic cocaine users, and these abnormalities exist in the absence of any visible structural changes as assessed by MRI. Chang, L., Mehringer, C.M., Ernst, T., Melchor, R., Myers, H., Forney, D., and Satz, P. Neurochemical Alterations in Asymptomatic Abstinent Cocaine Users: A Proton Magnetic Resonance Spectroscopy Study. *Biol. Psychiatry*, 42, pp. 1105-1114, 1997.

Differential Cognitive Functioning in 9-12 Years Olds Relative to Prenatal Cigarette and Marijuana Exposure

In an examination of cognitive performance of 131 9-12 year-old children participating in a Carleton University longitudinal study since birth, discriminant function analysis indicated a dose-dependent association between higher prenatal cigarette exposure in utero and lower performance on global intelligence test scores, with the verbal subtests of the intelligence test discriminating maximally among levels of in utero exposure. In contrast, prenatal marijuana exposure was not associated with global intelligence or the verbal subtests, but rather was negatively related to executive function tasks that require impulse control and visual analysis/hypothesis testing, and with a number of the intelligence subtests requiring these same abilities. The cigarette results extend observations made in

this sample and others at earlier ages. The marijuana findings, combined with results observed at earlier ages, lead the authors to suggest that in utero exposure to marijuana may have a negative impact on aspects of neurocognitive competence that fall under the domain of executive function. Fried, P.A., Watkinson, B.M. and Gray, R. *Neurotoxicology and Teratology*, 20 (3), pp. 293-306, 1998.

Mechanisms of Cardiovascular Effects of Cocaine in Humans

Cocaine use is associated with catastrophic cardiovascular events, ranging from cardiomyopathies, myocardial infarction to sudden death. Victor and his colleagues at the University of Texas Southwestern Medical Center conducted studies to understand the underlying mechanisms of cardiovascular effects of cocaine in humans. In their earlier studies, they found that intranasal cocaine (2 mg/kg-systemic route) increased myocardial oxygen demand and decreased oxygen supply. Later they (Jacobsen et al. 1997) showed that intranasal cocaine increased the sympathetic nerve discharge (recorded via intraneural microelectrodes in the peroneal nerve) to the skeletal muscle vascular bed. The authors hypothesized that the sinoaortic baroreflexes may be playing a pivotal role in modulating the cocaine-induced sympathetic excitation, and that the interplay between these excitatory and inhibitory neural influences determines the net effect of cocaine on sympathetic discharge targeted to the human skeletal muscle circulation. On the other hand, intracoronary infusion of cocaine at high concentrations (1 mg/min over a 15 min period, total dose of 15 mg cocaine) caused a deterioration of LV systolic and diastolic performance in humans (Pitts et al. 1998) without producing any epicardial coronary arterial vasoconstriction or alterations in the blood flow suggesting myocardial effects of cocaine (Daniel et al. 1996). Effects of Intracoronary Infusion of Cocaine on Coronary Arterial Dimensions and Blood Flow in Humans, Daniel, W.C., Lange, R., Landau, C.,Willard, J. and Hills, D. Am J Cardiol., 78, pp. 288-291, 1996; Effects of Intranasal Cocaine on Sympathetic Nerve Discharge in Humans, Jacobsen, T.N., Grayburn, P.A., Snyder, R.W., II, Hansen, J., Chavoshan, B., Landau, C., Lange, R.A., Hills, D., and Victor, R., J. Clin Invest., 99, pp. 628-634, 1997; Effects of Intracoronary Infusion of Cocaine on Left Ventricular Systolic and Diastolic Function in Humans, Pitts, W., Vongpatanasin, W., Cigarroa, J.E., Hills, D., and Lange, R. *Circulation*, 97, pp. 1270-1273, 1998.

A Comparison of Daily and 3-Day Buprenorphine/Naloxone Dosing Schedules

Dr. Leslie Amass an MDD sponsored grantee, compared the clinical efficacy of the combination tablet of buprenorphine and naloxone administered daily with that of two different 3-day dosing schedules. Under one 3-day schedule (3-day clinic), clients ingested 16, 16, and 24 mg of the combination tablet at the clinic each Monday, Wednesday and Friday, respectively. On the other 3-day schedule (3-day take-home), clients received an 8 mg tablet every Monday, Wednesday and Friday and 8 mg tablets to take at home on days between clinic visits. The data showed that there were no significant differences across conditions in rates of illicit drug use. Subjects "liked" both 3-day schedules significantly more than the daily schedule ($p=.002$), and ratings of "good" were significantly higher for the 3-day take-home as opposed to 3-day clinic condition ($p=.04$). The data suggest that reducing clinic attendance improves medication compliance and increases client satisfaction without impacting illicit drug use.

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National Institute on Drug Abuse

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

September, 1998

Research Findings

AIDS Research

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

Serum samples from 300 IDUs, 300 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. Anti-HAV was not significantly associated with high-risk drug-using behaviors ($p>.10$), but 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 contribute more to the occurrence of HAV infection among IDUs than does injection drug use. Data also indicate that IDUs and persons at risk for injection drug use should receive HAV vaccine. Villano, S.A., Nelson, K.E., Vlahov, D. et al., *Clin. Infect. Dis.*, 25, pp.726-728, 1997.

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.

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 x 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.

Unique Volume Presents Findings from the NIDA CA on Women's Drug Use and HIV Risk

A recent volume brings together empirical findings from NIDA's multisite CA research program which highlight a number of factors related to HIV infection among women who inject drugs and/or smoke crack cocaine, or who are the sex partners of individuals who use these drugs. Bringing their risk factors to light is timely and critical at this point in the epidemic, when women's vulnerability to HIV disease is becoming increasingly apparent. Worldwide, women account for 42% of adults living with HIV/AIDS, but women's acquisition of the virus has begun to grow more rapidly than it has for men. Drug use is well recognized as playing a major role in the spread of this disease: up to 46% of women's AIDS cases have been directly attributed to injection drug use and as much as 18% to women's heterosexual contacts with injection drug users. The papers in this volume are presented in five major sections: an overview of findings and research needs on women drug users and HIV prevention; HIV risk behavior change of female drug users; single CA site descriptions; contextual variables in women's HIV risk behaviors; gender differences in HIV risk behavior and health status of drug users; and a unique population of women at risk -- women who trade sex for money and drugs. Stevens, S.J., Tortu, S., and Coyle, S.L. (Eds.). Women, Drug Use, and HIV Infection. Binghamton, N.Y.: Haworth Medical Press, 1998 (co-published simultaneously as Women and Health, 27 (_), 1998).

Special Issue Devoted to HIV Prevention for Injection Drug Users

Recently, a special supplement on HIV prevention for injection drug users was published by the Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology. Edited by David Vlahov, Ph.D. of Johns Hopkins School of Hygiene and Public Health and T. Stephen Jones, M.D. of the Centers for Disease Control and Prevention, the supplement focuses on issues related to use of sterile syringes as an HIV prevention measure by drug users who continue to inject. A number of NIDA-sponsored researchers contributed articles to the supplement, including Drs. C. McCoy, L. Metsch, D. Chitwood et al., who assessed the frequency of multiperson use of needles, syringes, cookers, cotton, and water relative to the transfer of blood and blood-borne infections in approximately 4,000 IDUs. They report that nearly two-thirds of potential exposures to blood-borne infections among the IDUs were from multiperson use of cookers, cotton, and water, indicating the importance of considering all drug preparation and injection practices that could allow transfer of blood-borne infections among IDUs at parenteral transmission in any intervention programs. Drs. R. Heimer, K. Khoshnood, J. Guydish, and B. Junge contributed an article on the effects of syringe exchange programs on syringe use and reuse. They used multiple methods to estimate injections per syringe by SEP clients in San Francisco, Chicago, Baltimore, and New Haven, and found that SEP participation was significantly associated with increases in once-only use of syringes. The findings add to the weight of evidence which shows that SEPs reduce the transmission of syringe-borne infections such as HIV and hepatitis. Drs. P. Keyl, L. Gruskin, K. Casano et al., describe findings from their study on community attitudes toward Needle Exchange Programs (NEPs) in Baltimore. They conducted household interviews with a random sample of residents in six census tracts in the city, and found that, even though 72% of the respondents thought NEPs would attract IDUs to the neighborhood, 65% favored NEPs and 47% favored pharmacy sales without prescriptions. Factors independently associated with acceptance of NEPs were the perceptions that they decrease the numbers of discarded needles on the street, do not encourage a person to inject drugs, and decrease the incidence of HIV. Jones, T.S. and Vlahov, D. (Eds.). *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology: HIV Prevention for Injection Drug Users*, 18(supplement 1), July 1998.

Psychosocial Interventions and the Prevention of HIV Risk Behaviors in IDUs

Researchers examined the scientific evidence on the effectiveness of psychosocial interventions in reducing the risk of infection with HIV in IDUs. They reviewed 19 published studies on the effectiveness of individual counseling, HIV testing, group interventions, street outreach, and a "social" intervention designed to change norms for safer behaviors. Eight of 15 studies that examined behavioral outcomes provided evidence of the effectiveness of an experimental intervention, compared with a control or comparison group. Yet, there were a number of competing hypotheses which may have explained the findings (e.g., participation in an intervention evaluation itself may be a valuable intervention). The researchers discuss the importance of examining the efficacy of health risk assessment

when developing interventions, and the need to develop unobtrusive measures and to assess the impact of behavioral assessments when evaluating them. Because a substantial proportion of subjects receiving interventions report unacceptably high levels of risk behaviors, more potent interventions are needed, such as those designed to change the norms of entire communities of drug users concerning safer injection and safer sex. Gibson, D.R., McCusker, J., and Chesney, M. Effectiveness of Psychosocial Interventions in Preventing HIV Risk Behavior in Injecting Drug Users. *AIDS*, 12, pp. 919-929, 1998.

Condom Use Among Filipina Sex Workers

Until fairly recently, the Philippines did not witness the epidemic proportions of the AIDS virus that have been seen in certain parts of Asia such as Thailand and India; however, recent statistics indicate that there may be 18,000 adult carriers of the AIDS virus in the Philippines. Furthermore, commercial sex work promotes the spread of HIV, and there are about 265,000 sex workers in the Philippines. Findings are presented from the baseline assessment of a community-based HIV/STD prevention intervention among registered commercial sex workers (N = 1394) and managers of the establishments that employ them in the Philippines in this study. The primary goal of the intervention is to promote safer sexual practices among Filipina sex workers. The sex workers' knowledge, attitudes, behaviors, and perceptions of establishment policies concerning HIV prevention were assessed. Results indicated that most establishments do not have clear policies and practices for condom use between the sex workers and their clients. The best predictor for use of condoms with clients was whether condoms were available at the establishment. The findings point to the importance of an intervention that stresses changes in establishment policies and expectations as a means of reducing risk behaviors associated with HIV/STD transmission. Morisky, D.E., Tiglao, T.V., Sneed, C.D., Tempongko, S.B., Baltazar, J.C., Detels, R., & Stein, J.A. The Effects of Establishment Practices, Knowledge and Attitudes on Condom Use Among Filipina Sex Workers. *AIDS Care*, 10, pp. 213-220, 1998.

Drug-Involved Women Prefer Female-Controlled Protection from HIV and Other STDs

A multisite research project was initiated in 1996 to examine the acceptability of the female condom among women at high risk for HIV and other STDs and determine its potential utility as an additional risk-reduction tool for drug-involved women. Six research sites that were part of the collaborative, cross-site NIDA CA participated in the study: San Antonio, St. Louis, Washington, DC, Rio de Janeiro, Lexington/Louisville, and Raleigh/Durham. The study sought to introduce the female condom to a large sample of women drug users, to explore its acceptability as a risk-reduction device among these women, and to examine correlates of its use. This article reports findings from three of the six sites: San Antonio, St. Louis, and Rio de Janeiro. All of the female respondents participated in a female condom education program, and were asked to report their experiences at two points of contact. Outcome data indicated that a sizable proportion of the women who were followed up reported use of the female condom on one or more occasions of heterosexual contact, and that many women preferred the female condom to the male condom in terms of overall satisfaction, suggesting that there is a viable role for this device in the HIV prevention field. Surratt, H.L., Wechsberg, W.M., Cottler, L.B., Leukefeld, C.G., Klein, H., and Desmond, D.P. Acceptability of the Female Condom Among Women at Risk for HIV Infection. *American Behavioral Scientist*, 41(8), pp. 1157-1170, May 1998.

Street Research with Cocaine Users in Brazil Reported as Feasible and Effective

Researchers assessed the impact of an HIV risk reduction program on risky behaviors in a population of street cocaine users in Rio de Janeiro, Brazil. Pre- and post-intervention data were collected, and changes in the frequency of drug use, sexual risk behaviors, and other life-situation variables were examined. Participation in the program was associated with a significant decrease in the average number of days of cocaine use and a significant increase in employment and income. Significant increases in condom use were also documented. The data suggest that this population of street cocaine users was capable of understanding the severity of AIDS as well as learning and applying specific risk-reduction techniques to their behavior. The results further demonstrate the feasibility of conducting street research among an at-risk population of cocaine users in Brazil and in other countries in which there is little tradition of research with out-of-treatment drug users. McBride, D.C., Inciardi, J.A., Surratt, H.L., et al. The Impact of an HIV Risk-Reduction Program Among Street Drug Users in Rio de Janeiro, Brazil. *American Behavioral Scientist*, 41(8), pp. 1171-1184, May 1998.

Rational Model Links Needs, Impoverishment, and an Increase in HIV Risk Behaviors

Researchers considered a rational model where the needs of the HIV+ population are met by individual resources, plus public resources, and network resources (contributions by family and friends). They examine the argument made by some economists that since HIV transmission is embedded in a pattern of risk, the fact that AIDS shortens the life expectancy of the chronically indigent amounts to an economic (if not an ethical) boon as a cost-containment mechanism for social welfare expenditures. The rational model suggests otherwise because, as levels of social welfare expenditures or public transfers decrease and fail to meet the needs of HIV+ persons, the risky behavior and HIV infection rate among network altruists spiral upward as they become impoverished in meeting the shortfall in public transfers. The emotional dynamics of networks (family, friends) are potentially an important resource in the construction of an adequate public response to social problems. Bell, D.C., Richard, A.J., Montoya, I.D., et al. Social Network Utility and the Economics of Risk: The Case of HIV. *Journal of Economic Behavior and Organization*, 33, pp. 195-205, 1998.

Amphetamine, Substance Use and Its Relationship to Depression, Anxiety, and Isolation Among Youth Living With HIV

In a series of three papers, drug use and correlates were examined in youth living with HIV (YLH). Amphetamine use, other HIV-related risk acts, T-cell counts, emotional distress, coping style, and symptoms of HIV were examined in 337 HIV+ youth aged 13 to 24 (20% female; 22% African American, 27% Anglo, 35% Latino) from four cities (LA, NY, San Francisco, and Miami). One third of youth were found to have engaged in amphetamine use in their lifetime, and 21% of youths reported current use (i.e. in the last three months). Compared to non-users, users initiated other drug use at younger ages, used more types of drugs, reported more emotional distress, and employed escape coping significantly more often. Substance use pervaded the lives of these YLH. Among this sample, males had used more drugs, more often, and for longer periods than females. However, there had been major reductions in use. Being male, having high emotional distress, and having fewer negative social supports were significantly associated with greater reductions in substance use. The longer an individual had been diagnosed seropositive tended to be associated with reductions in use ($p=.06$). Compared to non-users, users also had more sexual partners and more sexual encounters. While users and non-users do not differ on physical symptoms or whether they have been diagnosed with AIDS, users of amphetamines report significantly higher T-cell counts than non-users. Despite poor psychosocial functioning, amphetamine users were found to have higher T-cell counts than other YLH. The continued high-risk profile of transmission acts among users suggests that preventive interventions must target specific drugs used by YLH. As the number of youths infected with HIV rises, secondary prevention programs are needed to help youths living with HIV meet three goals: 1) increase self-care behaviors, medical adherence, and health-related interactions; 2) reduce transmission acts; and 3) enhance their quality of life. Based on modifications of the social action model, a small group intervention was developed and tested in this population. Rotheram-Borus, M.J., Mann, T., and Chabon, B. Amphetamine Use Among Youths Living with HIV. AIDS Education and Prevention, In Press; Rotheram-Borus, M.J., Murphy, D.A., Swendeman, D., Chao, B., Chabon, B., Zhou, S., and Birnbaum, J. Substance Use and its Relationship to Depression, Anxiety, and Isolation Among Youth Living with HIV. International Journal of Behavioral Medicine, In Press; Rotheram-Borus, M.J., and Miller, S. Secondary Prevention for Youths Living with HIV. *AIDS Care*, 10(1), pp. 17-34. 1998.

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National Institute on Drug Abuse

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

September, 1998

Research Findings

Epidemiology, Etiology and Prevention Research

Community Epidemiology Work Group

In the Past 6 Months

- Heroin indicators have shown increases in many cities, in some cases overshadowing cocaine.
- Marijuana indicators have continued to escalate across the country.
- Cocaine indicators have continued to level or decline, except for some isolated potentially emerging problems (in Miami and Texas).
- Methamphetamine indicators have increased in most western areas, following some declines last year.
- "Club drugs" have continued to proliferate in the drug scene in several areas.

The 44th meeting of the Community Epidemiology Work Group (CEWG) was held in Boston, Massachusetts on June 23-26, 1998.

The CEWG is a network of researchers from 21 U.S. metropolitan areas and selected foreign countries 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. The following are highlights of the meeting:

- **Cocaine** - While crack cocaine remains the Nation's predominant illicit drug problem, indicator data continue to show leveling off in many urban areas: cocaine-related deaths were down or stable* in 7 of the 8 areas where such information was reported (Philadelphia was the exception); 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 or remained stable* in 14 of the 16 areas where such data were available (Newark and New Orleans had slight increases); cocaine-positive urinalysis percentages declined or remained stable in all 15 CEWG cities in the Arrestee Drug Abuse Monitoring (ADAM) program; and prices and purity remained stable in most areas. Supplies remain abundant in nearly every city. Demographic data continue to show most cocaine users as older, inner-city crack addicts, with two exceptions: in Miami, poison center, school survey, and anecdotal data continue to indicate some adolescents initiating cocaine use in combination with other drugs; and in some Texas communities, white and Hispanic street youth are reportedly using crack as an alternative to poor methamphetamine quality. Cocaine continues to be used in combination with other drugs, such as marijuana in Atlanta, Chicago, Miami, and Philadelphia; heroin in Atlanta, Boston, Philadelphia, St. Louis, and Seattle; and methamphetamine in Denver and parts of Texas. In some areas, such as Boston and Denver, users

dissolve crack for injection. Some shifts from crack to cocaine hydrochloride (HCl) are reported: among treatment admissions in Atlanta and Texas; and in street-level sales in New York. Cocaine is reported to be involved in 50 percent of homicides in New Orleans.

- **Heroin** - Indicators in many cities continue to show increases: heroin-related deaths increased in 6 of the 8 cities where mortality was reported (they remained stable in Honolulu and declined in Seattle); ED mentions increased significantly* in 8 cities; and treatment percentages increased* in 10 of the 16 areas where trend data were available. Heroin now overshadows cocaine in some cities: it ranks first among ED drug mentions in three cities, and it is the primary drug of abuse among treatment admissions in six areas. More than 10 percent of male arrestees tested heroin-positive in six CEWG cities.

  Heroin continues to increase among new and young users in a number of cities because of its easy availability, low price, high purity, and favorable reputation compared with crack. Indicator and anecdotal data suggest increases among young adults in Boston, Chicago, Denver, and San Francisco and among both youth and young adults in Baltimore, Miami, Minneapolis/St. Paul, Philadelphia, San Diego, and parts of Texas. The suburbs are increasingly mentioned: in Baltimore, young white professionals, laborers, and high school students from the suburbs are being noted in the inner city buying drugs; in some Texas suburbs, youth and young adults have been involved in overdose deaths; and a recent Chicago study of injecting drug users included a large proportion of suburban residents. Younger heroin users tend to snort the drug. The percentage of snorters among treatment admissions continues to increase in several cities, including Atlanta, Baltimore, Detroit, Minneapolis/St. Paul, Philadelphia, and San Diego. Atlanta ethnographic reports continue to indicate an increasing number of recently initiated snorters shifting to injection; in New York City, by contrast, snorters do not seem to be shifting to injection, except for a population of young immigrants from the former Soviet Union. Smoking remains relatively rare, but it is reported by 7 percent of admissions in both Miami and San Diego. Young adults in Phoenix reportedly use heroin to "come down" from methamphetamine-induced highs. In San Francisco, heroin-marijuana combinations are sold as "canade." In New York City, many crack sellers are switching to heroin sales due to the high profit potential.

  *mortality, treatment, and ADAM comparisons are for 1996 versus 1997; DAWN comparisons are for 1995 versus 1996, reliable at $p<0.05$.

- **Marijuana** - Marijuana accounted for more than 10 percent of total ED mentions in four cities, and it was the primary drug of abuse among treatment admissions in Denver, Minneapolis, and Seattle. Treatment admissions remained at elevated levels: percentages increased in five cities, remained stable in nine, and decreased in one. Among adult male arrestees, marijuana-positive findings exceeded cocaine-positives in seven ADAM cities. Despite declines in nine cities between 1996 and 1997, marijuana levels in this population were generally higher than in 1995. Marijuana remained readily available in many CEWG areas, although it was expensive and hard to find in San Francisco. Seizures increased in Boston, Detroit, and Hawaii, while marijuana-related arrests increased in New York City and Washington, DC. Qualitative and quantitative data from most CEWG cities indicate widespread marijuana use among youth. For example, among primary marijuana treatment admissions, the average age at first use was 13.9 in Minneapolis and 14 in Denver. In Washington, DC, the number of marijuana treatment admissions in the 12-17 age group increased 70 percent between 1995 and 1997. In each of the seven cities where ADAM tests juvenile males, the percentage of positive urinalyses was much higher for juveniles than for adults. While alcohol remains the most common secondary and tertiary drug among marijuana treatment admissions, other drug combinations continue to be reported. Blunts are combined with cocaine HCl in Atlanta and Philadelphia ("turbo") and with crack in Chicago ("diablito," "primo," or "3750,") and Miami ("geek joint"). Other combinations include phencyclidine (PCP) in Chicago ("wicky stick" or "donk") and Philadelphia ("love boat" or "dust blunt") and embalming fluid in Minneapolis. In Texas, blunts are dipped in embalming fluid laced with PCP ("fry," "amp," or "water-water") or in codeine cough syrup ("candy blunts").

- **Stimulants** - Indicators of **methamphetamine** use - mortality, treatment, and arrestee urinalysis-and ethnographic research continue to show increases in the West. After declining in 1996, mortality figures in San Diego, Hawaii, and Phoenix have risen. Similarly, the 1997 ADAM data indicate increases in all the western CEWG cities, returning the rates of arrestees testing positive to 1994-95 levels. Treatment figures show increases in all reporting western cities, except for Seattle, where they have stabilized, and Phoenix, where they have declined since 1994. Methamphetamine remains the most common primary drug among treatment admissions in Hawaii and San Diego. Smoking remains the primary route of administration for methamphetamine in San Diego and for "ice" in Hawaii, and it has become more common in Denver and San Francisco, although injecting still predominates. Inhalation still predominates in Los Angeles. In San Francisco, "speed" use is increasing among blue collar workers, young professionals, and college students. In Denver, where methamphetamine is often used with crack, some former crack users may have crossed over to exclusive methamphetamine use. Elsewhere in the country, methamphetamine appears in indicators in Minneapolis/St. Paul, Philadelphia, and parts of Texas. The number of treatment admissions has increased in Baltimore, Boston, Detroit, New Orleans, and St. Louis. In

Missouri, statewide meth-amphetamine admissions began to outnumber heroin admissions in 1996. State police report increased seizures of the drug in and near Boston, and it is associated with the club or rave scenes in Atlanta, Miami, and New York City.

Methylphenidate (Ritalin) abuse is reported, mostly among school-aged adolescents, in Boston, Detroit, Minneapolis/St. Paul, Phoenix, Seattle, Washington, DC, and areas of Texas; in Chicago, it is the drug of choice for some stimulant users or is mixed with heroin as a "speedball." **Methylenedioxymethamphetamine** (MDMA or "ecstasy") availability is reported in eight CEWG areas, primarily as a club drug at raves and dance parties. Increases are reported in Boston. **Ephedrine**-based products remain a concern, with products such as "herbal ecstasy" widely available at convenience stores and truck stops in many CEWG areas, including Atlanta, Minneapolis/St. Paul, and Phoenix; in Texas, at least eight deaths have been associated with ephedrine since 1993. Seizures of **khat**, a flowering evergreen shrub also known as "qat" or "Somali tea," continue in Detroit and Minneapolis/St. Paul. **Fenfluramine and phentermine** (Fen-Phen) are reportedly brought into Texas via legal prescriptions from Mexico.

- **Depressants - Gamma-hydroxy butyrate (GHB)**, referred to as a "stove-top drug" in Phoenix because of its ease of manufacture, has been involved in poisonings and over-doses in Boston, Detroit, Miami, and New Orleans. It is also part of the club scene in Baltimore, San Francisco, and Texas, and is popular as a synthetic steroid in Atlanta. Another club drug, **ketamine** ("Special K" or "vitamin K"), was involved in overdose cases in New Orleans. Some ketamine availability was reported in Boston (where police report it is becoming more prevalent), Detroit, Miami (where it was involved in DUI cases along with other drugs), Minneapolis, Seattle, and Washington, DC. **Flunitrazepam (Rohypnol)** availability and use appears to have decreased substantially in some CEWG areas: Detroit (where hotline inquiries have declined since 1996), Miami (where it has been replaced by GHB combined with alcohol), and Texas (where submissions to the crime laboratory declined 71 percent between 1996 and 1997); however, seizures and anecdotal data in New Orleans indicate that distribution and abuse is increasing. **Clonazepam** (marketed as Klonopin in the United States and Rivotril in Mexico) is frequently used as a substitute for flunitrazepam in Texas; in Atlanta it is used to enhance the effects of methadone; and police in Boston report it frequently accompanies heroin use. Benzodiazepines such as **diazepam** are appearing in crack houses in Atlanta and are used by heroin and cocaine abusers in Miami to self-medicate for withdrawal symptoms. Treatment admissions for depressants in Chicago, while remaining small proportionally, have more than doubled recently.

- **Hallucinogens** - Contrary to declining ED and treatment indicators, ethnographic data indicate increased **lysergic acid diethylamide (LSD)** use among youth in Atlanta and Boston and increased **phencyclidine (PCP)** use in Chicago and San Francisco. LSD also remains popular among youth in Detroit, Miami, and Minneapolis. Treatment admissions, however, remain low for all hallucinogens. In Washington, DC, PCP treatment admissions decreased by more than 50 percent between 1995 and 1997 (1.4 percent of all admissions). In addition to LSD and PCP, **psilocybin mushrooms** were reportedly available in Boston, Minneapolis, and Seattle, while some availability of **mescaline** was reported in both Baltimore and Boston.

- **Viagra** - The potency pill sildenafil citrate (Viagra) may be appearing in the club scene. Los Angeles treatment officials describe "Viagra parties" at gay bars and report that three young men have died after combining the drug with "poppers," a recreational nitrate. Researchers are also concerned about two other areas of potential abuse: sale of the drug over the Internet; and a black market for the drug in other countries, such as Japan and the United Kingdom, where the drug is not approved for prescription sale.

Age of First Use: Its Reliability and Predictive Utility

In a study of the early-onset issue, researchers at Rutgers University posed three questions: (1) Is age of first licit use a predictor of differences in alcohol and drug use intensity during the period (age 20) when normative patterns of use reach a peak?, (2) Is age of first licit use a predictor of differences in use intensity in young adulthood (age 30) when most individuals have moderated their use? and (3) How consistent are adolescents in retrospectively recalling age of first use? Subjects (N=839) from the Rutgers Health and Human Development Project provided four waves of longitudinal data spanning the age range from 15 to 31. The vast majority of adolescents exhibited a sequential pattern of drug use initiation consistent with that found in previous studies. Retrospective recall of age of onset revealed a fair degree of relative agreement but a lack of absolute agreement; that is, as adolescents became older, recalled ages on onset exhibited an upward shift approximately equal across most individuals. Age of first licit use as recalled at age 18 did not predict differences in alcohol or drug use intensity at age 20. Age of first illicit use was a fairly strong predictor of drug use at 20 but a weak predictor of alcohol use at that age. Age of first licit use and age of first illicit use did not predict difference in useor use consequences at age 30. Regardless of age of onset, illicit

drug use and heavier alcohol use constitute an adolescence-limited phenomenon for most individuals. The findings suggest that intervention efforts need to be aimed not only at delaying the onset of illicit use in adolescence but also at reducing use levels among young adult users by facilitating the maturing out process. Labouvie, E., Bates, M. E., and Pandina, R. J. Age of First Use: Its Reliability and Predictive Utility. *Journal of Studies on Alcohol*, 58(6), pp. 638-643, 1997.

Repeat Pregnancies Among Adolescent Mothers

Findings from an event history analysis of rapidly repeated pregnancies (i.e., within 18 months) among a sample of 170 adolescents who had experienced a nonmarital birth is presented. Study participants were school-aged adolescents (<18 at enrollment) from lower-to middle-income families who were recruited from social and health service agencies in an urban area of the Northwest. Just over half the sample were persons of color. Respondents were interviewed at five points from pregnancy through 18 months postpartum. The best fitting model included two proximate determinants of pregnancy, contraceptive use and frequency of intercourse, as well as a history of school problems, drug use, fighting, living with parents, length of relationship with boyfriends, best friends experiencing pregnancies, and age at first birth. Gillmore, M., Lewis, S., Lohr, M., Spencer, M., and White, R. *Journal of Marriage and the Family*, 59, pp. 536-550, 1997.

Gender and Psychotropic Drug Use

Although studies have documented women's greater use of prescribed psychotropic drugs, few have explicitly examined how women and men differ in psychotropic drug use. This study examines gender differences in aggregate psychotropic drug use, as well as use of specific therapeutic categories, and explores how other factors explaining psychotropic drug use vary by gender. Using 1989 National Ambulatory Medical Care Survey (NAMCS) data, logistic regression analysis is used to estimate the probability of psychotropic drug use in aggregate and for four therapeutic categories-anxiolytics, sedative-hypnotics, antidepressants, and antipsychotics. For equations where gender is statistically significant, separate logistic regression equations are estimated to determine the explanatory variables that vary by gender. Results of this study indicated that the probability of receiving any psycho-tropic drug is 55% greater in office visits by women than those by men, all else constant. Further, gender is a positive and significant predictor of anxiolytic and antidepressant use. Variables estimating anxiolytic and antidepressant use that differ by gender include diagnosis, physician specialty, and payment source for the office visit. Findings confirm research that has demonstrated that women are more likely than men to receive any psychotropic drug in office-based care. This gender differential holds only for anxiolytics and antidepressants. In addition, there were significant differences in the predictors of drug use for women and men. Simoni-Wastila.L. *Medical Care*, 36(1), pp. 88-94. 1998.

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

This study examined treatment outcome as a function of program modality, clients' lifetime patterns of drug dependence, and their interaction, controlling for current level of drug use at treatment intake. Data were based on almost 3,000 clients who were interviewed at intake and one-year follow-up as part of the national Drug Abuse Treatment Outcome Study (DATOS). Subjects' lifetime patterns of drug dependence were classified into nine groups according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R; American Psychiatric Association; 1987) diagnostic criteria and time of onset of drug use career. Outcome measure was the reduction of heroin use or cocaine use. The presence of dependence diagnosis was associated with less improvement when current use level at intake was controlled. Clients dependent on heroin but not currently daily users benefited most from inpatient and residential programs. Methadone programs were also relatively ineffective in reducing cocaine use. Characteristics of the client's drug dependence history, in addition to the current or presenting drug problem, should be assessed to guide treatment planning. The high rate of cocaine dependence among methadone clients, most of whom were dependent on heroin, poses considerable challenge to contemporary opiate substitution treatments. Hser, Y.I., Anglin, M.D., and Fletcher, B. *Journal of Substance Abuse Treatment* 15(1), pp. 1-11, 1998.

The Impact of Maternal Drinking During and After Pregnancy on the Drinking of Adolescent Offspring

The impact of prenatal maternal drinking on alcohol consumption in adolescent offspring was examined among boys and girls separately. A prospective longitudinal sample of 185 mother-firstborn child dyads was used to examine the impact of maternal self-reported lifetime and current drinking, controlling for potential confounding factors. In this representative general population sample, maternal drinking during pregnancy, particularly continuous moderate to heavy consumption, had a significant positive effect on adolescent daughters' current drinking, but a slight negative effect on sons' lifetime drinking. The sex-specific prenatal effect on current drinking persisted with controls for prenatal maternal cigarette smoking, current maternal drinking, child-rearing practices (i.e. maternal child closeness, monitoring and a rule against drinking) and adolescent's problem behaviors in childhood. Prenatal maternal smoking was also associate with elevated rates of adolescent drinking, particularly current drinking. Of the child-rearing variables, only a rule against drinking decreased adolescent drinking. Thus, selected prenatal factors may constitute risks for alcohol consumption among adolescent daughters. Griesler, P.C., Kandel, D.B. *Journal of Studies on Alcohol*, 59(3), pp. 292-304, 1998.

Ethnic Identity has Protective Effect on Risks for Drug Use

Five year follow-up data were collected from structured interviews with 555 male and female Puerto Rican adolescents who were originally interviewed in 1990 in New York City. At time of follow-up, the average age of the respondents was 19. The interview data were analyzed to determine the relationship of multiple drug risks, Puerto Rican identity, and drug use. In addition, the risk/protective and protective/protective paradigms for examining interactive effects of ethnic identity and drug risks on drug use were assessed. Each risk and two ethnic variables were related to drug use. Regressions showed that cultural knowledge, being culturally active, group attachment, and identification with Puerto Ricans offset the impact of risks on drug use. Ethnic variables also enhanced the protective effect of other protective factors. The findings substantiate expanding risk-buffering models to include ethnic identity and the protective role of ethnic identity for Puerto Rican Youth. Brook, J.S., Whiteman, M., Balka, et al. Drug Use Among Puerto Ricans: Ethnic Identity as a Protective Factor. *Hispanic Journal of Behavioral Sciences*, 20(2), pp. 241-254, 1998.

Statistical Methods in Genetic Research on Smoking

A growing body of evidence suggest that genetic factors have an important influence on the onset and course of smoking. Various statistical methods that have been used to test for genetic influences on smoking behavior, with a particular focus on studies of large national twin samples were reviewed. It is shown how many of the hypotheses that have been tests using a genetic model-fitting approach may be reformulated using logistic regression models that are more familiar to epidemiologists. Such an approach is more easily extended to allow for sociocultural, as well as genetic, influences on smoking behavior. Using either approach, data obtained from Scandinavian, Australian, and U.S. adult twins were consistent in indicating that certainly in men, and possibly in women, genetic factors play an important role in predicting which individuals who become cigarette smokers progress to being long-term persistent smokers. Heath, A.C., Madden, P.A.F., and Martin, N.G. *Statistical Methods in Medical Research*, 7, pp. 165-186, 1998.

Maternal Smoking in Pregnancy, Child Behavior Problems, and Adolescent Smoking

This study used a longitudinal sample of mother-child dyads to examine the role of child behavior problems in explaining the effect of maternal prenatal smoking on adolescent daughter's smoking. Maternal smoking during pregnancy is associated with higher levels of child behavior problems, particularly among girls. Childhood behavior problems increase the likelihood of lifetime smoking among daughters but do not explain the effect of prenatal maternal smoking on their current smoking. Maternal smoking in pregnancy, especially heavy use of a pack or more a day, retains a unique effect on girls' current smoking with controls for current maternal smoking, child behavior problems, and maternal monitoring of the child. The effect of maternal prenatal smoking is suggestive of a biological component, which may have direct or indirect influences on adolescent smoking. The small number of cases in the study calls for the replication of these findings in large samples that would incorporate prospective measures of prenatal nicotine exposure from mother and father and additional biological and psychosocial covariates. Griesler, P.C., Kandel, D.B., Davies, M. *Journal of Research on Adolescence*, 8(1), pp. 159-185, 1998.

Smoking, Smoking Cessation, and Tooth Loss

Smoking is associated with an increased risk of tooth loss, but it is not known if this risk decreases significantly when individuals quit smoking. The objectives of this study were to describe the rate of tooth loss by smoking status in two populations of medically healthy men and women. Among the men, rates of tooth loss and edentulism in relation to smoking cessation were also evaluated. The subjects were drawn from a group of 584 women (aged 40 to 70) recruited from the Boston, MA, area and a separate population of 1231 male veterans (aged 21 to 75) who participated in the VA Dental Longitudinal Study in Boston. In cross-sectional baseline analyses, current cigarette smokers of either had significantly more missing teeth than never-smokers or former smokers. Former smokers and pipe or cigar smokers tended to have an intermediate number of missing teeth. Current male smokers had more teeth with calculus, but the differences in plaque, tooth mobility, probing depth >2 mm, filled and decayed teeth, and bleeding on probing by smoking history were not significant. Prospective observations of 248 women (mean follow-up time=6.2 years) and 977 men (mean=18.7 years) indicated that individuals who continued to smoke cigarettes had 24-fold (men) to 3.5 fold risk (women) of tooth loss compared with non-smokers. The rates of tooth loss in men were significantly reduced after they quit smoking cigarettes but remained higher than those in non-smokers. Men who smoked cigarettes had a 4.5-fold increase in risk of edentulism, and this risk also decreased upon smoking cessation. These findings indicate that the risk of tooth loss is greater among cigarette smokers than among non-smokers. Smoking cessation significantly benefits an individual's likelihood of tooth retention, but it may take decades for the individual to return to the rate of tooth loss observed in non-smokers. Krall, E.A., Dawson-Hughes, B., Garvey, A.J., and Garcia, R.I. *Journal of Dental Research*, 76(10), 1997.

Gender Difference In The Outcome Of An Unaided Smoking Cessation Attempt

There is conflicting evidence concerning gender differences in success at quitting smoking. Information is especially lacking regarding gender differences among unaided quitters who make up the vast majority of those attempting to quit. One hundred thirty-five smokers who made an unaided attempt at quitting were interviewed before quitting and were followed for 1 year after cessation. Relapse rates were extremely high both for men and women with 62% of participants returning to regular smoking within 15 days after cessation. Women and men were equally likely to maintain short-term abstinence (through 15 days), but women were more than three times as likely to relapse subsequently. Nine percent of men, but no women, had biochemically verified sustained abstinence throughout the 1-year follow-up-period. For both men and women, any smoking after the quit attempt inevitably led to full-blown relapse. Most participants resumed regular smoking within 24 hours after the first episode of smoking. Gender differences were observed for several variables related to smoking history, demographics, social support, perceived stress, and motivational factors, but these differences did not explain the increased risk of relapse for women. Results clearly indicate that women are less likely than men to maintain long-term smoking abstinence following an unaided quit attempt, but reasons for this gender difference need further exploration. Ward, K., Klesges, R., Zbikowski, S., Bliss, R., and Garvey A. *Addicted Behaviors*, 22(4), pp. 521-533, 1997.

Hepatitis C Virus Transmission Dynamics in IDUs Challenges Prevention Efforts

Holly Hagan, Ph.D., reviewed published studies on the seroepidemiology of hepatitis C (HCV) in drug injectors in relation to HIV and hepatitis B (HBV) epidemiology, and related HBV, HIV, and HCV infections to a model of infectious disease transmission dynamics. She describes the unique features of HCV that define the epidemiology and natural history of the infection, and shows how HCV may be an important biological indicator of chains of viral transmission in an injection drug-user population. HCV presents several challenges to the development of prevention programs for IDUs. The infection in up to 80% of cases is persistent, and viremic individuals may transmit infection to others. With 65-90% of IDUs anti-HCV positive, a large reservoir of infection exists in most drug injector populations. Studying the genetic variability of HCV infections could permit researchers to reconstruct chains of viral transmission in IDUs. However, the relationship of HCV to HIV epidemiology remains unclear and may depend on whether the proportions of infectious persons in the population are similar for both viruses. Hagan, H. Hepatitis C Virus Transmission Dynamics in Injection Drug Users. *Substance Abuse and Misuse*, 33(5), pp. 1197-1212, 1998.

Patterns of Noninjecting Heroin Use and Risks for Transitions to Use by Injection

In a recent article, researchers review ethnographic data they have collected and the published literature in describing possible factors linked to an increased prevalence in noninjecting heroin use. Heroin use by noninjecting routes of administration has become more widespread worldwide, to the extent that its prevalence now equals or exceeds heroin use by injection in some cities (e.g., Rotterdam in The Netherlands and London in the United Kingdom). Methods of noninjected heroin use include oral ingestion, intranasal use by sniffing the powdered form,

smoking (either by itself or in a mixture with other drugs or substances, such as marijuana or tobacco), and inhaling the vapor after heating the drug on aluminum foil (colloquially known as "chasing the dragon"). Several reasons are discussed to explain why noninjecting heroin use has increased: the supply of high purity heroin is abundant (the worldwide production of opium has nearly doubled since the late 1980s and the purity of street-level heroin is at an all-time high); the wholesale price has fallen, as has the retail price; heroin distribution has become much more efficient, sophisticated, and "high tech" (e.g., use of electronic beepers with special codes, home delivery, more nonstreet sales); and users perceive noninjecting use as protective against HIV (in addition to reporting a fear of AIDS from needles, and anxiety about the use of needles themselves, noninjectors report being socially and morally different from highly stigmatized injectors or "dope fiends"). Another factor is that many heroin noninjectors use crack cocaine and report mixing crack with heroin as a way to modulate crack's stimulant effect and soften its "crash." The risks for transitioning from noninjecting heroin use to heroin injection are complex, and are characterized as falling along a continuum. Some people report using it strictly on social occasions, and not between, to stabilize their use and prevent themselves from developing a dependency. But of 202 new injectors in New York City between 1991 and 1993, 53% had sniffed heroin in the 30 days before their first injection, and 83% reported heroin as the drug they first injected. Factors which appear to predict transitions to injection use are the influence of social network members and those with whom they engage in drug and sexual behaviors, sociodemographic status (especially gender, race/ethnicity), and the extent of social integration within (or marginalized from) social institutions. Neaigus, A., Atillasoy, A., Friedman, S.R., et al. Trends in the Noninjected Use of Heroin and Factors Associated with the Transition to Injecting. In: J. Inciardi and L. Harrison (Eds.). Heroin in the Age of Crack-Cocaine. Thousand Oaks, CA: SAGE Publications, Inc.; Volume 6 of the drugs, health, and social policy series: pp. 131-159, 1998.

Current and Emerging Heroin Use Trends in the Age of Crack-Cocaine

A state-of-the-art volume has just been released which presents articles by experts in the field on current developments and emerging trends, in addition to a historical overview, of heroin use in the United States. The volume fills a void in the current literature on what's known about the "new" heroin users today, and provides an update on the status of aging heroin addicted populations who initiated use of the drug prior to the "age of cocaine." Having moved from the stereotypical "shooting galleries" of back alleys in inner city neighborhoods, heroin addiction continues to rise in mainstream culture and new ways of administration have come into use. A relative abundance of purer Southeast Asian heroin, the rapid rise in popularity of crack-cocaine, treatment controversies, and the realized role that injection drug use plays in the transmission of HIV all suggest increased dimensions of the heroin problem and in their saliency for the 1990s and beyond. Inciardi, J.A. and Harrison, L.D. (Eds.). Heroin in the Age of Crack-Cocaine. Thousand Oaks, CA: SAGE Publications, Inc.; Volume 6 of the drugs, health, and social policy series, 1998.

Heavy Caffeine Use and the Beginning of the Substance Use Onset Process: An Illustration of Latent Transition Analysis

This chapter has two objectives, the introduction of a relatively new methodology, latent transition analysis (LTA) and the demonstration of its usefulness in alcohol prevention research. LTA is an extension of latent class theory that allows the user to estimate and test models of stage-sequential development. Researchers may be more accustomed to thinking in terms of strictly quantitative development, in which change can be characterized by increases and decreases in a particular variable, such as test scores, self-esteem, or amount of alcohol consumed per week. Stage-sequential development is distinguished from quantitative development by the involvement of qualitatively different stages. Individuals develop by passing through these stages. In this study, LTA was used to investigate whether heavy use of caffeine would be a predictor in the early part of the substance use onset process. Heavy use of caffeine was defined in several different ways, in terms of both coffee and cola soft drinks. By all the definitions of heavy caffeine use, those in the high-caffeine-risk latent class were more likely to have initiated the substance use onset process by seventh grade, and those who had not initiated by seventh grade were more likely to do so by eighth grade. The increased risk of onset related to caffeine use was greater for coffee than for cola. For coffee, the probability of onset was greater for the more extreme definitions of caffeine risk. The level of caffeine consumption required to elevate risk was surprisingly low. Increased risk was found for as little caffeine consumption as 6 cups of coffee in one's lifetime and 6 cola drinks in the past week. The results replicated well and consistently across two cross-validation subsamples. In K. Bryant, M. Windle, and S.West (Eds.), The Science of Prevention: Methodological Advances from Alcohol and Substance Abuse Research (pp. 79-99). Washington, DC: American Psychological Association, 1998.

Problem and Conventional Behaviors Among American Indian Adolescents

Investigators from the National Center for American Indian and Alaska Native Mental Health Research at the University of Colorado Health Sciences Center report two related factor analytic studies that take Problem-Behavior Theory as a starting point. They examined the latent structure of problem and positive behaviors in a sample of 1894 American Indian adolescents (n=1894 in the first study and 2250 in the second study) and found a 2-factor 2nd-order structure in which problem behaviors (alcohol use, drug use, antisocial behavior, risky sexual behavior) and positive behaviors (school success, cultural activities, competencies, community-mindedness) represented two relatively uncorrelated aspects of behavior. The positive behaviors construct contributed significant incremental construct validity in the prediction of psychosocial outcomes (e.g., depression, competencies), relative to the problem behavior construct alone. Factor structures differed across gender primarily for alcohol use and school success. The second-order alcohol use factor was more closely related to "problem drinking" for girls, but for boys it was more closely related to "negative consequences following drinking". "Doing schoolwork carefully" was more closely related to school success for girls than for boys, reflecting others' reports that girls tend to attribute their successes in school to their own hard work whereas boys tend to attribute their school successes to greater intellectual ability. Across four sampled communities, the structures differed only slightly, suggesting commonalities on such dimensions as positive behaviors, possibly from consistent messages adolescents receive about appropriate ways to act. Results highlight the need to include a focus on positive behaviors in prevention/promotion activities, and community members need to understand not only how to circumvent the processes that result in maladaptive outcomes but also how to promote the development of successful adolescents. Mitchell, C.M., and Beals, J. The Structure of Problem and Positive Behavior Among American Indian Adolescents: Gender and Community Differences. American Journal of Community Psychology, 25, pp. 257-288, 1997; and Mitchell, C.M. and O'Nell, T.D. Problem and Conventional Behaviors Among American Indian Adolescents: Structure and Validity. *Journal of Research on Adolescence*, 8, pp. 97-122, 1997.

Affectivity and Impulsivity: Temperament Risk for Adolescent Alcohol Involvement

Researchers at Arizona State University studied the joint effects of impulsivity, positive affectivity, and negative affectivity on adolescent alcohol use and alcohol-related impairment. Participants were 427 adolescents (aged 12-18, mean age=14.6) from the third wave of an ongoing study of adolescent children of alcoholics and demographically matched controls. Data were gathered using in-person interviews with adolescents and their parents. Results showed that impulsivity moderated the effects of positive affectivity on both alcohol use and alcohol-related impairment. Impulsive adolescents who were also characterized by low levels of positive affectivity showed higher alcohol involvement and more alcohol-related impairment than did either impulsive adolescents with high levels of positive affectivity or non-impulsive adolescents. These results suggest that multiple dimensions of temperament (and their interaction) must be taken into account in trying to predict alcohol involvement, and that positive affectivity is important above and beyond negative affectivity. Practically, the results suggest that positive affectivity is a potentially important target for intervention programs. Although intervention programs often focus on teaching adolescents how to cope with negative affect, less attention has been paid to interventions that increase positive affect, and strategies that target positive affect may be helpful additions to prevention programs. Colder, C.R., and Chassin, L. *Psychology of Addictive Behaviors*, 11, pp. 83-97, 1997.

Effects of Stress on Delinquency and Drug Use Similar for Males and Females

In a test of Agnew's revised individual-level strain theory, which postulates a mediating role for negative relationships and resulting negative affect (primarily anger) that propels adolescents toward deviant adaptations, investigators at the National Opinion Research Council (NORC) assessed the effects of stressful life events on male and female adolescents' subsequent delinquent and drug-using behaviors. They hypothesized the relationships would vary by sex because of previously observed differences in males' and females' reactions to stress. They used structual equation modeling with two waves of data from 11-to 17-year old adolescents in the High Risk Youth Study (N = 803), a sample that includes heavy representation of offsprings of parents with psychological disorders. Modeling variables reflecting stressful life events, school and family attachment, grades, and indicators of delinquency and substance use, they found that stressful life events have a similar, short-term impact on delinquency and drug use among females and males and that changes in life events were associated with greater delinquency and drug use. The authors presented several possible reasons for the failure to find a sex difference, including the possibility that stress associated with parental psychological disorders may affect males and females similarly. Hoffman, J.P., and Su, S.S. The Conditional Effects of Stress on Delinquency and Drug Use: A Strain Theory Assessment of Sex Differences. *Journal of Research in Crime and Delinquency*, 34 (1), pp. 46-78, 1997.

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

The impact of maternal and adolescent factors on initial and increased levels of drug use by adolescents was examined in two groups of adolescents: 210 younger adolescents (ages 12-14 at initial assessment) and 199 older adolescents (ages 15-18). The adolescents and their mothers were interviewed at 2 points in time, 3 years apart. The results indicated that adolescent unconventionality is a crucial determinant for both initial and increased levels of drug use for both age groups, but intrapsychic distress is more important for the younger adolescent's initial use. Lack of maternal attachment and poor control techniques were associated with initial levels of drug use for both groups. However, the mother-child relationship and models of the mother's unconventionality had a greater impact on the older than on the younger group's increased involvement. Interactive results suggest that adolescents from both age groups who are well adjusted can offset the potential risks of maternal models of drug use. Brook J.S., Cohen P., and Jaeger, L. *The Journal of Genetic Psychology*, 159(2), pp. 179-197, 1998.

Drug Use and Parenting in Adolescence

This project at the University of Washington conducted longitudinal analyses of 241 adolescent mothers' use of 3 substances -- marijuana, alcohol and tobacco -- from the time of pregnancy through 1 year post-partum. Variables measured for each substance included use, verified with urinalysis; intentions to use; attitudes and perceived norms about using; and specific outcome and normative expectations about use of each substance. Substance use increased dramatically from pregnancy to 6 months post-partum, leveling off between 6 and 12 months post-partum. Consistent with the Theory of Reasoned Action model, as substance use increased after pregnancy, so did intentions to use, favorable attitudes toward use, perceived norms regarding use, and beliefs favorable to use. Changes in specific outcome and normative beliefs were observed and that, over time, the young mothers saw bad outcomes of using substances (such as negative effects on their health) as less likely, and positive outcomes (such as helping them to forget their problems) as more likely. They also perceived less disapproval from their families, friends, and doctors after their babies were born. These findings suggest that young mothers are heeding warnings about the danger to their babies of using substances during pregnancy, but are less convinced that substance use has negative effects on parenting or on their own health. The contrast between the abundance of messages warning about substance use during pregnancy and the very few messages aimed at reduce substance use among parents may unwittingly reinforce a notion that substance use is not very harmful when one is not pregnant. A promising intervention approach for young mothers may be to capitalize on their concerns for their babies' health. Morrison, D.M., Spencer, M.S., and Gillmore, M.R. *J. Res. Adoles.*, 8, pp. 69-95, 1998.

Sibling Antisocial Behavior, Substance Use, and Intra-family Conflict

Conventional covariance structure analysis, such as factor analysis, is often applied to data obtained in a hierarchical fashion, such as siblings observed within families. Multivariate modeling of such data, however, is most frequently done as if the data were obtained as a simple random sample from a single population. An alternative specification is presented that explicitly models the within-level and between-level covariance matrices in family antisocial behavior. Data from the National Youth Survey included 1076 adolescents from 450 households. The age of participants ranged from 11 to 17 years with a mean age of 13.9 years. Antisocial behavior included theft, aggression, vandalism, and minor violations. Predictors of family antisocial behavior included life transitions, parent marital status, and whether the family was receiving public assistance. Results showed homogeneity in antisocial behavior within sibling clusters and heterogeneity across families. Between-family variation in antisocial behavior represented approximately 31% of the total variation in antisocial behavior scores. Families experiencing greater numbers of life transitions had higher family levels of antisocial behavior. Findings highlight potential pitfalls of ignoring issues of dependence and demonstrate the importance of examining family-level clustering of specific problem behaviors, such as antisocial behavior.

Another paper on sibling behavior demonstrates a more appropriate specification which explicitly models the within-level and between-level covariance matrices of sibling substance use and intra family conflict. Participants were 267 target adolescents (mean age=13.11 years) and 318 siblings (mean age=15.03 years). The level of homogeneity within sibling clusters, and heterogeneity among families, was sufficient to conduct a multilevel covariance structure analysis (MCA). Parent and family-level variables consisting of marital status, socioeconomic status, marital discord, parent use and modeling of substances, were used to explain heterogeneity across families. Marital discord predicted

intra family conflict, and single-parent families and families with higher levels of parent displayed substance use had higher levels of sibling substance use. Duncan, T.E., Alpert, A., and Duncan, S.C. Multilevel Covariance Structure Analysis of Sibling Antisocial Behavior. Structural Equation Modeling, 5, pp. 211-228, 1998; Duncan, T.E., Alpert, A., Duncan, S.C., and Hops, H. *Journal of Psychopathology and Behavioral Assessment*, 18, pp. 347-369, 1997.

Social Context Predictors of Adolescent Substance Use Development

This study examined the form of growth in alcohol, cigarette, and marijuana use among adolescents and covariates influencing this growth. Participants were 664 male and female adolescents (ages 14 to 17 years) assessed at three time points. A common trajectory existed across the developmental period with significant increases in all three substances. Second-order multivariate extensions of the basic latent growth modeling framework indicated that associations among the individual differences parameters representing growth in the various substance use behaviors, could be adequately modeled by a higher-order substance use construct. Inept parental monitoring, parent-child conflict, peer deviance, academic failure, gender, and age, were significant predictors of initial levels and the trajectory of substance use. Results indicate considerable similarity in the development of alcohol, cigarettes and marijuana during adolescence, and suggest that it may be possible to reduce the upward trajectory of adolescent substance use if we improve the prevalence of effective parental monitoring, reduce parent-child conflict and associations with deviant peers, and increase academic success. Duncan, S.C., Duncan, T.E., Biglan, A., and Ary, D.V. Contributions of the Social Context to the Development of Adolescent Substance Use: A Multivariate Latent Growth Modeling Approach. *Drug and Alcohol Dependence*, 50, pp. 57-71, 1998.

Behavioral and Emotional Problems Among Children of Cocaine and Opiate Dependent Parents

Children of cocaine and opiate dependent parents are compared with demographically matched referred and nonreferred children. Cocaine and opiate dependent parents completed the Child Behavior Checklist for 410 children (218 boys, 192 girls) between the ages of 2 and 18 years (mean=7.9 years). Children of drug abusers (CDAs) were matched to referred (RCs) and nonreferred children (NCRs) on age, gender, informant, ethnicity, and SES. RCs scored lower than CDAs and NCRs on all competence scales, and higher than CDAs and NRCs on all problem scales. CDAs scored lower than NRCs on social, school, and total competence, and higher than NRCs on withdrawn, thought problems, delinquent behavior, aggressive behavior, internalizing, externalizing, and total problems. More CDAs than NRCs also scored in the clinical range on school and total competence, withdrawn, anxious/depressed, thought problems, delinquent behavior, aggressive behavior, internalizing, externalizing, and total problems. Preschool CDAs were at risk of both internalizing and externalizing problems, and adolescent CDAs were at greatest risk of externalizing problems. CDAs were at risk of internalizing and externalizing psychopathology relative to demographically matched NRCs, but showed significantly less psychopathology than shown by matched RCs. Stanger, C., Higgins, S.T., Bickel, W.K., Elk, R., Grabowski, J., Schmitz, J., Amass, L., Kirby, K.C., Seracini, A. *Journal of the American Academy of Child and Adolescent Psychiatry*, 1998.

Alcohol-Related Homicides Committed by Women

In an analysis of data derived from interviews conducted with female homicide offenders as part of the FEMDREIM (Female Drug Relationships in Murder), cases in which respondents believed the offense was related to their use of alcohol at the time of the homicide were examined (N=35). Four basic types of homicides based on victim-offender relationships and the circumstances of the incidents were found. The first and most common type (n=11 or 31% of the alcohol-related homicides) was a non-domestic dispute (i.e., a dispute where the victim was not a spouse, lover, or other family member). The second type (n=7 or 20% of the homicides) was a domestic dispute (i.e., a dispute that was domestic in nature in that the victim was an intimate or family member). The third type (n=7 or 20% of the alcohol-related homicides) occurred during a robbery. The fourth type of alcohol-related homicide (n=4 or 11% of the homicides) was a DWI (driving while intoxicated) case. (Also, there were six alcohol-related homicides (17%) that could not be categorized as one of the four basic types. These involved a variety of other circumstances, including child abuse and neglect, arson, and infanticide.) Women who committed each type of alcohol-related homicide reported a variety of motives for committing these acts. There were also similarities and differences between the types not only in the kinds of motives reported but also in the extent to which planning was involved. Likewise, there were similarities and differences between the different types of homicides regarding the type and amount of alcohol and other drugs used by respondents on the day of the incident, and regarding respondents' perceptions of the alcohol-relatedness of the events. Spunt, B., Brownstein, H., Crimmins, S., Langley, S., Spanjol, K. *Journal of Psychoactive Drugs*, 30, pp. 33-43, 1998.

Aggression Classification and Treatment Response

This preliminary study investigated whether the aggression subtypes derived from the Aggression Questionnaire (AQ) are related to treatment response. Subjects were 28 aggressive conduct-disordered children (25 males, 3 females), ranging in age from 9.8 to 17.0 years (mean=12.69 years), who participated in a double-blind, placebo-controlled study of lithium as a treatment for reducing aggression. The Predatory-Affective Index of the AQ was used to classify subjects into predatory (planned) or affective (explosive) subtypes of aggression and then related this classification to treatment response. This index did not differentiate placebo baseline responders from non-responders but did significantly differentiate responders and non-responders during the experimental treatment period, regardless of whether they received lithium or placebo. Treatment response was associated with a more affective and less predatory subtype of aggression. Authors report that, to the best of their knowledge, this is the first study in children to show an association between aggression subtype and treatment response. Malone R., Bennett D., Luebbert, J., Rowan, A., Biesecker, K., Blaney, B., Delaney, M. *Psychopharm*. Bulletin, 34(1), pp. 41-45, 1998.

Using Developmental Processes to Predict Substance Use Outcomes

Latent growth models have been used to describe developmental growth and to identify factors that influence growth in predictable ways. However, there are few examples of research that use characteristics of growth trajectories as predictors of developmental outcomes. This report provides an illustration of this type of study, where the development of ego resiliency (a sequence of stages of functioning across the domains of personal relationships, impulse control, moral develop-ment and cognitive style) over the adolescent years is modeled as a predictor of alcohol and tobacco use in early adulthood. Ego development was assessed six times during a ten year interval in a sample of 123 adolescents. Previous work with these data show that growth in ego development can be described as a curvilinear trajectory over this ten year period. This paper extends prior work to examine the extent to which ego level at three different points along the ten year trajectory (the initial assessment, midway through the study, and the final assessment), the rate of growth at these three points, and the extent to which curvature in ego growth predicted subjects' substance use status in the final year of the study. Results show that steady growth in ego development during early adolescence is associated with nonsmoking status in early adulthood. In addition, youths with steady ego development are more likely than those with delayed development to report moderate drinking habits. Sayer, A.G. and Allison, T.J. Using Developmental Processes to Predict Substance Use Outcomes. The Methodology Center Technical Report Number 98-25, College of Health and Human Development, The Pennsylvania State University, 1998.

Raising Healthy Children

In 1993, ten schools were randomly assigned to program or control conditions resulting in a sample of 562 program and 478 control first and second grade students. Students are currently in grades 5 and 6. Teachers, parents and students have been surveyed annually, teachers are observed twice a year, and school records are collected. The intervention includes teacher staff development, parenting workshops, and individual work with students. After 1.5 years of the intervention, teacher reports indicated academic and behavioral improvements for children in the experimental condition. Recent analyses focused on students in the top tertiles on antisocial behavior and depression. High anti-social students demonstrated higher academic achievement compared with their control group counterparts. Among the depressed children, those in the experimental group maintained their baseline level of social competence, whereas those in the control group decreased. Analyses focused on the hypothesized processes of development revealed significant prediction of family attachment (in year 3) from earlier protective processes (involvement, opportunities, and rewards) and child social, emotional and cognitive skills. Additional analyses examined the long-term effects of parental transitions and family stress on the development of anti-social behavior in children. Results suggest that family bonding partially mediates the effects of parental transitions on antisocial behavior. Haggerty, K.P., Catalano, R.F., Harachi, T.W., and Abbott, R.D. *Criminology*, 31(1), pp. 25-48, 1998.

Modeling of Longitudinal and Multilevel Alcohol Use Data

Using Multilevel Latent Growth Modeling (LGM), levels of alcohol use and development of alcohol use over four years were examined among individuals (adolescents and parents) nested within families. The sample comprised 435 families (435 target adolescents, 203 siblings and 566 parents) assessed annually for four years. The effects of family

status (single-parent, two-parent intact, and stepparent families) and socioeconomic status (SES) on family levels and development of alcohol use were examined. Approximately 29% of the total variation in initial levels of alcohol, and 37% of the developmental trajectories for alcohol use could be explained by family membership. Stepparent families, and less educated and more economically disadvantaged families, had higher family levels of alcohol use and developed in their use of alcohol at a faster rate. Findings suggest that the alcohol use of individuals in the same family is more alike than that of individuals from different families and that family alcohol use may be influenced by family-level variables such as family composition or SES. Duncan, T.E., Duncan, S. and Hops, H. Latent Variable Modeling of Longitudinal and Multilevel Alcohol Use Data. *Journal of Studies on Alcohol*, 59, pp. 399-408, 1998.

Beliefs About Substance Use Among Pregnant and Parenting Adolescents

Substance use among pregnant and parenting adolescents has health implications for both mother and baby. Utilizing the Theory of Reasoned Action, a social psychological model, this research investigates the cognitive structure underlying substance use, based on longitudinal analyses of data from 3 waves of interviews with a cohort of young mothers who were 17 years old or younger during pregnancy. Use of cigarettes, alcohol, and marijuana were lowest during pregnancy, increased sharply at 6 months postpartum, and remained level at 12 months postpartum. Changes in intentions, attitudes, perceived social norms, outcome beliefs, and normative beliefs followed the same pattern. The content of changing beliefs about substance use is examined and implications for substance use interventions among postpartum adolescent mothers is discussed. Morrison, D., Spencer, M., and Gillmore, M. *J. Res. Adoles.*, 8(1), pp. 69-95, 1998.

An Ecological Model for School-Based Mental Health Services for Urban Low-Income Aggressive Children

An ecological model for school-based mental health services that targets urban low-income aggressive children--a highly vulnerable and underserved population--is presented. The goals of the model are to increase children's and teachers' involvement in the delivery of services and to increase the integration of these services into existing school resources and activities. The model proposes that mental health service providers work in collaboration with teachers to deliver services that (1) can be managed by existing school resources and personnel, (2) are related to empirically based factors associated with reduced aggression and increased social functioning, and (3) are group administered to increase the number of children served and to reduce stigmatization associated with mental health services. The model is individualized and flexible by acknowledging that contexts for aggression differ across classrooms and children by providing services specific to those contexts. Two studies are presented illustrating the application of this model to decrease aggression and increase academic engagement in low-income urban public schools. Atkins, M.S., McKay, M.M., Arvantis, P., London, L., Madison, S., Costigan, C., Haney, P., Zevenbergen, A., Hess, H., Bennett, D., and Webster, D. *The J. of Behav. Health Serv. & Res.*, 5(1), pp. 64-75, 1998.

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^{31}P MRS and ERP Investigations of Substance Abuse Liability

Researchers at the University of Pittsburgh report two recent neurobiological studies elucidating components of liability to substance abuse. The first was an exploratory study to determine the heuristic potential of Phosphorus-31 magnetic resonance spectroscopy (MRS) employing chemical shift imaging (CSI), a procedure that reveals the presence of low molecular weight phosphorus containing metabolites critical in the transformation and use of energy by neurons and glia. Four distinct anatomic brain locations (i.e. frontal, occipital, right parietal, left parietal) were imaged in three groups of peripubertal children hypothesized to be at varying levels of familial SUD risk: children with a positive paternal history of SUD and a disruptive behavior disorder (DBD) diagnosis (SUD+/DBD+; n=10), those with a positive paternal SUD history in the absence of other psychopathology (SUD+/DBD-; n=13), and matched control children from normal families (SUD-/DBD-; n=13). In addition, investigators examined subjects' neuro-cognitive test results to determine any associations between cognitive capacities and regional ^{31}P1 MRS spectra. The highest-risk sample (SUD+/DBD+) demonstrated a diminished proportion of phosphodiesters confined to the right parietal voxel. This right parietal phosphodiester proportion correlated only with the Information Scale score on a standard intelligence test for children. This suggested a relationship between general learning ability and motivation for academic achievement and right parietal physiology in the highest-risk sample. Variations in synaptic pruning could account for this observation. Moss, H.B., Talagala, S.L., and Kirisc, I.L. Phosphorus-31 Magnetic Resonance Brain Spectroscopy of Children at Risk for a Substance Use Disorder: Preliminary Results. *Psychiatry Research-Neuroimaging*, 76(2-3), pp. 101-112, 1997.

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

Evaluating the Perceived Quality of Drug Treatment Programs

Key personnel in 294 drug treatment facilities in Los Angeles County were surveyed to provide objective program information and subjective evaluations of various aspects of their treatment programs. These ratings were obtained as part of the UCLA Drug Abuse Research Center Treatment Referral Network Survey which has the goal of matching drug users' treatment needs to appropriate services. Using latent variable models, a subset of the objective measures was used to predict perceived quality of the treatment programs. Perceived quality was indicated by ratings of the effectiveness of counseling services, staff, and overall program. At the latent variable level, significant predictors of greater perceived quality included a programmatic focus (philosophy and emphasis), and program intensity (greater frequency and number of psychological and social services). Group therapy and methadone program (including detoxification and maintenance) had significantly negative effects. Individual therapy had a slightly positive but not statistically significant effect on perceived quality. There were also significant relationships among measured variables: More individual counseling and a skills-building approach predicted higher ratings of overall program, supportive group therapy predicted higher ratings of treatment staff, and a change-oriented emphasis predicted higher ratings of counseling services. Measured variables representing staff turnover ratio, caseloads, and ratio of licensed staff to total staff did not significantly predict quality and did not increase the amount of variance accounted for by the final path model. The variables were, however, significantly correlated with some of the predictors which in turn predicted quality. Hser, Y.I., Stein, J.A., Maglione, M., & Polinsky, M.L. Predicting Perceived Quality of Drug Treatment Programs Using Latent Variable Models. *Evaluation and Program Planning*, 21, pp. 1-10, 1998.

Information Exposure

A theoretical model of attention to messages has been used to guide an extensive series of laboratory and field experiments involving the mass media and, more recently classroom instruction and health interventions. The model draws on individual differences in need for novelty as a basis both for identifying target audiences most likely to engage in a number of health risk behaviors, such as drug and alcohol abuse and risky sex, and as a guide for designing messages to attract and hold the attention of some individuals who make up the prime target audience for many campaigns. These strategies have been successful in bringing about changes in attitudes and behavioral intentions in experimental studies and in reaching at-risk audience segments in field studies through novel televised public service announcements placed in appropriate television programming. Donohew, L.R., Lorch, E.P., and Palmgreen, P. Applications of a Theoretical Model of Information Exposure to Health Interventions. *Health Communication Research*, 24(3), pp. 454-468, 1998.

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National Institute on Drug Abuse

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

Research Findings

Intramural Research

Behavioral Neuroscience Section, Behavioral Neuroscience Branch

An Antagonist of the Psychotomimetic Effects of Phencyclidine (PCP) has been Identified

PCP is a drug of abuse which produces bizarre behavioral and toxic effects. A selective agonist for dopamine D3 receptors, PD 128,907, has recently been shown to prevent the psychotomimetic-like effects of PCP in animal models. Interestingly, PD 128,907 also demonstrates the pharmacological profile of an atypical antipsychotic agent. This is the first report that has identified a D3 receptor drug as a potential antipsychotic drug candidate and an antagonist of effects of PCP. Likewise, the pharmacological management of schizophrenia, a disorder affecting about 1% of the general population, is not well-advanced. IRP researchers demonstrated that the PCP-blocking effects of PD 128,907 are due to effects of the drug on a very specific class of dopamine receptors that has precise localization in the brain. This paper is also the first to report on a new antagonist for these receptors that is the most selective agent known to date. These data will be useful for understanding the pathophysio-logical states of schizophrenia and the effects of PCP. This knowledge may result in the ultimate development of clinically useful drugs based upon this novel strategy. Witkin, J.M., Acri, J., Beekman, M., DeBoer, P., Wikstrom, H., and Dijkstra, D. Atypical Antipsychotic-like Effects of the Dopamine D3 Receptor Agonist, (+)-PD 128,907. *Eur. J. Pharm*. 347, R1-R3, 1998.

Pharmacotherapy Section, Treatment Branch

Sociodemographic Characteristics of Subjects in Cocaine Studies

Intramural scientists have reviewed the English-language, peer-reviewed literature on clinical studies of cocaine abuse pharmacotherapy to evaluate the sociodemographic characteristics of research subjects. Their major findings were that (1) many published studies do not fully report the sociodemographic characteristics of their subjects, and (2) research subjects are fairly comparable in basic sociodemographic characteristics to the larger population of treatment-seeking individuals with cocaine-related problems (assessed in the National Comorbidity Survey), except for race/ethnicity (African-Americans over represented) and geographic location (Northeast region over represented). Gorelick, D.A., Montoya, I.D., & Johnson, E.O. Sociodemographic Representation in Published Studies of Cocaine Abuse Pharmacotherapy. *Drug and Alcohol Dependence*, 49, pp. 89-93, 1998.

Behavioral Pharmacology Section, Preclinical Pharmacology Laboratory

Upregulation of Nicotine Receptors following Chronic Nicotine is Mediated by NMDA Receptor Activation

Chronic exposure to nicotine can result in sensitization to the stimulant effects of nicotine and produce an increase in the number of CNS nicotine receptors. A number of studies have shown that activation of NMDA receptors mediates the behavioral adaptations that occur following psychomotor stimulant administration. IRP investigators have recently shown that NMDA receptors also mediate the behavioral and neurochemical adaptations observed following chronic nicotine. Rats treated chronically with nicotine showed clear evidence of sensitization to the locomotor activating effects of nicotine. This sensitization could be blocked by pretreatment with the NMDA receptor antagonist MK801. The same treatment regimen of chronic nicotine upregulated nicotine receptors, as shown by [3H]-cystine binding. The upregulation of nicotine receptors was also attenuated by MK-801 treatment. These results suggest that, like other drugs of abuse, sensitization following chronic nicotine exposure is mediated, at least in part, through NMDA receptors. Shoaib, M., Schindler, C.W., Goldberg, S.R. and Pauly, J.A. Behavioural and Biochemical Adaptations to Nicotine in Rats: Influence of MK801, an NMDA Receptor Antagonist. *Psychopharmacology*, 134, pp. 121-130, 1997.

Cocaine Infusion Rate Can Influence Self-administration in Rhesus Monkeys

Substitution therapy has proven to be one of the most effective treatments for drug abuse. Typically, substitution drugs are delivered slowly over period of time (like a nicotine patch) or have a much longer duration of action (like methadone). The slow infusion or long duration of action are thought to mitigate against the abuse of the treatment agent. It follows then that the slow infusion of cocaine at a non-reinforcing dose may well block cocaine self-administration. To test this hypothesis, investigators varied the infusion rate of cocaine delivery to rhesus monkeys lever pressing for cocaine. As infusion rate decreased, self-administration rate also decreased to placebo levels. However, when this non-reinforcing infusion rate of cocaine was delivered throughout a self administration session, responding for cocaine was not affected. If fact, there was evidence to suggest that this slow infusion actually primed or reinstated drug seeking rather than decreased it. Thus, to be successful, substitution therapy for cocaine will likely require dosage levels well above those which are themselves not reinforcing. Panlilio, L.V., Goldberg, S.R., Gilman, J.P., Jufer, R., Cone, E.J., & Schindler, C.W. Effects of Delivery Rate and Noncontingent Infusion of Cocaine on Self-administration in Rhesus Monkeys. *Psychopharmacology*, 137, pp. 253-258, 1998.

Brain Imaging Section, Neuroimaging Branch

The Enantioselective Radiotracer [11C]A-84543 May Have Utility for the Noninvasive Imaging of Nicotinic Acetylcholine Receptors using PET

[11C]A-84543, 3-[(1-[11C] methyl-2(S)-pyrrolidinyl)methoxy]pyridine, is a specific and enantioselective neuronal nicotinic acetylcholine receptor (nAChR) radiotracer. The in vivo biodistribution of this radiotracer in mice showed high brain uptake and a distribution consistent with the density of nAChRs. The nAChR agonists (-)nicotine, cytisine, and (+) epibatidine reduced the radioactivity due to [11C]A-84543 in the superior colliculus by 41%, 38%, and 27%, respectively. The noncompetitive nAChR ligand, mecamylamine displayed no inhibitory effect. Ketanserin (5-HT2/5-HT2C), scopolamine (mAChR antagonist), (+)butaclamol (DA receptor antagonist), and haloperidol (D2/sigma) also displayed no inhibitory effect. The pharmacologically less active (R) enantiomer, also exhibited a high brain uptake, but had a low thalamus/cerebellar ratio of 1.4 which contrasts with a higher value of 2.3 for the more active (S) enantiomer. Since [11C]A-84543 displays enantioselectivity for nAChRs, it may deserve further investigation as a possible PET radiotracer. Kassiou, M., Scheffel, U.A., Ravert, H.T., Mathews, W.B., Musachio, J.L., London, E.D., and Dannals, R.F. Pharmacological Evaluation of [11C]A-84543: An Enantioselective Ligand for In Vivo Studies of Neuronal Nicotinic Acetylcholine Receptors. *Life Sci*. 63(1), PL13-8, 1998.

Cue-Elicited Craving for Cocaine Does Not Represent a Simple State of Cortical Arousal as Assessed by Signs of EEG Activation

Relationships between the spontaneous electro- encephalogram (EEG), self-reports of cocaine craving, and cerebral glucose metabolism, determined using 2-[18F]fluoro-2-deoxy-D-glucose and positron emission tomography, were assessed during the presentation of either neutral or cocaine-related environmental stimuli. In cocaine users but not non-drug-abusing controls, EEG power in the alpha1 and alpha2 frequency bands was significantly lowered during presentation of the drug-related stimuli when compared to the neutral test session. Decreases in alpha1 power were negatively correlated with increases in global glucose metabolism but were not correlated with either the time course or the magnitude of craving throughout the 30-min test session. Although EEG desynchron-ization is related to global brain metabolism, the difference in the time courses between EEG power and craving suggests that self-reports of

cue-elicited cocaine craving do not simply reflect increases in the state of cortical arousal. Liu, X., Vaupel, D.B., Grant, S. and London, E.D. Effect of Cocaine-Related Environmental Stimuli on the Spontaneous Electroencephalogram in Polydrug Abusers. *Neuropsychopharmaoclogy* 19, pp. 192-199, 1998.

Locus Coeruleus Neurons from Morphine-treated Rats Do Not Show Opiate Withdrawal Hyperactivity In Vitro - A Challenge to Current Theory of Opiate Withdrawal

In vitro studies have not consistently demonstrated naloxone-precipitated opiate-withdrawal hyper-activity of locus coeruleus neurons, possibly because some withdrawal may occur during the locus coeruleus slice preparation. NIDA scientists measured opiate withdrawal-related hyperactivity in neurons recorded from locus coeruleus slices while ensuring the maintenance of dependence by keeping morphine present in all solutions to which the tissue is exposed until naloxone-precipitated withdrawal. The firing rate of the drug-naive controls was 0.93 Hz. Bath application of morphine almost completely suppressed firing in drug naive controls (0.058 Hz), whereas in solutions containing morphine the cell firing rate from morphine-treated rats averaged 0.71Hz indicating considerable, but incomplete tolerance. In the same slices, naloxone increased the spontaneous firing to 0.96 Hz. Thus, naloxone did not produce withdrawal hyperactivity even when dependence was maintained, but returned the cells from morphine-treated rats to control rates. It was concluded that locus coeruleus cells in slice preparations from morphine-treated rats do not demonstrate withdrawal-related hyperactivity. Thus, the results do not support a role for adaptations intrinsic to locus coeruleus neurons in withdrawal hyperexcitability, but instead imply the necessity of functional afferent activity. Bell, J.A. and Grant, S.J. Locus Coeruleus Neurons from Morphine-treated Rats Do Not Show Opiate-withdrawal Hyperactivity In Vitro. *Brain Res*., 788(1-2), pp. 237-244, 1998.

A New High Affinity Ligand for Nicotinic Acetylcholine Receptors, [125I]5-I-A-85380, has Excellent Potential as a Noninvasive Imaging Radioligand Using SPECT

5-[125I]iodo-3-(2(S)-azetidinylmethoxy)pyridine, [125I]5-I-A-85380, was evaluated in the mouse as a potential in vivo imaging ligand for central nicotinic acetylcholine receptors (nAChRs). After intravenous administration of [125I]5-I-A-85380, peak brain levels of radioactivity were measured within 1 h and declined slowly over 4 h. [125I]5-I-A-85380 binding was saturable, and both its pharmacology, based upon inhibition studies, and its pattern of accumulation in brain regions having high nAChR densities were consistent with an interaction at (4(2 nAChR agonist binding sites. The thalamus:cerebellum radioactivity ratio, a measure of specific labeling, reached 37. Therefore, radiolabeled 5-I-A-85380 has excellent potential as an imaging radiotracer for nAChRs, particularly with single photon emission computed tomography (SPECT), when 123I is incorporated into the molecule. Vaupel, D.B., Mukhin, A.G., Kimes, A.S., Horti, A.G., Koren, A.O. and London, E.D. In Vivo Studies with [125I]5-I-A-85380, A Nicotinic Acetylcholine Receptor Radioligand. *NeuroReport*, 9, pp. 2311-2317, 1998.

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

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

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

NIDA IRP radiochemists have used a new chemical series of 3-pyridyl ethers synthesized by Abbott Laboratories and having subnanomolar affinity for the nAChR to develop a new fluorinated radioligand. The radiosynthesis of 2-[18-F]A-85380 has yielded a radiotracer with a high specific activity (1050 mCi/(mol). It is noteworthy that the parent compound, A-85380, has a substantially wider margin of safety than epibatidine-type compounds in animal studies. Therefore, a high specific activity combined with the potential for a wider margin of safety suggest that of 2-[18-F]A-85380 that may be an excellent positron emission tomography (PET) imaging radiotracer for nAChRs. Horti, A.G.,

Koren, A.O., Ravert, H.T., Musachio, J.L., Mathews, W.B., London, E.D. and Dannals, R.F. Synthesis of a Radiotracer for Studying Nicotinic Acetylcholine Receptors: 2-[18F]fluoro- 3-(2(S)-azetidinylmethoxy)-pyridine (2-[18F]A-85380). J. Label Compds. *Radiopharm*. XLI, pp. 309-318, 1998.

Molecular Neurobiology Section, Molecular Neurobiology Branch

Conditioned Place Preference Established in Dopamine- and Serotonin-Transporter Knockout Mice

Cocaine and methylphenidate block uptake by neuronal plasma membrane transporters for dopamine, serotonin, and norepinephrine. Cocaine also blocks voltage-gated sodium channels, a property not shared by methylphenidate. Several lines of evidence have suggested that cocaine blockade of the dopamine transporter (DAT), perhaps with additional contributions from serotonin transporter (5-HTT) recognition, was key to its rewarding actions. Investigators now report that knockout mice without DAT and mice without 5-HTT establish cocaine-conditioned place preferences. Each strain displays cocaine-conditioned place preference in this major mouse model for assessing drug reward, while methylphenidate- conditioned place preference is also maintained in DAT knockout mice. These results have substantial implications for understanding cocaine actions and for strategies to produce anticocaine medications. Sora, I., Wichems, C., Takahashi, N., Li, X.F., Zeng, Z., Revay, R., Lesch, K.P., Murphy, D.L., and Uhl, G.R. Cocaine Reward Models: Conditioned Place Preference Can Be Established in Dopamine- and in Serotonin-Transporter Knockout Mice. *Proc. Natl. Acad. Sci. USA* 95, pp. 7699-7704, 1998.

Cellular Neurophysiology Section, Cellular Neurobiology Branch

Trophic Factors in Neurodegeneration

Intranigral transplantation of fetal ventro- mesencephalic grafts and nigrostriatal administration of GDNF from nigra to striatum regenerates the nigrostriatal dopaminergic pathway and restores striatal dopamine release in 6-hydroxydopamine lesioned rats. In addition, ischemic brain injury elicits an upregulation of GDNF and GDNF receptors. Exogenous GDNF administration markedly attenuates ischemic brain injury, suggesting an endogenous neuroprotective role for this trophic factor. Tang, F.I., Tien, L.T., Zhou, F.C., Hoffer, B.J., and Wang, Y. Intranigral Ventral Mesencephalic Grafts and Nigrostriatal Injections of Glial Cell Line-Derived Neurotrophic Factor Restore Dopamine Release in the Striatum of 6-hydroxydopamine-lesioned Rats. *Exp. Brain Res.*, 119, pp. 287-296, 1998.

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National Institute on Drug Abuse

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

September, 1998

Program Activities

Program Announcements/RFAs

On June 9, 1998, NIDA, in conjunction with numerous other NIH Institutes including NIGMS, NIEHS, NIAMS, NIA, NIMH, NIAAA, NICHD, NHGRI and NHLBI, issued a Program Announcement to encourage research on the **Genetic Architecture of Complex Phenotypes (PA-98-078)**. The purpose of this initiative is to support new studies on the architecture of complex phenotypes, including research using human and model systems as well as research using theoretical approaches. The studies targeted by this Program Announcement are expected to expand understanding of the roles of genetic and environmental variation and their interactions in causing phenotypic variation in populations; increase the quantity and quality of population-based data; lead to development of mathematical and statistical tools for analyzing measured genotype data; lead to improvements in study design; and create biologically relevant models for understanding the origins, roles and implications of genetic variation in causing variation in phenotypes.

On June 10, 1998, NIDA issued an RFA entitled **Basic Behavioral and Cognitive Science Research: Approaches to the Study of HIV/AIDS and Drug Abuse (DA-99-002)**. This RFA is intended to encourage applications for research projects in the basic behavioral and cognitive sciences that can address the complex relationship between drug abuse/addiction and HIV/AIDS transmission and progression. Research is needed to characterize the antecedent variables and processes associated with increased risk for contracting HIV/AIDS and to determine the behavioral and cognitive consequences caused by potential combined effects of the virus, drugs of abuse, drug abuse pharmacotherapies, and anti-HIV medications. In addition, the recent development of anti-HIV medications requires adherence to complex medication regimens. It is important, therefore, to understand the basic cognitive and behavioral processes associated with treatment compliance, and the influence of drug abuse and addiction on these fundamental processes. Knowledge gained from basic behavioral and cognitive science research will aid in the development and refinement of treatment and prevention interventions. Letter of Intent Receipt date for this RFA is December 15, 1998; Application Receipt date is January 15, 1999.

Other Program Activities

Cocaine Rapid Efficacy Screening Trials (CREST) Program

The Medications Development Division, Clinical Trials Branch has initiated a Cocaine Rapid Efficacy Screening Trials (CREST) Program at 5 Medications Development Research Unit (MDRU) sites. Under direction of Dr. Deborah Leiderman, these Phase II trials evaluate the safety/efficacy of currently marketed medications for potential treatment of cocaine dependence. Each CREST protocol evaluates 2-3 marketed medications versus placebo in a controlled, 8 week double paradigm targeted to enroll 50-60 patients per site.

NIDA/NeuroSearch CRADA

The Cooperative Research and Development Agreement (CRADA) between NIDA/MDD and NeuroSearch has progressed to the point where NeuroSearch has begun Phase I clinical trials of its proprietary compound as a potential treatment for cocaine addiction.

Drug Dependence Items on National Gambling Impact Study

NIDA is supporting inclusion of drug dependence items on a national survey of gambling behavior being fielded by the National Gambling Impact Study Commission (NGISC). The NGISC was created by the 104th Congress to conduct a comprehensive study of the social and economic impacts of gambling on individuals, families, communities, and social institutions. The national survey, which will be collected by telephone, will include, inter alia, questions to assess problem or pathological gambling according to the criteria in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV); the Commission mandate also covers consideration of illicit drug use. NIDA will also support a supplement to the NGISC to include drug items to allow ascertainment of drug dependence using DSM-IV criteria. The final Commission report, due to Congress in June 1999, will incorporate findings based on these NIDA-sponsored items, and the data files will be provided to NIDA staff for analysis of co-occurring pathological gambling patterns and drug dependence.

NIDA/IRP Summer Research Program for Students

Since 1986, the IRP has had a summer research program for students. During the summer of 1998, a total of 41 students representing 35 high schools, colleges, and medical and graduate schools participated in the program through either the NIH Summer Internship Program or the Minority Research and Training Program. Each student participant was assigned to work with an IRP scientist on a research project. The students' training program is individually developed and includes directed readings, tutorials, attendance at seminars, and actual laboratory experience under the direction of the scientist. The culmination of the summer program is the students' presentation of their research at the NIH Student Poster Session held at the Bethesda campus in early August. Because of outstanding contributions and effort, some students will be co-authors on published papers or abstracts. The NIH Summer Internship Program is coordinated by Dr. Stephen Heishman, and the Minority Research and Training Program is coordinated by Dr. Jean Cadet and Ms. Mary Affeldt.

NIDA/IRP Fellows Committee

Within the intramural program, a NIDA Fellows Committee has been established, consisting of fellows elected from each of NIDA's intramural branches. The committee is modeled after the highly successful NIH Fellows Committee. Its mission is to work for the enhancement of the intramural research experience at NIDA, to serve as liaison between NIDA's fellows and the NIDA Administration, and to promote the fellows' future scientific careers. As its first major project, the NIDA Fellows Committee created and conducted the NIDA Fellows Survey, a one-hundred item questionnaire which polled the fellows' satisfaction with many aspects of their fellowship experience (e.g. Physical Resources, Technical Support, Mentor Relations, the NIDA Administration). This survey was completed by forty of NIDA's forty-eight fellows, and its findings were presented in the NIDA Fellows Survey Results Summary, which identified those areas receiving praise and criticism, both NIDA-wide and broken down by NIDA branch. From these findings, and subsequent discussions which took place in both Branch and Committee meetings, the NIDA Fellows Committee Action Plan was generated and presented to NIDA's Scientific Director, Dr. Barry Hoffer, in July of 1998. This Action Plan consisted of ten specific recommendations for the NIDA Administration to undertake to improve the intramural fellowship experience, and included suggestions to hire a professional consulting firm to improve the subject recruitment process, allocate an FTE slot for a full-time statistician, make successful mentorship a formal part of each senior staff's evaluation, and mandate that each fellow receive the basic necessities of a personal work space, a personal computer, and the funds to attend one scientific conference and one scientific workshop per year.

Summer Research Placements in Drug Abuse for Underrepresented Minority Students

For the second consecutive year, NIDA's Special Populations Office (with support from the Office of Research on Minority Health) sponsored summer research placements in drug abuse for underrepresented minority high school and undergraduate students. Twenty-two students participated in this year's program, which enabled them to work closely with NIDA investigators.

NIDA'S New/Competing Awards Since May 1998

Adinoff, Bryon --- University of Texas Southwestern Medical Center
Limbic Sensitivity in Cocaine Addiction

Aldrich, Jane V. --- University of Maryland
Opioid Peptide Analogs as Probes of Opioid Receptors

Arria, Amelia M. --- Johns Hopkins University/Dept. of Mental Hygiene
Suspected Influences on Methamphetamine Use

Aston-Jones, Gary --- Allegheny University of the Health Sciences
Norepinephrine, Extended Amygdala and Opiate Withdrawal

Basbaum, Allan I. --- University of California
Spinal Mechanisms of Opioid Analgesia and Tolerance

Bechara, Antoine --- University of Iowa
Cognitive and Neural Mechanisms of Substance Abuse

Benowitz, Neal L. --- San Francisco Hospital/Langley Porter Psychiatric Institute
Pharmacokinetics and Pharmacodynamics of Nicotine

Bidlack, Jean M. --- University of Rochester
Opioid Receptors on Lymphocytes and Brain

Bigelow, George E. --- Johns Hopkins University Bayview Campus
Treatment Research Center: Behavioral Pharmacology

Borchardt, Ronald T. --- University of Kansas
Cyclic Prodrugs of Opioid Peptides

Branch, Marc N. --- University of Florida
Behavioral Determinants of Cocaine Tolerance

Brooner, Robert K. --- Johns Hopkins University -- Bayview Medical Center
Comparing Complementary Behavior Therapies

Carroll, Frank I. --- Research Triangle Institute
Novel Pharmacotherapies for Cocaine Dependence

Celentano, David D. --- Johns Hopkins University
Epidemiology of HIV-1 among Opiate Users in N Thailand

Chavez, Ernest L. --- Colorado State University
Mexican-American Dropouts and Drug Use

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

Chen, Kewen --- University of Medicine and Dentistry New Jersey Medical School
Delay of Gratification: Substance Use/Abuse/Dependence

Cherek, Don R. --- University of Texas Health Sciences Center
Altering Behavioral Risk for Drug Dependence

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

Childers, Steven R. --- Wake Forest University School of Medicine
Molecular Regulatory Mechanisms of Brain Opioid Systems

Collins, Allan C. --- University of Colorado
Pharmacogenetic Regulation of Sensitivity to Nicotine

Collins, Linda M. --- Pennsylvania State University
Drug Abuse Prevention Research Methodology Conferences

Crystal, Stephen --- Rutgers University
Drug Treatment and Care During Pregnancy in HIV+ Women

Csuhai, Eva --- University of Kentucky
Regulation of N-arginine Dibasic Convertase

Curran, James W. --- Emory University/Rollins School of Public Health
Emory/Atlanta Center for AIDS Research

D'Aunno, Thomas A. --- University of Chicago
Drug Abuse Treatment System Survey

D'Esposito, Mark --- University of Pennsylvania
Drug Studies of Dopamine and Prefrontal Function

Devi, Lakshmi A. --- New York University Medical Center
Posttranslational Regulation of Opioid Receptors

Duncan, Terry E. --- Oregon Research Institute
Random Coefficient Models of Family Substance Use

Edgar, Dale M. --- Stanford University
Sleep Homeostasis and Stimulant Drugs of Abuse

Edlin, Brian --- University of California
HIV Prevalence and Incidence Trends among IDUs 1986-1997

Edlin, Brian --- University of California
Randomized Hepatitis B Vaccine Delivery Trial for IDUs

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

Evans, Christopher J. --- University of California, Los Angeles
Mutational Libraries to Study Opioid Receptor Function

Fiorentine, Robert --- UCLA Drug Abuse Research Center
Client Needs and Drug Treatment Effectiveness

Fischman, Marian W. --- Research Foundation for Mental Hygiene, Inc.
Drug Effects on Behavior: Workplace Implications

Foltin, Richard W. --- Research Foundation for Mental Hygiene, Inc.
Laboratory Analysis of Cocaine Abstinence

Forman, Steven D. --- Western Psychiatric Institute & Clinic
Neurobiology of Cognitive Gains with Opiate Maintenance

Foung, Steven K. H. --- Stanford University
Immunologic Response of Intravenous Drug Users to HTLV

Gastfriend, David R. --- Massachusetts General Hospital
Validity of the ASAM Criteria for Drug Abuse Treatment

Gawin, Frank H. --- Friends Research Institute, Inc.
Novel Neuroregulation of Crack Dependence

Gentry, W. Brooks --- University of Arkansas
Mechanisms of Onset & Offset of Rapid Stimulant Effects

Gifford, Andrew N. --- Brookhaven Science Assoc.
Modulation of Neurotransmitter Release by Cannabinoids

Grandy, David K. --- Oregon Health Sciences University
Transgenic Mice for Studying Drugs of Abuse

Grandy, David K. --- Oregon Health Sciences University
OFQ Modulation of Opioid Effects

Greenfield, Shelly F. --- McLean Hospital
Drug Use Disorders and Health Services Utilization

Grella, Christine E. --- University of California
Context & Effectiveness of Two Models of Service Delivery

Griffin, James P. --- Rollins School of Public Health
BRAVE (Building Resiliency and Vocational Excellence)

Griffiths, Roland R. --- Francis Scott Key Medical Center
Abuse Liability of Benzodiazepines and Caffeine

Grimes, Tresmaine R. --- South Carolina State University
Rural Black Youth in Transition: Impact on Drug Use

Groves, Philip M. --- University of California
Novel Modes of Action of Abused Drugs

Hanson, Glen R. --- University of Utah -- Dept. of Pharmacology & Toxicology
Pharmacology and Toxicology of Methamphetamine Abuse

Hans, Sydney L. --- University of Chicago
Infant Attachment: Maternal Trauma and Drug Use

Harachi, Tracy W. --- Social Development Research Group
Cross-Cultural Families Study

Hargreaves, Kenneth M. --- University of Texas Health Sciences Center
Peripheral Cannabinoids and Neurogenic Inflammation

Henderson, Earl E. --- Temple University School of Medicine
Effects of Opioids on HIV-1 Replication and Reactivation

Horvitz, Jon --- Columbia University
Mechanisms of Drug Abuse: DA and CS-Reward Learning

Howlett, Allyn C. --- St. Louis University
Cannabinoid Receptor Structure Activity Relationships

Hughes, John R. --- University of Vermont
Reduced Smoking to Prompt Smoking Cessation

Kalman, David W. --- Brown University
Smoking Cessation Treatment for Substance Abusers

Kendler, Kenneth S. --- Virginia Commonwealth University
A Twin-Family Study of Drug Use, Abuse, and Dependence

Kish, Stephen J. --- Clarke Institute of Psychiatry
Brain Neurochemistry of Human Methamphetamine Users

Kurtz, Stephen E. --- Northwest Neurologic, Inc.
A Method to Identify Pharmacotherapies for Cocaine Abuse

Lester, Robin A. --- University of Alabama
Subunit-Specific Regulation of Nicotinic Receptors

Levin, Edward D. --- Duke University
Chronic Nicotine-Infusion Induced Memory Improvement

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

Liberty, Hilary J. --- Social Sciences Innovations
Self-Report/Biological Measures Database of Drug Use

Lindberg, Iris --- Louisiana State University Medical Center
Opioid Peptide Processing Enzymes

Logan, T. K. --- University of Kentucky -- Center for Drug and Alcohol Research
HIV Risk Behavior and Violence among Crack Users

Luetje, Charles W. --- University of Miami School of Medicine
Binding Site Structure of Neuronal Nicotinic Receptors

Madden, John J. --- Emory University School of Medicine
6th Conference: Drug Abuse, Immunomodulation and AIDS

Madras, Bertha K. --- Harvard Medical School
Molecular Probes for Specific Cocaine Recognition Sites

Malow, Robert M. --- University of Miami
Reducing HIV Risk in Drug Abusing Youth

Mandeville, Joseph B. --- Massachusetts General Hospital
fMRI Study of CNS Physiology During Cocaine Response

Mantyh, Patrick W. --- University of Minnesota Twin Cities
Neurochemistry of Nociception

Mark, Gregory P. --- Oregon Health Sciences University
Nucleus Accumbens Involvement in Cocaine Reinforcement

Martin, Catherine A. --- University of Kentucky
Drug Abuse Pubertal Hormones and ADHD in Adolescence

Mattingly, Bruce A. --- Morehead State University
Receptor-Dependent Sensitization to Cocaine

McLaughlin, Robert J. --- Baylor College of Medicine
Efficacy of Teacher-Facilitated Student Support Groups

McMahon, Thomas J. --- Yale University School of Medicine
Drug-Dependent Fathers: A Developmental Perspective

Miczek, Klaus A. --- Tufts University
Psychomotor Stimulants and Aggression in Animals

Montoya, Isaac D. --- Affiliated Systems Corporation
A Field-Based Treatment Model for Hispanic Cocaine Users

Moore, Richard D. --- Johns Hopkins University
HIV Disease Outcomes in Drug Users in Clinical Practice

Morgan, James P. --- Beth Israel Deaconess Hospital
Cellular Mechanisms of Crack Cocaine's Cardiac Toxicity

Murphy, Sheigla --- Institute for Scientific Analysis
A Study of New Heroin Users

Nair, Prasanna --- University of Maryland
Program for Drug Abusing Women and Their Children

Nestler, Eric J. --- Yale University School of Medicine
Molecular Neurobiology of Drug Addiction

Nishith, Pallavi --- University of Missouri, St. Louis
Substance Use and Dissociation in Female Trauma Victims

Norman, Andrew B. --- University of Cincinnati
Passive Immunity to Cocaine Using Novel Human Antibodies

North, Carol S. --- Washington University
Homeless Drug Abuse: Service Use, Costs, Consequences

Nurco, David N. --- Friends Research Institute
Community-Based Intervention for Children

Nyamathi, Adeline M. --- University of California
TB/HIV Risk Reduction with Homeless and Drug-Addicted

O'Brien, Charles P. --- University of Pennsylvania
Efficacy of Three Models of Nicotine Patch Treatment

Oswald, Robert E. --- Cornell University
Cocaine & Nicotine Action on CNS Acetylcholine Receptors

Paone, Denise --- Beth Israel Medical Center
Sexual Abuse and HIV Risk

Patrick, James W. --- Baylor College of Medicine
Molecular Approaches to Nicotine Addiction

Pilling, Gary M. --- Albany Molecular Research Inc.
18-mc Analogs as Potential Anti-addictive Agents

Pingitore, Regina A. --- Hines VA Hospital
Effects of Tryptophan Depletion on Cigarette Cravings

Pintar, John --- UMDNJ/Robert W. Johnson Medical School
Prenatal Differentiation of the Pituitary Gland

Piomelli, Daniele --- University of California, Irvine
Characterization of Anandamide Transport in Brain

Platt, Jerome J. --- Allegheny University of the Health Sciences
Substance Use and the Transition from Welfare to Work

Prokai, Laszlo --- University of Florida
Neuropeptide Ff Antagonists for Treating Opiate Abuse

Pugatch, David --- Rhode Island Hospital
HIV Testing among Adolescents with Substance Abuse

Roehrs, Timothy A. --- CWRU Henry Ford Health Sciences Center
Sleepiness and the Reinforcing Effect of Methylphenidate

Rounsaville, Bruce J. --- Yale University/Center for Substance Abuse Treatment
Diagnosis & Treatment of Substance Use Disorders

Rowlett, James K. --- Harvard Medical School
Anxiolytic Effects and Abuse of Benzodiazepine Receptor Ligands

Schechter, Martin --- University of British Columbia
Role of Syringe Access & Risk Factors on HIV Transmission

Schenk, James O. --- Washington State University
Drugs of Abuse and Bidirectional Transport of Dopamine

Schmitz, Joy M. --- University of Texas at Houston
Prevention of Smoking Relapse in Women

Schoenbaum, Ellie E. --- Montefiore Medical Center
HIV Therapy Adherence and Viral Resistance in Drug Users

Schumacher, Joseph E. --- University of Alabama
Cost Effectiveness of Drug Treatment for Homeless

Shorter, Simon --- Adeza Biomedical Corporation
HLA-G Test for Rupture of Membranes and Preterm Delivery

Shumsky, Jed S. --- Allegheny University of the Health Sciences
Prenatal Cocaine Exposure & Seizure Susceptibility

Singer, Lynn Twarog --- Rainbow Babies & Childrens Hospital
Cocaine Exposed Infants and Their Mothers

Singer, Merrill --- Hispanic Health Council
Longitudinal Study of AIDS Risk among Drug Users

Singhal, Pravin C. --- Long Island Jewish Medical Center
HIV-Associated Nephropathy in Drug Addicts

Slesnick, Natasha --- University of New Mexico
Treatment Outcome for Runaway Adolescents

Song, Zhao-hui --- Texas A & M University
Structure and Function of CB2 Cannabinoid Receptor

Spealman, Roger D. --- New England Regional Primate Research Center
Primate Model of Speedball Abuse: Mechanisms & Treatment

Stewart, Jane --- Concordia University
Neurobiology of Relapse Induced by Stress and Drugs

Stinchcomb, Audra L. --- Albany College of Pharmacy
Naltrexone Prodrugs for Transdermal Delivery

Stormshak, Elizabeth A. --- Counseling Psychology Program
High-Risk Siblings as Predictors of Substance Use

Stranger, Catherine --- University of Vermont
Outcomes for Children of Drug Abusers: a Multisite Study

Sullivan, Jane M. --- Salk Institute for Biological Studies
Cannabinoid Effects on Synaptic Function and Plasticity

Swisher, John D. --- Pennsylvania State University
Life Skills Infusion/Prevention in Rural Junior High

Szeto, Hazel H. --- Cornell University Medical College
Pharmacokinetics and Fetal Exposure to Narcotics

Tecott, Laurence --- University of California, San Francisco
Serotonin 5HT2c Receptors and the Actions of Cocaine

Thomas, Mary L. --- University of Texas
Cocaine, Sex Hormones & 5-HT: Molecular & Behavioral Analyses

Toga, Arthur W. --- UCLA School of Medicine
A Conference on Brain Mapping Addiction Neurobiology

Turner, Barbara J. --- Jefferson Medical College
Medical & Substance Abuse Care for HIV+ Drug Users

Valentine, James D. --- Minneapolis Medical Research Foundation
Stress & Reinstatement of Nicotine-Seeking Behavior

Vazquez, Delia M. --- University of Michigan
Postnatal Stress: HPA Axis and Vulnerability to Drug Use

Waterhouse, Barry D. --- Allegheny University of Health Sciences
Cocaine Modulation of Sensory Neuron Function

Weerts, Elise M. --- Johns Hopkins Bayview Campus
Vocalizations: A Model of Subjective Drug Effects

Welch, Sandra P. --- Virginia Commonwealth University
Career Development in Drug Abuse Research

Wells, Elizabeth A. --- University of Washington
Stages of Change and Cocaine Treatment

West, Charles H. --- Emory University/Dept. of Psychiatry & Behavioral Sciences
Amphetamine Sensitization & Response to Natural Rewards

West, James B. --- Bend Research, Inc.
Technology for Generation of Drug-Candidate Libraries

West, Mark O. --- Rutgers/State University of New Jersey
Cocaine Self-Administration Mesolimbic Neurophysiology

Wilkins, Diana G. --- University of Utah -- Center for Human Toxicology
Hair Analysis to Monitor Drug Abuse Treatments

Winters, Ken C. --- University of Minnesota -- Research & Technology Transfer Adm.
Assessment and Treatment of Adolescent Drug Abusers

Woodward, Erna J. --- Biographics, Inc.
System to Test Medications Developed to Treat Drug Abuse

Zwaan, Rolf A. --- Florida State University
Smoking Addiction and Higher-Level Cognitive Processes

Review Activities

Staff Development

NIDA's Office of Extramural Program Review (OEPR) continues active involvement in providing staff training for NIDA and other NIH staff. In June, Dr. Teresa Levitin, Director, OEPR, presented at two sessions that were sponsored by the NIH Office of Extramural Research to address the implementation of the new policy on inclusion of children in research. These were attended by staff from many NIH Institutes, and Dr. Levitin addressed how the new policy will be implemented in review groups.

In July, Dr. William C. Grace, Deputy Director, OEPR, spoke on the various roles of the review administrator in extramural administration and facilitated case studies as part of the core training for new NIH employees provided through the NIH Office of Extramural Research.

Meetings/Conferences

At a grant writing workshop at the American Psychiatric Association's annual meeting in Toronto in June, Dr. Teresa

Levitin presented on the Role of the Scientific Review Administrator in the peer review process. She gave a similar presentation to the Society of Biological Psychiatry convention in May and at the College on Problems of Drug Dependence (CPDD) meeting in Scottsdale in June, where she also led a mock Scientific Review Group meeting. Dr. Rita Liu co-presented a CPDD workshop titled "Merger of NIDA Science into the NIH Center for Scientific Review."

Dr. Mark Swieter presented an Update on Fellowship Review Procedures at the Third Annual NIDA Training Directors' Meeting held in Bethesda in May.

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National Institute on Drug Abuse

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

September, 1998

Congressional Affairs

FY 99 Appropriations

On July 15, 1998, the FY 1999 Labor-HHS-Education Appropriations bill was reported out of the full House Appropriations Committee. The House Appropriations Committee's report on the bill also was filed (HRpt. 105-645). The full House has yet to act on the Committee recommendation.

House Report Language for the National Institute on Drug Abuse

"The Committee provides $575,426,000 for ... NIDA, which is $49,234,000 above the fiscal year 1998 comparable level and $859,000 above the Administration request.

Mission

NIDA supported science addresses questions about drug abuse and addiction, which range from its causes and consequences to its prevention and treatment. NIDA research explores how drugs of abuse affect the brain and behavior and develops effective prevention and treatment strategies; the Institute works to ensure the transfer of scientific data to policy makers, practitioners and the public.

Children and Adolescents

Drug abuse affects the children of this country in devastating ways, through prenatal exposure, through growing up in drug abusing households, and through drug abuse by young people themselves. The Committee urges NIDA to continue research on preventing or diminishing the health and developmental consequences associated with drug abuse and addiction, particularly on prenatally exposed children to find out what the long-term consequences of prenatal drug exposure are in later childhood and adolescence. The Committee is particularly interested in the differential effects of drugs on the brain and the behavior of children at different ages.

Clinical Trials

The Committee commends NIDA's extensive progress in developing drug abuse treatments, both behavioral and psychological. NIDA's investment in behavioral and neuroscience research has brought the science of addiction treatment to a point of broad practical application. The Committee encourages NIDA to continue to move forward by supporting research to clarify more specifically what works for which patients, under what circumstances, and for how long. The Committee also encourages NIDA to examine behavioral and pharmacological therapies that are shown to be effective in small scale studies and evaluate them in large multi-site clinical trials.

Coordinating Efforts

The Committee urges NIDA to take the lead in coordinating its research efforts with those of the Knowledge and Development Application programs of the Substance Abuse and Mental Health Services Administration. The Committee requests that NIDA be prepared to give the Committee a progress report on this effort, including recommendations on how to improve the outcomes of this research, at its fiscal year 2000 appropriations hearing.

Drug Abuse Treatment

The Committee commends the progress NIDA has made in neuroscience research and encourages NIDA to continue its efforts to develop pharmacological and behavioral drug abuse treatments.

Methamphetamine

NIDA research has shown that methamphetamine is a powerfully addictive stimulant associated with many physical and behavioral changes. Recognizing that there continues to be a significant problem in methamphetamine use in specific areas of the country, the Committee encourages NIDA to study the development of an anti-methamphetamine medication, to clarify the long-term neurological and behavioral consequences of the use of this drug, and to continue to study the epidemiological trends of methamphetamine use. The Committee also encourages NIDA to support research to develop prevention programs specifically geared toward the unique characteristics of the methamphetamine user as well as research on treatment approaches specifically tailored for polydrug addiction to methamphetamine and other substances.

Nicotine Research

The health consequences of tobacco/nicotine use in this country will not be eliminated until the addiction to nicotine itself is effectively prevented and those currently addicted are effectively treated. The Committee encourages NIDA to: (1) expand its support for basic research on the biological, behavioral, and pharmacological bases of nicotine addiction; (2) conduct basic and applied behavioral research targeting children and adolescents to improve strategies to prevent smoking initiation; and (3) increase support for research that will lead to more effective long-term smoking cessation by developing both nicotine and non-nicotine replacement medications in combination with behavioral strategies. The Committee encourages NIDA to support behavioral research on nicotine and smoking and epidemiological studies that monitor patterns of drug use, including nicotine.

Prevention

NIDA has demonstrated the usefulness of its research to prevention of drug use by developing and distributing over 100,000 copies of the first ever research-based prevention guide, "Preventing Drug Use Among Children and Adolescents." This booklet is the first research-based guide which articulates the principles learned from 20 years of NIDA supported prevention research. It gives practical guidance on how communities can apply these principles to address local drug problems. The Committee urges NIDA to continue to support this useful research and to produce more tools translating research findings into useful guides for parents, educators, treatment providers, and policy makers.

Social Work Research

The Committee commends NIDA's support for social work research and dissemination on behavioral and psychological treatment and prevention related to drug abuse, addiction, and HIV/AIDS. The Committee also commends NIDA's efforts to support the development of drug abuse treatment and health services research within graduate schools of social work.

On September 3, 1998, the Senate Appropriations Committee approved the HHS-Labor-Education bill.

Draft Senate Report Language for NIDA:

"The Committee recommends an appropriation of $603,274,000 for the National Institute on Drug Abuse [NIDA]. This is $28,164,000 more than the budget request and $77,082,000 more than the fiscal year 1998 appropriation." In their draft report the Committee emphasized the following areas:

Nicotine Research - encourages NIDA to expand its support for basic research on the biological, pharmacological, and behavioral bases of nicotine addiction.

Clinical Trials - commends NIDA for having launched a major treatment initiative and encourages NIDA to develop a clinical trials infrastructure, and to move rapidly to test the efficacy of promising pharmacological, behavioral, and

psychosocial treatment through large-scale, multi-site clinical trials.

Children & Adolescents - urges NIDA to continue research on preventing or diminishing the health and developmental consequences associated with drug abuse and addiction, looking particularly at prenatally exposed children to understand the long-term consequences of drug exposure in later childhood and adolescence.

Methamphetamine - encourages NIDA to study the development of antimethamphetamine medication, to clarify the long-term neurological and behavioral consequences of the use of these drugs, and to continue to study the epidemiological trends of methamphetamine use. The Committee is pleased that NIDA plans a conference in Des Moines, IA, to focus attention and expand understanding of this growing problem.

Treatment - commends NIDA for progress in neuroscience research, and encourages NIDA to continue its efforts to develop pharmacological and behavioral drug abuse treatments.

Social Work - commends NIDA for supporting social work research and for dissemination on behavioral and psychosocial treatment and prevention related to drug abuse, addictions, and HIV/AIDS.

Behavioral Science Research - continues to support NIDA's expansion of its behavioral science portfolio and views NIDA as a model of how to approach its behavioral science and public health responsibilities. OUTLOOK FOR THE FALL 1998:

In many instances, the two chambers' bills contain dramatically different provisions. In addition, the President has issued veto warnings on the Labor-HHS bill. Should Congress and the President not come to agreement by the October 1 deadline, a continuing resolution is considered likely to keep the agencies running.

Hearings/Briefings

July 28, 1998
At the invitation of the Chairman, Senator Jeffords (R-VT), Dr. Alan I. Leshner, Director, NIDA, testified before the Senate Committee on Labor and Human Resources on "The Science of Addiction and Options for Treatment."

- Members Present: Senators Jim Jeffords (R-VT), Chairman; Mike Dewine (R-OH), Tim Hutchinson (R-AR), Paul Wellstone (D-MN), Jack Reed (D-RI).
- Witnesses: Panel 1: Representative Jim Ramstad (R-MN). Panel 2: Alan I. Leshner, Ph.D., Director, National Institute on Drug Abuse, NIH. Panel 3: David Lewis, M.D., Project Director, Physician Leadership on National Drug Policy; Robert Morse, M.D., Professor of Psychiatry, Mayo Medical School; Ted Suhl, Deputy Director, The Lord's Ranch. Panel 4: June Gertig, J.D., parent; Richard Frank, Ph.D., Professor of Health Economics, Harvard University; Bill Gradison, President, Health Insurance Association of America (HIAA); John S. Saylor, M.D., AMR Corporation.
- Dr. Leshner's testimony focused on the current state of the science of addiction. He noted that brain changes produced by heavy drug use can last a very long time after an individual stops using drugs and that brain physiology is only one component of addiction. Behavioral and social context elements are also important factors related to addiction and relapse. Research has shown that the integration of behavioral and pharmacological treatments, in ways specific to an individuals's needs, is likely the best way to treat addictive disorders. Dr. Leshner stressed that NIDA is committed to working intensively with the drug abuse professional community to actively transfer scientific knowledge in a proactive way into the community setting to improve addiction treatment in this country. To accomplish this, NIDA is planning to launch a National Drug Treatment Clinical Trials Network that will provide the infrastructure to ensure that all potential addiction treatments are tested in real life settings. He said, "Moving treatments from the laboratory, to the clinic, to the community is the next rung of the ladder for national treatment improvement."
- In response to an inquiry from Senator Jeffords regarding difficulties involved in treating long-time addicts, Dr. Leshner responded that treatment before someone is "fully addicted" is preferable. Senator Wellstone asked about the efficacy of prescription treatment for substance abuse. Dr. Leshner responded that the best treatments address both pharmacological and behavioral problems. Senator Dewine asked Dr. Leshner what policy implications we should take from his testimony. He responded that there is no question that drug addiction is an illness. Once addicted, a person is ill, and he or she must be treated.

July 23, 1998
The House Commerce Subcommittee on Oversight and Investigations (Chairman Joe Barton R-TX) held a hearing on

drug testing policy issues. Dr. Ed Cone, Acting Chief, Clinical Pharmacology Branch, NIDA testified. SAMHSA and FDA also testified.

July 21, 1998
At the request of staff to Senator Edward Kennedy (D-MA), Dr. Alan I. Leshner participated in a briefing for Senate staff on the science of needle exchange.

July 10, 1998
At their request, Dr. Frank Vocci, Director, Division of Medications Development, NIDA, briefed the Majority Staff of the House Committees on Commerce and Judiciary on the science of buprenorphine.

Miscellaneous Bills of Interest

S. 2347 --On July 23, 1998, Senator Tom Harkin (D-IA) introduced S. 2347, the Comprehensive Methamphetamine Abuse Reduction Act of 1998, to provide for a coordinated effort to combat methamphetamine abuse, including expanded interdisciplinary research by NIDA related to methamphetamine abuse and addiction issues. The bill (in part) would amend Section 464N of the Public Health Service Act (PHSA) by adding a section on expanding methamphetamine research and would authorize appropriations for NIDA in the amount of $16 million for FY 99 and such sums as may be necessary in succeeding fiscal years to carry out that section. The bill was referred to the Senate Committee on Labor and Human Resources.

H.Res. 423 --On May 12, 1998, H.Res. 423, a resolution "expressing the sense of the House with respect to winning the war on drugs to protect our children", was passed by the House. The resolution was introduced on May 7 by Representative J. Dennis Hastert (R-IL).

H.R. 4135 --On June 24, 1998, Representative Edolphus Towns (D-NY) introduced H.R. 4135, a bill that would amend Section 491(a), PHSA, by requiring the HHS Secretary to establish a program for the collection of information relating to the use of children and individuals with mental disabilities as subjects in biomedical and behavioral research. The program may include a requirement that Institutional Review Boards submit reports containing information related to: a description of the research subjects, the nature of the research, the objective of the research, the reasons for the use of these subjects, and the source of funding. The Secretary must make this information available to the public on a regular basis, and in an annual report. The bill was referred to the House Committee on Commerce.

H.R. 4170 --On June 25, 1998, Representative Gil Gutknecht (R-MN) introduced a bill to amend Title IV of the PHSA to establish a National Center for Bioengineering Research. This legislation would establish, within NHLBI, a National Center for Bioengineering Research, and would authorize appropriations for the center in the amount of $750,000 for each fiscal year for the general operation of the Center. For general bioengineering activities, the legislation would authorize to be appropriated $20,000,000 for each of the fiscal years 1998 through 2007, to be allocated at the discretion of the Director of NIH among the bioengineering activities being carried out by the national research institutes and other agencies of NIH. H.R. 4170 was referred to the House Committee on Commerce.

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International Activities

On June 8-10, Dr. Alan Leshner, Director, NIDA, was part of the official U.S. delegation for the **United Nations General Assembly Session on Drug Abuse** in New York which featured approval by 150 nations for international coordination of demand reduction. The Special Session included speeches by heads of state and leading government officials of 47 nations.

Drs. Patricia Needle, International Office, Robert Battjes, DCSR, and Peter Hartsock, DEPR, attended the **Sixth International Conference on AIDS, Cancers and Related Problems** in St. Petersburg, Russia, May 18-22, 1998. In conjunction with the Conference, NIDA staff participated in the Second Annual Russia-US Workshop, "Emerging and Re-emerging Infectious Diseases," co-organized and chaired by Drs. A.P. Kozlov, Biomedical Center, Research Institute of Pure Biochemicals, St. Petersburg, Karl Western, NIAID, and Peter Hartsock, which provided an opportunity for Russian scientists to explore funding opportunities with participating NIH staff. While in St. Petersburg, Drs. Needle and Battjes also met with Dr. Edwin Zvartau, Pavlov State Medical University, St. Petersburg, and several HIV prevention researchers regarding planning for the upcoming U.S.-Russian Conference on Drug Abuse and HIV Prevention, planned for Spring 1999.

NIDA hosted an international satellite meeting on **Building International Research on Drug Abuse: Global Focus on Youth** at the June Annual Scientific Meeting of the College on Problems of Drug Dependence. More than 70 people from 25 countries participated. The keynote address was presented by Dr. Andrew Ball of the Programme on Substance Abuse, World Health Organization (WHO), who reported on findings from the 20-nation WHO Street Children Project. Dr. Michael Clatts, National Development and Research Institutes, New York, provided an overview of research on homeless youth in the United States, with particular emphasis on New York City. In addition, the meeting featured panel discussions on trends in drug use and methodology for research with children and youth, and discussion groups focused on publishing in peer-reviewed journals, NIH research guidelines, funding mechanisms and preparation of successful grant applications.

NIDA has selected two **INVEST research fellows for 1998-99**. They are Dr. You Wan of the Beijing Medical University, Beijing, China, and Dr. Neo Morojele of the Medical Research Council, Cape Town, South Africa. Dr. Wan will conduct research on the biological mechanisms underlying acupuncture analgesia at the University of Illinois, Champaign-Urbana. Dr. Morojele will conduct epidemiological research on the etiology of drug abuse at Mt. Sinai School of Medicine in New York.

Dr. Elizabeth Rahdert, DCSR, participated in the **14th International Congress of the International Association for Child and Adolescent Psychiatry and Allied Professions** in Stockholm, Sweden, on August 2-6, 1998. She chaired a symposium presented by NIDA-supported researchers Drs. James Hall, Judith Landau, William Latimer, Paula Riggs and Paul Marques.

NIDA, the NIH's Office of AIDS Research, the World Health Organization/Programme on Substance Abuse (WHO/PSA), and the Joint United Nations Programme on HIV/AIDS teamed together in sponsoring the inaugural meeting of the **Global Research Network on HIV Prevention in Drug-Using Populations**, held June 25-26, 1998 in Geneva, Switzerland, just prior to the 1998 World AIDS Conference. The meeting represented the first step

toward the long-term goal of establishing a self-sustaining global communications infrastructure for rapid international communication, dissemination, and utilization of HIV/AIDS epidemiology and prevention research information, including the exchange and interpretation of research findings from intervention studies with drug-using populations at high risk for HIV and other blood-borne diseases; the translation and dissemination of research findings on prevention principles and practices which slow the rate of spread of HIV; and the development of new cross-national, collaborative research efforts to prevent the spread of HIV and other infections among drug users. The international participants at the meeting represented more than 25 countries and every region of the world. Dr. Richard H. Needle, Chief of NIDA's Community Research Branch, took the lead in planning, organizing, and chairing the inaugural meeting. Also participating in the meeting for NIDA were Dr. Zili Sloboda and Helen Cesari, DEPR, and Patricia Needle, NIDA International Program.

Mr. Nicholas Kozel, DEPR, co-chaired a joint meeting of the **East and South Asian Multi-City Epidemiology Work Group** meeting held in Penang, Malaysia on May 4-7, 1998. Researchers from Malaysia, the Philippines, Thailand, Burma, China, Laos, Cambodia, Vietnam, Bangladesh, India, Pakistan, and Sri Lanka participated in the meeting and reported on patterns and trends of drug abuse in their countries and on emerging problems and related issues. Major drugs of abuse include: opium smoking and injection, heroin injection and Ôchasing the dragon', buprenorphine injection, cannabis smoking, inhalation of volatile substances, and the recent and substantial emergence of methamphetamine, MDMA and ketamine abuse in a number of countries in the region.

Ms. Ann Blanken, Deputy Director, DEPR, represented NIDA at the 28th meeting of the **Pompidou Group** of substance abuse epidemiologists June 8-9, 1998 at the Council of Europe in Strasbourg, France. She presented information on recent drug use trends in the United States and on NIDA conferences addressing changing patterns of drug abuse in the United States. The Pompidou Group includes representatives from cities in nations in the European Union, Eastern bloc countries of the former soviet Union, and selected other locations.

Mr. Richard A. Millstein, NIDA Deputy Director, met with Mr. Herbert Barnard, Counselor for Health of the Netherlands Embassy, on collaborative health research on June 5, 1998.

On May 19, 1998 Dr. Elizabeth Robertson, DEPR, met with Widar Andersson, Member of Parliament, Sweden, to discuss prevention interventions in the United States and Sweden.

On July 5, 1998, Drs. Patricia Needle, International Program, and Elizabeth Robertson, DEPR, met with Mr. Spencer Sui Hong So, Director of the Community Drug Advisory Council in Hong Kong for an overview of NIDA organization and research and to discuss prevention issues in the United States, Hong Kong Special Administrative Region, and China. Dr. Meyer Glantz met with several members of Britain's Home Office to consult on issues related to the establishment of Britain's drug abuse and prevention research program.

In a collaboration with Dr. Lars Olson at the Karolinska Institute, Sweden, Drs. Barry J. Hoffer, Marisela Morales and Ms. Arezou Sarabi, NIDA IRP, are studying the regulation of GDNF and GDNF receptor gene expression in the brain. This will have therapeutic implications for treatment of Parkinson's Disease.

In a collaboration with Dr. S. Lin, Chairman of the Neurosurgery Dept. of the National Defense Medical Center (NDMC) in Taiwan, Drs. Barry J. Hoffer and Yun Wang, NIDA IRP, are studying trophic factors of the TGF_ superfamily as therapeutic agents for ischemic brain injury.

Drs. Svetlana Chefer, Barry Hoffer, and Jean Lud Cadet presented at the 12th General Meeting of the European Society for Neurochemistry, St. Petersburg, Russia, July 19-24, 1998. Dr. Chefer presented a paper on nicotinic and dopamine receptors in monkey brain. Drs. Hoffer and Cadet participated in the NIDA-sponsored colloquium on the **Neurochemistry of Drug Abuse** along with NIDA extramural researchers. Dr. Cadet presented his research on the neurodegenerative effects of methamphetamine.

Dr. David A. Gorelick, Pharmacology Section, Treatment Research Branch, presented papers entitled "Characteristics of Marijuana Users Presenting to an Urban Hospital Emergency Department" and "Marijuana Dependence Among Inpatients at a Regional Trauma Center" at the **1998 Symposium on the Cannabinoids of the International Cannabinoid Research Society**, La Grande Motte, France, July 23-25, 1998.

Dr. Jag Khalsa of the Center for AIDS and Other Medical Consequences of Drug Abuse, was invited to co-chair a pre-conference satellite symposium entitled Update on Wasting, Metabolism, and Altered Body Shape in HIV/AIDS, held at the **12th World AIDS Conference** in Geneva, Switzerland, June 28, 1998. This symposium was a tri-partite collaborative effort of researchers from drug industry (Sorono Labs and Bristol Meyers), academia (Tufts University School of Medicine) and the National Institutes of Health (NIDA and NIDDK) on this important topic of AIDS Wasting, in an international forum. Dr. Khalsa also moderated a session on Nutritional Considerations where the speakers discussed the role of macro- and micronutrients in HIV/AIDS disease progression in drug abusers.

Dr. Tsung-Ping Su, Cellular Pathobiology Unit, IRP, presented a lecture at the **XXIst Congress of the Collegium Internationale NeuroPsychopharmacologicum (CINP)** held July 12-16, 1998 in Glasgow, Scotland. Dr. Su's talk entitled "Sigma Receptors and Intracellular Calcium Signaling" was part of the symposium "Sigma Receptors: From Cloning to Their Clinical Importance".

Dr. Tsruo Hayashi, Cellular Pathobiology Unit, IRP, presented an award-winning poster entitled "Sigma1 Receptor Ligands Modulate Intracellular Calcium Mobilization in NG-108 Cells" at the **XXIst Congress of the Collegium Internationale NeuroPsychopharmacologicum (CINP)** held July 12-16, 1998 in Glasgow, Scotland.

Dr. Tsung-Ping Su of the IRP was invited by the world-reknown neurosteroid researcher Professor Etienne-Emile Baulieu of the **French INSERM at Institut National de la Sante, et de la Recherche Medicale**, Paris, France, to present a seminar on July 17, 1998, entitled "Sigma Receptors Regulated Calcium Signaling on the Endoplasmic Reticulum and Plasma Membrane in NG-108 Cells".

On July 25, 1998, Dr. Tsung-Ping Su of the IRP was chosen by the **International Narcotic Research Conference (INRC)**, to participate in a symposium entitled "Opioids in Development and Apoptosis" and present a talk entitled "Delta Opioid DADLE Blocks Dopamine Transporter (DAT) Loss and p53 mRNA Increase Induced by Methamphetamine (METH): By Acting as a Free Radical Scavenger?" at Garmisch Partenkirchen, Germany.

Dr. Svetlana Chefer, IRP, presented a paper on nicotinic and dopamine receptors in monkey brain at the **12th General Meeting of the European Society for Neurochemistry** held in St. Petersburg, Russia, July 19-24, 1998.

Dr. Jean Lud Cadet, Clinical Director of the IRP, recently attended the meeting of the **European Society for Neurochemistry** in St. Petersburg, Russia. There, he presented data on the effects of methamphetamine-induced neurotoxicity. This was contrasted to the neurotoxic effects of dopamine which was shown by Dr. Cadet's group to cause apoptosis. These data support the idea that methamphetamine is causing its effects through the increase release of dopamine in the brain.

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Meetings/Conferences

Cognition and Emotion: Applications to Drug Abuse was a satellite mini-conference to the American Psychological Society meeting held on May 21, 1998. The meeting, chaired by Dr. Jaylan Turkkan, was sponsored by NIDA's Behavioral Science Working Group. Panel chairs were Drs. Joseph Frascella, Steven Sparenbourg, and Teresa Levitin of NIDA. NIDA Council member Dr. G. Alan Marlatt was discussant for the conference, which featured several noted researchers.

Wired for Addiction was presented on June 22, 1998 as part of NIDA's *Frontiers in Neuroscience* seminar series. The theme of these presentations centered on the neuronal remodeling that emerges after repeated substance use and withdrawal, with particular emphasis on the possibility of altered cognitive function as a consequence of the neural remodeling. A summary and discussion of implications for humans were presented by Dr. Steve Grant of NIDA. Presenters, their affiliations, and the titles of their presentations follow: Ann Graybiel, Massachusetts Institute of Technology, "Chronic Exposure to Psychomotor Stimulants may Rewire Your Brain"; Anthony Grace, University of Pittsburgh, "Neuronal Interactions Within the Limbic System of Rats: Alteration During Amphetamine Sensitization"; John Marshall, University of California at Irvine, "Cortical and Striatal Circuits Influenced During Repeated Methamphetamine Administration"; Janet Neisewander, Arizona State University, "Neurochemical Correlates of Cocaine-Seeking Behavior"; and Regina Carelli, University of North Carolina, "The Nucleus Accumbens and Reward: Electrophysiological Studies in Behaving Animals."

Addicted to Nicotine: A National Research Forum was a NIDA conference held on July 27 and 28, 1998. Vice President Al Gore gave the keynote address which highlighted the staggering mortality from nicotine addiction and tobacco use. Written summaries, slides, and video clips of all presentations can be found at /Meetings/Nicotine/Nicotineagenda.html. Also, a special issue of Nicotine and Tobacco Research (edited by Dr. Gary Swan) will be forthcoming. The conference was co-sponsored by The Robert Wood Johnson Foundation, the National Cancer Institute, and the CDC Office on Smoking and Health. Conference Chairs were Drs. Jaylan Turkkan and Timothy Condon.

On August 3-4, 1998, Drs. Jag Khalsa, Sander Genser and Henry (Skip) Francis of the Center for AIDS and Other Medical Consequences of Drug Abuse conducted the NIDA's first workshop on the subject **Metabolic, Endocrine, and Gastrointestinal Disorders in Drug Abuse and HIV/AIDS**. It was co-sponsored by the Office of Dietary Supplements, NIH. A group of 16 expert scientists/clinicians presented and/or reviewed current findings on the subject and recommended future research. The subjects covered at the workshop ranged from lipid, carbohydrate, and protein metabolic problems, endocrine and GI problems, nutritional deficiencies, assessment tools, and various intervention strategies being tested for HIV-infected drug abusers. An executive summary for publication in JAIDS is in preparation.

On June 3-5, 1998, NIDA's Special Populations Office sponsored a three-day meeting entitled **Cannabinoid and Opiate Vascular Neuroimmunology** as part of its Research Development Seminar Series in Chicago, Illinois. The seminar, co-sponsored by the State University of New York at Old Westbury, featured lectures and demonstrations by NIDA staff and researchers on nitric oxide, image analysis, and neuroimmunology.

The Medications Development Division hosted a meeting on August 14, 1998 in Reston, VA to discuss the

development of a multi-center protocol involving the investigational treatment of opiate dependence in the office-based setting with buprenorphine/naloxone. Representatives from the American Society of Addiction Medicine, the American Academy of Addiction Psychiatry, and the American Psychiatric Association and the site investigators discussed the protocol and operations issues.

The Intramural Research Program's Library hosted a meeting of the Maryland Association of Health Science Libraries (MAHSL) group in May, 1998. Approximately 40 librarians toured the new library and viewed a demonstration of online journals, new document delivery/interlibrary loan system and online catalog.

A meeting of **NIDA's Hispano/Latino Researchers and Scholars Work Group**, chaired by Ana Anders, was held in conjunction with the annual College on Problems of Drug Dependence meeting in Scottsdale, Arizona, June 12-13, 1998. The meeting's focus was "Violence Research Among Hispanic Populations". The Institute Director and Deputy Director, Dr. Alan Leshner and Mr. Richard Millstein, also participated and presented.

On May 28-29, 1998, the Special Populations Office sponsored an **HBCU Technical Assistance Meeting** in Rockville, Maryland.

Drs. James Cooper, David Gorelick, and Frank Vocci attended a meeting on July 10, 1998 sponsored by The Center for Substance Abuse Treatment (CSAT) on **Office-Based Opioid Therapy (OBOT) for Opiate Addicts**. CSAT and NIDA have recognized a growing interest around the country on behalf of physicians and patients who want methadone treatment to be made more widely accessible. Connecticut has recently passed legislation establishing a pilot project (to begin this summer) in one community where patients from a methadone maintenance treatment program would be transferred to the care of private practitioners. Discussions have taken place in other communities toward a similar end including Seattle where the Robert Wood Johnson Foundation has funded such a project. The American Methadone Treatment Association adopted criteria for implementing physician based methadone practices. There was considerable discussion about the various models of OBOT and the risks/benefits and existing obstacles for implementation of each. CSAT plans to develop this year a "strategic plan" outlining the issues, various models for possible implementation etc. Future reasearch was proposed to evaluate the feasability (risks/benefits) of OBOT's in various rural, suburban settings around the country where physicians, trained in narcotic maintenance treatment, would treat new patients in their offices. NIDA and CSAT staff have since met to further explore this research issue.

Dr. Alan I. Leshner, NIDA Director, and Ana Anders, Senior Advisor on Special Populations, participated in a July 8, 1998 WORLDNET town meeting broadcast from Roswell, New Mexico, on the subject of "Drugs, Gangs, and Violence". Jack Stein, Acting Deputy Director, OSPC, organized NIDA cooperation with the United States Information Agency to plan this event which was broadcast to Mexico City, San Salvador, and Tegucigalpa.

Mr. Richard A. Millstein, NIDA Deputy Director, met with the Board of Directors of the College on Problems of Drug Dependence on June 12, 1998.

Mr. Richard A. Millstein, NIDA Deputy Director, participated in the meeting of the Society for the Advancement of Women's Health Research and the 1998 Achievement Awards in Women's Health held June 22-23, 1998.

Mr. Richard A. Millstein, NIDA Deputy Director, and Ms. Ana Anders, Senior Advisor on Special Populations, met with Dr. Jane Delgado, President of COSSHMO, on NIDA programs and projects of particular relevance to Latinos on June 24, 1998.

Mr. Richard A. Millstein, NIDA Deputy Director, participated in activities relating to the DHHS press conference to release SAMHSA's National Household Survey on Drug Abuse, August 18-21, 1998.

Mr. Richard A. Millstein, NIDA Deputy Director, spoke on recognizing and treating drug abuse at the U.S. Office of Personnel Management's National Conference on Federal Employee Assistance and Health Enhancement Programs on September 3, 1998.

Dr. Timothy P. Condon, Associate Director NIDA, conducted a media event on June 2, 1998 entitled "Substance Abuse and Youth: A Scientific Discussion of the Film Trainspotting".

Dr. Timothy Condon made a presentation entitled "Alcohol, Tobacco, and Other Drugs (ATOD)-TV and Community Attitudes Regarding Drug Abuse" on June 4, 1998 at the American Psychiatric Association's Annual Meeting held in Toronto, Canada.

Dr. Condon and Jack Stein, Acting Deputy Director, OSPC, made a presentation entitled "Using Research to Improve Clinical Practice" at the National Association of Alcoholism and Drug Abuse Counselors Annual Meeting, July 2, 1998, in Chicago, Illinois.

On June 16, 1998, Dr. Condon gave a televised presentation on "Methamphetamine Abuse and Addiction" as a guest on the Iowa cable television program "Ask Senator Harkin." Dr. Condon discussed the effects of methamphetamine on the brain and body and answered caller questions.

Dr. Andrea Baruchin, Chief, Science Policy Branch, OSPC, held a workshop at the 1998 American Psychiatric Association Annual Meeting in Toronto, Canada entitled, "Dos and Don'ts in Writing Your First NIH Grant." Representatives from both NIDA and NIMH discussed funding opportunities for psychiatrists at their respective institutes.

Dr. Andrea Baruchin and Dr. Cindy Minor, Deputy Research Training Coordinator, OSPC, presented the "NIDA Grant Writing Workshop" at the 60th Annual meeting of the College on Problems of Drug Dependence held in Scottsdale, Arizona, June 16, 1998.

Dr. Andrea Baruchin represented NIDA at the Second Annual Surgeon General's Report on Mental Health Meeting, June 1-2, 1998 at the Madison Hotel.

On June 8, 1998, Jan Lipkin, Deputy Chief, Public Information Branch, Office of Science Policy and Communications, presented information on NIDA publications and materials at a meeting of the National Addiction Technology Transfer Centers in Washington, D.C.

On June 28-July 1, 1998, Beverly Wyckoff Jackson, Chief, Public Information Branch, Office of Science Policy and Communications, and Sheryl Massaro, Deputy Press Officer, Public Information Branch, participated in the 1998 National Media Education Conference, "A Paradigm for Public Health," in Colorado Springs, CO. Ms. Jackson was part of the planning committee for this event.

Dr. Cora Lee Wetherington, DBR, gave an invited presentation entitled "Behavioral Science Research Opportunities at the National Institute on Drug Abuse" at the Twenty-fourth Annual Meeting of the Association for Behavior Analysis held in Orlando, FL, May 23, 1998.

On May 27, 1998, Lula Beatty presented a session on NIDA's funding opportunities to a national group of minority researchers at Morgan State University in Baltimore, Maryland.

On June 4, 1998, Lula Beatty presented an overview of NIDA and its programs to incoming members of the NIH Extramural Associates Program in Bethesda, Maryland.

On July 26-28, 1998, Lula Beatty attended the annual planning retreat of the Board of the NIH Extramural Associates Research Development Award Program in St. Michael's, Maryland.

On July 13-16, 1998, Ana Anders represented the Special Poulations Office at a training conference for Hispanic Researchers entitled "Preparing the Next Generation of Hispanic Researchers" in San Diego, California. The conference was sponsored by the National Latino Research Center at San Diego State University.

On August 3-4, 1998, Ana Anders presented a workshop entitled "Making the Right Connection" (Networking) to the National Association of Professional Asian American Women (NAPAW) in Bethesda, Maryland.

On August 19-22, 1998, Ana Anders represented NIDA at SAMHSA/CSAP's Regional Alcohol and Drug Awareness Resource (RADAR) Network Meeting in Miami, Florida.

Dr. Elizabeth Rahdert, DCSR, chaired a symposium entitled "Psychiatric Comorbidity Among Adolescents with a Substance Use Disorder," and was the discussant on the symposium, "Family Therapy for Drug Abusing Hispanic Youth," at the 106th Annual Convention of the American Psychological Association held in San Francisco, CA, August 14-18, 1998.

Dr. Stephen Zukin, Director, DCSR, and Dr. Dorynne Czechowicz, Treatment Research Branch, DCSR, presented information on the Institute's Treatment Initiative and the Behavioral Therapies Development Program to the Committee on Research on Psychiatric Treatments, at the American Psychiatric Association Annual Meeting in Toronto, Canada in June 1998.

Dr. Robert Battjes, DCSR, chaired a panel presentation entitled "Drug Abuse Treatment Outcomes: Effects of Services and Settings," at the 15th Annual Meeting of the Association for Health Services Research held June 21-23, 1998, in Washington, DC.

Dr. Jack Blaine and Dr. Betty Tai, co-chairs of NIDA's Treatment Research Workgroup, held a symposium entitled "Interaction of Psychosocial Treatments and Pharmacotherapies" at the annual NCDEU meeting that took place on

June 10, 1998, in Boca Raton, Florida.

Drs. Lisa Onken and Jack Blaine of the Treatment Research Branch, DCSR, co-chaired a meeting of the Stage 1 Behavioral Therapy Investigators held in Tysons Corner,VA, July 13-14, 1998.

Dr. Lisa Onken, Treatment Research Branch, DCSR, gave a presentation at the American Psychological Association Meeting in August 1998 on NIDA's Treatment Initiative, a major Institute-wide activity aimed at improving the quality of drug addiction treatment.

On July 27-29, 1998, Drs. Robert Battjes, DCSR, and Teri Levitin, OEPR, participated in the NIMH Clinical Treatment and Services Research Workgroup meeting in Santa Fe, New Mexico. The workgroup, which is a subcommittee of the NIMH Council and chaired by Dr. John Rush, is charged with reviewing NIMH's efforts in supporting research to improve treatment and systems of care and developing an action plan to enhance the utility of research for consumers, practitioners, and policy makers.

Dr. Arthur MacNeill Horton, Jr., ECNB, DCSR, presented a lecture entitled "Research Initiatives within the Clinical and Services Research Division" at the Conference on Hispanics and Drug Use: A Training Conference for Hispanic Researchers, on July 13, 1998, at San Diego State University in San Diego, California.

Dr. Arthur MacNeill Horton, Jr., ECNB, DCSR, co-chaired a poster session entitled "Eating Disorders and the Treatment of Drug Abuse" on August 17, 1998 and served as a discussant for the Symposium entitled "Psychiatric Comorbidity among Adolescents with a Substance Abuse Disorder" on August 18, 1998, at the American Psychological Association Convention in San Francisco, California.

Dr. Steven Grant, ECNB, DCSR, was a discussant at the meeting entitled "Brain Imaging in Development of Medications for Drug Abuse" held on June 19, 1998 in Scottsdale, Arizona. Dr. Joseph Frascella, ECNB, DCSR, chaired a session on "Drug Abuse and Emotion" at the symposium on "Cognition and Emotion Applications to Drug Abuse" that was a satellite held at the annual meeting of American Psychological Society in Washington DC, May 21, 1998.

Dr. Joseph Frascella, ECNB, DCSR presented a poster entitled "Clinical Neurobiology Research Opportunities at NIDA" at the annual meeting of the American Psychological Society held in Washington, DC on May 22, 1998.

Dr. Joseph Frascella, ECNB, DCSR gave a presentation at the annual meeting of the Society for Biological Psychiatry on Grant Writing Strategies and Process in Toronto, Canada on May 30, 1998.

Dr. Joseph Frascella, ECNB, DCSR made two presentations at the Special Populations Research Development Seminar Series: Cannabinoid and Opiate Vascular Neuroimmunology held in Rosemont, Illinois, June 3-5, 1998.

Dr. Joseph Frascella, ECNB, DCSR was a discussant at the symposium entitled "Magnetic Resonance Applications in Substance Abuse" held at the CPDD meeting in Scottsdale, Arizona, on June 15, 1998.

Drs. Stephen Zukin, Steven Grant, and Joseph Frascella of the Division of Clinical and Services Research presented at and participated in a portion of the Summer Institute on Cognitive Neuroscience held in Squaw Valley, California, July 8-13, 1998.

NIDA Staff from the Division of Epidemiology and Prevention Research (DEPR) presented poster sessions on NIDA funded research at the American Psychological Society meeting held in Washington, DC, May 2, 1998.

Dr. Elizabeth Robertson was a participant in a symposium at the Society for Prevention Research annual meeting held in Park City, Utah, on June 7, 1998. The title of the symposium was "Dissemination Systems Collaboration Across Multiple Phases of Prevention Research".

Drs. Elizabeth Robertson and Bennett Fletcher and Ms. Susan Azeka presented a panel titled "NIDA Research Update" at the Association for Health Services Research, in Washington, D.C. on June 21, 1998.

Drs. Elizabeth Robertson, Jacques Normand, and James Colliver of DEPR presented poster sessions on the PRB, CRB, and ERB research agendas and funding opportunities at the annual meeting of the American Psychological Society held in Washington May 22-24, 1998.

Dr. Elizabeth Robertson attended the Family Research Consortium meetings in Blaine, Washington, June 27-30, 1998. The topic of the discussions was family-based prevention interventions.

Dr. James Colliver of DEPR and Dr. Lucinda Miner of OSPC represented NIDA at a meeting entitled Stages and Pathways of Drug Involvement: Examining the Gateway Hypothesis, held in Los Angeles, CA, June 27-30, 1998. Chaired by Drs. Denise Kandel and Richard Jessor, this meeting brought together a multidisciplinary group of

researchers to present and evaluate evidence on various aspects of the gateway phenomenon.

Peter Hartsock, Dr. P.H., CRB, DEPR represented DHHS at a special meeting of the Federal Interagency Arctic Research Policy Committee (IARPC) on June 23, 1998 to begin planning federal Arctic research efforts for the next century.

Dr. Frank Vocci presented on Pharmacotherapy for Opiate and Cocaine Dependence at a symposium on Medications Development for Addictive Disorders at the American Psychiatric Association meeting held in Toronto, Canada, on June 1, 1998.

Dr. Frank Vocci spoke on MDD- Industry Interactions in the Development of Medications for Substance Abuse Disorders at a symposium: Drug Abuse Pharmacotherapy Development in the Private Sector in Scottsdale, Arizona on June 15, 1998.

Drs. Anna Rose Childress and Frank Vocci co-chaired a June 15, 1998 workshop entitled "The Duality of Drug-Craving States: Implications for the Development of Anti-Craving Medications" at the College on Problems of Drug Dependence meeting in Scottsdale, Arizona. Drs. George Koob, David Roberts, Mark Albanese, and Anna Rose Childress presented on the implications of drug withdrawal, negative affect states, and alleviation of such states as motivators for drug use.

Dr. Frank Vocci presented on the Requirements for the Development of Medications for Addictive Disorders at a satellite symposium: Brain Imaging in Development of Medications for Drug Abuse in Scottsdale, AZ, June 19, 1998. Dr. Vocci's presentation focused on the role of neuroimaging techniques in clinical pharmacology studies to increase effectiveness and efficiency in medications development. The symposium proceedings will be published in the CPDD monograph.

Dr. Frank Vocci gave a plenary lecture at the New England School for Addiction Studies in Amherst, MA on June 2, 1998. His presentation focused on the current benefits associated with the use of methadone and LAAM and the prospective role of buprenorphine in the treatment of opiate dependence.

Dr. Peter J. Cohen, MDD, presented Grand Rounds at the Intramural Research Program on May 28, 1998 with a discussion of Institutional Review Boards and Clinical Investigation. An Ethical Conundrum: Inclusion Of (Pregnant) Women.

Dr. Alane S. Kimes, IRP, presented "In Vivo Imaging of Nicotinic Acetylcholine Receptors" at the University of Kansas Medical Center Society for Neuroscience Local Chapter Meeting held in Kansas City, KS on May 18, 1998.

Dr. John Matochik, IRP, presented "Using PET and MRI to Understand Brain Function" at the Neuroscience Research Program, Eli Lilly and Company, Indianapolis, IN on June 25, 1998.

Dr. Andrew Horti, IRP, presented "Development of Radiotracers for In Vivo and In Vitro Central Nicotinic Acetylcholine Receptors" at the NIDA IRP Seminar Series, Baltimore, MD, on June 30, 1998.

Dr. Edythe D. London, IRP, organized a satellite meeting entitled "Brain Imaging in Development of Medications for Drug Abuse" and presented "Imaging the Underlying Pathology of Drug Abuse" at The College on Problems of Drug Dependence's Sixtieth Annual Scientific Meeting held in Scottsdale, AZ, June 13-18, 1998.

Dr. D. Bruce Vaupel, IRP, presented "Effects of Cocaine-Related Environmental Stimuli on the Spontaneous EEG and Craving in Polydrug Abusers" at The College on Problems of Drug Dependence's Sixtieth Annual Scientific Meeting held in Scottsdale, AZ, Jun. 13-18, 1998.

Dr. Evan D. Morris, IRP, presented "Comparison of Quantitative Measures of Neurotransmitter Changes Based on PET: A Simulation Study" at the Functional Neuroreceptor Mapping of Living Brain Conference held in Ann Arbor, MI, June 12-14, 1998.

Dr. D. Bruce Vaupel, IRP, presented "Preclinical Evaluation of [123/125I]5-IODO-A-85380, a New SPECT Ligand for Nicotinic Acetylcholine Receptors" at the PET Interest Group, NIH, Bethesda, MD on July 17, 1998.

Dr. Amy Newman was invited to give a lecture to the Drug Discovery Group at Georgetown University Medical Center, Washington, D. C. in June 1998. The title of her talk was "Novel 3aŽ-(Diphenylmethoxy) Tropane Analogs as Probes for the Dopamine Transporter".

David A. Gorelick, M.D., Ph.D., organized and chaired a symposium on "Detection and Treatment of Stimulant Abuse" at the American Psychiatric Association's annual meeting held in Toronto, Canada on June 3, 1998.

Dr. Evan D. Morris, IRP, presented "Effect of Age on D2 Dopamine Receptor Binding Measured with 11-C Raclopride and PET in Rhesus Monkeys. Partial Volume Correction Reduces the Apparent Rate of Decline with Age" at the Society of Nuclear Medicine 45th Annual Meeting held in Toronto, Canada, June 7-11, 1998.

Dr. David Newlin, IRP, organized and chaired a symposium on the "Cardiovascular Psychophysiology of Alcohol and Cocaine" at the Research Society on Alcoholism 1998 meetings in Hilton Head, SC. As part of this symposium he presented a paper on "The Effect of Alcohol and Cocaine on Chaos and Complexity Measures of Cardiovascular Function."

Gorelick, D.A., Bencherif, B., Nelson, R.A., Stauffer, R., Ravert, H., Dannals, R., & Frost, J.J. Mu-Opioid Receptor Binding During Cocaine Abstinence. Presented at the American Psychiatric Association annual meeting, Toronto, Canada, June 1998.

Gorelick, D.A., Carriero, N.J., Simmons, M.S., & Tashkin, D.P. Antecedents of Smoked Cocaine Use in Male Cocaine Smokers. Presented at the College on Problems of Drug Dependence annual meeting, Scottsdale, AZ, June 1998.

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Media and Education Activities

Science Education

On July 27, 1998, NIDA released the seventh in its "**Mind Over Matter**" series for middle school students. "**The Brain's Response to Nicotine**," developed through NIDA's Science Education Program, follows the same format as the earlier components of the series in which the young character Sara Bellum takes the reader on an exploration of the brain's response to drugs. At the end of Sara's investigation of the effects of nicotine on the brain, the magazine unfolds to display on the reverse side an artistic photograph of neurons with a quotation designed to inspire curiosity about science. Concurrent with the development of the student magazine, a chapter on nicotine was added to the teacher's guide that accompanies the series. All of the "Mind Over Matter" materials are available free through the National Clearinghouse for Alcohol and Drug Information (1-800-729-6686).

Press Releases

June 22, 1998 - Cocaine Reward Does Not Require Dopamine or Serotonin Transporters--The Brain Sites Previously Implicated Cocaine's action in the brain requires more or other sites than researchers previously believed, or an unidentified means of action. A team led by Dr. George Uhl and Dr. Ichiro Sora of NIDA's Intramural Research Program found that cocaine could still elicit drug-seeking behavior in mice lacking the genes for either the dopamine or serotonin transporter. This study was published in the June 23 *Proceedings of the National Academy of Science*.

As a result of this news release, articles appeared in *The Wall Street Journal*, *Science Magazine*, *ABC News.Com*, and *The Washington Times*.

June 24, 1998 - Gene Variant Found That Can Help Protect Against Nicotine Addiction. According to a study published in the June 25 issue of *Nature*, some individuals carry a gene variant that may help protect them from becoming addicted to nicotine. Dr. Rachel F. Tyndale, University of Toronto found that individuals with a genetic variant in a particular enzyme break nicotine down more slowly than those who do not. These individuals have greater resistance to nicotine addiction and if they do smoke, they smoke fewer cigarettes than individuals without the impairment.

As a result of this news release, articles appeared in *USA Today*, *Associated Press (Online)*, *The Washington Times*, *The New York Times*, *The San Jose Mercury News*, *Science Daily*, *New Scientist*, and *Nature* magazine.

June 24, 1998 - First Global Meeting On HIV Prevention and Drug-Using Populations To Be Held in Geneva, Switzerland, June 25-26, 1998. NIDA, in collaboration with the World Health Organization's Programme on Substance Abuse and the Joint United National Programme on HIV/AIDS, will convene a meeting of researchers for the first time to establish a Global research Network on HIV Prevention in Drug-Using Populations. Approximately

50 HIV/AIDS prevention researchers from 23 countries have been invited to attend. In addition, a special June supplement of Public Health Reports will focus on the current status of national and international drug abuse and HIV/AIDS prevention research, much of which has been sponsored by NIDA.

July 20, 1998 - Nicotine Addiction Focus of National Conference. Facts about nicotine addiction, based on the latest scientific research, will be the focus of a national conference, Addicted to Nicotine, A National Research Forum, sponsored by NIDA and the Robert Wood Johnson Foundation.

As a result of this news release and press coverage at the event, articles appeared in *Reuters*, *CBS.Com*, *Associated Press* and numerous trade publications.

Media Exposure

June 4, 5, & 8, 1998 - Dr. Leshner, Dr. Hoffer, and several NIDA research staff at the IRP were interviewed by *BBC Radio* reporter Sue Armstrong for a 30-minute science news show on drug addiction and neuroscience. The show will air internationally in September.

June 6, 1998 - *Wall Street Journal*. Dr. Leshner and Dr. Frank Vocci were interviewed for an article "Researchers Push Many New Weapons Against Cocaine Habit" which focused on medications for treating addiction.

June 25, 1998 - Dr. Leshner was interviewed by several media outlets including, *USA Today and Associated Press*, regarding the NIDA funded study on defective genes and nicotine addiction.

Sunday, July 26, 1998 - *The New York Times*. Dr. Leshner was quoted in an article about efforts to develop medications to treat drug addiction. This article was prepared following negative comments about methadone by New York City Mayor, Rudolph Giuliani.

Monday -Tuesday, July 27-28, 1998 - *Addicted to Nicotine Conference*. Dr. Leshner, Dr. Vocci, and several conference speakers were interviewed by several member of the press, resulted in national coverage by *CBS This Morning* and *CBS Radio*, *NBC Radio*, *Associated Press*, *Reuter's*, and *Knight Ridder*, and upcoming coverage by *JAMA*, and *U.S. News & World Report* among others.

August 4, 1998 - Dr. Leshner was interviewed by several media outlets, including *CBS and NBC Nightly News*, *Wall Street Journal* and *New York Times* for articles and news segments on a NIDA funded study at Brookhaven National Laboratory on a new medication for treating cocaine addiction. Paramount Stations nationwide aired a documentary on teen smoking, "Smoking Truth or Dare" which included information from an interview with Dr. Edythe London, IRP.

Press Briefings

NIDA sponsored a press briefing during the **Addicted to Nicotine Conference**, June 27, 1998. The briefing was hosted by Dr. Alan I. Leshner who was joined by 5 researchers who have brief presentations related to their areas of expertise. A question and answer period followed the presentations. About 20 individuals representing print and broadcast media attended.

Awards

NIDA's video, **"The Great Disconnect,"** has won a Gold Certificate in the Questar Awards given by MerComm, Inc. for video communications. MerComm, Inc., is affiliated with the International Academy of Communication Arts and Sciences. "The Great Disconnect" highlights the power of science in the battle against drug abuse and addiction.

NIDA's **Mind Over Matter** (MOM) Magazine Series has won the distinguished Bronze Anvil Award given by the Public Relations Society of America (PRSA). MOM won the award in the Magazine Series category for Excellence in Tools and Tactics in public relations. PRSA is the world's largest organization of public relations professionals. The MOM series consists of seven full-color glossy magazines and a teacher's guide designed to teach middle school students how drugs of abuse act in the brain.

NIDA **INFOFAX** has won the prestigious Banner Award given by the American Hospital Association's Society for Healthcare Strategy and Market Development. INFOFAX won the award in the "Use of Emerging Media" category. The Banner Awards program recognizes fundamental skills in the disciplines of planning, strategy development, marketing, public relations and communications. The NIDA Infofax system uses network-based telecommunications to provide a toll-free, 24-hour information service to a broad range of users.

Exhibits

The following are meetings where NIDA has exhibited its publications and program announcements in recent months:

June 3-7, 1998 - Society for Prevention Research

June 4-6, 1998 - National Association of Drug Court Professionals (NADCP)

June 10-14, 1998 - National Coalition of Hispanic Health and Human Services Organizations

June 13, 1998 - NIH Health Forum

June 16-17, 1998 - NIH Health Fair

June 13-18, 1998 - College on Problems of Drug Dependence (CPDD)

June 21-23, 1998 - Association for Health Services Research (AHSR) and the Foundation for Health Services Research (FHSR)

June 21-23, 1998 - Congress on Women's Health: Advances in Research & Therapy

June 28-July 2, 1998 - Media Education Conference

June 28-July 3, 1998 - International AIDS Conference

July 1-4, 1998 - National Association of Alcoholism and Drug Abuse Counselors (NAADAC)

July 28-31, 1998 - Association on Higher Education and Disability (AHEAD)

August 1-6, 1998 - National Medical Association (NMA)

August 14-18, 1998 - American Psychological Association (APA)

August 21-25, 1998 - American Sociological Association

September 16-20, 1998 - American Academy of Family Physicians (AAFP)

Planned Meetings

NIDA is sponsoring the meeting **Understanding Drug Abuse and Addiction: Myths Vs. Reality**, a town meeting in Des Moines, Iowa on October 14, 1998. NIDA Director, Dr. Alan I. Leshner and NIDA researchers will discuss ways that state policy makers, organizations, schools and communities can utilize the latest scientific research to assess state and local drug problems and develop programs to meet their needs.

NIDA will conduct a **Training Track at the Community Anti-Drug Coalitions of America** (CADCA) National Leadership Forum on November 18-21, 1998 at the Omni Shoreham Hotel, Washington, DC. This year's Forum will focus on the critical need to improve the quality and effectiveness of community coalitions. NIDA's track will provide practical guidance to coalitions about the science of drug abuse and addiction.

NIDA will be participating in the **Primary Care/Behavioral Healthcare Summit** in St. Louis, MO, November 4 and 5, 1998. The summit is designed to acquaint primary care physicians and managed care organizations with behavioral healthcare issues. NIDA is a cosponsor of the event, and has developed a drug abuse tract for conference attendees.

The NIDA, NIMH and the NIH Office of Medical Applications of Research will cosponsor a **Consensus Development Conference on the Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder (ADHD)** on

November 16-18, 1998. Despite the substantial progress in the assessment, diagnosis, and treatment of children and adults with ADHD, the disorder has remained controversial in many public and private sectors leaving many families, health care providers, educators, and policy-makers uncertain about the status of the disorder, its treatment and its long-term consequences. Psychostimulants, including dextroamphetamine, methylphenidate, and pemoline, are by far the most widely researched, clinically effective, and commonly prescribed treatments for ADHD. These medications are regarded by many in the medical community as constituting the psychopharmacologic treatment of choice for ADHD. Nonetheless, considerable controversy exists, both in the public at large and within segments of the medical community, about the common use of these medications for treating children diagnosed with ADHD. The use of methylphenidate and amphetamine nationwide has increased significantly in recent years. This increased availability and use of psychostimulants has intensified the concerns about use, overuse, and abuse. This 21/2-day conference will bring together national and international experts as well as representatives from the public. After these presentations and audience discussion, an independent, non-Federal consensus panel chaired by Dr. David J. Kupfer, Thomas Detre Professor and Chair, Department of Psychiatry, University of Pittsburgh, will weigh the scientific evidence and prepare a statement on ADHD and its treatment. The Conference sessions will be held in the Natcher Conference Center (Building 45). You may register for this conference by Internet @ http://consensus.nih.gov or send an e-mail message to Brain@ProspectAssoc.com

A symposium entitled **Amygdala and More** will be held in November 1998. Participants will include: Dr. Roger Brown, NIDA (Chair); Dr. L. Heimer, University of Virginia; Dr. George Koob, Scripps Research Institute; Dr. B.J. Everitt, University of Cambridge, UK; and Dr. H.C. Breiter, Massachusetts General Hospital. Marked neuroadaptations in monoaminergic and neuropeptide systems occur in the extended amygdala and in the shell of the nucleus accumbens after the repeated administration of abused substances. These limbic structures form a large forebrain continuum connecting virtually every part of the brain. The anatomical limits and connections, the regional dysregulation of neurotransmitters and neuropeptides, and the functional and cognitive consequences that emerge in this region after repeated exposure to drugs of abuse in animals and humans will be discussed.

The Behavioral Science Working Group (Chair, Dr. Jaylan Turkkan) is planning a number of New Investigator events at national conferences this coming year including CPDD; the American Psychological Society; the Society for Research on Nicotine and Tobacco; the Society for Prevention Research; the Society for Neuroscience; the Society for Research on Child Development; and the AIDS Impact Meeting. Each venue will highlight achievements by new NIDA investigators, provide useful information about training and career mechanisms, and offer mentoring advice from senior NIDA investigators.

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Publications

Research Monograph

Cost-Benefit/Cost-Effectiveness Research of Drug Abuse Prevention: Implications for Programming and Policy--Research Monograph 176, NIH Pub. No. 98-4020.
This monograph provides definitions of prevention program types, discusses effect sizes to be expected from program delivery, assesses in financial and social terms the benefits to society that result from effective drug abuse prevention programs and policies. The monograph will have a variety of important uses to include guiding future developments in prevention programming, informing policy makers, legislators, and program managers concerning advanced prevention program strategies that work, and disseminating to the scientific research community an overview of the state-of-the-art of drug abuse prevention as reflected by a critical review of extant drug abuse prevention research.

Other Publications

National Conference on Drug Abuse Prevention: Presentations, Papers, and Recommendations NIH Pub. 98-4293.
This publication represents the outcome of more than 20 years of research that could be put to use in community prevention programs. The purpose of this publication is to present a compilation of keynote speeches, plenary presentations, and work group recommendations.

National Survey Results on Drug Use From the Monitoring the Future Study 1975-1997: Volume I: Secondary School Student, NIH Pub. 98-4345, NCADI BKD300.
Volume I of this report provides data from the 1995-1996 and the 1996-1997 school year. The Monitoring the Future data is one of the key indicators of trends in substance use among adolescents and young adults. It is the only national survey of its kind in the U.S. that collects data from 8th, 10th, and 12th graders.

National Survey Results on Drug Use From the Monitoring the Future Study 1975-1997: Volume II: College Students and Young Adults, NIH Pub. 98-4346.
This is the second volume in a two-volume set reporting the results of all surveys through 1997 from the Monitoring the Future study of American secondary school students, college students, and young adults. This second volume presents the results of the 1977 through 1997 follow-up surveys of the graduating high school classes of 1976 through 1996 as these respondents have progressed through young adulthood.

Epidemiologic Trends in Drug Abuse: Community Epidemiology Work Group, December 1997: Volume I, NCADI BKD266, NIH Pub. 98-4297.
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.

Slide Teaching Packet II: The Neurobiology of Drug Addiction, NCADI MS626.
This teaching packet was developed to provide health practitioners, neuroscientists, and teachers a tool to aid in discussions with high school students, the general public, and recovering drug addicts about the basic function of the brain, the neurobiological basis for addiction and the actions of heroin and cocaine. It includes a set of 30 slides, a "hard copy" print of the slide set (to aid in previewing) and a narrative script to accompany the slide set.

Economic Cost on Alcohol and Drug Abuse in the United States 1992, NIH Pub. 98-4327, NCADI 265.
This publication was developed as a result of a study conducted to update information on the cost of alcohol and drug abuse in the United States. This publication reporting the data and its analysis will be of considerable interest to policy makers as well as to drug abuse practitioners. This publication provides to the field of drug and alcohol demand and supply reduction the most current findings and interpretations of data in the areas of cost and cost analysis. The publication will be vitally important to the discussion of all aspects of drug and alcohol use reduction, including health care services, financing, and service delivery.

Mind Over Matter Series
This eye-catching series encourages young 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 is included on the back of each magazine.

- **The Brain's Response to Marijuana, NIH Pub. 98-3859 NCADI PHD801L.**
- **The Brain's Response to Inhalants, NIH Pub. 98-4038 NCADI PHD800L.**
- **The Brain's Response to Steroids, NIH Pub. 98-3860 NCADI PHD804L.**
- **The Brain's Response to Stimulants, NIH Pub. 98-3857 NCADI PHD805L.**
- **The Brain's Response to Opiates, NIH Pub. 98-3856 NCADI PHD802L.**
- **The Brain's Response to Hallucinogens, NIH Pub. 98-3858 NCADI PHD803L.**
- **The Brain's Response to Nicotine, NIH Pub. 98-, NCADI PHD807.**

Marijuana: Facts for Teens, NIH Pub. 98-4037 (Revised).
This revised publication provides adolescents, teenagers, and young adults with answers to some frequently asked questions about marijuana. The teen booklet explains the current knowledge about marijuana, what it is, who uses it, how it affects a person physically and mentally through short-term and long-term usage, and where to seek help. It also includes reactions to marijuana use by teenage users and nonusers.

Marijuana: What Parents Need to Know, NIH Pub. 98-4036 (Revised).
This revised publication provides valuable information gained from research on the dangers of marijuana and gives parents details about the drug so they can better communicate dangers to their children. The booklet also includes answers to some of the most frequently asked questions about marijuana, explanations of the latest scientific information, and suggestions about how to talk to teenagers about marijuana. Audiences for this publication include parents, grandparents, care givers, teachers, and recreation and community leaders who work with young people.

Research Report Series

Nicotine Addiction, NCADI PHD762, NIH Pub. No. 98-4342.
This publication describes what nicotine is; current epidemiological research data regarding its use; the medical consequences of nicotine use, with an emphasis on the effects of nicotine on the brain; current research findings about use during pregnancy, and treatment approaches.

NIDA NOTES

NIDA NOTES, Vol. 12, Issue No. 5, NCADI NN0025.
This issue features results from NIDA's Drug Abuse Treatment Outcome Study. The issue also reports findings that morphine shrinks nerve cells in the brain. NIDA's cooperative work with Latin American countries to advance drug abuse research is also reported. An article also describes drug abuse education materials for middle school students.

NIDA NOTES, Vol. 12, Issue No. 6, NCADI NN0027.
The lead article in this issue reports on NIDA's Heroin Conference in Washington, D.C. Other articles discuss the conclusions of two panels: one on effective medical treatment of heroin, and the other on the need for research on

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

NIDA NOTES -Vol. 13, Issue No. 1, NCADI NN0028.
NIDA's Methamphetamine Initiative is featured in this issue, as well as highlights from NIDA's 1997 Constituent Conference. Another feature article describes how NIDA uses interagency pacts and collaborations with other NIH institutes to extend its research reach. This issue's Tear off compares methamphetamine and cocaine.

NIDA NOTES -Vol. 13, Issue No. 2, NCADI NN0029.
A number of articles and the Director's Column in this issue discuss the links between child abuse and the victim's later abuse of drugs. A NIDA-sponsored international meeting of epidemiologic researchers is covered, including findings on international trends in drug abuse that were reported at the meeting. Another article reports on brain imaging studies that are providing information on cocaine's effects on the brain. Results from NIDA's annual Monitoring the Future study of drug use among high school students are detailed as well.

NIDA NOTES -Vol. 13, Issue No. 3, NCADI NN0030.
NIDA's National Conference on Drug Addiction Treatment is the lead story in this issue. The Director highlights NIDA's nicotine addiction research in his column, and a pair of articles looks at new findings in that area. Another feature reports on evidence showing that cocaine abuse may lead to strokes and mental deficits. NIDA-funded studies on how to stem tuberculosis among injecting drug abusers are covered as well.

A volume entitled **Cocaine: Effects on the Developing Brain** was published by the New York Academy of Sciences (NYAS) in June 1998. The volume is edited by John A. Harvey and Barry E. Kosofsky, and contains a Foreword by Dr. Leshner. A result of a NYAS meeting held in September 1997 with partial support from NIDA, the book brings together contributions from basic and clinical researchers, and includes discussion of research that has attempted to identify the molecular, neurochemical, physiologic, and neuropathologic processes that may mediate toxicity of in utero cocaine exposure, as well as behavioral and clinical correlates of that exposure.

Special Issue Chronicles NIDA's Prevention Research Response to Drug Abuse, HIV, and AIDS
In June 1998, the U.S. Public Health Service published a special supplement on the origins, evolution, and current status of the HIV prevention science knowledge base that was derived, in large part, from the HIV research and intervention programs supported by the National Institute on Drug Abuse's (NIDA) Community Research Branch. The special issue's Guest Editor is Richard H. Needle, Ph.D., MPH, Chief of NIDA's Community Research Branch, and the Guest Associate Editors are Susan L. Coyle, Ph.D., Chief of OEPR's Clinical, Epidemiological, and Applied Sciences Review Branch, and Helen Cesari, M.S., of the Community Research Branch. The special supplement chronicles NIDA's prevention research response to the epidemics of drug abuse, HIV, and AIDS since the Public Health Service first established a comprehensive plan in 1985 to control and prevent the spread of the infection. Public Health Reports, 113 (Suplmt. #1), June 1998.

Special Issue Provides Findings from NIDA's Cooperative Agreement for AIDS Research
A recent special issue provides findings from NIDA's Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program (CA) which, as of February 1997, included over 28,000 participants from as many as 23 urban and rural research sites in the U.S., Puerto Rico, and Brazil. The special issue makes clear that drug users are highly heterogeneous and difficult to categorize into any one group. In addition, while macro-level factors such as region or size of metropolitan area may influence drug use patterns and risks for HIV/AIDS, local contextual factors which define the conditions of daily lives (e.g., the local distribution and control of drugs, HIV seroprevalence levels, access to health care, living conditions, local traditions and customs regarding drug use, peer norms, and other social and cultural influences) have immediate and direct impacts as well. The special issue contains eight papers by NIDA-sponsored Principal Investigators, Co-PIs, and colleagues in the CA, and the Guest Co-Editors of the issue are David Himmelgreen and Merrill Singer, of the Hispanic Health Council in Hartford, Connecticut. The American Journal of Drug and Alcohol Abuse (Special Issue on the NIDA Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program); 24 (2), 1998.

Gorelick, D.A., Montoya, I.D. & Johnson, E.O. Sociodemographic Representation in Published Studies of Cocaine Abuse Pharmacotherapy. Drug and Alcohol Dependence, 49, pp. 89-93, 1998.

Carmona, G.N., Schindler, C.W., Shoaib, M., Jufer, R., Cone, E.J., Goldberg, S.R., Greig, N.H., Qian-Sheng, Y., and Gorelick, D.A. Attenuation of Cocaine's Behavioral Activity by Butyrylcholinesterase. Experimental and Clinical Psychopharmacology, 6, pp.274-279, 1998.

Gorelick, D.A. The Rate Hypothesis and Agonist Substitution Approaches to Cocaine Abuse Treatment. In Goldstein, D. (Ed.), Catecholamines: Bridging Basic Science with Clinical Medicine. (Advsnces in Pharmacology, Vol 42), (San Diego, Academic), pp. 995-997, 1998.

Sloboda, Z. What We have Learned from Research about the Prevention of HIV Transmission among Drug Abusers. Public Health Reports, 113, pp. 194-204, 1998.

Sloboda, Z. Drug Abuse among College Students: Part I. Impaired Driving Update, II(3), March/April 1998.

Sloboda, Z. Drug Abuse among College Students: Part II. Impaired Driving Update. II(4), May/June 1998.

Sloboda, Z. State of the Art of Prevention Research in the United States. Evaluating Drug Prevention in the European Union. EMCDDA Scientific Monograph Series, No. 2, 1998.

Cohen, P.J. The Placebo is not Dead: Three Historical Vignettes, IRB 20, pp. 6-8, 1998.

Dr. Jonathan Katz, IRP, has recently completed editorial work on a book summarizing recent research on the pharmacology and psychology of cocaine abuse. This book includes chapters by recognized experts in the field of cocaine abuse and covers areas from the basic pharmacology of cocaine, basic behavioral pharmacology of cocaine (co-authored by Katz), clinical pharmacology of cocaine, drug discovery efforts directed at cocaine abuse therapeutics, cocaine induced teratology, genetic underpinnings of cocaine abuse, treatment approaches to elimination of cocaine abuse, as well as sociologic issues involved in cocaine abuse.

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

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

Dr. Amy Newman served as guest editor of a special issue of the Journal Medicinal Chemistry Research. The issue focused on the recent advances in the medicinal chemistry of novel dopamine transporter ligands and their relationship to the development of a cocaine pharmacotherapeutic. Dr. Newman also contributed the invited guest editorial Novel Dopamine Transporter Ligands: The State of the Art. Med. Chem. Res. 8, pp. 1, 1998. The special issue was published in June, 1998.

Dr. Amy Newman prepared an invited review of her research efforts on the development of novel dopamine transporter ligands, based on benztropine. The review entitled "Novel Benztropine [3aŽ-(Diphenylmethoxy)tropane] Analogs as Probes for the Dopamine Transporter" will appear in Current Medicinal Chemistry, 5, pp. 301-315, 1998.

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Staff Highlights

Honors and Awards

1998 Blue Cross/Blue Shield Award

Charles Sharp, DBR
Ann Montgomery, MDD

1998 Quality of Worklife Award

Carol Cushing

1998 Secretary's Award for Distinguished Service

Elizabeth Robertson, DEPR (as a Member of the Secretary's Initiative on Youth Substance Abuse Prevention)
Beverly Jackson, OSPC (as a Member of the Secretary's Initiative on Youth Substance Abuse Prevention)
William Bukoski, DEPR (as a Member of the Secretary's Initiative on Youth Substance Abuse Prevention)

1998 NIH Director's Award

Group Award
David Gorelick, IRP (part of the NIH Institutional Review Boards Group)

Individual Awards
Henry Francis, CAMCODA
Susan Herbert, MDD
Mary Affeldt, IRP

1998 Commissioned Corp Awards

Peter Delaney, DCSR - Commendation Medal
Kesinee Nimit, OEPR - Commendation Medal
Steven Sparenborg, MDD - Commendation Medal
Betty Tai, MDD - Commendation Medal
Anti-Cocaine Addiction Medication Development Group - Unit Commendation
NIDA IRP Pharmacy - Unit Commendation
CDR Janice M. Carico, IRP - Outstanding Service Medal

Other Awards

Lee Cummings, J.D., of the Medications Development Division, was elected as chairman of the NIH-wide Technology Development Coordinators, effective September 1998.

Drs. Newman, Allen, Kline, Izenwasser and Katz, were awarded a U.S. Patent #8,667,024, on April 15, 1998 entitled 3a*-Diphenylmethoxytropane Analogs as Cocaine Therapeutics.

Dr. Amy Newman has received an HHS Special Service Award in April 1998 for serving as an invited guest editor for a special issue of Medicinal Chemistry Research, focused on recent advances in medicinal chemistry at the dopamine transporter.

On July 12, 1998, **Dr. Teruo Hayashi**, a visiting fellow working with **Dr. Tsung-Ping Su** of the IRP, was honored as one of the ten Rafaelsen Fellows selected from young scientists in the opening ceremony of the XXIst Congress of the Collegium Internationale NeuroPsychopharmacologicum (CINP) which was held from July 12 to 16, 1998 at Glasgow, Scotland. Dr. Hayashi was awarded with a two thousand dollars travel scholarship to attend the XXIst CINP meeting. Dr. Hayashi was honored for his ongoing study with Dr.Tsung-Ping Su on the role of sigma receptors in the modulation of calcium signaling in cells.

Dr. Jonathan Links, Technical Director of NIDA's Brain Imaging Center, has been elected President of the Society of Nuclear Medicine and has been promoted to Professor with tenure, Environmental Health Sciences (SPH), School of Public Health, Johns Hopkins University.

Staff Changes

Kathleen Etz, Ph.D. joined the Prevention Research Branch, DEPR, as a Program Official in August 1998. She comes to NIDA from a Post Doctoral Fellowship at the University of Kentucky Center for Drug Abuse Prevention. She received her doctorate from the Human Development and Family Studies program at the University of North Carolina at Greensboro where she participated in the Carolina Consortium on Human Development.

Steven Grant, Ph.D. has recently joined the Etiology and Clinical Neurobiology Branch, Division of Clinical and Services Research. Before coming to NIDA's extramural program, Dr. Grant spent 5 years at NIDA's Intramural Research Program in Baltimore studying the clinical neurobiology of drug addiction. He will direct the ECNB's program in cognitive neuroscience.

Richard Kline, Ph.D. was selected for the position of Chemist in the Chemistry and Pharmaceutics Branch, MDD, effective May 24, 1998. Dr. Kline is a medicinal chemist, with a background in the medicinal chemistry of novel cocaine addiction therapeutics. Prior to employment with MDD, Dr. Kline worked with Information Management Consultants developing a 3D chemical structural information database system. Dr. Kline was a NIDA Research Fellow at the Intramural Research Program, and the recipient of a National Research Council Fellowship in 1994.

Jeffrey Merrill, M.P.H. is serving on a detail to DEPR under an Intergovernmental Personnel Assignment (IPA) from the University of Pennsylvania Medical School effective July 6, 1998. At NIDA, Mr. Merrill has assumed the duties of a senior level Public Health Advisor and Special Assistant to the Director, DEPR, and will provide expertise and guidance to DEPR and its Prevention Research Branch in the area of prevention health services research and managed care.

Moo Kwang Park, Ph.D. was selected for the position of Chemist in the Chemistry and Pharmaceutics Branch, MDD, effective June 18, 1998. Dr. Park is a pharmaceutical scientist with special expertise in research and development of pharmaceutical dosage forms and bioequivalance studies. Dr. Park was most recently employed by the FDA Division of Bioequivalance, and formerly held positions with Formulation Development Company, Bristol-Myers Squibb, and Ayerst Laboratories.

Mr. Keith Van Wagner, Presidential Management Intern, began his rotation in the Public Information Branch, Office of Science Policy and Communications, in July. Mr. Van Wagner earned his Masters of Public Administration from North Carolina State University and is nearing the end of his first year in the 2-year program.

Marina Volkov, Ph.D. joined NIDA's Office of Extramural Program Review as a Scientific Review Administrator in the Clinical, Epidemiological, and Applied Sciences Review Branch in early September 1998. Dr. Volkov comes to NIDA from the NIH Office of Behavioral and Social Sciences Research (OBSSR). Activities in which she was involved while at OBSSR included developing a standard NIH definition of these sciences, creating trans-institute and trans-agency funding initiatives, and improving communications among the behavioral and social science communities, as well as information exchange between the research community and biomedical scientists, health care providers, the media, the public and policy makers.

Ms. Kathleen Wilson has moved from NIDA's Intramural Research Program to work in the Public Information Branch, Office of Science Policy and Communications, as a communications assistant. Ms. Wilson participates in the NIH Temporary Employment Program and is a telecommunications major at Morgan State University.

Henry Francis, M.D. was reassigned to the position of Director for the Center on AIDS and Other Medical Consequences of Drug Abuse effective June 7, 1998.

Elizabeth Robertson, Ph.D. was selected to be Chief, Prevention Research Branch, DEPR. Dr. Robertson holds a Ph.D. in human development and family studies from the University of North Carolina at Greensboro. She first joined NIDA staff as a Program Official in the Prevention Research Branch in November, 1995.

Jaylan Turkkan, Ph.D. was selected as Chief of the Behavioral Sciences Research Branch, Division of Basic Research, in July 1998.

Ms. Mona Brown, Public Information Specialist with NIDA's Public Information Branch, OSPC, and NIDA's Press Officer for 10 years, left the Institute to assume a position in the Health Resources and Services Administration's (HRSA), Office of Communications.

Ms. Andrea Kopstein of the Epidemiology Research Branch, DEPR, is leaving NIDA to join the Division of Population Surveys in the Office of Applied Studies at the Substance Abuse and Mental Health Services Administration (SAMHSA). Ms. Kopstein, who came to NIDA in 1988, will work on the National Household Survey on Drug Abuse (NHSDA).

Dr. Alan Trachtenberg, Medical Officer in the Office of Science Policy and Communications left NIDA to assume a position at SAMHSA.

Edward J. Cone, Ph.D. retired from government service on August 31, 1998 after more than 26 years of service. Dr. Cone joined NIDA's Intramural Research Program (Addiction Research Center) in Lexington, KY on July 1, 1972 where he served as Chief of the Chemistry and Drug Metabolism Section until 1998. Dr. Cone was a Commissioned Officer in the U.S. Public Health Service and had the rank of Permanent Director Grade (CO-06). Dr. Cone's research on the kinetics and dynamics of smoked drugs, effects of environmental exposure to drugs of abuse, and the use of alternative specimens like saliva, sweat and hair for drug testing has been recognized world-wide and has resulted in the publication of numerous chapters and over 200 scientific articles on the analysis of drugs in biological media. Dr. Cone was cited by Science Watch, a journal that tracks trends and performance in basic research, as being the most highly cited author in Forensic Science over the period of 1981-1993. Presently, Dr. Cone is serving as a consultant to private industry, government and the military on matters relating to drug testing and drug delivery systems. In addition, he holds appointments as Adjunct Professor in the Toxicology Program, University of Maryland at Baltimore and as Visiting Professor at Johns Hopkins School of Medicine.

Zili Sloboda, Sc.D., Director of NIDA's Division of Epidemiology and Prevention Research will be leaving October 1, 1998. Dr. Sloboda was responsible for uncounted major innovations and successes of the prevention, epidemiology, etiology and AIDS related programs of the Division, the Institute, and the field. At NIDA, she previously served as the Associate Director for Planning and Service Coordination of the Division of Clinical Research, as Chief of the Prevention Research Branch, and as a Research Epidemiologist emphasizing the natural history of HIV infection among drug abusers. Dr. Sloboda was one of the founders of the Society for Prevention Research and the professional journal, Prevention Science. She is the author of numerous scientific articles and chapters and her early work on the validity of self-report of drug abusers is still often cited--more than twenty years after its publication. Trained first as a medical sociologist at New York University and later as an epidemiologist at the Johns Hopkins University School of Hygiene and Public Health, Dr. Sloboda came to the federal government in 1987 as an expert and experienced researcher in both epidemiology and prevention research. She relocates to Ohio leaving an unmatched legacy of professional accomplishment in the research and public health fields; she takes with her the highest personal regard, respect and appreciation of her colleagues and her many friends. Dr. Sloboda will pursue her research interests in the area of drug abuse services research.

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