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

May, 2001

Index

[Office of Director] [First Report Section]

See our **Contact Information**. .

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Research Findings

Basic Research

Experiences During Drug Withdrawal Alter Brain Chemistry

Researchers from Texas Southwestern Medical Center recently showed significant changes in the brain enzyme tyrosine hydroxylase (TH) in rats following withdrawal from cocaine. TH is the rate-limiting enzyme for the synthesis of the brain neurotransmitter dopamine. In the experiment, rats pressed a response lever to self-administer cocaine over twelve consecutive days. Following this phase of "acquisition," one group of rats went through cocaine withdrawal for one week in their home cage. A second group of rats was returned to the chamber where they previously received cocaine each day for one week, but this time lever presses did not result in cocaine infusions (a procedure known as "extinction"). When TH was measured in these two groups, the rats that went through withdrawal in the home cage had lower TH levels in the nucleus accumbens and ventral tegmental area, two brain regions implicated in drug addiction, than rats who experienced "extinction" training. Importantly, these data suggest that experiences during cocaine withdrawal can result in differential neuroadaptations in neurotransmitters affected by drugs of abuse. The investigators hypothesized that the experience of seeking cocaine and not obtaining it increased TH levels, and presumably dopamine levels, leading to accelerated recovery from the negative effects associated with cocaine withdrawal. These results have important implications for treating cocaine addiction and understanding the role of experiential factors in reversing drug-induced brain changes. Schmidt, E.F., Sutton, M.A., Schad, C.A., Karanian, D.A., Brodkin, E.S., and Self, D.W. Extinction Training Regulates Tyrosine Hydroxylase during Withdrawal from Cocaine Self-Administration, The Journal of Neuroscience, 21, pp. 1-5. 2001.

Neurotoxic Effects of Nicotine

The laboratory group of Gaylord Ellison has previously shown that a variety of addicting drugs (e.g. cocaine, methamphetamine, MDMA), when given continuously to rats so as to mimic "binging" in people, all induce degeneration of axons. These axons run from the lateral habenula through the sheath of the fasciculus retroflexus to midbrain nuclei such as the ventral tegmental area, substantia nigra, and raphe nuclei. With some of these drugs, such as cocaine, this is virtually the only degeneration induced in all of the brain. Dr. Ellison's group very recently found that nicotine given continuously for five days at relatively low doses which induce plasma levels of nicotine comparable to heavy smokers, also selectively induces degeneration in fasciculus retroflexus. However, with the nicotine, this damage is in the other half of the fasciculus retroflexus tract - the cholinergic axons running from medial habenula in the core of the tract to the interpeduncular nucleus.

Humans generally begin their smoking habits by smoking only a few cigarettes each day, and thus probably rapidly induce a great deal of tolerance to this potential neurotoxicity. For this and other reasons, it is uncertain to what degree these observations in rats can be applied to humans. However, it is now apparent that, at least, the fasciculus retroflexus may be a "weak link" in the brain for diverse stimulant drugs of addiction. Damage to this tract may be involved in the induction of various behaviors associated with progressive addiction and relapse. Since fasciculus retroflexus provides negative feedback from the limbic forebrain back onto the midbrain monoaminergic "reward" cells that innervate it, it is predicted that its degeneration may be linked to a loss of higher brain control over behavior. Carlson, J., Armstrong, B., Switzer, R.C. 3rd, and Ellison, G. Selective Neurotoxic Effects of Nicotine on Axons in Fasciculus Retroflexus Further Support Evidence That This is a Weak Link in Brain Across Multiple Drugs of Abuse. Neuropharmacology, 39(13), pp. 2792-2798, 2000. In addition to the NIDA grant, this study was also funded in part by the Tobacco Related Disease Research Program, which is funded by California's tobacco tax.

Endomorphins and CNS Sites

Endomorphins (EM-1 and EM-2) have been shown to act as endogenous agonists for the mu-opioid receptor. However to date, the sites within the CNS that are activated by these two peptides have not been elucidated. Recently, Dr. Sulie Chang and her co-workers published a study in Brain Research that examined the sites of action of these EM in the rat brain using EM-induced FOS immunoreactivity (FOSir) as an anatomic marker of neuronal activation. They observed dose-dependent EM-1 and EM-2 activation of FOSir in various nuclei through out the rostral-caudal axis of the rat brain and the activation was correlated with mu-opioid receptor location in brain areas except in caudate putamen and the accumbens nucleus. The differential activation of structures by these two novel peptides, EM-1 and EM-2, suggests that these molecules may be involved either in separate physiological functions or may play different roles within the same physiological processes. Jiang, Y., Klodesky, C.M., and Chang, S.L. Endomorphine-1 and Endomorphine-2 Induce the Expression of c-FOS Immunoreactivity in the Rat Brain. Brain Research, 873, pp. 291-296, 2000.

Anti-Inflammatory and Analgesic Action of a Cannabinoid Compound

A number of studies have shown that THC and structurally related synthetic cannabinoids are capable of modulating pain sensitivity in animal models at the level of brain or spinal cord CB1 receptor activation. This, in part, has generated an interest in finding cannabinoids that may activate peripheral CB1 receptors, resulting in both anti-inflammatory and antihyperalgesic effects. Of particular interest has been to search for a metabolite of THC that might have the indicated actions, but without psychotropic effects, and which could be delivered topically or orally. One of the first such compounds studied was the 11-nor-delta-9-THC-9-carboxylic acid (also known as THC-11-oic acid), which is a major metabolite of THC. This has been shown to inhibit prostaglandin synthesis by inhibiting cyclo-oxygenase activity, and to have antinociceptive activity in mice at 20-40 mg/kg orally. The metabolite was found to bind only weakly to the CB1 receptor. More recently, a synthetic analog of THC-11-oic acid, known as ajulemic acid, or CT-3, has been similarly investigated by Dr. Sumner Burstein. The compound is also under patent to Atlantic Pharmaceuticals Inc. In mice, CT-3 showed approximately equal potency with morphine in the hot plate test when administered intragastrically, and similar potency to morphine over several hours observation in the mouse tail clip test administered intragastrically or intraperitoneally. Dose-dependent analgesia was also observed in the rat tail clip procedure. The compound also demonstrated anti-inflammatory effects in an adjuvant-induced rat model for arthritis, with a lower ulcerogenic potential than shown by other anti-inflammatory agents, including indomethacin. Additionally, CT-3 reduced the accumulation of leukocytes induced by injection of pro-inflammatory cytokines into subcutaneous air pouches on the backs of mice, as a model of acute inflammation. In preliminary data, CT-3 did not produce signs of strong dependency in rats tested over fourteen days at oral doses of 10-40mg/kg, administered in an oil-based formulation. Burstein, S.H. Current Pharmaceutical Design, 6, pp. 1339-1345, 2000.

Design, Synthesis, and Monoamine Transporter Binding Site Affinities of Methoxy Derivatives of Indatraline

In this study, a series of methoxy-containing derivatives of indatraline, a nonselective monoamine reuptake inhibitor capable of antagonizing methamphetamine-induced neurotransmitter release, were synthesized. The structure of some intermediate compounds such as indanone, and trans-1-azido-3-(3,4-dichlorophenyl)-5-methoxyindan was confirmed by single crystal X-ray analysis. The binding affinity of these compounds for dopamine, serotonin, and norepinephrine transporter binding sites was determined. Out of several methoxy group-containing derivatives, 6-methoxy displayed the highest affinity for both serotonin and norepinephrine transporters, however this compound also retained reasonable affinity for the dopamine transporter. This high affinity compound might eliminate methamphetamine's reinforcing effects by blocking the transporters that are thought to contribute or modulate the effects of stimulant-like drugs. The authors concluded that this compound would be a promising template for the development of a long acting inhibitor of monoamine transporters. Such inhibitors have high potential as medications for treatment, as a substitution medication, or for prevention of the abuse of methamphetamine-like stimulants. Gu, X-H, Yu, H., Jacobson, A.E., Rothman, R.B., Dersch, C.M., George, C., Flippen-Anderson, J.L. and Rice, K.C. Design, Synthesis, and Monoamine Transporter Binding Site Affinities of Methoxy Derivatives of Indatraline, J. Med. Chem., 43, pp. 4868-4876, 2000.

Coupled Plasmon-Wavelengh Resonance (CPWR) Technology for Receptor

Structural changes accompanying the binding of ligands to the cloned human sigma-opioid receptor immobilized in a solid-supported lipid bilayer have been investigated using coupled plasmon-waveguide resonance(CPWR). This highly sensitive technique directly monitors mass density, conformation, and molecular orientation changes occurring in anisotropic thin films and allows direct determination of binding constants. Although both agonist binding and

antagonist binding to the receptor cause increases in molecular ordering within the proteolipid membrane, only agonist binding induces an increase in thickness and molecular packing density of the membrane. This is a consequence of mass movements perpendicular to the plane of the bilayer occurring within the lipid and receptor components. These results are consistent with models of receptor function that involve changes in the orientation of transmembrane helices. This methodology has the unique capability of independently examining the real-time changes in the structure of the receptor both parallel and perpendicular to the lipid membrane in response to receptor-ligand interactions. CPWR also provides greatly enhanced sensitivity and spectral resolution as compared to conventional surface plasmon resonance (SPR). In addition, the method should be readily adaptable to high-throughput screening, in view of the minute amounts of receptor and ligand needed for complete dose-response binding assay and for evaluation of receptor structural changes. In the present paper, the highly selective sigma-opioid receptor agonist DPDPE was incorporated into the preformed lipid layer and studied by CPWR. Salamon, Z., Cowell, S., Varga, E., Yamamura, H.I., Hruby, V.J. and Tollin, G. Biophysical Journal, 79, pp. 2463-2474, 2000.

Role of Positive Charge on the N-Terminal Amino Group of Opioid Peptides

To investigate the role of positive charge on the N-terminal amino group of opioid peptides in the interaction with their receptors, Schiller and colleagues undertook the synthesis and pharmacological characterization of enkephalin analogs in which the amino group is replaced with the neutral methyl group. As the parent compound, the potent enkephalin analog H-Dmt-D-Ala-Gly-Phe-Leu-NH2 was selected as it exhibits potent mu and delta agonist activities. The replacement of amino group in this analog with a methyl group required the development of a stereospecific synthesis of (2s)-2-methyl-3-(2,6-dimethyl-4-hydroxyphenyl)-propionic acid (Mdp). Following the synthesis of Mdp, the pentapetide, (2S)-Mdp-D-Ala-Gly-Phe-Leu-NH2, was prepared by the solid-phase method and the purity and structural identity were established by analytical HPLC and FAB-MS. The enkephalin analog was pharmacologically characterized. The enkephalin analog turned out to be a quite potent delta opioid antagonist and somewhat less potent mu antagonist, indicating that a positively charged N-terminal group is not a *condition sine qua non* for the binding of opioid peptides to delta and mu receptors. Based on the results, Schiller and colleagues proposed that the elimination of the positive charge through substitution of the N-terminal group with a methyl group, leads to a peptide that is no longer capable of binding to and stabilizing an active conformation of the mu or delta receptor. In the future, this concept might lead to the synthesis of new opioid peptide antagonists that are very much needed as research probes. Lu, Y., Weltroska, G., Lemieux, C., Chung, N.N. and Schiller, P.W. Bioorganic and Medicinal Chemistry Letters, 11, pp. 323-325, 2001.

Cannabinoids' Role in Infection

Some health consequences of smoking marijuana can be explained through analysis of basic studies on the role of endogenous cannabimimetic ligands in immune regulation. Two major cannabinoid receptor subtypes exist; subtype 1 (CB1) is expressed primarily in the brain whereas subtype 2 (CB2) is expressed primarily in the periphery, including the immune system. Most immune studies therefore focus on CB2, which is primarily expressed in T cells. However, a recent report identifies a role for CB1 in B cells. When B-cells are stimulated, the CB1 receptor is upregulated; this may show an importance of this receptor in antigen processing or to secondary immune responses to infection. In this study authors show that splenic B cells express more CB1 mRNA than T cells. Furthermore, splenocytes stimulated with the T cell mitogens, PMA/Io and anti-CD3, showed a decrease in CB1 message while cultures stimulated with the B cell mitogen, anti-CD40 antibody, showed an increase in message. In addition, co-treatment with mitogens and IL-2 uniformly caused an increase in CB1 mRNA. It is suggested that signaling pathways activated by T cell mitogens lead to decreased CB1 gene activation while pathways activated by B cell mitogens and IL-2 lead to increased CB1. Noe, S.N., Newton, C., Widen, R., Friedman, H. and Klein, T.W. Anti-CD40, Anti-CD3, and IL-2 Stimulation Induced Contrasting Changes in CB1 mRNA Expression in Mouse Splenocytes. J. Neuroimmun., 110, pp. 161-167, 2000.

Opioid Receptors and Immunity

Researchers from the University of Tennessee have investigated the role of delta type opioid receptors on immune cells. Most investigators study the regulation of cells by measuring actions in vitro in cell cultures. However, a recent paper has shown that these receptors are increased in number following an immune stimulant administered to whole animals. Thus, these receptors are increased as a result of a foreign substance and may be important in infections. Delta opioid receptors (DORs) are known to modulate multiple T-cell responses. However, little is known about the expression of these receptors. These studies evaluated the expression of DOR mRNA and protein after a single in vivo exposure to staphylococcal enterotoxin B (SEE). SEE enhanced splenocyte DOR mRNA expression 8 and 24 h after injection. SEE also increased the fractions of the total splenocyte and T-cell populations expressing DOR protein. Thus, SEE significantly increased DOR expression in vivo, affecting both mRNA and protein levels primarily within the T-cell population. To determine whether T-cell DORs modulate the activity of extracellular-regulated kinases (ERKs),

the phosphorylation of ERKs 1 and 2 was studied using splenocytes from SEE-treated mice. D-AlaD-leu-enkephalin, a selective DOR agonist, significantly inhibited anti-CD3-epsilon-induced phosphorylation of the ERKs. Therefore, the DORs expressed by activated T-cells are capable of attenuating T-cell activation that depends on ERK phosphorylation. Shahabi, N.A., McAllen, K., Matta, S.G., and Sharp, B.M. Expression of Delta Opioid Receptors by Splenocytes from SEB-Treated Mice and Effects on Phosphorylation of MAP Kinase. Cell Immunol., 205, pp. 84-93, 2000.

Receptor Clustering on the Presynaptic Membrane

Glutamate receptors mediate most excitatory neurotransmission in the central nervous system, and the metabotropic class of glutamate receptors specifically regulate many aspects of neuronal function, including synaptic plasticity and memory formation. One theme of increasing importance in neurobiology is that clustering of neurotransmitter receptors in synaptic regions is crucial for efficient neuronal communication. In a recent paper, Dr. Ann Marie Craig and NIDA grantee Dr. Paul Worley and their colleagues demonstrate that the PICK1 protein is required for aggregating the mGluR7a metabotropic glutamate receptor at presynaptic sites. They showed that the PDZ domain of PICK1 interacts with the C-terminal region of mGluR7a to mediate this aggregation. While clustering and assembly of receptors and signaling molecules at excitatory post-synaptic sites has been well studied, this is one of the first demonstrations of the role of a clustering protein in the distribution of a receptor expressed on presynaptic membranes. The authors hypothesize that PICK1 may act as a scaffolding molecule at presynaptic sites organizing mGluR7a receptors with specific signal transduction complexes. Boudin, H., et al. Presynaptic Clustering of mGluR7a Requires the PICK1 PDZ Domain Binding Site. Neuron, 28, pp. 485-497, 2000.

The Human Genome and Drug Abuse Research

The publication of the sequence of the entire human genome was one of the most significant events in biological research in recent years. In a short article that appeared in the human genome issue of Nature, NIDA grantee Dr. Eric Nestler and Dr. David Landsman discussed the implications of genome sequencing for understanding drug addiction. They point out that the sequence will further understanding of the biology of addiction by allowing researchers to identify genes that contribute to individual risk for addiction and genes that mediate the addictive response to drugs. To illustrate their point, the authors scanned the human genome and found several new potential genes related to those known to be involved in the cellular response to drugs. Nestler, E.J. and Landsman, D. Learning about Addiction from the Human Genome. Nature, 409, pp. 834-835, 2000.

Using Proteomics to Study the Mechanism of Nitric Oxide Signaling

Nitric oxide (NO) affects many physiological processes, including neurotransmitter release, and has been implicated in mediating responses to various drugs of abuse. NO is known to work via stimulation of the enzyme guanylyl cyclase, but this mechanism cannot explain all of NO's effects. Dr. Solomon Snyder and his colleagues hypothesized that NO can also act by forming nitrosothiol adducts at cysteine residues in proteins (S-nitrosylation). Using mass spectrometry to test whether proteins are endogenously nitrosylated, Dr. Snyder and his colleagues analyzed the mice lacking neuronal nitric oxide synthase. Endogeneous s-nitrosylation was observed for GAPDH, glycogen phosphorylase, creatine kinase, Rb, Hsp72, Na+/K+ ATPase alpha-2 subunit, the NMDA glutamate subunits (NR1 and NR2A), beta-tubulin, actin, and NF-H in wild type mice but not in mutant mice. Nitrosylation of these proteins may affect such physiological functions as membrane potential, cytoskeletal reorganization, neurite outgrowth, and cell growth. Thus, this paper establishes S-nitrosylation as a physiological signaling mechanism, and opens the way for studies of mechanisms that regulate S-nitrosylation signaling. Jaffrey, S.R. et al. Protein S-Nitrosylation: A Physiological Signal for Neuronal Nitric Oxide. Nature Cell Biol., 3, pp. 193-196, 2001.

Effects of Chronic Exposure to Cocaine are Regulated by the Neuronal Protein Cdk5

Cocaine acts by blocking uptake of dopamine released from presynaptic terminals that synapse onto medium spiny neurons in the striatum. Repeated exposure to cocaine causes long lasting changes in the nervous system that play a role in addiction. One of the changes observed following chronic cocaine administration is the induction of delta FosB, a transcription factor that persists in striatum long after the end of cocaine exposure. The induction of delta FosB has been shown to mediate increased behavioral sensitization to cocaine, characterized by augmentation of locomotor activity following repeated injections of cocaine. Behavioral sensitization is considered by some to be a model for the intensification of drug craving in humans that characterizes addiction and promotes relapse. In a recent paper in Nature, the Greengard and Nestler laboratories report that overexpression of delta FosB in mice or repeated exposure to cocaine results in increased expression of cyclin dependent kinase 5 (cdk5). This suggests that delta FosB regulates the expression of cdk5. To test the role of cdk5 in sensitization, the Nestler and Greengard laboratories treated animals with cdk5 inhibitors. These cdk5 inhibitors resulted in an even greater locomotor response following

repeated exposure to cocaine. Thus, increases in cdk5 expression act to attenuate the responses to subsequent cocaine exposure and oppose other biochemical pathways induced by delta FosB that mediate behavioral sensitization. Cdk5 attenuates the response to cocaine by regulating the dopamine signaling pathway in the dendrites of medium spiny neurons in the striatum. Dopamine binding to the D1 receptor activates adenylate cyclase to increase cAMP production. Increased levels of cAMP lead to the phosphorylation of proteins by protein kinase A. One of the proteins that is phosphorylated by protein kinase A is DARPP-32. Phosphorylation of DARPP-32 at threonine 34 by protein kinase A causes DARPP-32 to inhibit the activity of protein phosphatase-1 and augments the phosphorylation of proteins by protein kinase A. In contrast, the activation of cdk5 leads to the phosphorylation of DARPP-32 at threonine75. Phosphorylation of this threonine in DARPP-32 prevents DARPP-32 from blocking the activity of protein phosphatase-1. Increased protein phosphatase-1 activity leads to a decrease in the amount of phosphorylation in medium spiny neurons in the striatum. One of the physiological consequences of decreased phosphorylation is diminished currents elicited by AMPA receptor agonists. The role that cdk5 plays as a homeostatic mechanism in attenuating the rewarding effects of cocaine and in drug seeking behavior remains to be determined. Bibb, J.A., et al. Effects of Chronic Exposure to Cocaine are Regulated by the Neuronal Protein Cdk5. Nature, 410, pp. 376 - 380, 2001.

Cannabinoid Effects on the Neural Encoding of Short-Term Memory in the Hippocampus

Cannabinoids, the principal psychoactive agents in marijuana, are known to have disruptive effects on memory processes in humans. In this study, the memory-disruptive effects of 9-tetrahydrocannabinol (9-THC) and the synthetic cannabinoid WIN 55,212-2 (WIN-2) were assessed in rats exposed to varying doses of each drug during performance of a spatial delayed non-match to sample (DNMS) task. In the DNMS task, the animal is first presented with a lever on either the right or left, which it is required to press (sample phase). After a variable delay interval, both levers are extended and the animal must press the lever opposite to the one extended in the sample phase. If the animal performs the correct non-match response, it is rewarded with water. Cannabinoids affected DNMS performance in a dose _ delay-dependent manner, and these effects on performance were eliminated if the cannabinoid CB1 receptor antagonist SR141617A was pre-administered. Cannabinoid receptors are particularly dense in the hippocampus, a brain structure that has been implicated in the performance of the DNMS task and other memory tasks that involve the encoding ("holding in mind") of specific information. The investigators have developed a method for recording the activity of ensembles of hippocampal neurons during the performance of the DNMS task. In previous studies, they found that hippocampal neurons increase their firing rate in specific patterns during various phases, or combinations of phases, of this task. In this study, both WIN-2 and 9-THC produced dose-dependent reductions in the amount of ensemble firing in the hippocampus during the sample phase of the task, but not during the non-match phase. This pattern of a selective decrease in firing during the sample phase, is similar to patterns seen when animals make natural (i.e., not drug-induced) mistakes in behavioral responses. These findings indicate that activation of CB1 receptors renders animals less able to retain item-specific information during a memory task. Hampson, R.E. and Deadwyler, S.A. Cannabinoids Reveal the Necessity of Hippocampal Neural Encoding for Short-Term Memory in Rats. Journal of Neuroscience, 20, pp. 8932-8942, 2000.

Individual Differences in Baseline Activity of Midbrain Dopamine Neurons are Correlated with Enhanced Vulnerability to Cocaine Self-Administration in Rats

In both humans and animals, there are considerable individual differences in sensitivity to the reinforcing effects of addictive drugs. Previous studies have shown that rats that respond with more locomotor activity when placed in a novel environment also tend to show greater behavioral and neurochemical responses to psychostimulant drugs. Specifically, rats with a high locomotor response to a novel environment (HRs) exhibit enhanced self-administration (SA) behavior, sensitization, and basal or drug-induced dopamine release in the nucleus accumbens as compared with rats with a low response to the novel context (LRs). In this study, the investigators asked whether such differences in vulnerability to drug addiction might be related to differences in dopamine (DA) neuron activity. Rats were divided into HRs and LRs according to their response to a novel environment and then tested for acquisition of cocaine self-administration. HRs rapidly acquired cocaine SA, whereas LRs did not. In a separate group of animals not exposed to any drugs, they recorded the activity of individual dopamine neurons with extracellular electrodes and found that HRs exhibit higher basal firing rates and bursting activity of DA neurons in the ventral tegmental area and, to a lesser extent, in the substantia nigra pars compacta. The greater activity of midbrain DA cells in HRs was accompanied by reduced sensitivity to the inhibitory effects of a DA D2-class receptor agonist, indicating possible sub-sensitivity of DA autoreceptors that are known to regulate the firing rate of these neurons. These results demonstrate that differences in the basal activity of DA neurons may be critically involved in determining individual vulnerability to drugs of abuse. Marinelli, M. and White, F.J. Enhanced Vulnerability to Cocaine Self-Administration is Associated with Elevated Impulse Activity of Midbrain Dopamine Neurons. Journal of Neuroscience, 20, pp. 8876-8885, 2000.

Altered Gating of Opiate Receptor-Modulated K+ Channels on Amygdala Neurons of Morphine-Dependent Rats

The molecular mechanism of tolerance to opiate drugs is poorly understood. Dr. Jonathan E. Freedman of the Northeastern University and his research team have used single-channel patch-clamp recordings to study opiate receptor effects on dissociated neurons from rat amygdala, a limbic region implicated in addiction processes. A 130-pS inwardly rectifying K+-preferring cation channel was activated by mu opioid receptors in a membrane-delimited manner. After chronic treatment with morphine, channel gating changed markedly, with an approximately 100-fold decrease in open probability at a given morphine concentration. The change in channel gating correlated both in time course and in dose of morphine treatment with the development of functional opiate dependence and appeared to arise at a step after G-protein activation and before channel permeation by K+. This decreased receptor-channel coupling appears to be large enough to account quantitatively for opiate tolerance and may represent one of the mechanisms through which tolerance occurs. Chen, X., Marrero, H.G., Murphy, R., Lin, Y.J., and Freedman, J.E. Proc. Natl. Acad. Sci., USA, 97(26), pp. 14692-14696, 2000.

Cannabinoid Receptors Activation Produces Coupling to Multiple G Protein Alpha-Subunits with Different Potencies

Previously it was shown that the amplification factors for cannabinoid receptors, defined as the number of total G proteins activated per occupied receptor, differs between several rat brain regions. Dr. Paul Prather at the University of Arkansas for Medical Sciences and his colleagues sought to determine which specific Gi/Goa subunits were activated by CB1 receptors in several rat brain regions and if this coupling might explain the regional differences in receptor/G protein amplification factors. Furthermore, they examined whether cannabinoid agonists might activate different subtypes of Ga subunits with varying degrees of efficacy and/or potency. Activation of specific G proteins by cannabinoid receptors was evaluated by the ability of the agonist WIN 55212-2 to stimulate incorporation of [alpha-32P]azidoanilido-GTP into Ga subunits in membranes. Photolabeled G proteins were either directly resolved using urea/SDS-polyacrylamide gel electrophoresis or first immunoprecipitated with specific antisera for different Ga subunits before electrophoresis. Individual Ga subunits were separated into distinct bands on a single gel and the amount of agonist-induced increase in radioactivity was quantified by densitometry. Stimulation of CB1 receptors by WIN 55212-2 resulted in the activation of a distinct pattern of at least five different Gia/Goa subunits in several brain regions. Furthermore, although the pattern of G proteins activated by WIN 55212-2 appeared to be similar across brain regions, slight differences were observed in both the percentage of increase and the amount of the individual Ga subunits activated. Most importantly, the amount of WIN 55212-2 required to half-maximally activate individual G proteins in the cerebellum varied over a 30-fold range for different Ga subunits. These results suggest that cannabinoid receptors activate multiple G proteins simultaneously in several brain regions and both the efficacy and potency of cannabinoid agonists to activate individual Ga subunits may vary considerably. Prather, P.L., Martin, N.A., Breivogel, C.S. and Childers, S.R. Mol. Pharmacol., 57(5), pp. 1000-1010, 2000.

Cocaine Relevant Stimuli Activate the Limbic Brain Regions

It is well accepted that environmental cues are a major factor in drug relapse. Recent work has implicated the extended amygdala in the development of salient stimuli to drug use. In this report, Dr. Friedbert Weiss and co-workers at Scripps Research Institute showed that the presentation of stimuli previously paired with cocaine availability elicited strong recovery of responding in rats that had been extinguished on cocaine self-administration behavior. The stimuli were effective even after 4 months confinement to the home cage. In addition, exposure of the rats to the cocaine-salient cues produced a strong neural activation (fos immunoreactivity) in the basolateral amygdala and medial prefrontal cortex. Treatment with the D1 dopamine antagonist SCH 23390 dose-dependently reversed the effects of the cocaine cue. These data show that the ability of cocaine cues to elicit drug-seeking remains intact over a prolonged time period. Data also implicate the medial prefrontal cortex and amygdala for mediating the cue-induced relapse and suggest that the D1 receptor may be an important substrate for the motivating effects of cocaine-related stimuli. Ciccocioppo, R., Paolo, P. and Weiss, F. Cocaine-Predictive Stimulus Induces Drug-Seeking Behavior and Neural Activation in Limbic Brain Regions After Multiple Months of Abstinence: Reversal by D1 Antagonists. PNAS, 98(4), pp. 1976-1981, 2001.

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Research Findings

Behavioral Research

How Persistent is the Effect of Smoking Urges on Cognitive Performance?

Recent work from Dr. R. Zwann's program has provided empirical support for the hypothesis that drug urges interfere with cognitive performance. That is, the speed and/or accuracy of cognitive performance deteriorates in the presence of external smoking cues such as the smell of smoke, or of internal cues such as the thought of smoking. There is, however, little information about the time course of these interference effects. Different theoretical formulations predict that the effect of urges on cognitive performance might remain constant, dissipate, or increase over time. The present study was designed to distinguish among these predictions. Smoking urges were elicited by listening to descriptions of smoking-related information and cognitive performance was evaluated using a sentence comprehension task. Exposure to the urge script decreased comprehension accuracy in smokers but not in nonsmokers. This effect was short-lived, appearing only in the first block of 25 trials. Thus, smoking urges interfere with cognitive performance, but the effect dissipates over time. However, it is still not known if dissipation of the urge effect is due to decay of the urge itself, or to an improved ability to perform in the face of a constant urge. Zwann, R.A., Stanfield, R.A. and Madden, C.J. How Persistent is the Effect of Smoking Urges on Cognitive Performance? Experimental and Clinical Psychopharmacology, 8, pp. 518-523, 2000.

Effects of Cocaine Self-Administration in a Complex Behavioral Task

Dr. Peter Winsauer has been using a three-component multiple schedule of reinforcement to assess cocaine's reinforcing effects separately from its effects on learning (acquisition of an operant response), and performance in monkeys. In the first component of the schedule, monkeys respond for intravenous infusions of cocaine. In the second component, monkeys learn a response sequence to receive food reinforcement. The sequence required in the second component changes from day-to-day; thus, animals must learn a new sequence each day (repeated acquisition). In the third component, monkeys also perform a response sequence to receive food reinforcement. However, the sequence required in the third component remains the same each day and thus provides a measure of effects on performance. The effects of 4 doses of cocaine (0.01, 0.032, 0.1, 0.32 mg/kg) on responding under the multiple schedule were studied. Increasing the unit dose of cocaine dose-dependently decreased overall response rates in all three components of the multiple schedule and increased the total amount of drug obtained per session. In addition, increasing the unit dose of cocaine disrupted acquisition but had little effect on performance. These data indicate that learning is generally more sensitive than performance to the disruptive effects of self-administered cocaine. These experiments also demonstrate the utility of multiple schedules for studying effects of self-administered drugs on the acquisition and performance of complex behaviors. Winsauer, P.J., Silvester, K.R., Moerschbaecher, J.M. and France, C.P. Cocaine Self-Administration in Monkeys: Effects on the Acquisition and Performance of Response Sequences. Drug and Alcohol Dependence, 59, pp. 51-61, 2000.

Motivation to Obtain Nicotine Is Higher in Female Rats

Research on smoking behavior and responsiveness to nicotine suggests that nicotine's effects may depend on the sex of the organism. Researchers in the Department of Psychology, University of Pittsburgh, led by Dr. Anthony R. Caggiula allowed male and female rats to self-administer nicotine at one of four doses (0.02-0.09 mg/kg, free base) on both fixed and progressive ratio schedules of reinforcement. Progressive ratio schedules measure how much an

animal will work to obtain reinforcement - an infusion of nicotine in this case. Males and females acquired nicotine self-administration across the entire range of doses. Acquisition of self-administration at the lowest dose was faster in females than males. However, few sex differences were found in the number of active responses, number of infusions, or total intake of nicotine during stable fixed ratio self-administration. In contrast, females reached higher break points on the progressive ratio; that is, they worked harder than the males to obtain the same dose of nicotine. For both schedules, females had shorter latencies to earn their first infusion of each session and demonstrated higher rates of both inactive and timeout responding. There was no effect of estrous cycle on self-administration during either fixed or progressive ratio sessions. Self-administered nicotine resulted in average arterial plasma nicotine levels between 53 and 193 ng/ml and left hemi-brain levels between 174 and 655 ng/g, depending on dose. Nicotine self-administration produced similar up-regulation of nicotinic receptor binding sites in males and females, as reflected by increased right hemi-brain binding of [3H]-epibatidine, when compared to the brains of untreated control rats. These results suggest that the motivation to obtain nicotine is higher in females. Donny, E.C., Caggiula, A.R., Rowell, P.P., Gharib, M.A., Maldovan, V., Booth, S., Mielke, M.M., Hoffman, A. and McCallum, S. Nicotine Self-Administration in Rats: Estrous Cycle Effects, Sex Differences and Nicotinic Receptor Binding. Psychopharmacology (Berl) 151(4), pp. 392-405, 2000.

Sex-Related Differences in the Antinociceptive Effects of Opioids

Sex differences in morphine-induced antinociception (reduction of pain) have been described previously using thermal, chemical and electrical stimuli. The present study examined the role of nociceptive stimulus intensity and relative efficacy (magnitude of binding required for effect) of opioids on sex differences in opioid-induced antinociception. Results indicated that sex differences in potency and effectiveness increased with [1] decreases in the opioid's relative efficacy, and [2] increases in the intensity of the nociceptive stimulus. For example, high efficacy opioids were 2.5 times more potent in males than females, whereas low efficacy opioids were 8.9 times more potent in males than females. These findings suggest that the failure to find sex differences in antinociception using high efficacy opioids may not predict whether a sex difference will be found for low efficacy opioids. In fact, the use of lower efficacy opioids may provide a sensitive assay for investigating the role of sex hormones on opioid sensitivity. Cook, C.D., Barrett, A.C., Roach, E.L., Bowman, J.R. and Picker, M.J. Sex-Related Differences in the Antinociceptive Effects of Opioids: Importance of Rat Genotype, Nociceptive Stimulus Intensity, and Efficacy at the _ Opioid Receptor. Psychopharmacology, 150, pp. 430-442, 2000.

A Dopamine Agonist Attenuates the Development of Morphine Tolerance but not Physical Dependence in Rats

Chronic administration of mu opioids such as morphine and heroin produces tolerance and physical dependence. In addition to their direct effects on the opioid system, chronic administration of mu opioids affect other neurotransmitter systems, in particular the dopaminergic (DA) system. The present study was undertaken to investigate the effects of a DA D2/D3 receptor agonist, 7-OH-DPAT, on the development of morphine tolerance and physical dependence in the rat. Results indicate that 7-OH-DPAT attenuates the development of morphine tolerance in a time- and dose-dependent manner in both na•ve and morphine-tolerant rats. This effect was not the result of increased sensitivity to morphine. However, 7-OH-DPAT did not attenuate signs of physical dependence to morphine and did not precipitate withdrawal in morphine-dependent rats. Thus, it appears that the effects of 7-OH-DPAT on tolerance versus physical dependence can be pharmacologically dissociated. This study adds to a growing body of literature showing that non-opioid mechanisms can differentially modulate the acute effects of morphine as well as the development of tolerance and dependence. Cook, C.D., Barrett, A.C., Syvanthong, C. and Picker, M.J. The Dopamine 3/2 Agonist 7-OH-DPAT Attenuates the Development of Morphine Tolerance but not Physical Dependence in Rats. Psychopharmacology, 152, pp. 93-104, 2000.

Role of Endogenous Stress Systems in the Acute Effects of Psychostimulants

Animals with experimenter-manipulated or stress-induced increases in corticosterone are more prone to acquire drug self-administration. Both locomotor and reinforcing effects of these drugs are blocked by interfering with the HPA (hypothalamic-pituitary-adrenal) axis or by inhibiting corticosterone synthesis. Stress has also been reported to influence acute responses to psychostimulants in humans and to enhance reports of craving reported by cocaine abusers. NIDA grantee Dr. Stephen Wachtel and colleagues recently evaluated the effects of hydrocortisone (HC) on the effects of acute d-amphetamine in drug experienced human subjects. These investigators pre-treated subjects with 100 mg HC (or placebo) prior to administering either 20 mg d-amphetamine or the amphetamine placebo in a cross-over design. HC by itself produced few subjective effects on the Addiction Research Center Inventory, on visual analog scales (e.g., "stimulated", "sedated", etc.), on a drug effects questionnaire (DEQ, e.g., "do you feel any drug effects", "are you high", etc.) or on a version of the POMS (profile of mood states). The acute physiological (increased

heart rate and blood pressure), psychomotor performance (enhanced digit symbol substitution test performance), and subjective effects (stimulation, arousal, and positive mood) of d-amphetamine were not altered by prior HC treatment, with the exception of a decrease in reports of "want more drug" on the DEQ. These observations with human subjects do not parallel the existing body of literature on an importance for endogenous stress systems in the reinforcing effects of psychostimulant drugs. However, this study examined only acute effects of d-amphetamine and did not directly assess choice behavior for the drug. It is also possible that activation of other components of this endogenous HPA system may be involved in vulnerability and relapse, or that a more prolonged activation is required to detect these influences. Wachtel, S.R., Charnot, A. and de Wit, H. Acute Hydrocortisone Administration Does not Affect Subjective Responses to d-amphetamine in Humans. Psychopharmacology, 153, pp. 380-388, 2001.

Behavioral Reactivity to Cocaine as a Predictor of Social Status

Researchers at the Wake Forest University School of Medicine examined a number of variables as potential predictors of social rank in 20 individually-housed Cynomologus monkeys; among them were body weight, serum cortisol and testosterone levels, and locomotor activity in an open-field apparatus following a low dose of cocaine (0.01 mg/kg). Subsequently, the 20 monkeys were placed in social groups (five pens of four monkeys each) and social rank was determined on the basis of dyadic agonistic encounters. Heavier body weight predicted higher social rank and cocaine-induced high locomotor activity predicted subordinance. Social rank was unrelated to serum cortisol and testosterone levels. Morgan, D. Grant, K.A., Prioleau, O.A., Nader, S.H., Kaplan, J.R. and Nader, M. Predictors of Social Status in Cynomolgus Monkeys (Macaca Fascicularis) After Group Formation. American Journal of Primatology, 52, pp. 115-131, 2000.

Increased Sensitivity to Alprazolam in Females with a Paternal History of Alcoholism

In a study of 28 women characterized as light drinkers, the anxiolytic drug alprazolam impaired performance in a dose-related manner on psychomotor, cognitive and memory tasks. At the highest alprazolam dose, women with a paternal history of alcoholism were more impaired on these measures than women without a paternal history of alcoholism. The authors also report greater alprazolam-produced increases in ratings of "difficulty concentrating" and "unmotivated behavior" as well as fewer positive subjective effects (e.g. positive mood, elation, friendliness, "drug liking") and more negative subjective effects (e.g., "bad drug effect") in women with a paternal history of alcoholism. Evans, S.M., Levin, F.R., and Fischman, M.W. Increased Sensitivity to Alprazolam in Females with a Paternal History of Alcoholism. Psychopharmacology, 150, pp. 150-162, 2000.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Research Findings

Treatment Research and Development

Differences between Methamphetamine and Cocaine Users

At the Matrix Institute on Addictions, in Los Angeles, CA, two large cohorts of cocaine and methamphetamine (MA) users sought outpatient treatment during the same four-year period. The 224 cocaine users spent more money on their drugs, more frequently had severe financial problems or bankruptcy (37.9%), and more frequently used alcohol with their drug of choice (46.9%). The 500 methamphetamine users included a higher proportion of women (40%) and Whites (80.5%), more frequently used their drug on a daily basis (43.6%), more frequently had used marijuana (56.2%) and hallucinogens (6.4%) in the past year, and more frequently had current psychiatric symptoms at admission. However, the two groups did not differ significantly in treatment retention. Retention in treatment for >90 days was most significantly correlated with reported years of heavy drug use. No significant correlation with retention was found for use of methamphetamine, gender, marital status, age, years of education, or prior drug treatment. Rawson, R., Huber, A., Brethen, P., Obert, J., Gulati, V., Shoptaw, S., and Ling, W. Methamphetamine and Cocaine Users: Differences in Characteristics and Treatment Retention. Journal of Psychoactive Drugs, 32(2), pp. 233-238, 2000.

Baseline Urine Test Predicts Cocaine Use during Treatment

At the Philadelphia Veterans Affairs Medical Center, 61 male participants completed a protocol for a 4 week, outpatient treatment for cocaine dependence, using ritanserin or placebo. Altogether, these completers provided an average of more than 11 of their 12 scheduled urine samples. During a 1-3 week baseline placebo period, all participants provided one urine sample, which tested negative or positive for >300 ng/ml benzoylecgonine. Baseline urine was cocaine-positive in 24 men, and cocaine-negative in 37 men. The baseline-positive group had an average of twice as many positive urine samples during treatment as the baseline-negative group. The baseline-positive group also had less than half as many men who were completely abstinent during the 4-week trial, and the group took longer to achieve 3 consecutive cocaine-free urines. These differences in outcome suggest that future evaluations of treatment efficacy should stratify group assignment by results of a baseline urine test. Ehrman, R.N., Robbins, S.J., and Cornish, J.W. Results of a Baseline Urine Test Predict Levels of Cocaine Use during Treatment. Drug and Alcohol Dependence, 62(1), pp. 1-7, 2001.

Propranonol Reduces Symptoms of Cocaine Withdrawal

Dr. Kyle Kampman and colleagues from the University of Pennsylvania have published a paper demonstrating the effectiveness of propranolol in reducing symptoms of cocaine withdrawal and its effectiveness in improving treatment retention and reducing cocaine use in patients with high withdrawal scores. Currently the investigators are evaluating the combination of propranolol and amantadine in the treatment of cocaine dependence. Drug and Alcohol Dependence, 63, pp. 69-78, 2001.

Effects of In-Utero Cocaine Exposure on Brain of Children

Dr. Smith and colleagues at Harbor-UCLA Medical Center investigated the effects of prenatal cocaine exposure on brain metabolism using proton magnetic resonance spectroscopy (1H-MRS). The aim of this work was to examine the

possible neurotoxic effects of prenatal cocaine exposure on the developing brain. Cocaine-exposed children and age-matched control subjects were evaluated with structural MRI and localized 1H-MRS. Preliminary findings revealed no structural abnormalities in either group, but children exposed to cocaine *in utero* had significantly higher (+13%) levels of creatine (Cr, a measure of high-energy phosphate stores) in the frontal white matter, suggesting biochemical alterations may occur in response to early exposure to cocaine. No differences were seen in n-acetyl-containing compounds (NA) that suggest no significant neuronal loss or damage in the basal ganglia or frontal white matter (the two areas assessed in all children). These findings are consistent with findings in abstinent adult cocaine abusers, and these results suggest the clear need to investigate further possible abnormalities of energy metabolism in the brain of children exposed to cocaine prenatally. Smith, L.M. et al. Brain Proton Magnetic Resonance Spectroscopy and Imaging in Children Exposed to Cocaine In-Utero. Pediatrics, 107(2), 2001.

Decision-Making Deficits in Alcohol and Stimulant Abusers Linked to Dysfunctional Ventromedial Prefrontal Cortex

Dr. Bechara and colleagues at the University of Iowa compared the performance of substance abusers, normal controls and patients with ventromedial prefrontal lesions on a decision-making task. This task (Gambling Task) was originally designed to assess cognitive deficits in patients with ventromedial prefrontal lesions. In the task, subjects are presented with 4 decks of cards and told to choose the cards that will yield the best monetary outcome. All of the decks provide immediate reward, but also occasional penalties. Two of the decks yield higher immediate rewards than the other two decks. However, the high-reward decks are disadvantageous in the long run since the penalties eventually outweigh the gains yielding net loss. Unlike neurologically intact subjects who tend to pick more cards from the advantageous, low immediate reward decks, subjects with ventromedial prefrontal lesions tend to persist in choosing the disadvantageous high immediate reward. Substance abusers also tended to pick more cards from the disadvantageous decks, and nearly two thirds of the substance abusers performed as poorly as the ventromedial lesioned patients. Performance of the substance abusers was not related to age, IQ, level of education or performance on other cognitive tasks related to executive or frontal lobe function, but was related to duration of abstinence, years of drug use, number of times of relapse, treatment attempts, and ability to hold gainful employment. These data suggest that drug abuse may be related to dysfunction of the orbitofrontal cortex, at least in a sub-group of drug abusers. Bechara, A. et al. Decision-Making Deficits, Linked to a Dysfunctional Ventromedial Prefrontal Cortex, Revealed in Alcohol and Stimulant Abusers. Neuropsychologia, 39, pp. 376-389, 2001.

Predictability Modulates Human Brain Response to Reward

Dr. Berns and colleagues at Emory University used fMRI to map the responses to predictable and unpredictable delivery of liquid rewards in normal humans. Subjects received small drops of either fruit juice or water under two conditions. In the first condition, juice and water were delivered in a fixed alternating sequence at 10-second intervals. In the second condition, juice and water were delivered in a random sequence at varying intervals. After the sessions were over, subjects stated whether they preferred water or juice (80% preferred juice). This design allowed analysis of brain responses to 1) delivery of the preferred versus non-preferred solution, 2) predictable versus unpredictable delivery, and 3) interaction of preference and predictability. Activity in the nucleus accumbens was associated with unpredictable delivery of liquid, irrespective of whether or not the liquid was preferred. In contrast, only the mouth region of the somatosensory cortex was associated with delivery of the preferred solution. These results provide a new perspective on the functional role of the nucleus accumbens in humans. Rather than being activated in proportion to the hedonic value of stimuli per se as has been previously thought, activity in the nucleus accumbens may reflect attempts to resolve uncertainty about the delivery of rewards. Berns, G.S. Predictability Modulates Human Brain Response to Reward. J. Neuroscience, 21(8), 2001.

The Internet is a Vast New Source of Hallucinogens and Underground Drugs

Drs. Halpern and Pope at McLean Hospital surveyed the information available on the Internet regarding hallucinogens as of December 1998. Using a common search engine (Yahoo), they identified over 80 web sites related to the synthesis, identification, procurement, or subjective effects of hallucinogens. Many of these sites had been heavily accessed; one site had nearly 3 million visitors over the past 3 years, whereas a second site had over 800,000 visitors within the past year. The authors commented on the extraordinary wealth of on-line information about hallucinogenic drugs on the Internet relative to the information available from government or biomedical sources (e.g. MEDLINE). Halpern, J.H. and Pope, H.G. Hallucinogens on the Internet: A Vast New Source of Underground Drug Information. American Journal of Psychiatry, 158, pp. 481-483, 2001.

Cortical Effects of Bromocriptine in Human Subjects Revealed by fMRI

Dr. Kimberg and colleagues at the University of Pennsylvania used fMRI to determine the neurocognitive effects of D-

2 receptor stimulation in normal humans. Subjects performed 3 tasks during the fMRI scanning sessions. Two were cognitive tasks related to working memory (two-back) and set-formation and shifting (Wisconsin Card Sorting task). The third task was a simple bimanual motor response task. Subjects were also given a test of reading span during an initial practice session. The effects of bromocriptine on task performance were related to the subject's initial cognitive capacity, as indexed by performance on the reading span task. Bromocriptine improved performance on the Wisconsin Card Sorting task in subjects who had high initial reading span capabilities, but decreased performance in subjects with low reading span scores. There were no effects of bromocriptine or interactions with reading span on the two-back or motor response tasks. The effects on brain activity varied according to the task. The effect of bromocriptine was to attenuate task-related fMRI signals across all three tasks. That is to say, the bromocriptine only affected those brain regions activated during performance of each individual task. Kimberg, D.Y. et al. Cortical Effects of Bromocriptine, a D-2 Dopamine Receptor Agonist, in Human Subjects, Revealed by fMRI. Human Brain Mapping, 12, pp. 246-257, 2001.

Functional Organization of the Brain for Working Memory Differs by Gender

Gender differences in brain activation during working memory tasks were examined with fMRI. Seventeen right-handed adult subjects were studied with four different verbal working memory tasks of varying difficulty using whole brain echo-planar fMRI. Consistent with prior studies, activation of the lateral prefrontal cortices (LPFC), the parietal cortices (PC), and additionally caudate activation was observed in both sexes. The volume of activated brain tissue increased with increasing task difficulty. For all tasks, the males showed bilateral activation or right-sided dominance (LPFC, PC and caudate), whereas females showed activation predominantly in the left hemisphere. Performance data demonstrated higher accuracy and slightly slower reaction times for females. Results show highly significant gender differences in the functional organization of the brain for working memory. These variations in functional organization of the brain may be due to gender-differences in problem solving strategies or in neurodevelopment. Therefore, gender matching or stratification is necessary for studies of brain function using imaging techniques. Speck, O., Ernst, T., Braun, J., Koch, C., Miller, E., Chang, L. Gender Differences in the Functional Organization of the Brain for Working Memory. Neuroreport, 11(11), pp. 2581-2585, 2000.

Cerebral Perfusion Abnormalities in Abstinent Cocaine Abusers

Drs. Ernst, Chang and colleagues at Harbor-UCLA Medical Center used perfusion magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT) to evaluate regional cerebral blood flow abnormalities in abstinent cocaine abusers. Abnormalities were evaluated and compared in 25 asymptomatic abstinent cocaine users and 15 healthy controls without a history of drug use. After co-registration of SPECT with MRI, the relative rCBF (from perfusion MRI and SPECT) and absolute rCBF (from SPECT) were determined in 10 brain regions in each hemisphere. There was a statistically significant interaction between drug use and brain region on SPECT alone (relative and absolute rCBF), and on SPECT and perfusion MRI combined, but not on perfusion MRI alone. There also was a significant interaction among gender, drug use, and brain region. Compared to the controls, abstinent cocaine abusers showed increased rCBF in the frontal white matter and in the globus pallidus, and decreased rCBF in the putamen and the temporal cortex. Female, but not male, cocaine abusers showed significantly reduced relative rCBF in the parietal gray matter and increased relative rCBF in the frontal and temporo-parietal white matter, whereas male, but not female, cocaine abusers showed significantly increased rCBF in the thalamus. SPECT and perfusion MRI detect a regional pattern of rCBF abnormalities in cocaine users that is consistent across the two methods. The hypoperfusion in the cortex and deep gray matter of the cocaine users is consistent with previous results. The increased rCBF in the white matter of cocaine users may be due to the presence of reactive glia. Ernst, T., Chang, L., Oropilla, G., Gustavson, A., Speck, O. Cerebral Perfusion Abnormalities in Abstinent Cocaine Abusers: A Perfusion MRI and SPECT Study. Psychiatry Research: Neuroimaging, l99(2), pp. 63-74, 2000.

Effects of Route of Administration on Cocaine-Induced Dopamine Transporter Blockade Using PET

Dr. Volkow and colleagues at the Brookhaven National Laboratory assessed differences in the efficacy of cocaine to block the dopamine transporter (DAT) as a function of route of administration. Positron emission tomography (PET) was used to compare the levels of DAT blockade induced by intravenous, smoked, or intranasal cocaine administration in 32 current cocaine abusers. They found that the levels of blockade were comparable across all routes of administration, and a dose effect was observed for intravenous and intranasal cocaine but not for smoked cocaine. For equivalent levels of cocaine in plasma and DAT blockade, smoked cocaine induced significantly greater self-reports of "high" than intranasal cocaine and showed a trend for a greater effect than intravenous cocaine. The time to reach peak subjective effect was significantly faster for smoked (1.4 min) than for intravenous cocaine (3.1) or for intranasal cocaine (14.6 min). It was found that differences in the reinforcing effects of cocaine as a function of

the route of administration were not due to differences in the efficacy of cocaine to block the dopamine transporters. The faster time course for the subjective effects for smoked than intravenous and for intravenous than for intranasal cocaine highlights the importance of the speed of cocaine's delivery into the brain on its reinforcing effects. Volkow, N.D. et al. Effects of Route of Administration on Cocaine Induced Dopamine Transporter Blockade in the Human Brain. Life Sciences, 67, pp. 1507-1515, 2000.

An fMRI Study Reveals Sex Differences in Response to Visual Stimulation: Implications for Dopamine System Function

Drs. Cowan, Renshaw and colleagues at McLean Hospital investigated the visual system response to blue light as a marker of CNS dopamine tone. Given that numerous sex-related differences in CNS dopamine function have been found previously, it was predicted that blue (470 nm) and red (660 nm) light stimulation would produce sex-specific patterns of response in the primary visual cortex using the blood oxygen level dependent (BOLD) functional magnetic resonance (fMRI) method. BOLD response to red and blue light was analyzed in male and female volunteers. Results showed that near threshold, males and females showed similar BOLD signal change to red light, but males showed a threefold greater increase to blue light stimulation when compared to females. These findings support a sex- and color-dependent differential pattern of primary visual cortical response to photic stimulation and further suggest a viable method for assessing the influence of specific dopamine agonist/antagonist medications on visual function. Cowan, R.L. et al., Sex Differences in Response to Red and Blue Light in Human Primary Visual Cortex: A BOLD fMRI Study. Psychiatry Research: Neuroimaging, 100, pp. 129-138, 2000.

Effects of Nicotine and Caffeine on EEG Topography and Other Measures

The effects of nicotine and caffeine were assessed separately and in combination, in 12 male habitual smokers (aged 19-31 yrs) using a repeated-measures design. Caffeine (0-mg versus two 150-mg doses were administered in a decaffeinated/sugar-free cola drink following baseline and 90 min later) and was crossed with nicotine (*ad libitum,* self dosing versus 1.00-mg machine-delivered dose versus 0.05-mg machine-delivered dose). Subjects smoked 5 cigarettes at 30-min intervals over a 2-hr period. Caffeine and nicotine had large effect sizes on EEG power; however, these effects were modulated by whether the eyes were open or closed, the other drug, and the electrode site. EEG effects of open versus closed eyes tended to be of the same size and direction as those of nicotine and caffeine. However, whereas nicotine increased EEG power in some higher frequency bands in some conditions, caffeine decreased EEG power across almost all conditions. Serum cortisol concentration, vigor, and pleasantness were increased by nicotine, but not by caffeine. Level of depressive mood depended on an interaction of caffeine and nicotine. Vigilance performance was enhanced significantly by caffeine and was increased almost significantly by nicotine. The findings were interpreted in terms of common and differential mechanisms of the two drugs. Gilbert, D.G, Dibb, W.D., Plath, L.C., and Hiyane, S.G. Effects of Nicotine and Caffeine, Separately and in Combination, on EEG Topography, Mood, Heart Rate, Cortisol, and Vigilance. Psychophysiology, 37(5), pp. 583-595, 2000.

Impact of Temperature on METH-Induced Neurotoxicity via DAT

Hyperthermia exacerbates and hypothermia attenuates methamphetamine (METH)-induced dopamine (DA) neurotoxicity. The mechanisms underlying these temperature effects are unknown. Given the essential role of the DA transporter (DAT) in the expression of METH-induced DA neurotoxicity, it was hypothesized that the effect of temperature on METH-induced DA neurotoxicity is mediated, at least in part, at the level of the DAT. To test this hypothesis, the effects of small, physiologically relevant temperature changes on DAT function were evaluated in two types of cultured neuronal cells: (1) a neuroblastoma cell line stably transfected with human DAT cDNA and (2) rat embryonic mesencephalic primary cells that naturally express the DAT. Temperatures for studies of DAT function were selected based on core temperature measurements in animals exposed to METH under ambient (22o C) and hypothermic (6o C) temperature conditions, where METH neurotoxicity was fully expressed and blocked, respectively. DAT function, determined by measuring accumulation of radiolabeled DA and 1-methyl-4-phenyl-pyridinium (MPP+), was found to directly correlate with temperature, with higher levels of substrate uptake at 40o C, intermediate levels at 37o C, and lower levels at 34o C. DAT-mediated accumulation of METH also directly correlated with temperature, with greater accumulation at higher temperatures. These findings indicate that relatively small, physiologically relevant changes in temperature significantly alter DAT function and intracellular METH accumulation, and suggest that the effect of temperature on METH-induced DA neurotoxicity is mediated, at least in part, at the level of the DAT. Xie, T., McCann, U.D., Kim, S., Yuan, J., and Ricaurte, G. Effect of Temperature on Dopamine Transporter Function and Intracellular Accumulation of Methamphetamine: Implications for Methamphetamine-Induced Dopaminergic Neurotoxicity. Journal of Neuroscience, 20(20), pp. 7838-7845, 2000.

Strongest Evidence to Date Demonstrates a Single Nucleotide Polymorphism in DβH

Structural Gene Accounts for 35-52% of the Variation of Plasma Activity of Dopamine-*beta* hydroxylase

Dr. Joseph Cubells and colleagues at Yale have analyzed the dopamine beta-hydroxylase (DβH) gene in samples of African Americans, European Americans and Japanese and found that individuals with low levels of DβH activity have two copies (i.e., are homozygous) of the polymorphism in which there is a substitution of tyrosine for cytosine (C→T) in the 5' flanking region (-1021C→T). Individuals with only one copy (heterozygotes) had intermediate activity compared to the homozygotes who both had the unsubstituted allele. DβH catalyzes the conversion of dopamine to norepinephrine and released from sympathetic neurons into the circulation. While the clinical significance of low DβH activity is not settled, it is believed that it is a disease-modifying gene and may be related to addiction as well as other psychopathology. These results offer a new tool for testing hypotheses along this line. Zabetian, C.P., Anderson, G.M., Buxbaum, S.G., Elston, R.C., Ichinose, H., Nagatsu, T., Kim. K-S., Kim, C-H., Malison, R.T., Gelernter, J., and Cubells, J.F. A Quantitative-Trait Analysis of Human Plasma-Dopamine Beta-Hydroxylase Activity: Evidence for a Major Functional Polymorphism at the DβH Locus. Am. J. Hum. Genet. 68, pp. 515-522, 2001.

Heritability of Use and Abuse of Illicit Substances in Adolescents

Iacono and colleagues found in their longitudinal study on twins (Minnesota Twin Family Study, MTFS) that heritability of illicit substances was only 25% or less with heritability of tobacco use and nicotine dependence to be substantially higher: 40% and 60%, respectively. These estimates are lower than others found in adult twin studies and suggest a larger influence of environment at this younger age. Indeed, the contribution to the shared environment turned out to be a substantial 41% and 66% for illicit substance use and abuse, respectively. It was also found that, in general, these heritabilities were not different between males and females. McGue, M., Elkins, I., and Iacono, W.G.. Genetic and Environmental Influences on Adolescent Substance Use and Abuse. Am. J. Med. Genet. 96(5), pp. 671-677, 2000.

Identifying a Multivariate Endophenotype for Substance Use Disorders Using Psychophysiological Measures

Iacono and associates have achieved modest success in identifying individuals with substance dependence using performance on two uncorrelated psychophysiological measures: P300 evoked potentials and electrodermal modulation. These measures had been associated with risk for substance abuse in the past. Now subjects were selected based on their scores and compared for presence of abuse. In the high-risk group, defined as low P300 amplitudes and good electrodermal modulation, significantly more had "any" substance abuse (including alcohol) and significantly more nicotine dependence. There were no differences for illicit substances that may be due to low incidence in this adolescent cohort as well as low numbers of subjects. These data provide suggestions for physiological markers - endophenotypes - that characterize people who abuse psychoactive substances. Iacono, W.G., Carlson, S.R., and Malone, S.M. Identifying a Multivariate Endophenotype for Substance Use Disorders Using Psychophysiological Measures. Intl. J. Psychophysiol. 38(1), pp. 81-96, 2000.

Withdrawal Symptoms were Observed During 28-day Abstinence from Heavy, Chronic Marijuana Use

Drs. Kouri and Pope documented a number of behavioral changes reported in daily diaries by individuals who were temporarily abstaining from heavy marijuana smoking compared to controls, who either were never users or who were heavy marijuana users but who had quit at least 6 months prior to the study. Compared to baseline (day 0 for current users), anxiety, physical tension, and irritability increased; mood decreased over the length of the period. Scores on the Hamilton Depression Scale were maximal at about 1 week into abstinence. Appetite declined for the first few days and then resumed to baseline. Increases in physical symptoms were reported intermittently. This is the first prospective naturalistic investigation demonstrating a variety of symptoms in withdrawal from marijuana use. Kouri, E.M. and Pope, H.G. Abstinence Symptoms during Withdrawal from Chronic Marijuana Use. Exp. Clin. Psychopharm., 8(4), pp. 483-492, 2000.

Upregulation of Serotonin Transporters (SERT) in Chronic Cocaine Users

Mash and associates assessed the status of the serotonin transporter (SERT) in post-mortem tissue of cocaine overdose deaths. Significant increases were seen in the nucleus accumbens, anterior and posterior sectors of the striatum, and in areas of the orbitofrontal gyrus including the anterior portion of the insular cortex and cingulate gyrus. Also investigated were SERT changes in overdose victims who also were determined premorbidly to have excited delirium. In contrast to other victims, elevation was not seen in the substantia nigra and posterior striatum

suggesting a distinct phenotype for these individuals. Mash, D.C., Staley, J.K., Izenwasser, S., Basile, M., and Ruttenber, A.J. Serotonin Transporters Upregulate with Chronic Cocaine Use. J. Chem. Neuroanat., 20(3-4), pp. 271-280, 2000.

Procaine Challenge Produced a Bilateral Activation of the Orbitofrontal Cortex in Cocaine-Addicted Subjects

Adinoff and colleagues are trying to determine if repeated cocaine use induces permanent hyperexcitability in the limbic system, not unlike the kindling effect in an animal model. Using procaine as a probe and SPECT measures of regional cerebral blood flow, the cocaine patients demonstrated an increase in the orbitofrontal cortex while comparison subjects showed activation of the anterior cingulate, bilateral insula, and right amygdala. Of interest, the cocaine patients had a significantly lower activation in the orbitofrontal cortex after placebo. This pattern of findings in the cocaine patients was interpreted to be similar to the pattern of interictal hypoperfusion and ictal hyperperfusion that has been observed in subjects with epilepsy and thus may represent evidence of localized (orbitofrontal) sensitization. Adinoff, B., Devous, M.D., Best, S.M., George, M.S., Alexander, D., and Payne, K. Limbic Responsiveness to Procaine in Cocaine-Addicted Subjects. Am. J. Psychiatry, 158, pp. 390-398, 2001.

Prognostic Significance of Antisocial Personality Disorder in Cocaine-Dependent Patients Entering Continuing Care

Dr. McKay and colleagues at the University of Pennsylvania examined the relationship of antisocial personality disorder (APD) to response to continuing care treatments in cocaine-dependent patients (N=127). Patients with and without APD were randomly assigned to 20-week standard group or individualized relapse prevention continuing care interventions after the completion of an initial treatment episode and followed up at 3, 6, and 12 months. Patients with and without APD did not differ on retention in continuing care, substance use outcomes, social function outcomes, or experiences before or during cocaine relapse episodes. A diagnosis of APD was also not a predictor of differential response to the two continuing care interventions in the study. However, APD patients had worse medical psychiatric problem severity than non-APD patients at entrance to continuing care and during follow-up. The results suggest that cocaine patients with APD who are in the continuing care phase of outpatient rehabilitation might benefit from additional medical and psychiatric treatment services. McKay, J.R., Alterman, A.I., Cacciola, J.S., Mulvaney, F.D. and O'Brien, C.P. The Journal of Nervous and Mental Disease, 188, pp. 287-296, 2000.

Factors Accounting for Cocaine Use Two Years Following Initiation of Continuing Care

This study examined the relationship between various interpersonal, intrapersonal and situational factors assessed at 6, 12, and 18 months after entrance to continuing care, and cocaine use in subsequent periods. Cocaine-dependent male veterans (n=132) were randomly assigned to either 12 -step focused group treatment or to an individualized relapse prevention continuing care. Measurements of motivation, coping and mood, social support, co-morbid problem severity, treatment attendance, self-help participation and cocaine use were made at each follow-up. In multivariate analyses, degree of self-help participation emerged as the strongest and most consistent predictor of cocaine use. Continued self-help participation and early achievement of cocaine abstinence appear to be important factors in the maintenance of good cocaine use outcomes over extended periods. McKay, J.R., Merikle, E., Mulvaney, F.D., Weiss, R.V., and Koppenhaver. Addiction, 96, pp. 213-225, 2001.

Behavioral Couples Therapy for Male Methadone Maintenance Patients: Effects on Drug-Using Behavior and Relationship Adjustment

A total of 36 drug-abusing men entering methadone maintenance treatment were randomly assigned either to individual skill-based counseling or to behavioral couples therapy (BCT). Men participating in BCT had significantly fewer positive drug screens during treatment and reported greater reduction in drug use from baseline to post-treatment than did men participating in individual counseling. Further, although both groups showed significant reductions in drug-abuse severity and psychiatric symptoms after treatment, men receiving BCT also reported fewer family and social problems after treatment than did men receiving individual counseling. These findings suggest that BCT is an effective intervention for reducing both substance and family problems. Fals-Stewart, O'Farrell, and Birchler, Behavior Therapy, 32, pp. 391-411, 2001.

Predictors of Engagement in Adolescent Drug Abuse Treatment

Drs. Dakof, Tejeda, and Liddle from the University of Miami Center for Treatment Research on Adolescent Drug Abuse studied 224 adolescents referred for drug abuse treatment and their parents. These researchers compared

adolescents considered to be successfully engaged in treatment (n = 118) to those not successfully engaged (n = 106), defining successful engagement as participation in four or more sessions. Both parent and adolescent perceptions distinguished between successful and unsuccessful engagement. Adolescents who were successfully engaged in treatment had parents who described them as exhibiting significantly more "externalizing behavior", including delinquency and aggression, than adolescents who were not successfully engaged. Also, parents of successfully-engaged adolescents reported significantly higher expectations of academic success for their child than did unsuccessfully-engaged adolescents. Finally, adolescents who reported higher degrees of family conflict were more likely to be engaged successfully in treatment than adolescents who reported less family conflict. These results suggest a particular family profile at higher risk for treatment dropout, and inform clinical interventions aimed to engage drug-abusing adolescents and their families in treatment. Dakof, Tejeda, and Liddle, Journal of the American Academy of Child and Adolescent Psychiatry, 40, pp. 274-281, 2001.

Methods for Enhancing Transition of Substance Dependent Patients from Inpatient to Outpatient Treatment

Drs. Chutuape, Katz, and Stitzer at Johns Hopkins University examined methods for increasing the transition of substance dependent patients from inpatient detoxification to outpatient aftercare. One hundred and ninety-six patients were randomly assigned to, 1) standard referral (standard); 2) standard referral with an incentive (incentive); or 3) staff escort from detoxification to aftercare with an incentive (escort + incentive). Incentives (worth US $13.00) were dispensed for completing aftercare intake procedures on the day of discharge from detoxification. More escort + incentive participants (76%) than those in the incentive (44%) or standard conditions (24%) completed intake. The escort + incentive procedure may be useful for improving transition from detoxification to aftercare. Chutuape, M.A., Katz, E.C., and Stitzer, M. Drug and Alcohol Dependence, 61(2), pp. 137-143, 2001.

Development of a Skill Training Program for Parents of Substance-Abusing Adolescents

Dr. Neil McGillicuddy and colleagues at the Research Institute on Addictions, State University of New York at Buffalo, have developed a coping skill training program for parents of substance abusing adolescents. The behavioral-analytic model of program development was used to sample representative problematic situations experienced by parents of substance abusing adolescents, obtain an effectiveness-scaling of responses to these situation, and derive alternate forms of a situational role-play measure of parental coping. These situations and scoring guidelines were then used to create the skill training program. Parents of substance abusing adolescents not in treatment subsequently were randomly assigned in a pilot investigation to either a skill training or delayed treatment condition. Skill training resulted in significant improvement in parental coping skills relative to delayed treatment. Moderate to large improvement in the parent's report of their own functioning, family communication, and the teen's marijuana use also favored the skill training group. McGillicuddy, N.B., Rychtarik, R.G., Duquette, E.T., and Morsheimer, E.T. J Substance Abuse Treatment (20), pp. 59-68, 2001.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Research Findings

Research on AIDS and Other Medical Consequences of Drug Abuse

Regional Cerebral Blood Flow Abnormalities in Early Stages of HIV-Cognitive Motor Complex

Nineteen patients (aged 34-63 yrs) with early HIV-cognitive motor complex and 15 normal controls (aged 19-63 yrs) were evaluated for possible regional cerebral blood flow (rCBF) abnormalities on perfusion magnetic resonance imaging (MRI). Compared with controls, those with HIV had significantly decreased rCBF bilaterally in the inferior lateral frontal cortices and in the interior medial parietal brain region. In contrast, rCBF was increased bilaterally in the posterior inferior parietal white matter. Furthermore, rCBF abnormalities correlated significantly with clinical disease severity as measured by CD4 count, plasma viral load, Karnofsky score, and HIV dementia scale. Chang, L., Ernst, T., Leonido-Yee, M., and Speck, O. Perfusion MRI Detects rCBF Abnormalities in Early Stages of HIV-Cognitive Motor Complex. Neurology, 54(2), pp. 389-396, 2000.

Gender Differences in Behavioral and Psychosocial Predictors of HIV Testing and Return for Test Results in a High-Risk Population

Investigators at UCLA assessed gender differences in psychosocial and behavioral predictors of HIV testing and returning for results in a high-risk sample of 1,049 predominantly minority, impoverished, homeless and/or drug-abusing women (n=621) and men (n=428). Predictors included latent variables representing injection drug use, self-esteem, social support, AIDS knowledge, poor access to health services, perceived risk for AIDS, sexual risk behavior, and the mediators of positive and negative coping styles. Significant predictors of test and return for women included injection drug use, greater social support, more AIDS knowledge, a higher perceived risk for AIDS, and a positive coping style. Significant predictors for the men included injection drug use, greater AIDS knowledge, a higher perceived risk for AIDS, and a positive coping style. The significant predictors of HIV testing and return were generally similar for men and women, except that greater social support was not significant for the men. However, the men evaluated their risk of AIDS significantly lower than the women, although they reported more sexual risk behaviors and equally risky injection drug use behaviors. Results suggest that interventions designed to increase AIDS knowledge, raise the perceptions of risk and promote a positive coping style would be effective in encouraging more HIV testing for both men and women, but raising perceptions of what constitutes personal risk behaviors may need special emphasis when delivering prevention programs to men. Stein, J.A. and Nyamathi, A. Gender Differences in Behavioral and Psychosocial Predictors of HIV Testing and Return for Test Results in a High-Risk Population, AIDS Care, 12(3), pp. 343-366, 2000.

Correlates of HIV Risk-Taking Behaviors Among African American College Students: The Effect of HIV Knowledge, Motivation, and Behavioral Skills

Investigators from UCLA collaborated in a study identifying theoretically based predictors of condom use in a sample of 253 sexually active African-American college students recruited from two historically African-American colleges. The Information-Motivation-Behavioral (IMB) skills model of AIDS-preventive behavior was used to delineate the roles of HIV/AIDS knowledge, experiences with and attitudes toward condom use, peer influence, perceived vulnerability, monogamy, and behavioral skills. A predictive structural equation model revealed significant predictors of more condom use including: male gender, more sexual HIV knowledge, positive experiences and attitudes about

condom use, nonmonogamy, and greater behavioral skills. Results imply that attention to behavioral skills for negotiating safer sex and training in the proper use of condoms are key elements in reducing high risk behaviors. Increasing the specific knowledge level of college students regarding the subtleties of sexual transmission of HIV is important and should be addressed. Heightening students' awareness of the limited protection of serial monogamy, and the need to address gender-specific training regarding required behavioral change to reduce transmission of HIV should be an additional goal of college health professionals. Bazargan, M., Kelly, E.M., Stein, J.A., Hasaini, B.A., and Bazargan, S.H. Correlates of HIV Risk-Taking Behaviors Among African American College Students: The Effect of HIV Knowledge, Motivation, and Behavioral Skills, Journal of the National Medical Association, 92, pp. 391-404, 2000.

Efficacy of a Preventive Intervention for Youths Living with HIV

HIV transmission behaviors and health practices were examined among youth living with HIV (YLH) over 15 months after youth received a preventive intervention. YLH aged 13-24 years were assigned by small cohort to (1) a two-module intervention totaling 23 sessions ("Stay Healthy" and "Act Safe"), or (2) a Control condition. 73% in the Intervention Condition attended at least one session. Following the Stay Healthy module, females who attended the Intervention Condition increased their number of positive lifestyle changes and increased active coping styles more often than those in the Control Condition. Following the Act Safe Module, YLH who attended the Intervention Condition reported 82% fewer unprotected sexual acts, 45% fewer sexual partners, 50% fewer HIV-negative sexual partners, and 31% less substance use on a weighted index than those in the Control Condition. It was concluded that prevention programs can effectively reduce risk acts among YLH. Alternative formats need to be identified for delivering the intervention. Efficacy of a Preventive Intervention for Youths Living with HIV. Rotheram-Borus, M.J., Lee, M.B., Murphy, D.A., Futterman, D., Duan, N., Birnbaum, J.M., Lightfoot, M., and the Teens Linked to Care Consortium. American Public Health Association, 91(3), pp. 400-405, 2001.

Variation in Health and Risk Behavior Among Youth Living with HIV

Lifetime and current health practices and risk behaviors were examined among 350 youth living with HIV (YLH) aged 14-23 years from four AIDS epicenters (72.6% male; 26.2% African American, 36.9% Latino). YLH were relatively healthy (M CD4 cells = 499), had used substantial health care and were satisfied with the care. YLH's sexual and substance-use histories indicated substantial HIV related risk acts: the median number of lifetime partners was 25 with only 8% using condoms consistently; 14.9% had injected drugs, and 61.2% had used hard drugs. Compared with females, males had more lifetime and recent sexual partners and had used more drugs. Youth who were recently sexually active (81.3%) had multiple partners. Most of the sexually active YLH used condoms consistently (81.6%). YLH who were symptomatic or had an AIDS diagnosis were likely to have recently had more seropositive sexual partners than the asymptomatic youth. Youth disclosed their serostatus to about half of their sexual partners (53.9%). YLH with AIDS used fewer hard drugs than those without an AIDS diagnosis. Health and risk behaviors of the YLH varied significantly based on their disease stage, gender, and ethnicity, suggesting the need for tailoring interventions for subgroups of YLH. Rotheram-Borus, M.J., Lee, M., Zhou, S., O'Hara, P., Birnbaum, J.M., Swendeman, D., Wright, W., Pennbridge, J., and Wight, R.G. Variation in Health and Risk Behavior Among Youth Living with HIV. AIDS Education and Prevention, 13(1), pp. 42-54, 2001.

Drug-Using Women's Communication with Social Supporters About HIV/AIDS Issues

Communication about health issues such as HIV/AIDS is essential for people, especially women, to obtain the social support they need either to prevent illness or manage it. This article compares the kinds of HIV-related issues that HIV positive and HIV negative substance-abusing women (N=211) in New York City talk about with various types of supporters. Despite the stigma associated with AIDS and their unconventional lifestyles, both groups of women talked to a broad spectrum of supporters about a variety of HIV-related issues, though this was more the case for HIV positive women. Although the main topic that both groups discussed with their supporters was their HIV status, the women also talked about risk reduction, their supporters' HIV status, HIV testing, how to live with AIDS, information about HIV/AIDS, and the emotional impact of AIDS (e.g., fear of infection, reactions to learning test results, and the impact of knowing others who have died from the disease). Falkin, G.P., and Strauss, S.M. Journal of Drug Issues, 30(4), pp. 801-822, 2000.

An Alternative Program for Methadone Maintenance Dropouts: Description and Preliminary Data

Time in drug treatment has been shown to be one of the best predictors of post-treatment success. Since as many as half of the enrollees leave methadone treatment during the first year, the project described in this article was designed to test the effectiveness of an alternative program for individuals who have recently dropped out of methadone maintenance treatment. The goals of this "Alternative Program" are to help participants re-connect with

formal drug treatment and other community or medical programs, reduce their HIV risk behavior, decrease or eliminate drug use, join self-help groups, and obtain entitlements. Program components include: contacts by local outreach workers, cognitive-behavioral relapse-prevention group counseling, and individual counseling for needs assessment and referral. The authors describe the basis for development of the intervention, summarize the methodology being used, and provide preliminary data on participation in the Alternative Program. Goldstein, M.F., Deren, S., Beardsley, M., and Richman, B.L . Mt. Sinai J Med., 68 (1), pp. 33-40, 2001.

Hepatitis C Disease Among Injection Drug Users: Knowledge, Perceived Risk and Willingness to Receive Treatment

The authors surveyed 306 former injection drug users receiving methadone maintenance treatment in 1997-1998 in Providence, RI regarding, (1) knowledge of hepatitis C transmission: (2) the concordance of self-knowledge of hepatitis C virus (HCV) status versus actual status; (3) perceived risk of cirrhosis: and (4) willingness to receive therapy for hepatitis C. The seroprevalence of HCV was 87%. While 77%, of participants knew that HCV could be sexually transmitted, 30%, did not know that condoms are protective against transmission. Thirty of 45 persons who reported they were HCV seronegative were actually seropositive; 51 of 62 persons (82%) who reported they had never been HCV tested or did not know their HCV status were serologically HCV-positive. Over half of respondents (53%) would 'definitely' or 'probably' use interferon therapy for viral hepatitis when informed of the risks and benefits of treatment. The authors cite significant gaps in knowledge about HCV among IDUs. Serologic confirmation of HCV status is important among drug users, as self-report of HCV infection is often unreliable. This population, with its high prevalence of HCV, may be interested in treatments that include interferon. Stein, M.D., Maksad, J., and Clarke, J. Drug and Alcohol Dependence, 61(3), pp. 211-215, Feb 1, 2001.

Prevalence and Duration of Hepatitis C Among Injection Drug Users in San Francisco, California

Drs. Lorvick, Kral, Seal, Gee, and Edlin conducted a study to determine the prevalence of anti-HCV among IDUs in San Francisco in 1987, and to estimate how long prevalent cases have been infected. The subjects were originally recruited for an HIV prevalence study among street-recruited IDUs (the Urban Health Study). They found that injection drug users (IDUs) are the single population most affected by the hepatitis C virus (HCV). Progression to cirrhosis and/or hepatocellular carcinoma occurs in 20-30% of chronically HCV infected persons 20-30 years after infection. Stored serum samples collected from 372 IDUs in 1987 were tested for HCV antibody. They found that 353/372 (95%) samples were positive for HCV antibody. Prevalence was strongly associated with the duration of injection drug use. Of those injecting ≤ 2 years, 75.9% were infected (95% CI .56, .90). Of those injecting >10 years, 98.8% were infected (95% CI .96, .99). There were no significant differences in prevalence by race, gender or frequency of injection. The median year of commencing injection drug use was 1972 (interquartile range 1967, 1979). Because most HCV infections occur within two years of initiating injection drug use, the majority were likely infected by the mid-1970's. The vast majority of IDUs in this sample were infected with HCV in 1987. Many are entering their third decade of infection and may be progressing to liver disease at this time. Lorvick, J., Kral, A.H., Seal, K., Gee, L., and Edlin, B.R. Prevalence and Duration of Hepatitis C among Injection Drug Users in San Francisco, California. American Journal of Public Health, 91, pp. 46-47, 2000.

Neurobehavioral Outcomes of Cocaine-Exposed Infants

Singer et al. investigated the neurobehavioral outcomes associated with prenatal cocaine exposure. The sample included 319 infants (158 cocaine-exposed and 161 non-exposed) with a mean-corrected age of 43 weeks post-conception. Cocaine exposure was determined by a positive response to one of the following: infant meconium, urine or maternal urine positive for cocaine; maternal report to hospital staff, or; maternal self-report during clinical interview. Cocaine positive infants were further divided into heavy and light categories. When only cocaine-exposed and non-exposed infants were compared, the exposed infants exhibited significantly more abnormalities in movement and tone than the non-exposed, with a trend for greater jitteriness in the exposed infants. When the exposed group of infants was divided into those with heavy and light exposure, heavily exposed infants had significantly more attentional abnormalities and jitteriness than the lightly exposed and non-exposed groups. Heavily exposed infants were also more likely to be identified with any abnormality than non-exposed infants, had more movement and tone abnormalities and sensory asymmetries than non-exposed infants and were four times as likely to be jittery and nearly twice as likely to demonstrate any abnormality than lightly- and non-exposed infants. Singer, L.T., Arendt, R., Minnes, S., Farkas, K., and Salvator, A. Neurobehavioral Outcomes of Cocaine-Exposed Infants. Neurotoxicology and Teratology, 22(5), pp. 653-666, 2000.

Effects of Prenatal Cocaine/Crack and Other Drug Exposure on Electroencephalographic

Sleep Studies at Birth and One Year

Electroencephalographic (EEG) sleep patterns can be used to assess cerebral maturation and neurophysiologic organization of the developing central nervous system. Scher and colleagues conducted sleep studies of infants born to 37 women who used crack or one or more lines per day of powder cocaine during the first trimester of pregnancy. A control group of 34 infants had mothers who used neither cocaine nor crack during pregnancy. Maternal substance use was determined by self-report during interviews. Infants were eligible if they had gestations from 38-42 weeks, no general anesthesia, and 5 minute Apgar scores of >5. A total of 71 infants received 2 hour EEG sleep recordings at 24-36 hours after birth, with 57 infants returning for EEG sleep recordings at 1 year postpartum. The results indicated that after controlling for the significant covariates, prenatal cocaine exposure was associated with less well-developed spectral correlations between homologous brain regions at birth, and with lower spectral EEG power values at 1 year of age. Implications of these findings are that the neurotoxic effects of prenatal cocaine/crack use can be detected with quantitative EEG measures. Further research is needed to determine whether the abnormal brain patterns detected are associated with developmental abnormalities. Scher, M.S., Richardson, G.A., and Day, N.L. Effects of Prenatal Cocaine/Crack and Other Drug Exposure on Electroencephalographic Sleep Studies at Birth and One Year, Pediatrics, 105(1 Pt 1), pp. 39-48, 2000.

Drug Abuse Among Athletes

Pope and his colleagues from McLean Hospital/Harvard School of Medicine have observed a substantial drug abuse problem among athletes in the U.S. In a survey of 511 clients entering five gymnasiums (Kanayama et al. 2000), they found that among men, 18% report use of androstenedione and/or other adrenal hormones, 25% report ephedrine use, and 5% report anabolic steroid use within the past three years; while among women, these rates were 3%, 13%, and 0%, respectively. Extrapolating from these figures to the U.S. as a whole, the authors estimate that possibly 1.5 million American gymnasium clients have used adrenal hormones and 2.8 million have used ephedrine within the last three years. They further report that nalbuphine may represent a new drug of abuse among athletes, especially those using anabolic steroids. (Nalbuphine, a nonscheduled opioid agonist/antagonist analgesic, is used for the treatment of pain.). Authors (Wines et al., 1999) conducted interviews on 11 subjects who reported nalbuphine use. Eight subjects were clinically dependent on nalbuphine, and seven of these experienced tolerance and withdrawal symptoms. Further, eight subjects who had never injected drugs intravenously before, reported using nalbuphine by this route. Nalbuphine-related morbidity was extensive and included medical complications and psychiatric symptoms (comorbid Axis I disorders). These observations suggest that nalbuphine may represent a new drug of abuse among anabolic steroids abusing athletes. Finally, the investigators (Halpern and Pope, 2001) also report that there is a widespread use of the Internet among well-educated adults and teenagers for obtaining medical information about hallucinogens and how to obtain and use these drugs. Kanayama, G., Gruber, A.J., Pope, H.G., Borowiecki, J.J., and Hudson J.I. Over-the-Counter Drug Use in Gymnasiums: An Underrecognized Abuse Problem? Psychotherapy and Psychosomatics, May/June issue, 2001; Wines, J.D., Gruber, A.J., Pope, H.G., and Lukas, S. Nalbuphine Hydrochloride Dependence in Anabolic Steroid Abusers. Am. J. Addictions, 8, pp. 161-164, 1999; Halpern, J.H. and Pope, H.G. Hallucinogens on the Internet: A Vast New Source of "Underground" Drug Information. American Journal of Psychiatry, 158, pp. 481-483, 2001.

Identifying Prenatal Exposure to Illicit Drugs Using Meconium Testing and Maternal Self-Report

In the four-site Maternal Lifestyle Study (Detroit, Miami, Memphis, Providence) of in utero cocaine and/or opiate exposure, meconium specimens of 8,527 newborns were analyzed by immunoassay (EMIT) with GC/MS (gas chromatography/mass spectrometry) confirmation. Maternal self-report of drug use during pregnancy was determined during a hospital interview. Recruitment occurred between May 1993 and May 1995. Prevalence and observed metabolites showed considerable variation across the four sites, and exposure status was higher in low birth weight infants. Results indicated that accurate identification of exposure is likely to be improved with GC/MS confirmation and when the meconium testing is used in conjunction with a maternal hospital interview (e.g., 254 mothers denied use but their infants had positive meconium confirmation for cocaine/opiates, thus allowing identification of an additional 38% of the cocaine/opiate exposed infants by means of meconium testing). Importantly, had the study relied on maternal report only, these 254 infants would have been eligible for inclusion in the unexposed group. However, at the current stage of this new and useful technology, many questions still remain about the disposition of drugs in meconium, and the investigators caution against the use of quantitative analysis of drugs in meconium to estimate the degree of exposure. Lester, B.M., ElSohly, M., Wright, L.L., Smeriglio, V.L., Verter, J., Bauer, C.R., Shankaran, S., Bada, H.S., Walls, H.C., Huestis, M.A., Finnegan, L.P., and Maza, P.L. Pediatrics, 107, pp. 309-317, 2001.

Prenatal Marijuana Exposure - Emerging Theme of Executive Function Deficiencies

In a review of the scientific literature dealing with neurobehavioral consequences of prenatal exposure to marijuana, Fried and Smith identify a degree of consistency in the limited longer-term data that exist, both from cross-sectional reports and from the two available long-term cohort studies, one involving a low-risk sample (Fried, Carleton University) and the other a high-risk sample (Day, University of Pittsburgh). Aspects of executive function appear to be negatively associated with in utero cannabis beyond the age of 3 years, especially attentional behavior and visual analysis/hypothesis testing. Published data are available for children as old as 12 years of age. In addition, the authors note that in work by the Day research group, on the basis of path analysis, it appeared that poor attentional skills of the child mediated an association between maternal report of child delinquency at age 10 years and prenatal marijuana use. Fried and Smith discuss their literature review findings in the context of the broader research fields of marijuana and prefrontal brain function, and they emphasize the need for further, well-controlled investigations. Fried, P.A. and Smith, A.M. Neurotoxicology and Teratology, 23, pp. 1-11, 2001; Goldschmidt, L., Day, N.L., and Richardson, G.A. Neurotoxicology and Teratology, 22, pp. 325-336, 2000.

Drug Treatment is Beneficial, Even for Drug Users In Treatment Less Than 90 Days

Many studies have found that the longer a drug user remains in treatment, the more positive the outcome. The majority of studies on the effects of time in treatment have followed participants from the time they enter treatment. Participants in this study were IDUs and crack users who were out of treatment at the time of their recruitment. Between the initial and six-month follow-up interviews, some chose to enroll in drug treatment. The more time a person spent in treatment during the follow-up period, the more likely it was that s/he was not using heroin or cocaine at follow-up (OR=.51; 95% C.I., .39-.67; p<.001). Unlike the results of some prior studies, positive effects of time in treatment were found even when time in treatment was less than 90 days. The findings of the present study strongly suggest that treatment is beneficial even for those who remain for less than 90 days. Those who provide treatment services to drug users should attempt to maintain contact with dropouts, and support their return to treatment. Goldstein, M.F., Deren, S., Magura, S., Kayman, D., et al. Cessation of Drug Use. J Psychoactive Drugs, 32(3), pp. 305-310, 2000.

Initial Plasma HIV-1 RNA and Progression to AIDS in Men and Women

Differences in plasma HIV-1 RNA levels (viral load) have been observed in some studies comparing HIV-infected men and women, but conclusive results have been limited by study design or small sample sizes. In this new larger analysis in a prospective cohort study of 202 IDUs who underwent seroconversion, viral load was measured and the association of initial viral load with disease progression was assessed. Of these seroconverters, 156 (77%) were men and 46 (23%) were women. The median viral load after seroconversion was significantly lower in women vs. men (15,103 vs. 50,766 copies per millimeter; P<.001), but CD4+ lymphocyte counts (CD4) did not differ according to sex. The median initial viral load remained approximately 0.5 log lower in women vs. men after adjusting for age, time from estimated seroconversion to first viral load test (P=.001), and CD4 at seroconversion (P=.001). The difference in viral load between men and women persisted for several years after seroconversion. HIV infection progressed to AIDS in 29 men and 15 women; time to AIDS did not significantly differ in men vs. women (P=.18). While viral load had a similar qualitative predictive value for progression to AIDS in men vs. women, the same absolute viral load conferred different risks of AIDS in men vs. women, e.g., an initial viral load of 17,149 copies per milliliter was associated with progression to AIDS in women but not in men, while the median viral load among men who did not progress to AIDS was 40,634 copies. Given that viral load has been the basis for the current guidelines regarding initiation of antiretroviral therapy in HIV-infected patients, these findings have implications that require further study. Analyses to determine if there is a threshold viral load value that predicts progression, and research on the underlying biologic mechanism of the observed viral load differences are needed. Sterling, T.R., Vlahov, D., Astemborski, J., Hoover, D.R., Margolick, J.B., and Quinn, T.C. New England Journal of Medicine, 344, pp. 720-725, 2001.

Trends in HIV in Puerto Rican IDUs in Puerto Rico and New York: 1992-1999

Researchers investigated trends in HIV seroprevalence and needle-sharing behaviors among Puerto Rican injection drug users (IDUs) in Puerto Rico and New York City between 1992 and 1999. Data from two studies of IDUs conducted from 1992-1995 and 1998-1999 in Bayamon, Puerto Rico, and East Harlem, New York, were examined to assess trends over this period. Separate analyses were conducted for IDUs who were current crack smokers. Significant decreasing trends in seroprevalence were found among IDUs in the New York and Puerto Rico samples (p <.001). Significant decreasing trends in receptive and distributive needle sharing were found in the New York sample, and a significant decline in receptive sharing was found in the Puerto Rico sample. Overall, higher levels of needle-sharing behaviors were reported in Puerto Rico compared with New York. Decreasing trends in needle sharing and

seroprevalence in both communities are an encouraging finding. Ongoing epidemiologic studies to monitor the epidemic and continued prevention efforts to help maintain or further these declines are needed, particularly to address the higher rates of needle sharing in Puerto Rico. Deren, S., Robles, R., Andia, J., Colon, H., et al. Trends in HIV Seroprevalence and Needle Sharing Among Puerto Rican Drug Injectors in Puerto Rico and New York: 1992-1999. J AIDS, 26(2), pp. 164-169, 2001.

Study Examines the Social Network Context of HIV Risk Behavior Among IDUs

Researchers characterized social network context of HIV risk behaviors among injection drug users who participated in the Baltimore Needle Exchange Program (NEP) from 1995-1997. They conducted interviews with 1,184 IDUs in which they asked each respondent to give the initials of up to five of their closest friends and whether, with each friend, they had injected drugs, shared syringes, had sex, or drank alcohol. Of the 203 (17.1%) IDUs who reported using a syringe after someone else, 78.3% reported sharing with close friends, and the adjusted odds ratio of any sharing and sharing with close friends was 30.9. IDUs were more likely to report sharing with strong-tie close friends and less likely to report sharing with other close friends if those friends were weak ties and new to their network. Friendship ties were not stable, with fewer than 30% of the friends being repeat nominations. The findings from this study show that many IDUs engage in selective risk taking that may minimize their disease risk exposure in the short term. In other words, risk taking is not random but rather, is more likely to occur with strong-tie close friends than with weak-tie ones. However, the turnover in relationships among IDUs represents a risk potential for infection transmission that could be ongoing within this population. As a result, as part of a comprehensive HIV prevention program, NEPs need to do more than provide access to sterile syringes and drug treatment referral. Valente, T.W. and Vlahov, D. Selective Risk Taking Among Needle Exchange Participants: Implications for Supplemental Interventions. Am J Public Health, 91, pp. 406-411, 2001.

Research Enumerates a Variety of Sexual Risk Reduction Strategies by Active Drug Users

Recent studies have shown that active drug users continue to report inconsistent use of condoms to reduce their HIV risks from unprotected sexual activity. Interventions with IDUs have also been more effective in changing drug injection behaviors than in changing risky sexual practices; even after the intervention, drug users have shown little evidence of sustained condom use. In this study, researchers sought to understand whether drug users employ alternative strategies (i.e., other than condom use) that they believe will reduce or eliminate their personal risk of acquiring HIV through sexual contact. An ethnographer conducted unstructured, face-to-face interviews with 92 not-in-treatment IDUs and/or crack users (including 68% male; 52% in their 40s and 33% in their 30s; 75% African American, 20%Hispanic, 2% White; 33% homeless; and 15.4% HIV positive). Researchers identified three categories of alternative sexual risk reduction strategies from the drug users participating in the qualitative interviews: before sex, partner screening was used (visual inspection, observation, and reliance on an outside authority, including being shown an HIV negative certificate); during sex, personal hygiene was considered very important, as were selecting or refusing to participate in specific sex acts; and after sex, respondents reported douching (often with vinegar and water or bleach and water) or washing with alcohol, peroxide, or lemon juice to reduce their risks for HIV. This study found that active drug users are aware of their personal risks for HIV from sexual activity, but instead of using condoms consistently, they often report using ineffective strategies to reduce their risks. The finding of a pervasive folk model equating cleanliness and health underscores the challenge to public health researchers and HIV prevention programs to develop more effective, science-based risk reduction and health promotion messages to counteract prevailing myths and misconceptions about HIV/AIDS within specific risk groups. Metsch, L.R., McCoy, C.B., Wingerd, J., and Miles, C.C. Alternative Strategies for Sexual Risk Reduction Used by Active Drug Users. AIDS and Behavior, 5(1), pp. 75-84, 2001.

Relationships of Laws Prohibiting OTC Syringe Sales With Prevalence of IDUs and HIV

A secondary ecologic analysis was conducted of data presented by Holmberg (1996) to assess relationships of laws prohibiting over-the-counter syringe sales with population prevalence of IDUs and HIV prevalence or incidence among 96 U.S. metropolitan areas. In 1992, Holmberg had estimated the population sizes and HIV prevalence and incidence rates of metropolitan subpopulations at particular risk for HIV, including IDUs, and MSMs within each of the 96 largest metropolitan areas of the U.S. Researchers compared metropolitan areas with and without laws that prohibit OTC syringe sales in terms of their population densities of IDUs, HIV prevalence and incidence rates among IDUs, HIV prevalence among MSM, and distance from New York City (because New York has been the epicenter for the epidemic of HIV among IDUs in the U.S.). They found that IDUs accounted for more (0.94%) of the population in the 36 metropolitan areas in states with laws against OTC syringe sales than in the 60 metropolitan areas without these laws (0.82%). Mean HIV prevalence was 13.8% in metropolitan areas with laws against OTC syringe sales and 6.7% in other metropolitan areas. Median HIV prevalence was also greater in cities with OTC laws than in cities without them. In discussing the implications of their findings to public health, the authors conclude that laws prohibiting OTC syringe

sales are not associated with lower population proportions of IDUs, but are significantly associated with HIV prevalence and incidence. Friedman, S.R., Perlis, T., and Des Jarlais, D. Laws Prohibiting Over-the-Counter Syringe Sales to IDUs: Relations to Population Density, HIV Prevalence, and HIV Incidence. Am J Public Health, 91(5), 2001.

Study Examines Sex-Specific Behaviors and HIV Among IDUs in Montreal

The objective of this study was to examine sex-specific behaviors associated with HIV infection among injection drug users in Montreal. Researchers recruited a total of 2,741 active drug users (2,209 [80.6%] men) between 1988 and 1998 for interviews regarding sociodemographic characteristics, drug use history and current drug use, drug-related behavior, sexual behavior, and other information. Participants were also tested for HIV antibodies. Sex-specific independent predictors of HIV prevalence were assessed by stepwise logistic regression. The overall prevalence of HIV among study participants was 11.1%; the prevalence was 12.0% among men and 7.5% among women. In multivariate models, a history of sharing syringes with a known seropositive partner (odds ratio [OR] for men 2.44, 95% confidence interval [CI] 1.72-3.46; OR for women 3.03, 95% CI 1.29-7.13) and of sharing syringes in the past 6 months (OR for men 0.61, 95% CI 0.44-0.85; OR for women 0.32, 95% CI 0.14-0.73) were independently associated with HIV infection. Other variables associated with HIV infection were homosexual or bisexual orientation, cocaine rather than heroin as drug of choice, frequency of injection drug use, and obtaining needles at a pharmacy or through needle exchange programs (for men only) and obtaining needles at shooting galleries and being out of treatment (for women only). Findings support the hypothesis that risk factors and processes related not only to sexual behaviors, but also to the social contexts of drug use and service utilization, might differ with regard to HIV prevalence between men and women. These sex-related differences should be taken into account in the development of preventive and clinical interventions. Bruneau, J., Lamothe, F., Soto, J., Lachance, N., et al. Sex-Specific Determinants of HIV Infection Among Injection Drug Users in Montreal. Canadian Medical Assoc Journal, 164(6), pp. 767-73, 2001.

An Event Analysis of Drug-Using Women's Sexual Risk

Researchers used event analysis to describe the most recent sexual events of drug-using women and their male partners, and to identify relationship-specific and event-specific determinants of condom use. Women drug users (n=320) were recruited from the streets of East Harlem. After validation of drug use, they participated in structured interviews and were offered HIV testing and counseling. Data were collected on demographic characteristics, relationship factors (including age of partner, race/ethnicity concordance, and HIV serostatus of partners), and event-specific factors, including sexual repertoire, communication about condom use, and perception of HIV risk. Univariate and multivariate analyses identified 5 major variables associated with event-specific condom use: Closeness to partner, perceived dyadic serostatus, sexual repertoire, communication about condoms, and perceived control of condom use. Behavioral interventions to reduce sexual risk should focus on dyads with long-standing sexual relationships and on the dynamics of the relationship, especially the issues of dyadic serostatus, intimacy, communication, and control. Tortu, S., McMahon, J., Hamid, R., and Neaigus, A. Drug-Using Women's Sexual Risk: An Event Analysis. AIDS and Behavior, 4(4), pp. 329-340, 2000.

Women IDUs Who Have Sex With Women Exhibit Increased HIV-Related Risk Behaviors

Researchers reviewed the published literature on HIV seroprevalence and HIV-related risk behaviors among women IDUs who have sex with women. They report that, since the late 1980s, published studies have converged into a consistent pattern concerning this population. Specifically, compared to other IDUs, women IDUs who have sex with women report higher levels of HIV-related risk behaviors (risky injection practices, unprotected sex), and in many cases exhibit higher levels of HIV seroconversion or seroprevalence. For example, a large study of 9,621 out-of-treatment IDU women found that women IDUs who had sex with both men and women during the prior six months were more likely than the other women to inject cocaine at least daily and score higher on a summary index on needle risk. Data from these and additional studies suggest that a relatively large proportion of women IDUs are women who have sex with women. Information regarding women injectors who have sex with women are widely collected but infrequently reported, indicating the need to apply promising research and analysis strategies to explore the meaning behind this pattern of increased vulnerability to HIV. Young, R.M., Friedman, S.R., Case, P., Asencio, M.W., and Clatts, M. Women Injection Drug Users Who Have Sex With Women Exhibit Increased HIV Infection and Risk Behaviors. J Drug Issues, 30(3), pp. 499-524, 2000.

Drug User Characteristics Related to HIV Testing and Returning for Test Results

As part of the 23-site NIDA cooperative agreement for the prevention of HIV/AIDS, researchers examined demographic and behavioral factors related to taking an HIV test and returning for test results. They recruited out-of-treatment IDUs and crack smokers in East Harlem, New York City (N=1,682) and administered the Risk Behavior

Assessment (RBA). Almost 56% (n=934) of the participants agreed to test for HIV; persons reporting no prior HIV testing were more likely to test, as were persons reporting having had drug injecting sex partners in the prior 30 days ($p<.05$). Drug-related risks, including frequency of injection or crack use in the prior 30 days, were not related to testing vs. not testing. Eighty-one percent of those who tested (n=753) returned for their results. Persons who were HIV positive were less likely to return for their results, as were persons who reported exchanging sex for money or drugs, and persons who considered themselves homeless ($p<.05$). Those more likely to return for their test results included African Americans, older drug users, persons with a high school or GED diploma, persons reporting unprotected vaginal sex in the past 30 days, current crack smokers, and persons who had been previously incarcerated ($p<.05$). The findings from this study demonstrate that it is possible to get high-risk individuals to get tested for HIV. However, they also show that younger high-risk drug users were less likely to get tested and to return for test results than older persons, and that high-risk subgroups (e.g., those who exchange sex for money or drugs) may be less likely to return for results. The data suggest that targeted strategies, including community-based outreach HIV risk reduction strategies, should be assessed and if necessary, improved, to enhance their effectiveness in encouraging persons at risk to seek HIV testing and return for their test results, particularly younger drug users and others at high risk for HIV. Ziek, K., Goldstein, M., Beardsley, M, Deren, S., and Tortu, S. Factors Associated with HIV Testing and Returning for Test Results in a Sample of Out-of-Treatment Drug Users. J Drug Issues, 30(3), pp. 675-686, 2000.

Neurotoxicity of HIV Proteins and Drugs

Little is known about the neurologic impairment resulting from mixed drug administration and HIV exposure. Some recent papers have brought new insight into this area. This study describes neurotoxicity of HIV proteins in select neural areas and the potentiation by stimulant drugs. Infection with the human immunodefiency virus (HIV) selectively targets the basal ganglia resulting in loss of dopaminergic neurons. Although frequently asymptomatic, some patients may develop signs of dopamine deficiency de novo. Accordingly, they are highly susceptible to drugs that act on dopaminergic systems. Both neuroleptics and psychostimulants may exacerbate these symptoms. Experimental evidence suggests that viral proteins such as gp120 and Tat can cause toxicity to dopaminergic neurons, and this toxicity is synergistic with compounds such as methamphetamine and cocaine that also act on the dopaminergic system. In addition, other neurotransmitters that modulate dopaminergic function, such as glutamate and opioids, may also modify the susceptibility of the dopamine system to HIV. Therefore, a thorough understanding of the mechanisms that lead to this selective neurotoxicity of dopaminergic neurons would also likely lead to the development of therapeutic modalities for patients with HIV dementia. Nath, A., Anderson, C., Jones, M., Maragos, W., Booze, R., Mactutus, C., Bell, J., Hauser, K.F., and Mattson, M. Neurotoxicity and Dysfunction of Dopaminergic Systems Associated with AIDS Dementia. J Psychopharm., 14, pp. 222-227, 2000.

Neurotoxicity in the Presence of Opioids

Human immunodeficiency virus (HIV) infection selectively targets the striatum, a region rich in opioid receptor-expressing neural cells, resulting in gliosis and neuronal losses. Opioids can be neuroprotective or can promote neurodegeneration. To determine whether opioids modify the response of neurons to human immunodeficiency virus type 1 (HIV-1) Tat protein-induced neurotoxicity, neural cell cultures from mouse striatum were initially characterized for mu and/or kappa opioid receptor immunoreactivity. These cultures were continuously treated with morphine, the opioid antagonist naloxone, and/or HIV-1 Tat protein, a non-neurotoxic HIV-1 Tat deletion mutant protein, or immunoneutralized HIV-1 'toxic' Tat protein. Morphine significantly increased Tat-induced neuronal losses at 24h following exposure. The synergistic effects of morphine and Tat were prevented by naloxone, indicating the involvement of opioid receptors. Furthermore, morphine was not toxic when combined with mutant Tat or immunoneutralized Tat. Neuronal losses were accompanied by chromatin condensation and pyknosis. Astrocyte viability was unaffected. These findings demonstrate that acute opioid exposure can exacerbate the neurodegenerative effect of HIV-1 Tat protein in striatal neurons, and infer a means by which opioids may hasten the progression of HIV-associated dementia. Nath, A., Sun, Q., Zhang, J., Martin, K.M., Chen, Y., and Hauser, K.F. Synergistic Neurotoxicity of Opioids and Human Immunodeficiency Virus-1 Tat Protein in Striatal Neurons in Vitro. Neuroscience, 102, pp. 555-563, 2001.

Chemokine Receptor Function

Chemokine receptors are necessary for HIV entry into a cell. Therefore, morphine's modulation of chemotaxis, an action of chemokines may be important in HIV neurotoxicity. The beta-chemokine RANTES has recently been implicated in the neuropathogenesis of the human immunodefiency virus. Based upon previous studies of the effects of morphine on microglial cell production of cytokines and chemotaxis towards the activated complement component C5a, authors tested the hypothesis that this opiate would alter the production of and migration towards RANTES by human microglia. Treatment of microglial cells with morphine was found to suppress chemotaxis. The inhibitory

effects of morphine on RANTES production and on chemotaxis were blocked by naloxone and beta-funaltrexamine, indicating that morphine mediated its suppressive effects via activation of microglial mu-opioid receptors. Morphine's inhibitory effect on chemotaxis did not appear to be associated with an alteration in RANTES-induced [Ca2+] mobilization. While the clinical significance of these in-vitro findings is unknown, they suggest that mu-opioid receptor agonists could alter certain neurodegenerative and inflammatory processes within the brain. Hu, S.X., Chao, C.C., Hegg, C.C., Thayer, S., and Peterson, P.K. Morphine Inhibits Human Microglial Cell Production of, and Migration Towards, RANTES. J Psychopharm., 14, pp. 238-243, 2000.

Chemokine Receptors and Lymphoid Cells

In non-neural systems scientists presented evidence about the specific mechanisms whereby mu-type (morphine) compounds stimulate the growth of HIV in human blood cells. Strong evidence for the direct modulation of the immune system by opioids is well documented. Mu-opioids have been shown to alter the release of cytokines important for both host defense and the inflammatory response. Proinflammatory chemokines monocyte chemoattractant protein-1 (MCP-1), RANTES, and IFN-gamma-inducible protein-10 (IP-10) play crucial roles in cell-mediated immune responses, proinflammatory reactions, and viral infections. In this report, authors show that DAMGO, a mu-opioid-selective agonist, augments the expression in human PBMCs of MCP-I, RANTES, and IP-10 at both the mRNA and protein levels. Because of the proposed relationship between opioid abuse and HIV-1 infection, we also examined the impact of DAMGO on chemokine expression in HIV-infected cells. Results show that DAMGO administration induces a significant increase in RANTES and IP-10 expression, while MCP-I protein levels remain unaffected in PBMCs infected with the HIV-1 strain. In contrast, results show a dichotomous effect of DAMGO treatment on IP-10 protein levels expressed by T-and M-tropic HIV-infected PBMCs. The differential modulation of chemokine expression in T- and M-tropic HIV-1-infected PBMCs by opioids supports a detrimental role for opioids during HIV-1 infection. Modulation of chemokine expression may enhance trafficking of potential noninfected target cells to the site of active infection, thus directly contributing to HIV-1 replication and disease progression to AIDS. Wetzel, M.A., Steele, A.D., Eisenstein, T.K., Adler, M.W., Henderson, E.E., and Rogers, T.J. Mu-opioid Induction of Monocyte Chemoattractant Protein-1, RANTES, and IFN-gamma-inducible protein-10 Expression in Human Peripheral Blood Mononuclear Cells. J Immunol., 165, pp. 6519-6524, 2000.

A related paper reports the increased expression of CCR5 receptors in human derived cells used to culture SIV. This would indicate that morphine might enhance growth of these retro-viruses in specific cell types. All HIV-1 strains studied to date use CCR5, CXCR4, or both receptors to enter cells, Simian immunodeficiency virus (SIV) infection of non-human primates has served as a useful model for understanding AIDS pathogenesis in humans. Research on several genetically divergent SIV isolates has revealed that SIV uses CCR5, and not CXCR4, for entry. CEMx174, a human lymphoid cell line, has been routinely used to cultivate and maintain various SIV strains. However, questions have arisen about how CEMx174, which reportedly was unable to express detectable amounts of CCR5 transcripts, efficiently supports the growth of SIV. In searching for an answer, authors resorted to a sensitive competitive reverse transcriptase-polymerase chain reaction procedure in an attempt to detect as well as quantify the amount of CCR5 expression. Here findings are presented which indicate that CEMx174 indeed expresses CCR5 and that the amount of CCR5 is increased in cells pretreated with morphine. These results correlate well with previous observations that morphine treatment causes CEMx174 cells to be more susceptible to SIV infection. Similar morphine effect was not observed on CEMx174 cells infected with simian retroviruses, which do not depend on CCR5 for entry. These findings suggest a plausible mechanism whereby opiate drug users render themselves more susceptible to HIV infection, thereby explaining the vast prevalence of HIV infection among endemic drug use populations. Miyagi, T., Chuang, L.F., Doi, R.H., Carlos, M.P., Torres, J.V., and Chuang, R.Y. Morphine Induces Gene Expression of CCR5 in Human CEM x174 Lymphocytes. J Biol. Chem., 275, pp. 31305-31310, 2000.

Morphine Induced Sepsis

Recently, it was observed that sepsis produced by enteric bacteria entering into the peritoneum after opiate administration caused sepsis and death. A follow up study describes the possible action whereby morphine produces this disease enhancement through the activation of a cytokine. In this study authors investigated the capacity of morphine to modulate expression of cytokines in peritoneal macrophages. Mice were implanted subcutaneously with a 75-mg morphine slow-release pellet, and 48 h later resident peritoneal macrophages were harvested. Control groups received placebo pellets, naltrexone pellets, or morphine plus naltrexone pellets. Adherent cells were stimulated with lipopolysaccharide plus interferon-gamma to induce cytokine production. Morphine enhanced mRNA expression of interleukin (IL)-12 and tumor necrosis factor alpha (TNF-alpha) compared with controls, whereas IL-10 levels were unchanged by drug treatment. The enhancement of IL-12 at both the mRNA and protein levels was antagonized by naltrexone, indicating that the modulation of this cytokine by morphine is via a classic opioid receptor. These results are particularly interesting in light of the previous observation that 48 h after morphine pellet implantation, the peritoneal cavity is colonized with gram-negative and other enteric bacteria. The enhancement of IL-12 by morphine

might be related to morphine-induced sepsis. Peng, X.H., Mosser, D.M., Adler, M.W., Rogers, T.J., Meissler, J.J. and Eisenstein, T.K. Morphine Enhances Interleukin-12 and the Production of Other Pro-inflammatory Cytokines in Mouse Peritoneal Macrophages. J Leukocyte Biology, 68, pp. 723-728, 2000.

Substance P and Opiates

Substance P is a neurotransmitter in the central nervous system and it appears to play an important role in the immune system. Macrophages and other immune cells produce substance P. Substance P is also associated with higher levels of stress and anxiety and communicates between the central nervous system and the immune system, much the same as opiates do. In this study investigators observed an interaction between substance P and opiates. In vitro and in vivo studies have indicated that there is an important relationship between morphine and neuropeptide substance P (SP). This study investigated the interaction of morphine and cultured human immune cells on the expression of SP, a neuropeptide recently demonstrated to be produced by human monocytes and lymphocytes. Morphine up-regulated SP production in human mononuclear phagocytes and lymphocytes at both the mRNA and the protein level. In addition, morphine induced SP receptor (NK-1R) expression in human lymphocytes. The specific morphine receptor antagonist, (naltrexone) blocked morphine-induced SP expression in human mononuclear phagocytes, supporting the concept of authentic morphine receptor-mediated regulation. Since SP modulates neurogenic inflammation and immunologic events, these data suggest that morphine-induced SP expression in cells of the immune system may be of importance in the pathogenesis of immune-mediated diseases, including neuroimmunologic diseases and AIDS. Li, Y., Tian, S., Douglas, S.D. and Ho, W.Z. Morphine Up-regulates Expression of Substance P and its Receptor in Human Blood Mononuclear Phagocytes and Lymphocytes. Cell Immunol., 205, pp. 120-127, 2000.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Research Findings

Epidemiology, Etiology and Prevention Research

A Model of Smoking Among Inner-City Adolescents: The Role of Personal Competence and Perceived Social Benefits of Smoking

Based on current trends, smoking will remain a major public health problem in the 21st century. Effective smoking prevention approaches offer the best hope for decreasing the rise in adolescent smoking rates. Competence enhancement approaches to smoking prevention are among the most successful. Yet, there is not a full understanding of how effective prevention approaches work. This study tested whether a deficiency in competence (poor decision-making skills and low personal efficacy) is linked to acquiring beliefs in the perceived benefits of smoking and whether these perceived benefits are then related to subsequent smoking. A sample of 1,459 students attending 22 middle and junior high schools in New York City participated. Students completed surveys at baseline, 1-year follow-up and 2-year follow-up during a regular class period. They self-reported smoking, decision-making skills, personal efficacy and beliefs in the perceived benefits of smoking. The tested structural equation model had a good fit and was parsimonious and consistent with the theory underlying the competence approach to smoking prevention. This research highlights the importance of addressing decision-making skills, personal efficacy, and beliefs in the social benefits of smoking within adolescent smoking prevention programs. Epstein, J.A., Griffin, K.W. and Botvin, G.J. A Model of Smoking Among Inner-City Adolescents: The Role of Personal Competence and Perceived Social Benefits of Smoking. Preventive Medicine, 31(2), pp. 107-114, 2000.

Preventing Illicit Drug Use in Adolescents: Long-Term Follow-Up Data from a Randomized Control Trial of a School Population

National survey data indicate that illicit drug use has steadily increased among American adolescents since 1992. This upward trend underscores the need for identifying effective prevention approaches capable of reducing the use of both licit and illicit drugs. The present study examined long-term follow-up data from a large scale randomized prevention trial to determine the extent to which participation in a cognitive-behavioral skills-training prevention program led to less illicit drug use than for untreated controls. Data were collected by mail from 447 individuals who were contacted after the end of the 12th grade, 6.5 years after the initial pretest. Results indicated that students who received the prevention program (Life Skills Training) during junior high school reported less use of illicit drugs than controls. Prevention effects were also found for specific illicit drugs including the use of hallucinogens and narcotics. This study shows that significant prevention effects are observable 5.5 years after the primary year of intervention. Botvin, G.J., Griffin, K.W., Diaz, T., Scheier, L.H., Williams C. and Epstein, J.A. Preventing Illicit Drug Use in Adolescents: Long-Term Follow-Up Data from a Randomized Control Trial of a School Population. Addictive Behaviors, 25(5), pp. 769-774, 2000.

Family Risk and Resiliency Factors, Substance Use, and the Drug Resistance Process in Adolescence

Recent approaches to drug prevention have emphasized risk and resiliency factors. Two models have been developed to explain these factors, one which posits that separate elements make up each set and the other which posits that a single factor can be either a risk or a resiliency factor depending on, for example, if it is present (resiliency) or absent (risk). This study tested these models and attempted to compare the effects of risk and resiliency across gender and

ethnicity. Results support the model in which risk and resiliency are discrete sets of factors and demonstrate that overall resiliency factors play a larger role than risk factors in substance use and drug resistance processes. However, gender proved to be an important moderator of these effects. For adolescent males, resiliency has an indirect effect on overall substance use through age of first use, while risk has a direct effect on overall substance use. For adolescent females, resiliency has a direct effect on overall substance use and risk has an indirect effect through age of first use. This indicates that while early interventions are important for both genders, resiliency factors must be dealt with before initiation of substance use for males. Findings did not differ substantially across ethnicity, although the small African-American sample size may have limited power to detect differences. Moon, D.G., Jackson, K.M. and Hecht, M.L. Family Risk and Resiliency Factors, Substance Use, and the Drug Resistance Process in Adolescence. Journal of Drug Education, 30(4), pp. 373-398, 2000.

Verifying Drug Abuse Prevention Program Effects Using Reciprocal Best Friend Reports

Considerable research suggests that social influences-based drug abuse prevention programming has produced the most consistently successful preventive effects. However, a common criticism of this literature is that most prevention intervention studies rely solely on self-reported substance use. The purpose of this study was to assess the effects of normative education, arguably the most successful component of social influence based prevention programs, on alcohol and cigarette consumption using both self- and reciprocal best friend reports of substance use. Analyses of subsamples of data from 11,995 students participating in the Adolescent Alcohol Prevention Trial revealed that normative education significantly delayed the onset of alcohol use across the eighth, ninth, and tenth grades among public school students. A similar but somewhat less robust pattern was found for cigarette use. These results suggest that self-report bias does not account for previous findings and demonstrate rather convincingly that normative education is an effective drug prevention strategy for public school settings. Donalson, S.I., Thomas, C.W., Graham, J.W., Au, J.G. and Hansen, W.B. Verifying Drug Abuse Prevention Program Effects Using Reciprocal Best Friend Reports. Journal of Behavioral Medicine, 23(6), pp. 585-601, 2000.

Effectiveness of Monetary Incentives for Recruiting Adolescents to an Intervention Trial to Reduce Smoking

This study's objective was to evaluate the effect of monetary incentives on response rates of adolescents to a smoking-related survey as the first step toward participation in an intervention trial. A sample of 4,200 adolescent members of a managed care organization were randomized to one of four incentive groups: a $2 cash group, a $15 cash group, a $200 prize drawing group, or a no-incentive group. Group-specific response rates and willingness to be contacted about future study activities were compared. Incentives increased survey response rates (55% response without incentive verses a 69% response with incentives), with response of 74% in the $15 cash group, 69% in the token group, and 63% with a prize incentive. Incentives did not adversely affect willingness of adolescents to be contacted about a smoking intervention, (65% willing with incentives verses 60% without). In terms of costs per additional survey completed, token and prize groups were marginally more expensive than the no-incentive group ($0.40 and $1.42, respectively) while the large cash incentive was substantially more costly ($11.37). Monetary incentives improve response rates to a mailed survey, without adverse impact on willingness to further participate in intervention activities. However, a variety of issues must be considered when using incentives for recruitment to intervention studies. Martinson, B.C., Lazovich, D., Lando, H.A., Perry, C.L., McGovern, P.G. and Boyle, R.G. Effectiveness of Monetary Incentives for Recruiting Adolescents to an Intervention Trial to Reduce Smoking. Preventive Medicine, 31(6), pp. 706-713, 2000.

Television Campaigns Impact Adolescent Marijuana Use

This study evaluated the effectiveness of targeted televised public service announcement campaigns in reducing marijuana use among sensation-seeking adolescents. Sensation-seeking has been identified as a personality characteristic associated with the need for novel, complex, ambiguous, and emotionally intense stimuli and the willingness to take risks to obtain such stimulation. People ranked high on the need for sensation are more associated with the risk for drug use than those ranked low. This study designed special advertising to address sensation-seekers with anti-marijuana messages. Two televised anti-marijuana campaigns were conducted in 1 county and 1 campaign in the comparison community. Personal interviews were conducted with 100 randomly selected teenagers monthly in each county for 32 months. All 3 campaigns reversed upward developmental trends in 30-day marijuana use among high-sensation seekers. As expected, low-sensation seekers had low use levels and no campaign effects were evident. Televised campaigns with high reach and frequency that use PSAs designed for and targeted at high-sensation-seeking adolescents can significantly reduce substance use in this high-risk population. Palmgreen, P., Donohew, L., Lorch, P., Hoyle, R.H. and Stephenson, M.T. American Journal of Public Health, 91(2), pp. 292-296, 2001.

Ethnic Identity Among Early Adolescents

A measure of ethnic identity, the Multigroup Ethnic Identity Measure (MEIM; J.S. Phinney, 1992), was examined with a sample of 2,184 11-15 yr olds who self-identified with a single race or ethnic group (mono-racial, n=1,812) or with 2 or more racial or ethnic groups (multi-racial, n=372). The psychometric properties and mean differences on the MEIM for White, mono-racial minority, and multi-racial early adolescents were investigated. Two factors were identified: (1) identification and (2) exploration. Identification was represented by items that reflect a sense of belonging and pride in an individual's ethnic group. Exploration was represented by items that characterize a search for ethnic group identity and participation in ethnic practices. Results show reliabilities for the 2 subscales with alpha = .84 for most individuals from mono-racial minority groups and multi-racial subgroups scored similarly on overall ethnic identity. Spencer, M.S., Icard, L.D., Harachi, T.W., Catalano, R.F., and Oxford, M. Ethnic Identity among Mono-racial and Multi-racial Early Adolescents. J. Early Adolescence 20(4), pp. 365-387, 2000.

Predictors of Early High School Dropout

This study compared the adequacy of 5 theories for predicting dropping out of high school before grade 10. These theories include full mediation by academic achievement and direct effects related to general deviance, deviant affiliations, family socialization, and structural strains. Models were used to test these theories on prospective data from an ethnically diverse urban sample. Poor academic achievement mediated the effect of all independent factors, although general deviance, bonding to antisocial peers, and socioeconomic status also retained direct effects on dropping out. Therefore, none of the theories were fully adequate to explain the data, although partial support was obtained for each theory. Battin-Pearson, S., Newcomb, M.D., Abbott, R.D., Hill, K.G., Catalano, R.F., and Hawkins, J. D. Predictors of Early High School Dropout: A Test of Five Theories. J. Educational Psychology 92(3), pp. 568-582, 2000.

Male Adolescent Friendships and Aggression Toward Female Partners

Deviancy training was examined as a risk factor for physical and psychological aggression toward a female partner among boys and young men in the Oregon Youth Study. Hostile talk about women during videotaped male friendship interactions was hypothesized to indicate a process by which aggression toward women is reinforced within male peer networks with both antisocial behavior and hostile talk being predicted to be associated with later aggression toward a female partner. Prospective developmental models were tested from 9-20 years of age through young adulthood. Findings indicated that the relation of deviant peer association in adolescence and later aggression toward a partner was mediated by antisocial behavior; observed hostile talk about women with male peers explained additional variance in aggression toward a partner. Aggression Toward Female Partners by At-Risk Young Men: The Contribution of Male Adolescent Friendships. Capaldi, D.M., Dishion, T.J., Stoolmiller, M., and Yoerger, K. Dev. Psych., 37(1), pp. 61-73, 2000.

Deviant Friendships and Problem Behavior

This study examines adult reports of externalizing and internalizing psychopathology at home and school in a sample of 224 high-risk adolescent boys and girls (mean age 12 yrs). Four groups of young adolescents were defined, based on the consistency of teacher and parent Child Behavior Checklist reports: normal, internalizing, externalizing only, and co-morbid. Group comparisons revealed the co-morbid and externalizing groups were more engaged in a deviant peer group and were observed in higher levels of deviancy training with their friends, compared to other young adolescent groups. In general, elevated levels of arrest, drug use, and sexual promiscuity were associated with cross-setting consistency in externalizing disorders. Co-morbid youth, however, showed the highest levels of sexual promiscuity in middle adolescence, compared to all other groups. These findings are consistent with a developmental account of adolescent maladjustment and suggest that emotional disturbance in early adolescence might exacerbate youth vulnerability, especially to deviancy training within friendships. Dishion, T.J. Cross-Setting Consistency in Early Adolescent Psychopathology: Deviant Friendships and Problem Behavior Sequelae. J. Personality, 68 (6), pp. 1109-1126, 2000.

Family Engagement in Preventive Interventions

There has been limited investigation of family engagement in preventive interventions for general populations. Families in eligible general populations can differ to a significant degree in intervention preferences and beliefs that influence their motivation to engage in interventions or in intervention evaluations. Also, a number of stable family member characteristics, such as internalizing/externalizing problems, have not been predictive of family engagement. Educational attainment has been predictive, but the differences between participants and non-participants tend to be small. In addition, there are several common barriers to engagement, including family scheduling conflicts, which

place practical limits on participation levels and need to be carefully addressed through engagement techniques. Spoth, R. and Redmond, C. J. Research on Family Engagement in Preventive Interventions: Toward Improved Use of Scientific Findings in Primary Prevention Practice. Primary Prevention, 21(2), pp. 267-284, 2000.

Influences on Enrollment in Family-Focused Prevention Research

This study is an extension of a previously supported model of family context and health belief predictors of parents' inclination to enroll in preventive interventions. The extended model addresses limitations in the prior investigation: i.e. the role intervention-related beliefs and stated inclinations to actually enroll in a skills training intervention research project. Model testing was conducted with a sample of 635 parents of 6th graders who completed a prospective participation factor survey and were recruited for an intervention research project 6 months later. All but one of the primary hypothesized effects were supported. Both stated inclination to enroll in an intervention and in the research project had significant positive effects on actual project enrollment occurring 6 months later. Perceived intervention benefits and barriers had significant effects on both types of stated inclination to enroll. The model also suggests an additional path linking educational attainment with actual enrollment. Spoth, R., Redmond, C., and Chungyeol, S. Modeling Factors Influencing Enrollment in Family-Focused Preventive Intervention Research. Prevention Science, 1(4), pp. 213-226, 2000.

Community Readiness

Communities are at many different stages of readiness for implementing drug abuse prevention programs, and this readiness is a major factor in determining whether a local program can be effectively implemented and supported by the community. The community readiness model was developed to meet research needs (e.g., matching treatment and control communities for an experimental intervention) as well as to provide a practical tool to help communities mobilize for change. The model defines 9 stages of community readiness ranging from "no awareness" of the problem to "professionalization" in the response to the problem within the informant interviews, with questions on 6 different dimensions related to a community's readiness to mobilize to address a specific issue. Edwards, R.W., Jumper-Thurman, P., Plested, B.A., Oetting, E.R., and Swanson, L. Community Readiness: Research to Practice. J. Community Psychology, 28(3), pp. 291-307, 2000.

Methods to Decrease Attrition in Longitudinal Studies with Adolescents

This article presents a summary of methods to decrease attrition in longitudinal school-based studies conducted with adolescents beginning junior high schools or middle schools. These include collection of contact information about students, additional days to collect data from absentee students, data collection in new high schools once students graduate from junior high schools or middle schools, sending questionnaires by mail, and conducting telephone or home interviews. Epstein, J.A. and Botvin, G.J. Methods to Decrease Attrition in Longitudinal Studies with Adolescents. Psychological Reports, 87 (1), pp. 139-140, 2000.

Predicting Regular Cigarette Use Among Continuation High School Students

The objective of this study was to provide a 1-year prospective examination of social, behavioral, intrapersonal and demographic factors that predict transition from experimental to regular cigarette use among continuation high school students. A cohort of 252 students completed baseline and 1-year followup questionnaires on health behaviors. Results showed relatively low smoking prevalence estimates, intention to smoke in the next year, violence perpetration, perceived stress, sensation seeking, and male gender predicted the transition to regular use 1 year later. It was concluded that intrapersonal variables may be relatively important in predicting the progression from experimental to regular smoking. Skara, S., Sussman, S., and Dent, C.W. Predicting Regular Cigarette Use among Continuation High School Students. American Journal of Health Behavior, 25(2), pp. 147-156, 2001.

Concurrent Prediction of Drug Use Among High-Risk Youth

Correlates of drug use were examined in a continuation high school sample (n = 1.315), using canonical correlation analysis. Fourteen demographic, attitude/belief. and psychosocial pressure/anxiety-type variables were included as concurrent predictors. Eight drug-use-related measures were also placed into the analysis as outcome variables. Two factors were revealed. White ethnicity, not being Latino, all attitude/belief measures, and family conflict and depression showed relatively high loadings on the first predictor factor, and were associated with all drug-use measures. Latino ethnicity and being relatively unacculturated (i.e., tending to speak Spanish), most of the attitude/belief measures (but not sensation seeking or spirituality), and perceived peer approval to use drugs, trait anxiety, and depression showed relatively high loadings on the second predictor factor, and were associated with the hard-drug-use measures. These results suggest that there is a subgroup of unacculturated Latino youth who are

anxious, who perceive they will achieve peer approval by using drugs, and who tend to use hard drugs. Indicated drug abuse prevention strategies may need to be tailored to this subgroup when developing and implementing programming. McCuller, W.J., Sussman, S., Dent, C.W., and Teran, L. Concurrent Prediction of Drug Use Among High-Risk Youth. Addictive Behaviors, 26(1), pp. 137-142, 2001.

Implications of Aggressive Children's Positively Biased Relatedness Views for Future Relationships

The present study examined the tendency of aggressive children to generalize the positive bias in their perceptions of relatedness across different interpersonal relationships. Secondly, it examined the implications of distorted perceptions of relatedness for quality of aggressive children's future relationships. Subjects included 62 second and third grade children nominated and rated by teachers as aggressive. Self- and others' appraisals of relationship quality were gathered across four interpersonal domains (i.e., mother, teacher, mentor, and peer). Children's positively biased perceptions of social relatedness were concordant across adult relationship domains but not across the peer domain, suggesting that children's relationships with adults and peers represent somewhat distinct socialization contexts. As expected, children who inflate levels of social relatedness establish less close relationships with novel partners (mentors). The findings emphasize the need for clinicians to focus on mental representations while planning interventions with aggressive children. Prasad-Gaur, A., Hughes, J.N., and Cavell, T. Implications of Aggressive Children's Positively Biased Relatedness Views for Future Relationships. Child Psychiatry and Human Development, 31(3), pp. 215-231, 2001.

Social Cognitive Differences Between Aggressive-Rejected and Aggressive-Nonrejected Children

This study investigated differences in social cognitive processing between 2 subtypes of aggressive children: those rejected by their peers and those not rejected. Children in Grades 2-4 classified as aggressive-rejected (AR; n = 34) or aggressive-nonrejected (AN; n = 55), on the basis of teacher ratings of aggression, were administered the Social Cognitive Assessment Profile--Revised (SCAP--R) as a measure of attribution, solution type, outcome expectancy, and self-efficacy for aggressive solutions. The results indicate that aggressive children, in general, have a broad range of social cognitive deficits and distortions. Further, AN children are more likely to believe that aggression leads to positive outcomes and are more confident in their ability to use aggression toward a peer. The pattern of social cognitive differences between AR and AN children is similar to that typically found between proactively and reactively aggressive children. Also AN children appear to have a distinct pattern of social cognitive biases that reflect antisocial beliefs likely to support the use of aggression to obtain desired goals. Yoon, J.S., Hughes, J.N., Cavell, T.A., and Thompson, B. Social Cognitive Differences Between Aggressive-Rejected and Aggressive-Nonrejected Children. Journal of School Psychology, 38(6), pp. 551-570, 2000.

Patterns and Temporal Changes in Peer Affiliation Among Aggressive and Nonaggressive Children

The behavior and affiliation patterns of 118 highly, moderately, and nonaggressive 7-8 yr old children were examined over the course of a 6-week summer school program. During free play, participants did not selectively associate on the basis of behavioral similarity, but initial mutual friendship choices did show a preference for similarly behaved peers. Nonreciprocated friendships at the beginning and end of the program and mutual friendships at the end revealed a preference of all children to befriend non aggressive peers. Moderately aggressive children increased their number of mutual friendships and their association with nonaggressive peers during free play, whereas highly aggressive children lost mutual friends. The aggressiveness of a child's playmates predicted the likelihood of that child behaving inappropriately during free play. Results suggest that selective affiliation may be the result of peer rejection rather than an active process of seeking similarly aggressive peers. Hektner, J.M., August, G.J., and Realmuto, G.M. Patterns and Temporal Changes in Peer Affiliation Among Aggressive and Nonaggressive Children Participating in a Summer School Program. Journal of Clinical Child Psychology, 29(4), pp. 603-614, 2000.

Clinical Correlates of Heavy Tobacco Use Among Adolescents

Investigators affiliated with the CEDAR Center at the University of Pittsburgh conducted a study to determine the clinical factors differentiating adolescents with heavy smoking (10 cigarettes/day) from adolescents with light smoking. A study group of 812 adolescents were recruited from adolescent alcoholism treatment centers and from the community. Logistic regression analyses demonstrated that adolescents with heavy smoking, compared with adolescents with light smoking, were significantly more likely to be Caucasian American and to exhibit drug-use disorders, alcohol-use disorders, and conduct disorder. The findings suggest that the clinical correlates of heavy

smoking among adolescents are generally similar to those for smoking at any level (vs. nonsmokers), except that heavy smoking is more strongly associated with Caucasian American ethnicity. Also, depressive disorders were associated with smoking at any level in the sample, but depressive disorders were not associated with heavy smoking. Cornelius, J.R., Lynch, K., Martin, C.S., Cornelius, M.D., and Clark, D.B. Clinical Correlates of Heavy Tobacco Use Among Adolescents. Addictive Behaviors, 26, pp. 273-277, 2001.

Tobacco Use Among Argentinean High School Students

This study assessed the prevalence and correlates of tobacco use among high school students in Buenos Aires, Argentina. Anonymous, self-administered questionnaires were given to 3,909 8th and 11th graders in a stratified random sample of 49 public and private schools. The instrument included items from American surveys, translated and validated among Argentinean teens. Multiple logistic regression analysis was used to estimate possible effects on smoking behavior of environment, students' personal characteristics, and their knowledge, beliefs, and attitudes regarding smoking. Of 8th and 11th graders, 20% and 43%, respectively, were classified as current smokers. Overall, 29% of males and 32% of females were current smokers. Students attending public schools were more likely to smoke than those in private schools ($p < .05$). Current smoking was associated with having a best friend who smokes, reporting that more than 50% of friends of the same sex smoke, having positive attitudes and beliefs toward smoking, and having a positive intention to smoke within the next year (all $p < .001$). Over 20% of the 8th graders in our sample were current smokers; prevention efforts must therefore start early. Morello, P., Duggan, A., Adger, H. Jr, Anthony, J.C., and Joffe, A. Tobacco Use Among High School Students in Buenos Aires, Argentina. American Journal of Public Health, 91(2), pp. 219-224, 2001.

Drug Use By Adolescent Mexican Americans and Adolescents in Mexico

Investigators at UCLA compared high school students in Baja California Norte (BCN), Mexico (n = 775), with Mexican American students in Los Angeles (LA), California (n = 516). The students' use of cigarettes, alcohol, marijuana, cocaine, inhalants, and other illicit drugs were compared, because these vary by gender, country, and their age of first drug use and are influenced by demographic variables, individual characteristics, and environmental influences. More BCN students than LA students had used alcohol, but more LA than BCN students had used illicit drugs and initiated drug use earlier. When demographic variables were influential, they were most powerful and increased the risk for drug use more than environmental factors or individual characteristics. Environmental factors were most influential for boys' drug use, whereas environmental and demographic variables were most influential for girls' drug use. Felix-Ortiz, M., Villatoro-Velazquez, J.A., Medina-Mora, M.E., and Newcomb, M.D. Adolescent Drug Use in Mexico and Among Mexican American Adolescents in the United States: Environmental Influences and Individual Characteristics. Cultural Diversity and Ethnic Minority Psychology, 7(1), pp. 27-46, 2001.

Modeling Suspected Influences on Youthful Drug Involvement

In longitudinal behavioral studies it is common to have multiple categorical indicators for measuring a theoretical construct of interest. In this study, researchers at Johns Hopkins illustrate the application of a latent class model that accounts for the structure in a set of correlated, categorical variables measured at discrete time periods, drawing information from these variables to form a smaller number of latent classes. The dependence of the resulting latent class model parameters on suspected factors over time is simultaneously modeled using a baseline-category logistic regression model. Estimation of the model parameters is achieved using an estimating equations procedure. A motivating example is provided from a longitudinal study of suspected linkages between monitoring or supervision by parents and the occurrence of drug use behaviors in an epidemiologic sample of school-attending youths. The latent class analyses extracted three subgroups representing youths in different stages of drug involvement. At the beginning of the study, the cohort of 8 to 10 year olds with little or no drug involvement were the most prevalent subgroup. By the end of the study, when these youths were 11 to 13 years old, the majority of youths had not only tried alcohol but had opportunities to use tobacco cigarettes, marijuana and inhalants. The model showed that drug involvement developed over time, starting with alcohol and then progressing to opportunity to use tobacco cigarettes, use of cigarettes, and finally opportunities to use internationally controlled drugs such as marijuana. These results are consistent with the model proposed by Kandel of stages of drug use, but in addition, the results provide evidence that opportunity to use drugs deserves consideration in the pathway leading toward serious drug involvement. Reboussin, B.A. and Anthony, J.C. Latent Class Marginal Regression Models for Modeling Youthful Drug Involvement and its Suspected Influences. Statistics in Medicine, 20(4), pp. 623-639, 2001.

Correlates of Mental Health Service Utilization and Unmet Need Among Male Adolescents

Researchers at the University of Pittsburgh sought to identify the correlates of mental health services utilization and unmet need for these services among a sample of adolescent males. They hypothesized that their findings would

replicate and extend those of the recent Methods for the Epidemiology of Child and Adolescent Mental Disorders (MECA) study, which found that parental factors play a major role in their children's unmet mental health care needs. The study involved an evaluation of mental health service utilization and unmet need during the prior 2 years, as reported by the subjects at a follow-up assessment at age 16. Four factors were found to predict increased mental health services utilization, including attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) among the adolescent males, the father's alcohol use disorder, and the mother's amphetamine use disorder. One factor was found to predict decreased utilization, the father's cannabis use disorder. Four factors significantly predicted unmet treatment need, including conduct disorder, the mother's amphetamine use disorder, a higher number of siblings, and a parental history of having had a childhood anxiety disorder. The results of this study suggest that parental psychopathology, parental substance abuse, the presence of conduct disorder, and an increased number of siblings act as barriers to adequate mental health treatment among adolescents. These findings confirm the crucial role that parental factors play in the treatment utilization and the unmet treatment need of their children, and also suggest that an increased number of siblings can also be associated with unmet treatment need. Cornelius, J.R., Pringle, J., Jernigan, J., Kirisci, L., and Clark, D.B. Correlates of Mental Health Service Utilization and Unmet Need Among a Sample of Male Adolescents. Addictive Behaviors, 26(1), pp. 11-19, 2001.

Developmental Factors in Liability to Adolescent Substance Use Disorders

Investigators at CEDAR reviewed the literature on the complex sequence of maturational, psychosocial, and neuroadaptive processes that lead to substance use disorders (SUD) in adolescence and constructed a synthesis of findings. After introducing the concepts of liability to SUD and epigenesis, they present a theory of how affective, cognitive, and behavioral dysregulation in late childhood is exacerbated during early and middle adolescence by family and peer factors, as well as puberty, leading to substance use. Continued exacerbation of the three components of dysregulation by drug and non-drug stressors during late adolescence is posited to result in neuroadaptations that increase the likelihood of developing SUD, particularly in high-risk individuals. Implications for etiologic research as well as clinical and preventive interventions are discussed. Dawes, M.A., Antelman, S.M., Vanyukov, M.M., Giancola, P., Tarter, R.E., Susman, E.J., Mezzich, A., and Clark, D.B. Developmental Sources of Variation in Liability to Adolescent Substance Use Disorders. Drug and Alcohol Dependence, 61(1), pp. 3-14, 2000.

Role of Conduct Disorder in Neuropsychological Deficits in Female Adolescents with Substance Use Disorder

CEDAR-affiliated researchers sought to determine whether neuropsychological deficits in female adolescents are more closely related to a diagnosis of a substance use disorder (SUD) or a conduct disorder (CD). Subjects were 470 female adolescents between the ages of 14 and 18 years. They were categorized into one of four groups: (1) SUD-only (n =63), (2) CD-only (n = 58), (3) SUD+CD (n = 239) and (4) normal control (n = 110). The groups were compared on multiple neuropsychological measures covering four cognitive domains: general intelligence, executive functioning, language competence and academic achievement. The findings were consistent across all measures. Multivariate analyses of variance revealed significant group differences for all four neuropsychological domains. Univariate tests indicated that the two CD groups equally exhibited the poorest performance of all four groups on nearly all measures of intelligence, executive functioning, language competence and academic achievement. The SUD-only group performed better than the two CD groups but not as well as the control group. Socioeconomic status and chronological age were statistically controlled for in all analyses. These findings suggest that the neuropsychological deficits in this sample of female adolescents with SUD are more closely related to CD, or antisociality in general, than to SUD. Future studies assessing the neuropsychological functioning of persons with SUD should make efforts to measure comorbid antisociality. Giancola, P.R. and Mezzich, A.C. Neuropsychological Deficits in Female Adolescents with a Substance Use Disorder: Better Accounted for by Conduct Disorder? Journal of Studies on Alcohol, 61(6), pp. 809-817, 2000.

Antisociality, Substance Dependence, and the DRD5 Gene

Researchers at the University of Pittsburgh reported a pilot population-based study of a microsatellite polymorphism at the DRD5 locus in adult European-Americans that showed its association with childhood symptom counts for oppositional defiant disorder (ODD) in males and females and adult antisocial personality disorder (ASPD) in females. No association with childhood conduct disorder symptom count was observed. ODD mediated the genotype-ASPD relationship in females. Neither ODD nor ASPD significantly mediated the relationship between the genotype and the liability to substance dependence (SD). The data suggest involvement of the DRD5 locus in the variation and sexual dimorphism of SD liability and antisociality and in the developmental continuity of antisociality. Vanyukov, M.M., Moss, H.B., Kaplan, B.B., Kirillova, G.P., and Tarter, R.E. Antisociality, Substance Dependence, and the DRD5 Gene: A Preliminary Study. American Journal of Medical Genetics, 96(5), pp. 654-658, 2000.

"Recanting" Prior Drug Use Reports in a Longitudinal Survey

Investigators at the University of Illinois at Chicago examined follow-up data from surveys in 1988, 1992 and 1994 in order to estimate the prevalence and explore the correlates of retest artifact (denial) of drug use among National Longitudinal Survey of Youth respondents who disclosed lifetime cocaine or marijuana use in 1984. In the cocaine use cohort, 42% denied lifetime cocaine use during at least one follow-up wave. In the marijuana use cohort, about 29% denied lifetime marijuana use during at least one follow-up wave. Denial either leveled off (cocaine) or diminished (marijuana) between the second and third follow-up interviews. The most consistent predictors of denial in both longitudinal and cross-sectional models and across substances were race/ethnicity (black informants had increased rates of denial) and marital status (married respondents had increased rates of denial). Other predictors of denial included interviewer characteristics (social attribution), interview mode, and drug salience. The findings with respect to marijuana reporting trends parallel increased willingness of public officials to retrospectively disclose this behavior in the popular press. Fendrich, M. and Kim, J.Y.S. Multiwave Analysis of Retest Artifact in the National Longitudinal Survey of Youth Drug Use. Drug and Alcohol Dependence, 62, pp. 239-253, 2001.

Bystander Effects in CASI and PAPI Surveys of Substance Use

In a special issue of Substance Use and Misuse devoted to methodological issues in measurement of drug use, researchers at the University of Wisconsin at Madison reported an investigation of the influence of bystanders on self-administered interviews asking about the use of alcohol and illicit drugs. Interview participants were adolescents and young adults living in urban and suburban areas of the United States. Participants were assigned randomly to either a computerized or a paper-and-pencil self-administered interview. Results show that the impact of bystanders during the interview varies according to the identity of the bystander, age of the person interviewed, and the mode of interview. When a parent was present during the interview, survey participants were less likely to report the use of alcohol and marijuana. The influence of parents was stronger for adolescents than for young adults. The use of computer-assisted self-administered interviewing, compared to interviews with paper-and-pencil forms, reduced the effects due to the presence of parents during the interview. The presence of siblings during the interview had a small, negative effect on reports of using alcohol or illicit drugs. Among married or cohabiting respondents, the presence of the husband, wife, or live-in partner had no influence on reports of alcohol use or drug use. Aquilino, W.S., Wright, D.L., and Supple, A.J. Response Effects Due to Bystander Presence in CASI and Paper-and-Pencil Surveys of Drug Use and Alcohol Use. Substance Use & Misuse, 35(6-8), pp. 845-867, 2000.

The Association Between Cigarette Smoking and Drug Abuse in the United States

Cigarette smoking has been identified as an independent risk factor for many human diseases. However, the association between cigarette smoking and illegal drug use has not been thoroughly investigated. Investigators have analyzed the 1994 National Household Survey on Drug Abuse to clarify whether cigarette smoking has any effect on the initiation of illegal drug use. Data from 17,809 respondents completing the 1994 "new" (1994-B) questionnaire were analyzed. Logistic regression analyses were performed with the use of statistical package SUDAAN, taking into consideration the multistage sampling design. The results show that those who had smoked cigarettes were far more likely to use cocaine (OR = 7.5; 95% CI: 5.7-9.9), heroin (OR = 16.0; 95% CI: 6.8-37.9), crack (OR = 13.9; 95% CI: 7.9-24.5) and marijuana (OR = 7.3; 95% CI: 6.2-8.7). The associations are consistent across age-strata and remain after adjusting for race and gender. This study suggests that cigarette smoking may be a gateway drug to illegal drug use. Lai, S., Lai, H., Page, J.B., McCoy, C.B. The Association between Cigarette Smoking and Drug Abuse in the United States. J Addict Dis , 19(4) pp. 11-24, 2000.

Stalking as a Variant of Intimate Violence: Implications From a Young Adult Sample

There is a limited but growing literature which suggests that stalking is a variant of intimate violence. The purpose of this study was to examine physical, psychological, and stalking victimization and perpetration among males and females. Alcohol use was also examined. The sample was 46 male and 84 female undergraduate students who reported stalking victimization and perpetration after a difficult breakup, and psychological and physical victimization and perpetration during that specific relationship. Overall, 27% of the sample study was classified into the stalking victimization group, which is consistent with other stalking prevalence rates among college samples. For females, stalking victimization was significantly associated with physical and psychological abuse victimization. For males, stalking victimization was significantly associated with psychological abuse victimization. However, there was also a strong significant reciprocal relationship of stalking and psychological abuse victimization and perpetration, especially for males. Also, alcohol use was significantly associated with victimization and perpetration of stalking and psychological abuse for males. The data from this study contribute to the hypothesis that stalking is a variant of or extension of intimate violence, especially for females. Implications and recommendations for future research are discussed. Stalking as a Variant of Intimate Violence: Implications from a Young Adult Sample, Violence Vict, 15(1),

pp. 91-111, 2000.

Variation in Youthful Risks of Progression From Alcohol and Tobacco to Marijuana and to Hard Drugs Across Generations

Much research has documented that youthful substance use typically follows a sequence starting with use of alcohol or tobacco or both and potentially proceeding to marijuana and then hard drug use. This study explicitly examined the probabilities of progression through each stage and their covariates. A secondary analysis of data from the National Household Survey on Drug Abuse (1979-1997) was conducted with particular sensitivity to the nature of substance use progression, sampling procedures, and reliability of self-report data. Results showed that progression to marijuana and hard drug use was uncommon among persons born before World War II. The stages phenomenon essentially emerged with the baby boom and rose to a peak among persons born around 1960. Subsequently, progression risks at each stage declined. Progression risks were also higher among younger initiators of alcohol, tobacco, or marijuana use. The recent increase in youthful marijuana use has been offset by lower rates of progression to hard drug use among youths born in the 1970s. Dire predictions of future hard drug abuse by youths who came of age in the 1990s may be greatly overstated. Golub, A., and Johnson, B.D. Variation in Youthful Risks of Progression from Alcohol and Tobacco to Marijuana and to Hard Drugs Across Generations. Am J Public Health, 91(2), pp. 225-232 2001.

Trauma, Drugs and Violence Among Juvenile Offenders

Trauma typically occurs when one experiences a situation where life has been threatened or lost. If the trauma is not resolved, negative residual effects may result in alcohol and drug use, involvement in violent activities as well as the development of mental health problems such as posttraumatic stress disorder (PTSD). This study examined the link between trauma, drug use, and violence among youth. Results from interviews with 414 juveniles remanded to the Office of Children and Family Services (formerly New York State Division For Youth) for assault, sexual assault, robbery or homicide, document the trauma experienced by these youth, as well as how it correlated with their drug usage and participation in violent, illegal activities. Discussion of these findings, their implications for understanding and intervening, and recommendations for future research are highlighted. Crimmins, S.M., Cleary, S.D., Brownstein, H.H., Spunt, B.J., Warley, R.M. Trauma, Drugs and Violence Among Juvenile Offenders. J Psychoactive Drugs, 32(1) pp. 43-54, 2000.

Perceived Risk of Cocaine Use and Experience with Cocaine Are Found to Cluster in U.S. Neighborhoods but Findings Do Not Hold for Larger Geographic Areas

Population-based data from six years of the National Household Surveys on Drug Abuse public use files were employed to study whether experience with cocaine and the perception of risk associated with cocaine use cluster within neighborhoods and cities in the U.S. The alternating logistic regressions model was used to quantify the extent of geographic concentration. Perceptions of the harm associated with cocaine use and actual experience with cocaine tend to cluster within neighborhoods; once within-neighborhood concentration is taken into account, there is little evidence of residual concentration with cities. Petronis, K.R., and Anthony, J.C. Perceived Risk of Cocaine Use and Experience With Cocaine: Do They Cluster Within US Neighborhoods and Cities?, Drug and Alcohol Dependence, 57, pp. 183-192, 2000.

Drug Use 50% More Common Among Households with Welfare Recipients

This study examined the prevalence of drug use in a nationally representative sample of 1,989 recipients and 6,840 nonrecipients of four welfare programs. Data from the 1995 National Household Survey on Drug Abuse (NHSDA) were analyzed using the conditional form of multiple logistic regression with matching of respondents on neighborhood of residence. Weighted proportions and variances accounting for the complex sample design of the NHSDA survey were estimated using the Taylor series linearization method. The results indicate that drug use is 50% more common in household with welfare recipients than in nonwelfare households. Programs making welfare eligibility dependent on the recipient's working toward a drug-free lifestyle are worth examining, although a vigilant eye must be kept on the potential unintended consequences. Delva, J., Neumark, Y.D., Furr, C.D.M., and Anthony, J.C. Drug Use Among Welfare Recipients in the U.S. American Journal of Drug Alcohol Abuse, 26(2), pp. 335-342, 2000.

Panama: Odds of Drug Use Among School-Attending Youths Increases When Another in Same School Uses Drugs

The first epidemiological investigation of clustering of tobacco, alcohol, inhalant, and other drug involvement has been conducted using data from Panama's 1996 National Youth Survey on Alcohol and Drug Use. Clustering was

estimated with the Alternating Logistic Regression method. Adjusted estimates of pair-wise cross-product ratios (PWCPR), a measure of clustering, show modest clustering (i.e., PWCPR >1.0) at the school level for tobacco smoking (PWCPR = 1.41; 95% confidence internal, CI = 1.22-1.64), alcohol consumption (PWCPR = 1.33; 95% CI = 1.22-1.45), use of inhalants, (PWCPR = 1.35; 95% CI = 1.07-1.69), and other drug use (PWCPR = 1.38; 95% CI = 1.14-1.68). These findings provide preliminary evidence that the odds of drug use among school-attending youths increase when another in the same school uses drugs, and suggest a new line of research on within-school diffusion that should include the identification of school-level factors that contribute to student drug use. Delva, J., Bobashev, G., Gonzalez, G., Cedeno, M, and Anthony, J.C. Clusters of Drug Involvement in Panama: Results from Panama's 1996 National Youth Survey. Drug and Alcohol Dependence, 60, pp 251-257, 2000.

Childhood Depression and Adult Personality Disorder

This study extends previous findings of the risks posed by childhood major depressive disorder and other psychopathological features for later personality disorder (PD) in a random sample of 551 youths. Self-reports and mother reports were used to evaluate DSM-III-R (Axes I and II) psychiatric disorders at mean ages of 12.7, 15.2, and 21.1 years. Logistic regression was used to examine the independent effects of major depressive disorder in childhood or adolescence on 10 PDs in young adulthood. Results indicate that the odds of dependent, antisocial, passive-aggressive, and histrionic PDs increased by more than 13, 10, 7, and 3 times, respectively, given prior major depressive disorder. Those effects were independent of age, sex, disadvantaged socioeconomic status, a history of child maltreatment, nonintact family status, parental conflict, preexisting PD in adolescence, and other childhood or adolescent Axis I psychopathological features, including disruptive and anxiety disorders. In addition, odds of schizoid and narcissistic PD increased by almost 6 times and odds of antisocial PD increased by almost 5 times given a prior disruptive disorder, and odds of paranoid PD increased by 4 times given a prior anxiety disorder. Personality disorders may represent alternative pathways of continuity for major depressive disorder and other Axis I disorders across the child-adult transition. Kasen, S., Cohen, P., Skodol, A.E., Johnson, J.G., Smailes, E. and Brook, J.S. Childhood Depression and Adult Personality Disorder: Alternative Pathways of Continuity. Arch. Gen. Psychiatry, 58(3), pp. 231-236, 2001.

Network Therapy for Addiction

Network therapy was developed as a specialized type of combined individual and group therapy to ensure greater success in the office-based treatment of addicted patients by using both psychodynamic and cognitive-behavioral approaches to individual therapy while engaging the patient in a group support network composed of family members and peers. This article outlines the role of group cohesiveness as a vehicle for engaging patients in this treatment; the patient's family and peers are used as a therapeutic network, joining the patient and therapist at intervals in therapy sessions. This network is managed by the therapist to provide cohesiveness and support, to undermine denial, and to promote compliance with treatment. The author presents applications of the network technique designed to sustain abstinence and describes means of stabilizing the patient's involvement. Some specific techniques discussed include ambulatory detoxification, disulfiram and naltrexone administration, relapse prevention, and contingency contracting. Also discussed are recent research on the use of psychiatric residents and counselors for treatment, and use of the Internet in dissemination. Galanter, M. and Brook, D. Network Therapy for Addiction: Bringing Family and Peer Support into Office Practice. Int J Group Psychother, 51(1), pp. 101-122, 2001.

Marijuana Use Among Black and Puerto Rican Adolescents

This study used a longitudinal design to assess the relationship between Black and Puerto Rican adolescent generational status (first generation vs. second generation) and specific psychosocial factors predicting later marijuana use. In addition, the interactive effects of adolescent generational status and psychosocial risk and protective factors on later marijuana use were assessed. Structured interviews were conducted with 108 Black males and females and 392 Puerto Rican males and females whose mean age at Time 1 and Time 2 was 14 and 19, respectively. Correlation analyses showed that various psychosocial variables (i.e., personality, family, peer, and the ecological setting) were related to later marijuana use. Regression analysis showed that the personality and family domains had a direct relationship with young adult marijuana use. In contrast, the impact of the generational status of the adolescent on later marijuana use was mediated by the psychosocial variables. The findings also indicated that the risk for drug use among second generation American adolescents (American-born children of immigrant parents) was offset by a number of protective factors stemming from the domains of personality, family, and ecology. Chappin, S.R., and Brook, J.S. The Influence of Generational Status and Psychosocial Variables on Marijuana Use among Black and Puerto Rican Adolescents. Hispanic Journal of Behavioral Sciences, 23(1), pp. 22-36, 2001.

Sex and Drug-related Risk Among Younger and Older Injection Drug Users in San Francisco

Dr. Kral and colleagues compared injection and sex-related risk behaviors of younger and older injection drug users (IDUs) in two adjacent neighborhoods. IDUs were recruited from street settings in two adjacent neighborhoods in San Francisco in April 1997. All participants were interviewed using a standardized questionnaire and were tested for HIV antibodies. Injection and sex related risk behaviors were compared between younger IDUs (<30 years old; n=56) and older IDUs (30 years or older; n=116). Younger IDUs were more likely to be white, be homeless, have injected amphetamines, and have been arrested in the past year. Older IDUs were more likely to be African American and smoke crack cocaine, and they had injected a mean of 18 years longer. Younger IDUs were more likely to have shared syringes in the past month (52% vs. 10%; $p<0.05$), report drug overdose in the past 15 months (39% vs. 7%; $p<0.05$), and to have had unprotected vaginal intercourse in the past 6 months (77% vs. 53%; $p<0.05$). After control of confounding factors using logistic regression analysis, all these associations remained significant. There is an urgent need for innovative prevention programs that target younger, homeless IDUs. Kral, A.H., Lorvick, J., and Edlin, B.R. Sex and Drug-related Risk Among Younger and Older Injection Drug Users in San Francisco. Journal of Acquired Immune Deficiency Syndromes, 24, pp. 162-167, 2000.

The Suspected Association Between Methamphetamine ('ice') Smoking and Frequent Episodes of Alcohol Intoxication: Data from the 1993 National Household Survey on Drug Abuse

Drs. Furr, Delva and Anthony at Johns Hopkins University estimated the strength of association between frequent episodes of alcohol intoxication and recent smoking of methamphetamine ('ice'). Using the 1993 National Household Survey on Drug Abuse, a total of 101 ice smokers were matched on neighborhood of residence to 816 non-smokers. Based upon conditional logistic regression analyses, persons with daily episodes of alcohol intoxication were estimated to have been five times more likely to smoke ice, as compared with non-drinkers or drinkers with little or no history of alcohol intoxication. This estimate includes statistical adjustment for potential confounders (e.g. age, sex) and was statistically significant ($P=0.01$). The association between frequent alcohol intoxication and 'ice smoking' offers an intriguing lead for a broad range of new research. Furr, C.D., Delva J., and Anthony J.C. The Suspected Association Between Methamphetamine ('ice') Smoking and Frequent Episodes of Alcohol Intoxication: Data from the 1993 National Household Survey on Drug Abuse. Drug Alcohol Depend., 59(1)10, pp. 89-93, 2000.

The Use of the Case-Crossover Design in Studying Illicit Drug Use

Drs. Wu and Anthony, using a case-crossover design, studied time-varying exposures that cause transient excess risk of acute health events. It is a variant of case-control and subject-as-own-control research designs, involving use of information about exposure history of each case to estimate the transient effect. This design can help to reduce sampling bias otherwise introduced in the selection of controls, as well as confounding bias that might be derived from enduring individual characteristics, especially personality traits and other long-standing inherited or acquired vulnerabilities. Authors found that when the subject is used as his or her own control, these personal vulnerabilities can be matched. In this paper they discuss strengths and weaknesses of the case-crossover design and suggest applications of the case-crossover design in epidemiologic studies on suspected hazards of illicit drug use, and in studies of drug use and co-occurring psychiatric disturbances. They conclude that the case-crossover design can play a useful role, but it discloses a need to secure fine-grained measurements in epidemiologic research on psychiatric comorbidity. As explained in the paper, they believe the case-crossover method may be of use to several disciplines: criminologists who study the drugs-crime nexus; services researchers; clinicians who seek to understand treatment entry and compliance behavior; and to etiologists interested in polydrug use. Wu, L.T., and Anthony, J.C., The Use of the Case-Crossover Design in Studying Illicit Drug Use. Substance Use Misuse. May-Jun, 35(6-8), pp. 1035-1050, 2000.

Differential Recall of Intimate Partner Violence

Research on intimate partner violence (IPV) has found that partners often do not agree about the occurrence of IPV, with abusive male partners reporting lower levels than their abused female partners. Among the reasons suggested for these differences are: denial or self-deception, fear of legal sanctions, and gender differences in recall of interpersonal events. This qualitative study focused on the factors that account for gender differences in recall of male-to-female partner conflict. Interviews were conducted with battered women recruited from a shelter, male batterers in an intervention program, and equal numbers of men and women recruited from the community who had no history of IPV in their relationships. Subjects were asked an open-ended questionnaire and then asked questions based on their response. The main results of this study indicate that participants believe that women remember more than men, both choose what they want to remember, and both remember that they were right in the conflict. Participants suggested that women tend to focus on the emotional aspects of a fight and remember fights longer. 19% of respondents suggested that substance abuse might contribute to distorted recollections of partner violence.

The female victims group, in particular, mentioned the intentional forgetting of fights. The overall significance of this study is that it suggests mechanisms underlying partner disagreement about IPV that have not previously been considered. Armstrong, T.G., Heiderman, G., Corcoran, K.J., Fisher, B., Medina, K.L. and Schafer, J. Disagreement About the Occurrence of Male-to-Female Intimate Partner Violence: A Qualitative Study. J. Fam. Comm. Health, 24(1), pp. 55-75, April 2001.

Partner Violence Among Mexican American Women

The prevalence of intimate partner violence (IPV) and associated risk and protective factors among Mexican-American women was studied using data from a cross-sectional household survey of U.S. residents of Mexican origin. The analysis includes data from women who were involved in an intimate relationship with a male partner and who answered questions about violence (n=1155). Approximately two fifths of the women were U.S. born. The self-reported prevalence of physical abuse by a current partner was 10.7%. Multivariate analysis showed that U.S birthplace, young age, urban residence, and having 4 or more children were associated with physical abuse. Social support and regular church attendance were protective. A consistent association was found between IPV and higher acculturation, e.g., years in U.S., country of schooling, dominant language. It is suggested that aspects of traditional Mexican culture may serve a protective function for families. Lown, E.A. and Vega, W.A. Prevalence and Predictors of Physical Partner Abuse among Mexican-American Women, A. J. Pub. Health, 91, pp. 441-445, 2001.

Community Level Effects on Prevalence of Substance Use During Pregnancy

Multilevel logistic regression models were used to analyze individual and community correlates of prenatal substance use. This study analyzed a subset of data from the California Perinatal Substance Exposure Study (PSE), the subjects in this study (n=10,611) are the subset of women identified as white, non-Hispanic (n=10,611) and Black/African-American (n=2,669) from the larger multiethnic sample (n=29,494); Latinas were not included in this study. Using census data, the proportion of zip code residences receiving public assistance was attached to each respondent's data in the PSE data file. Analyses showed that, except for alcohol, levels of neighborhood public assistance had an independent, significant effect on prevalence of substance use; increasing levels of neighborhood poverty increased the likelihood of a pregnant woman testing positive. Black women had higher predicted prevalence rates for alcohol and cocaine, while White women had higher predicted risks for tobacco, marijuana, and amphetamines. After controlling for neighborhood public assistance levels, no racial differences were seen in the category overall illicit drug use or opiate use. Future more detailed studies are needed to determine if neighborhood poverty effects on substance use are due to compositional effects, e.g., greater access to drugs, greater overall deviance, etc. or contextual factors, e.g., increased stresses associated with poor housing, lack of social services, etc. Finch, B.K., Vega, W.A., and Koldny, B. Substance Use During Pregnancy in the State of California, USA, Soc. Sci. Med. 52, pp. 571-583, 2001.

High Potency Marijuana Use Among Urban Youth

This paper describes cultural factors associated with the use of high-potency marijuana among inner-city youth in a midsized northeastern city. The investigators note that while high-potency marijuana has been available and used nationally for over a decade, surveys of drug use do not include items on what "new marijuana" contains and how and under what circumstances it is used. This paper, based on data from an ethnographic and epidemiological study of pathways to heavy drug use among youth and young adults, examines the sociocultural context of new marijuana use as an emergent trend. After considering the street market for high-potency marijuana, social rituals and meanings surrounding its distribution and use, and links with hip hop culture, the paper concludes with a critical analysis of the ways in which the drug market drives drug sales, drug use and drug-use sequencing in inner-city neighborhoods. Schensul, J.J., Huebner, C., Singer, M., Snow, M., Feliciano, P., and Broomhall, L. The High, the Money, and the Fame: The Emergent Social Context of "New Marijuana" Use among Urban Youth. Medical Anthropology, 18, pp. 389-414, 2000.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Research Findings

Services Research

Persistence of Impaired Functioning and Psychological Distress after Medical Hospitalization for Men with Co-occurring Psychiatric and Substance Use Disorders

The objective of this study was to measure the persistence of impaired health-related quality of life (HRQL) and psychological distress associated with co-occurring psychiatric and substance use disorders in a longitudinal sample of medically hospitalized male veterans. A random sample was followed observationally for 1 year after study enrollment. The study setting included inpatient medical and surgical wards at three university-affiliated Department of Veterans Affairs Medical Centers. Patients/participants comprised a random sample of 1,007 admissions to medical and surgical inpatient services, excluding women and admissions for psychiatric reasons. A subset of participants (n = 736) was designated for longitudinal follow-up assessments at 3 and 12 months after study enrollment. This subset was selected to include all possible participants with study-administered psychiatric diagnoses (52%) frequency-matched by date of study enrollment to approximately equivalent numbers of participants without psychiatric diagnoses (48%). All participants were administered a computerized, structured psychiatric diagnostic interview for 13 psychiatric disorders (including substance use) and received longitudinal assessments at 3 and 12 months on a multidimensional measure of HRQL, the SF-36, and a measure of psychological distress, the Symptom Checklist, 90-item version. On average, HRQL declined and psychological distress increased over time ($P < .05$). Psychiatric disorders were associated with significantly greater impairments in functioning and increased distress on all measures ($P < .001$) except physical functioning ($p < .05$). These results were replicated in the patients (n = 130) who received inpatient or outpatient mental health or substance abuse services. The authors concluded that general medical physicians need to evaluate the mental health status of their hospitalized and seriously ill patients. Effective mental health interventions can be initiated post-hospitalization, either immediately in primary care or through referral to appropriate specialty care, and should improve health functioning over time. Booth, B.M., Blow, F.C., and Cook, C.A.L. Journal of General Internal Medicine 16(1), pp. 57-65, January 2001.

Screening and Intervention for Illicit Drug Abuse - A National Survey of Primary Care Physicians and Psychiatrists

Illicit drug abuse causes much morbidity and mortality, yet little is known about physicians' screening and intervention practices regarding illicit drug abuse. The authors mailed a survey to a national sample of 2,000 practicing general internists, family physicians, obstetricians and gynecologists, and psychiatrists to assess their screening and intervention practices for illicit drug abuse. Of 1,082 respondents (adjusted response rate, 57%), 68% reported that they regularly ask new outpatients about drug use. For diagnosed illicit drug abuse, 55% reported that they routinely offer formal treatment referral, but 15% reported that they do not intervene. In multivariate logistic regression models, more optimal screening and intervention practices were associated with psychiatry specialty, confidence in obtaining the history of drug use, optimism about the effectiveness of therapy, less concern that patients will object, and fewer perceived time constraints. Most physicians reported that they ask patients about illicit drug use, but a substantial minority inadequately intervene in diagnosed drug abuse. Initiatives to promote physician involvement in illicit drug abuse should include strategies to increase physicians' confidence in managing drug problems, engender optimism about the benefits of treatment, dispel concerns about patients' sensitivity regarding substance use, and address perceived time limitations. Friedmann, P.D., McCullough, D., and Saitz, R. Archives of Internal Medicine, 161(2), pp. 248-251, January 22, 2001.

Linkage to Medical Services in the Drug Abuse Treatment Outcome Study

An episode of substance abuse treatment is an opportunity to link substance-abusing patients to medical care at a time when management of medical problems might stabilize recovery and long-term health. However, little is known about the ability of organizational linkage mechanisms to facilitate the delivery of medical care to this population. The goal of this study was to examine whether organizational linkage mechanisms facilitate medical service utilization in drug abuse treatment programs. This was a prospective secondary analysis of the Drug Abuse Treatment Outcome Study, a national longitudinal study of drug abuse treatment programs and their patients from 1991 to 1993. Hierarchical linear models evaluated the effect of on-site delivery, formal and informal referral, case management emphasis, and transportation on the log-transformed number of medical visits at the 1-month in-treatment patient interview. Program directors' surveys provided organizational information, including the linkage mechanism used to deliver medical care. Patients reported the number of medical visits during the first month of drug abuse treatment. Exclusive on-site delivery increased medical utilization during the first month of drug abuse treatment (beta estimate, 0.22; standard error [SE], 0.06; P <0.001). Transportation services also increased 1-month medical utilization (beta estimate, 0.13; SE, 0.03; P <0.001). Transportation assistance warrants strong policy consideration as a facilitator of medical service delivery. Future research should clarify whether program-level linkage to medical services improves the patient-level outcomes of drug abuse treatment. Friedmann, P.D., Lemon, S.C., Stein, M.D., Etheridge, R.M., and D'Aunno, T.A. Med Care. 39(3), pp. 284-295, 2001.

Telephone Management in Substance Abuse Treatment

The purpose of this article is to describe the results of a clinical trial in which telephonic case management was evaluated as a supplement to substance abuse treatment. An interactive voice response system (IVR) was developed by the research team for use in the case management of randomly assigned participants in a clinical trial research project. The features of the software program facilitated a double caseload for the case manager as well as real-time data capture. At intake, no significant differences were found between participants in the telecommunication condition and the general project. Thus, the effectiveness of random assignment was supported. An IVR was useful for case management services, was less costly, and showed acceptability to clients. A reduction in time expenditure by using telecommunication occurred within three activity areas. Telecommunication facilitated client interaction and the use of case management, and it reduced provider time expenditure. As an alternative strategy, telecommunication ease management can enhance cost effectiveness improvements. Hall, J.A. and Huber, D.L. Telemedicine Journal And E-Health, 6(4), pp. 401-407, 2000.

The Effectiveness of Two Intensities of Psychosocial Treatment for Cocaine Dependence

Structured treatments for cocaine dependence have been shown to be effective despite high attrition rates. What is unclear is what level of treatment intensity is needed to improve and sustain patient outcomes, especially among low SES urban residents. This study evaluated whether there were differences between two levels of treatment intensities for cocaine dependence in reducing substance use and improving health and social indicators. Ninety-four cocaine dependent predominantly African-American male veterans were randomly assigned to either a 12 h/week day hospital program (DH12) or a 6 h/week outpatient program (OP6) and were evaluated at baseline, during treatment and at 4 and 7 months post-treatment. Both treatments stressed abstinence, behavior change and pro-social adjustment and only differed in level of treatment intensity. During-treatment measures included urine toxicologies, program attendance, treatment completion and aftercare attendance. Participants reported a 52% reduction in days of cocaine use and experienced significant improvements in employment and psychiatric functioning at seven months post-treatment. However, there was no significant difference between the DH12 and OP6 programs in terms of abstinence during treatment, treatment completion, treatment or aftercare attendance or any Addiction Severity Index (ASI)-related variable assessing level of functioning at 4 and 7 months. While future research with a larger community-based sample that includes female clients is necessary, the current findings demonstrate that a 6 h/week program is just as effective and thus has a significant cost savings compared to a 12 h/week treatment modality for cocaine dependence. Coviello, D.M., Alterman, A.I., Rutherford, M.J., Cacciola, J.S., McKay, J.R. and Zanis, DA. Drug and Alcohol Dependence, 61(2), pp. 145-154, 2001.

Relapse Outcomes in a Randomized Trial of Residential and Day Drug Abuse Treatment

Relapse outcomes at 6-, 12-, and 18-month intervals were compared between clients randomly assigned to day (n=114) versus residential (n=147) drug abuse treatment. Day clients were more likely than residential clients to relapse 6 months post-admission (OR=3.06, p<0.001); however, no setting differences at 12 or 18 months were found. Few baseline predictors were prospectively related to relapse at 12 and 18 months. These predictors were usual employment status (part-time OR=17.47, p<0.001; full-time OR=2.54, p<0.001), history of drug injecting

(OR=5.39, p<0.01), multiple sex partners (OR=1.16, p<0.01), and not having a gay sexual partner (OR=0.05, p<0.03) during 6 months prior to admission. Still, these baseline predictors, together with the existing literature, could be used by drug treatment professionals to identify individuals who may be at high risk for relapse over time, and to offer specialized treatment and aftercare resources as intervention and prevention measures. Greenwood, G.L., Woods, W.J., Guydish, J. and Bein, E. Journal of Substance Abuse Treatment, 20(1), pp. 15-23, 2001.

Therapeutic Communities - Enhancing Retention in Treatment Using "Senior Professor" Staff

Evaluation research documents a firm relationship between retention and treatment outcomes among substance abusers in therapeutic communities (TCs). However, most admissions leave treatment prematurely, particularly in the first months after admission. This paper reports findings from a controlled study that assessed the efficacy of an intervention to reduce early dropout in a residential TC. In the "Senior Professor" (SP) intervention, the most experienced clinical and managerial staff in a TC program were utilized to conduct program induction seminars during the first weeks of admissions, traditionally the period of the highest rate of dropout. Rates of short-term retention (30 days of treatment) were compared for the experimental cohort (N = 362), who received the intervention, and a cohort of admissions (N = 243), who received standard or non-enhanced treatment. The authors showed that the SP intervention significantly reduced the likelihood of early dropout compared with controls. The enhanced effects are most evident for the new inductees with the lowest levels of motivation. Some theoretical and clinical implications are discussed as to the utilization of experienced staff to increase retention among new inductees with relatively lower motivational levels, who are at greatest risk for early dropout. De Leon, G., Hawke, J., Jainchill, N., and Melnick, G. Journal of Substance Abuse Treatment, 19(4), pp. 375-382, 2000.

Twenty-Five Strategies for Improving the Design, Implementation and Analysis of Health Services Research Related to Alcohol and Other Drug Abuse Treatment

While some aspects of addiction can be studied in laboratory or controlled settings, the study of long-term recovery management and the health services that support it requires going out into the community and dealing with populations and systems that are much more diverse and less under our control. This in turn raises many methodological challenges for the health service researchers studying alcohol and other drug abuse treatment. The authors identify some of these challenges related to the design, measurement, implementation and effectiveness of health services research. They then recommend 25 strategies (and key primers) for addressing them: (1) identifying in advance all stakeholders and issues; (2) developing conceptual models of intervention and context; (3) identifying the population to whom the conclusions will be generalized; (4) matching the research design to the question; (5) conducting randomized experiments only when appropriate and necessary; (6) balancing methodological and treatment concerns; (7) prioritizing analysis plans and increasing design sensitivity, (8) combining qualitative and quantitative methods; (9) identifying the four basic types of measures needed; (10) identifying and using standardized measures; (11) carefully balancing measurement selection and modification; (12) developing and evaluating modified and new measures when necessary; (13) identifying and tracking major clinical subgroups; (14) measuring and analyzing the actual pattern of services received; (15) incorporating implementation checks into the design; (16) incorporating baseline measures into the intervention; (17) monitoring implementation and dosage as a form of quality assurance; (18) developing procedures early to facilitate tracking and follow-up of study participants; (19) using more appropriate representations of the actual experiment; (20) using appropriate and sensitive standard deviation terms; (21) partializing out variance due to design or known sources prior to estimating experimental effect sizes; (22) using dimensional, interval and ratio measures to increase sensitivity to change; (23) using path or structural equation models; (24) integrating qualitative and quantitative analysis into reporting; and (25) using quasi-experiments, economic or organizational studies to answer other likely policy questions. Most of these strategies have been tried and tested in this and other areas, but are not widely used. Improving the state of the art of health services research and bridging the gap between research and practice do not depend upon using the most advanced methods, but rather upon using the most appropriate methods. Dennis, M.L., Perl, H.I., Huebner, R.B., and McLellan, A.T. Addiction, 95, S281-S308, Suppl. November 3, 2000.

Sources of Motivation for Abstinence: A Replication Analysis of the Reasons for Quitting Questionnnaire

The Reasons for Quitting Questionnaire (RFQ) as modified by McBride and colleagues (C. M. McBride et al., 1994) for use with substance users other than tobacco smokers, was administered to individuals approved for public-sector addiction treatment. Four motivation dimensions, similar to those found by McBride et al., were identified: self-concept issues, health concerns, legal issues, and social influence. A forced two-component solution yielded dimensions interpretable as intrinsic and extrinsic motivation. Self-concept issues provided the highest levels of

motivation for abstinence in this sample, with moderate levels provided by health concerns, and the lowest levels provided by legal and social influence components. Intrinsic motivation was higher than extrinsic motivation. Logistic regression models, with adjustment for total motivation, tested the association of successful abstinence during a follow-up period with baseline extrinsic and intrinsic motivation, and with the difference between intrinsic and extrinsic levels. All three associations were significant: intrinsic motivation (positive association), extrinsic motivation (negative association), and the difference score (positive association). The results suggest the usefulness of the 20-item modified RFQ in evaluating motivation for abstinence among treatment seekers exhibiting severe negative consequences of addiction. Testing with samples varying in severity of addiction consequences is recommended. Downey, L., Rosengren, D.B., and Donovan, D.M. Addictive Behaviors, 26 (1), pp. 79-89, January-February 2001.

Placement Matching: Challenges and Technical Progress

Although it is highly desirable, standardized placement matching for substance use disorders poses challenges due to variability in settings, services, and syndromes; multidimensionality of clinical problems; multiplicity of outcome constructs; and temporal phenomena in the course of recovery. Despite these obstacles, progress is being made in developing patient placement criteria that are comprehensive with adequate reliability, feasibility, and resolution. With these methodological advances, it has been possible to initiate controlled research with placement criteria. The first such studies provide early evidence supporting such criteria and indicate areas for refinement. Gastfriend, D.R., Lu, S.H., and Sharon, E. Substance Use & Misuse 35(12-14), pp. 2191-2213, 2000.

Modeling Year 1 Outcomes with Treatment Process and Post-Treatment Social Influences

Follow-up studies of drug user treatment generally find significant improvements in client functioning, but information about the therapeutic components associated with client behavioral changes over time is limited. An integrative model developed previously to predict treatment retention was expanded and applied to post-treatment outcomes. This study is based on 321 daily opioid users treated in three methadone treatment clinics. Effects of pre-treatment motivation, treatment process measures representing therapeutic relationship, counseling session attendance, and length of treatment are examined in relation to measures of family relations, peer deviancy, return to treatment, drug use, and criminality in the year after treatment. Models were tested in two stages. The first was built on a during-treatment process model for predicting time in treatment to include post-treatment outcomes. The second model was expanded further to include the effects of intervening social support variables as predictors of post-treatment drug and criminality outcomes. The results supported both models and emphasize the importance of considering social influences and related community contextual factors that affect recovery dynamics. Simpson, D.D., Joe, G.W., Greener, J.M., and Rowan-Szal, G.A. Substance Use & Misuse, 35(12-14), pp.1911-1930, October-December 2000.

Drug Abuse Treatment on Demand in San Francisco: Preliminary Findings

This article reports on a process and capacity evaluation of San Francisco's Treatment on Demand Initiative, which was launched in 1997 to increase availability of publicly-funded substance abuse treatment. For the process evaluation, data from public documents, interviews with community key informants, and newspaper articles were analyzed. For the capacity evaluation, budget documents and admissions data for publicly-funded substance abuse treatment in San Francisco for fiscal years 1995-1998 were analyzed. Results from the process evaluation document the development of the community-oriented Treatment on Demand Planning Council, and its efforts to not only expand treatment, but to create a continuum of services to address the needs of San Francisco's richly diverse communities, to provide service enhancements, and to prioritize service needs. Process evaluation results also highlight the complexities of implementing treatment on demand, including the difficulty of opening new programs. Results from the capacity evaluation indicate that the San Francisco budget supporting publicly-funded treatment increased from $32 million to $45.2 million over four years. During the same period, the number of persons entering the system in a single year increased by 18%, and the number of admissions in a single year increased by 15%. Implications of these findings are discussed. Guydish, J., Moore, L., Gleghorn, A., Davis, T., Sears, E., and Harcourt, J. Journal of Psychoactive Drugs 32 (4), pp. 363-370, October-December 2000.

Adolescent Substance Abuse Treatment Outcome: The Role of Substance Abuse Problem Severity, Psychosocial, and Treatment Factors

A structural equation model incorporating substance abuse problem severity, psychosocial risk and protection, and treatment variables was used to examine adolescent drug abuse treatment outcome pathways across 6- and 12-month follow-up points. Findings on resiliency factors and an empirical method adapted from previous research were used to select and assign 10 psychosocial factors to either a multiple protective factor index or a risk factor index. Gender, substance abuse problem severity, treatment modality, treatment length, and aftercare participation were

also examined as outcome predictors. The findings suggest that treatment intensity decisions may be better informed by pretreatment psychosocial risk level rather than by substance abuse problem severity. The present study also suggests that drug-abusing adolescents who receive sufficiently long treatment, participate in aftercare, and possess at least 1 individual or interpersonal protective factor during their recovery process have the best chance to maintain gains made during treatment. Latimer, W.W., Newcomb, M., Winters, K.C., and Stinchfield, R.D. Journal of Consulting and Clinical Psychology, 68(4), pp. 684-696, August 2000.

Demographic, Individual, and Interpersonal Predictors of Adolescent Alcohol and Marijuana Use Following Treatment

A vulnerability model of adolescent substance abuse treatment outcome provided the basis for selection of demographic, individual, interpersonal, and treatment factors to predict the follow-up use of alcohol and marijuana in a sample of adolescents (N = 225) with psychoactive substance use disorders. Pretreatment levels of sibling substance use and aftercare participation predicted alcohol and marijuana use during the first 6 months post treatment. Pretreatment levels of deviant behavior also predicted the use of marijuana at 6-month follow-up. Peer substance use at intake and 6-month post treatment both predicted substance use frequency outcomes at 12-month follow-up. Alcohol and marijuana use frequencies at 6-month follow-up also predicted continued use for these substances throughout the remainder of the 1st post treatment year. Shorter treatment length and being male were risk factors for alcohol use during the 2nd half of the 1st post treatment year. Elevated psychological substance dependence at 6-month follow-up was a unique risk factor for subsequent marijuana use. Findings support conceptual models that attempt to explain adolescent substance abuse treatment outcome in terms of relationships among demographic, individual, interpersonal, and treatment factors. Latimer, W.W., Winters, K.C., Stinchfield, R., and Traver, R.E. Psychology of Addictive Behaviors, 14(2), pp. 162-173, June 2000.

Therapeutic Communities: Diversity in Treatment Elements

The authors address the need to describe the diversity-of therapeutic community (TC) programs. The Survey of Essential Elements Questionnaire (SEEQ) was used to develop a typology of TC programs based on 19 programs that identified themselves as traditional or modified TCs in the Drug Abuse Treatment Outcome Studies (DATOS). These traditional and modified TCs differed in adherence to the elements of TC treatment, on operational characteristics, and in client mix. Differences in treatment philosophy and approach included the emphasis on self-reliance and the use of work as a therapeutic agent for traditional TCs. There were also trends for traditional TC programs to utilize community-as-method, provide educational and vocational training, and include family members as part of therapy. Modified programs showed a greater tendency to rely on counselors. Implications of the findings for program quality, health care policy, and research are discussed. Melnick, G., De Leon, G., Hiller, M.L., and Knight, K. Substance Use & Misuse, 35(12-14), pp. 1819-1847, 2000.

Program Factors and Treatment Outcomes in Drug Dependence Treatment: An Examination Using Meta-Analysis

In comparison with studies of client characteristics and treatment processes, limited research has been conducted on how program features of drug dependence treatment programs may affect client outcomes. Of particular interest are those characteristics of programs that may have a clinically significant impact on outcomes and that are amenable to change within programs. The authors examine the impact of various program factors on client outcomes using data from a meta-analysis of drug dependence effectiveness studies (n = 143). Because of heterogeneity among studies, the data are analyzed in terms of type of outcome variable (drug use and crime), type of design (single-group and treatment-comparison group), and type of treatment (methadone maintenance, therapeutic communities, outpatient drug free, and detoxification). For the more valid treatment-comparison group studies, the weighted mean effect size was 0.29 for drug use outcomes and 0.17 for crime outcomes. Program factors found to be significantly correlated with effect size in one or more modalities were decade of treatment, researcher involvement in treatment delivery, maturity of the program, counselor/client ratio, treatment implementation, treatment exposure, and methadone dosage. Prendergast, M.L., Podus, D., and Chang, E. Substance Use & Misuse, 35(12-14), pp. 1931-1965, 2000.

Social Relationships of Crime-Involved Women Cocaine Users

Social relationships play a significant role in drug use and recovery, perhaps especially for women. Research on social relationships among crime-involved women drug users is reviewed, including both well established findings and more recent topics of inquiry. Several open questions about social relationships of women drug users are then examined in data from a study conducted in the Miami (Florida) metropolitan area in 1994-1996. For a study of barriers to drug treatment for crime-involved women cocaine users, over 400 women were interviewed in treatment programs and an

equal number were recruited on the street. Respondents were asked about their social relationships during the last 30 days on the street in regard to both legal and illegal activities. This included crime partnerships, help obtaining cocaine, living arrangements, help with living expenses, children and help with child care, help with several ordinary problems, and pressures to enter treatment. The analysis looks at how much social support crime-involved women cocaine users have in their ordinary daily activities and who provides this support. Pottieger, A.E., and Tressell, P.A. Journal of Psychoactive Drugs, 32(4), pp. 445-460, October-December 2000.

The Impact of Women's Family Status on Completion of Substance Abuse Treatment

This study examines the role of family status and demographic characteristics in explaining the nearly 60% dropout rate for women in substance abuse treatment. Data from the administrative record files of the Illinois Office of Alcoholism and Substance Abuse (OASA) for the fiscal year 1996-1997 were analyzed for women age 12 or older who completed intake for publicly funded substance abuse treatment and whose outpatient treatment records were closed at year-end. Multivariate logistic regression models found that the likelihood of not completing treatment was greatest for women who were African American, pregnant, had custody of minor children, or were younger than age 21. However, African American women who had children in foster care were more likely to complete treatment. Implications for treatment and research are discussed. Scott-Lennox, J., Rose, R., Bohlig, A., and Lennox, R. J Behav Health Serv Res, 27(4), pp. 366-379, November 2000.

The Relationship Between the Quality of Drug User Treatment and Program Completion: Understanding the Perceptions of Women in a Prison-based Program

To determine why some women offenders complete prison-based drug user treatment and others leave early, clients' (N = 101) perceptions of various aspects of the quality of the treatment experience were compared. Analyses of both quantitative and qualitative data indicate that clients who completed the program had a more favorable perception of staff and felt empowered by the experience in treatment. Most of the clients who left early did so because of conflicts or disagreements with the program's rules. We discuss how a supportive approach to personal development may enhance client perceptions of program quality and increase retention rates. Strauss, S.M., and Falkin, G.P. Substance Use & Misuse, 35(12-14), pp. 2127-2159, October-December 2000.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Research Findings

Intramural Research

Chemistry & Drug Metabolism Section, Clinical Pharmacology & Therapeutics Research Branch

Blockade of Effects of Smoked Marijuana by the CB1-Selective Cannabinoid Receptor Antagonist SR141716

SR141716, a recently developed CB1 cannabinoid receptor antagonist, blocks acute effects of Λ-9-tetrahydrocannabinol (THC) and other CB1 cannabinoid agonists in vitro and in animals. These findings suggest that CB1 receptors mediate many of the effects of marijuana, but this has not been evaluated in humans. Sixty-three healthy men with a history of marijuana use were randomly assigned to receive oral SR141716 or a placebo in an escalating dose (1, 3, 10, 30, and 90 mg) design. Each subject smoked an active (2.64% THC) or placebo marijuana cigarette 2 hours later. Psychological effects associated with marijuana intoxication and heart rate were measured before and after antagonist and marijuana administration. A single oral doses of SR141716 produced a significant dose-dependent blockade of marijuana-induced subjective intoxication and tachycardia. The 90-mg dose produced 38% to 43% reductions in visual analog scale ratings of "How high do you feel now?" "How stoned on marijuana are you now?" and "How strong is the drug effect you feel now?" and produced a 59% reduction in heart rate. SR141716 alone produced no significant physiological or psychological effects and did not affect peak THC plasma concentration or the area under the time X concentration curve. SR141716 was well tolerated by all subjects. SR141716 blocked acute psychological and physiological effects of smoked marijuana without altering THC pharmacokinetics. These findings confirm, for the first time in humans, the central role of CB1 receptors in mediating the effects of marijuana. Huestis, M.A., Gorelick, D.A., Heishman, S.J., Preston, K.L., Nelson, R.A., Moolchan, E.T. and Frank, R.A. Archives of General Psychiatry, 58, pp. 322-328, 2001.

Peptide-Peptide Interaction by MALDI

Matrix assisted laser desorption/ionization mass spectrometry (MALDI) was used to study peptide-peptide interaction. The interaction was seen when 6-aza-2-thiothymine was used for matrix (pH 5.4), but was disrupted when -cyano-4-hydroxycinnamic acid (pH 2.0) was used. In the present study we show that dynorphin, an opioid peptide, and 5 of its fragments that contain two adjacent basic residues (Arg6 and Arg7), all interact non-covalently with peptides that contain two to five acidic residues (Asp or Glu). Two other non-related peptides containing Two (Arg-Arg) or Three (Arg-Lys-Arg) adjacent basic amino acid residues show the same behavior. However peptides containing two adjacent lysines or histidines did not. The non-covalent bonding is so stable that digestion with trypsin, only cleaved the peptides at the carboxyl-terminus of basic residues that were not involved in hydrogen bonding with the acidic residues. In an equimolar mixture of dynorphin, its fragments and an acidic peptide (mini-gastrin), the acidic peptide formed ionic bonds preferentially with dynorphin. However, if the concentration of mini-gastrin was increased 10 fold, non-covalent interaction was seen with dynorphin and all its fragments. In the absence of dynorphin, mini-gastrin formed non-covalent complexes with all dynorphin fragments. These findings suggest that conformation, equilibrium and concentration do play a role in the occurrence of peptide-peptide interaction. The fact that the ionic bonds could not be disrupted by enzymatic digests, that conformation and concentration seem to influence the complex formation, and that the complex did not form with fragments of dynorphin that did not contain residues 6 and 7, and with fragments of dynorphin where Arg7 was mutated to a phenylalanine residue, strongly suggests that peptide-peptide

interaction does occur, and can be studied by MALDI if physiologic pH is maintained. Woods, A.S. and Huestis, M.A. Journal of Mass Spectrometry, 12, pp. 88-96, 2001.

Monitoring Opiate Use in Substance Abuse Treatment Patients

Although urine testing remains the standard drug use monitoring method, sweat testing for drugs of abuse is increasing, especially in criminal justice programs. One reason for this increase is that sweat testing offers the possibility for widening the detection window compared to urine testing. This study was designed to compare the efficacy of sweat versus urine for detecting drug use. Paired sweat patches that were applied and removed weekly (on Tuesdays) were compared to 3-5 consecutive urine specimens collected Mondays, Wednesdays, and Fridays (355 matched sweat and urine specimen sets) in 44 patients in a methadone maintenance outpatient treatment program. All patches (N = 1010) were extracted in 2.5 mL of solvent and analyzed by ELISA immunoassay (cutoff concentration 10 ng/mL). A subset (389) of patches was analyzed by GC/MS. Urine specimens were subjected to qualitative analysis by EMIT (cutoff 300 ng/mL). Opiates were detected in 22.5% of the sweat patches with the ELISA screen. Eighty-nine percent of the screen-positive sweat patches were confirmed by GC-MS for heroin, 6-acetylmorphine, morphine and/or codeine. Heroin and/or 6-acetylmorphine were detected in 78.1% of the GC/MS positive sweat patches. There were 13.5% false negative and 7.9% false positive sweat results as compared to urine tests. Analysis of sweat patches provides an alternate method for objectively monitoring drug use and provides an advantage over urine drug testing by monitoring an individual's drug use over an extended period of time. However, the percentage of false negative results, at least in this treatment population, indicates that weekly sweat testing may be slightly less sensitive than thrice weekly urine testing in detecting opiate use. Huestis, M.A., Cone, E.J., Wong, C.J., Umbricht, A. and Preston, K.L. Journal of Analytical Toxicology, 24, pp. 509-521, 2000.

Cocaine and Metabolite Elimination Patterns in Chronic Cocaine Users During Cessation

Several reports suggest a prolonged elimination of cocaine and metabolites after chronic use compared to single or occasional use. This study was designed to measure the half-lives of cocaine in plasma and saliva of individuals who consume cocaine on a frequent basis. We investigated the disposition and elimination patterns of cocaine and metabolites in the body fluids of chronic high-dose cocaine users during acute cessation of use. Plasma and saliva specimens were collected over a 12 h period during cessation and analyzed by gas chromatography-mass spectrometry. Pharmacokinetic parameters were derived by noncompartmental analysis of plasma and saliva data. Results indicated a cocaine terminal T1/2 of 3.8 hours in plasma and 7.9 hours in saliva. The terminal T1/2 of benzoylecgonine was 6.6 hours in plasma and 9.2 hours in saliva. Compared with prior studies of acute low-dose cocaine administration, these findings suggest that cocaine's half-life is longer in active street users than in occasional users though the half-life of its main metabolite benzoylecgonine remains similar (as do cocaine saliva-to-plasma ratios). Thus, regular use of cocaine appears to alter the disposition and elimination of cocaine when compared to single or occasional use. Moolchan, E.T., Cone, E.J., Wtsadik, A., Huestis, M.A., and Preston, K.L. Journal of Analytical Toxicology, 24, pp. 458-466, 2000.

Brain Imaging Section, Neuroimaging Research Branch

Volume of Lateral Ventricle in Bipolar I Patients is Nearly Twice as Large as the Volume in Patients with Bipolar II Disorder

A quantitative magnetic resonance imaging comparison of bipolar I and bipolar II patients was undertaken because no previous quantitative assessments of bipolar II patients have been documented and the number of quantitative studies of bipolar I patients is small. Magnetic resonance imaging was used to estimate volume of the temporal lobe, hippocampus, and the lateral ventricle in 25 bipolar I disorder, 22 bipolar II disorder, and 19 control subjects. There were no significant differences in volume estimates for the temporal lobe and hippocampus between groups. In contrast, the lateral ventricle area and the lateral ventricle to cerebrum area ratio were approximately twice as large in the bipolar I patients as the other groups in the left hemisphere only. The results suggest that subjects diagnosed with bipolar I disorder, particularly in males, may show neurobiological alterations different from patients with bipolar II disorder or control subjects. Hauser, P., Matochik, J.A., Altshuler, L.L., Denicoff, K.D., Conrad, A., Li, X., and Post, R.M. Journal of Affective Disorders, 60, pp. 25-32, 2000.

Methadone-maintained Former Heroin Addicts Have Lower Specific Binding of [18F] cyclofoxy, an Opioid Antagonist, in Brain Areas Related to Drug Addiction

Positron emission tomography using tracer amounts of [18F]cyclofoxy, an opioid antagonist that labels mu and kappa receptors, was used to measure opioid receptor binding in 14 stabilized methadone-maintained former heroin addicts

and 14 healthy controls. Specific binding of [18F]cyclofoxy was lower by 19 to 32% in methadone-maintained subjects compared to controls in the thalamus, amygdala, caudate nucleus, putamen, and the anterior cingulated cortex. Lower specific binding in the caudate nucleus and putamen was correlated with methadone plasma levels, suggesting that lower binding may be related to receptor occupancy with methadone and that significant numbers of opioid receptors may be available to function in their normal physiological roles. Kling, M.A., Carson, R.E., Borg, L., Zametkin, A., Matochik, J.A., Schluger, J., Herscovitch. P., Rice, K.C., Ho, A., and Kreek, M.J. Journal of Pharmacology and Experimental Theraputics, 295, pp. 1070-1076, 2000.

Development and Plasticity Section, Cellular Neurobiology Research Branch

Motor Activity-Mediates Partial Recovery in Ischemic Rats

Spontaneous partial recovery in motor and/or cognitive dysfunctions in stroke patients has been documented, but the factors that affect such functional improvement have not been well elucidated. The present study demonstrates that repeated behavioral testing (daily or once a week over a period of 4 weeks) promoted partial recovery from motor asymmetry in adult ischemic rats. In contrast, ischemic animals that were only tested once every 2 weeks or once after 4 weeks did not show such partial recovery. These results suggest that repeated behavioral testing (i.e., increased use of the ischemia-affected limbs and body parts) may contribute to partial recovery of motor deficits following an experimental stroke, even in the absence of pharmacological therapeutic intervention. Borlongan, C.V. NeuroReport, 18, pp. 4063-4067, 2000.

Cellular Neurophysiology Section, Cellular Neurobiology Research Branch

Methamphetamine Potentiates Ischemic Brain Injury

Previous studies have indicated that both methamphetamine (MA) and ischemia/reperfusion injuries involve reactive oxygen species formation and activation of apoptotic mechanism. It is possible that MA may have a synergistic or additive effect with stroke-induced brain damage. The purpose of this study was to investigate if administration of MA *in vivo* would potentiate ischemic brain injury. Adult CD-1 mice were treated with MA (10 mg/kg) or saline (i.p., 4 times, each dose two hours apart). Animals were later anesthetized with chloral hydrate and then placed in stereotaxic frame. A subset of animals received intracerebral administration of glial cell line-derived neurotrophic factor (GDNF). The right middle cerebral artery (MCA) and bilateral carotids were transiently occluded for 45 minutes. Regional cerebral blood flow was measured by Laser Doppler. Animals were sacrificed for tri-phenyl-tetrazolium chloride (TTC) staining and p53 mRNA Northern blot assay after 24 hours of reperfusion. Cortical and striatal GDNF levels were assayed by ELISA. Investigators found that pretreatment with MA increased ischemia-induced cerebral infarction. Ischemia or MA alone enhanced p53 mRNA expression. Moreover, MA potentiated the expression of p53 mRNA in the ischemic mouse brain. MA pretreatment decreased GDNF levels in ischemic striatum. Intracerebral administration of GDNF before ischemia reduced MA-facilitated infarction. These data indicate that MA exacerbates ischemic insults in brain, perhaps through the inhibition of GDNF-mediated pathways, and suggest that MA may antagonize endogeneous neuroprotective pathways as part of its mechanism of action. Wang, Y., Hayashi, T., Chang, C.F., Chiang, Y.H., Tsao, L.I., Su, T.P., Borlongan, C.V., and Lin, S.Z. Stroke, 32, pp. 775-782, 2001.

Molecular Neuropsychiatry Section, Cellular Neurobiology Research Branch

Delta Opioid Peptide [D-Ala2, D-Leu5]Enkephalin Causes a Near Complete Blockade of the Neuronal Damage Caused by a Single High Dose of Methamphetamine: Examining the Role of p53

The delta opioid peptide [D-Ala2, D-Leu5]enkephalin (DADLE) has been reported to block the neurotoxicity induced by multiple administrations of a moderate dose of methamphetamine (METH). IRP scientists examined in this study if DADLE might block the neurotoxicity caused by a single high dose of METH in CD-1 mice. The levels of dopamine transporter (DAT), tyrosine hydroxylase (TH), major biogenic amines including DA, 5-hydroxytryptamine (5-HT), and their metabolites were examined. In addition, since the tumor suppressor p53 has been implicated in the neurotoxicity of METH, this study also examined the levels of p53 mRNA and protein affected by METH and DADLE. METH (25 mg/kg, i.p.) caused significant losses of DAT, TH, DA, 3,4-dihydroxyphenylacetic acid (DOPAC), and 5-HT in the striatum within 72 h. The administration of a single dose of DADLE (20 mg/kg, i.p., 30 min before METH) caused a complete blockade of all losses induced by METH except for that of the DA content (an approximately 50% blockade). DADLE did not affect the changes of rectal temperature induced by the administration of the high dose of METH. METH increased p53 mRNA in the striatum and the hippocampus of CD-1 mouse. DADLE abolished the p53 mRNA increase caused by METH. METH tended to increase the p53 protein level at earlier time points. However,

METH significantly decreased the p53 protein level by about 30% at the 72-h time point. DADLE blocked both the increase of p53 mRNA and the decrease of p53 protein caused by METH. These results demonstrate a neuroprotective effect of DADLE against the neuronal damage and the alteration of p53 gene expression caused by a single high dose of METH. The results also indicate an apparent discordance between the protein level of p53 and the neurotoxicity caused by a high dose of METH. Hayashi, T., Hirata, H., Asanuma, M., Ladenheim, B., Tsao, L.I., Cadet, J.L. and Su, T.P. Synapse 39(4), pp. 305-312, 2001.

Peroxynitrite Plays a Role in Methamphetamine-induced Dopaminergic Neurotoxicity: Evidence from Mice Lacking Neuronal Nitric Oxide Synthase Gene or Overexpressing Copper-Zinc Superoxide Dismutase

The use of methamphetamine (METH) leads to neurotoxic effects in mammals. These neurotoxic effects appear to be related to the production of free radicals. To assess the role of peroxynitrite in METH-induced dopaminergic damage, IRP scientists investigated the production of 3-nitrotyrosine (3-NT) in the mouse striatum. The levels of 3-NT increased in the striatum of wild-type mice treated with multiple doses of METH (4 x 10 mg/kg, 2 h interval) as compared with the controls. However, no significant production of 3-NT was observed either in the striata of neuronal nitric oxide synthase knockout mice (nNOS -/-) or copper-zinc superoxide dismutase overexpressed transgenic mice (SOD-Tg) treated with similar doses of METH. The dopaminergic damage induced by METH treatment was also attenuated in nNOS-/- or SOD-Tg mice. These data further confirm that METH causes its neurotoxic effects via the production of peroxynitrite. Imam, S.Z., Newport, G.D., Itzhak, Y., Cadet, J.L., Islam, F., Slikker, W. and Ali, S.F. J Neurochem., 76(3), pp.745-749, 2001.

Effects of Methamphetamine-induced Neurotoxicity on the Development of Neural Circuitry: A Hypothesis

Exposure of the developing brain to methamphetamine has well-studied biochemical and behavioral consequences. IRP scientists reviewed: (1) the effects of methamphetamine on mature serotonergic and dopaminergic pathways; (2) the mechanisms of methamphetamine neurotoxicity and (3) the role of serotonergic and dopaminergic signaling in sculpting developing neural circuitry. Consideration of these data suggest the types of neural circuit alterations that may result from exposure of the developing brain to methamphetamine and that may underlie functional defects. Frost, D.O. and Cadet, J.L. Brain Res Rev., 34(3), pp. 103-118, 2000.

African-American Teen Smokers: Issues to Consider for Cessation Treatment

Previous reports have indicated ethnic differences in both tobacco-related morbidity and treatment outcome for smoking cessation among adults. IRP investigators assessed smoking-related characteristics in African-American and non-African American teenagers applying to a cessation trial. 115 teens (15.9 +/- 1.8 years, 68% females, 27% African-American) responded via telephone to media ads. Self-reported sociodemographic, medical and smoking-related data were obtained to determine pre-eligibility for a full intake screen prior to trial participation. Compared to non-African American, African American teen applicants were older (16.4 +/- 1.7 years versus 15.6 +/- 1.6; p = 0.015), had lower Fagerstrom Test for Nicotine Dependence (FTND) scores (5.3 +/- 2.3 versus 6.1 +/- 1.8; p = 0.018, ANOVA controlling for age) and smoked fewer cigarettes on the weekend (27 +/- 16 versus 38 +/- 17; p = 0.001). African American teens reported similar duration of smoking (3.3 +/- 1.4 versus 3.1 +/- 1.5 years) and time elapsed between first cigarette ever smoked and daily smoking (0.7 +/- 0.9 versus 0.6 +/- 0.7 years). African American and non-African American teens had similar motivation to quit scores and frequency of reported health problems (e.g., asthma, psychiatric conditions). These data suggest that cessation treatment programs designed for African American youth should include lower Fagerstrom-defined levels, and possibly other criteria for tobacco dependence. These observations also highlight the importance of ethnocultural issues in treatment research programs. Moolchan, E.T., Berlin, I., Robinson, M.L., and Cadet, J.L. J Natl Med Assoc., 92(12), pp. 558-562, 2000.

Behavioral Neuroscience Section, Behavioral Neuroscience Research Laboratory

Role of Leptin in Relapse to Heroin Seeking Induced by Food Deprivation

Studies in rats have shown that intermittent footshock stress reinstates drug seeking after prolonged drug-free periods. Recently, IRP investigators found that another environmental stressor, acute 1-day food deprivation, potently reinstates heroin seeking in rats. Here they report that this effect of food deprivation can be blocked by leptin, a hormone involved in the regulation of energy balance and food intake. Rats were trained to self-administer heroin (0.05-0.1 mg/kg/infusion, IV, three 3-hr sessions/day) for 8-10 days. The heroin-reinforced behavior was then extinguished for 10-13 days during which lever presses had no reinforced consequences. Subsequently, rats were

tested for reinstatement after one day of food deprivation (Experiment 1), or exposure to intermittent footshock (15 min, 0.6 mA) and heroin priming injections (0.25 mg/kg, SC) (Experiment 2). Acute food deprivation reinstated heroin seeking, an effect that was attenuated by leptin (2 or 4 µg/rat, ICV; 2 infusions, given 21 hr and 20-30 min before the start of the test sessions). In contrast, leptin had no effect on reinstatement of heroin seeking induced by intermittent footshock or priming injections of heroin. These data indicate that food deprivation can provoke relapse to heroin seeking via a leptin-dependent mechanism, which is not involved in relapse induced by footshock stress or reexposure to heroin. Shalev, U., Yap, J. and Shaham, Y. The Journal of Neuroscience, 21, RC129, pp. 1-5, 2001.

Preclinical Pharmacology Section, Behavioral Neuroscience Research Laboratory

Self-administration of Remifentanil, an Ultra-Short Acting Opioid, Under Continuous-Reinforcement and Progressive-Ratio Schedules

It has been proposed that there is a relationship between a drug's duration of action and its effectiveness as a reinforcer. Remifentanil is an opioid with a half-life of less than a minute. To evaluate the role of duration of action in drug self-administration we compared the ability of remifentanil to maintain self-administration with the longer acting opioid heroin. On a continuous reinforcement schedule, inter-infusion intervals for both drugs increased monotonically as a function of dose, with the remifentanil curve being considerably flatter. That is, at higher doses animals were able to respond at higher rates when remifentanil was used to maintain responding. Under a progressive ratio schedule, the highest break points maintained by remifentanil and heroin were similar. Therefore, although rates of self-administration are clearly influenced by a drug's duration of action, the ability for a drug to maintain responding under intermittent schedules of reinforcement may be independent of duration of action. Panlilio, L.V. and Schindler, C.W. Psychopharmacology, 150, pp. 61-66, 2000.

Medicinal Chemistry and Psychobiology Sections, Medications Discovery Research Branch

Highly Selective Chiral N-substituted 3α-[bis(4'-fluorophenyl)methoxy]Tropane Analogues for the Dopamine Transporter: Synthesis and Comparative Molecular Field Analysis

In a continuing effort to further characterize the role of the dopamine transporter (DAT) in the pharmacological effects of cocaine, a series of chiral and achiral N-substituted analogues of 3α-[bis(4'-fluorophenyl)methoxy]tropane (4',4"-diF-BZT) has been prepared, as selective DAT ligands. These novel compounds displaced [3H]WIN 35,428 binding from DAT, in rat caudate putamen, with Ki values ranging from 14.0 to 477 nM. Previously, it was reported that 4',4"-diF-BZT, demonstrated a significantly higher affinity for DAT than the parent drug, benztropine (BZT). However, 4',4"-diF-BZT remained nonselective over muscarinic m1 receptors (DAT, Ki=11.8 nM; m1, Ki=11.6 nM) which could potentially confound the interpretation of behavioral data, for this compound and other members of this series. Thus, significant effort has been directed toward developing analogs that retain high affinity at DAT but have decreased affinity at muscarinic sites. Recently, it was discovered that by replacing the N-methyl group of 4',4"-diF-BZT with the phenyl-n-butyl substituent, retention of high binding affinity at DAT (Ki=8.51 nM) while decreasing affinity at muscarinic receptors (Ki=576 nM) was achieved, resulting in a 68-fold selectivity. In the present series, a further improvement in the selectivity for the dopamine transporter was accomplished, with the chiral analog (*S*)-(*N*-2-amino-3-methyl-*n*-butyl)-3α-[bis(4'-fluorophenyl)methoxy] tropane, showing a 136-fold selectivity for DAT vs. muscarinic m1 receptors (Ki=29.5 nM vs. Ki=4020 nM, respectively). In addition, a Comparative Molecular Field Analysis (CoMFA) model was derived to correlate the binding affinities of all the N-substituted-4',4"-diF-BZT analogues prepared with their 3D-structural features. The best model (q2 = 0.746) was used to accurately predict binding affinities of compounds in the training set and in a test set. The CoMFA coefficient contour plot for this model, which provides a visual representation of the chemical environment of the binding domain of DAT, can now be used to design and/or predict the binding affinities of novel drugs within this class of dopamine uptake inhibitors. Robarge, M.J., Agoston, G.E., Izenwasser, S., Kopajtic, T., George, C., Katz, J.L., and Newman, A.H. Journal of Medicinal Chemistry, 43, pp. 1085-1093, 2000.

2D QSAR Modeling of Dopamine Transporter Inhibitor Affinity Using Genetic Algorithm Variable Selection of Molconn Z Descriptors

Novel approaches towards both understanding the activity of inhibitors of the dopamine transporter (DAT) and the identification of novel inhibitors that may be of therapeutic potential have been taken in order to further elucidate the role of the DAT in the pharmacology and abuse potential of cocaine. IRP scientists' most recent studies towards these ends have made use of two-dimensional (2D) Quantitative Structure Activity Relationship (QSAR) methods in order to develop predictive models that correlate structural features of DAT ligands to their biological activities. Specifically, they have adapted the method of Genetic Algorithms-Partial Least Squares (GA-PLS) to the task of variable selection

of the descriptors generated by the software Molconn Z. As the successor to the program Molconn X, which generated 462 descriptors, Molconn Z provides 749 chemical descriptors. By employing genetic algorithms in optimizing the inclusion of predictive descriptors, they have successfully developed a robust model of the DAT affinities of 70 structurally diverse DAT ligands. This model, with an exceptional q2 value of 0.85, is nearly 25% more accurate in predictive value than a comparable model derived from Molconn X-derived descriptors (q2 = 0.69). Utilizing activity-shuffling validation methods, they have demonstrated the robustness of both this DAT inhibitor model and their QSAR method. Moreover, they have extended this method to the analysis of dopamine D1 antagonist affinity and serotonin ligand efficacy, illustrating the significant improvement in q2 for a variety of data sets. Finally, they have employed their method in performing a search of the National Cancer Institute database based upon activity predictions from their DAT model. They report the preliminary results of this search, which has yielded five compounds suitable for lead development as novel DAT inhibitors. Hoffman, B.T., Kopajtic, T., Katz, J.L., and Newman, A.H. Journal of Medicinal Chemistry, 43, pp. 4151-4159, 2000.

Structure-Activity Relationships at the Monoamine Transporters and Muscarinic Receptors for N-substituted-3α-[3'-Chloro-, 4'-Chloro-, 4',4"-diChloro-substituted) diphenyl] Methoxytropanes

The design, synthesis and evaluation of benztropine (BZT) analogs have provided potent and selective probes for the dopamine transporter (DAT). Structure-activity relationships have been developed that contrast with those described for cocaine, despite significant structural similarity. Furthermore, behavioral evaluation of many of the BZT analogs in animal models of cocaine abuse, has suggested that these two classes of tropane-based dopamine uptake inhibitors have distinct pharmacological profiles. In general, the BZT analogs, do not demonstrate efficacious locomotor stimulation in mice, do not fully substitute for a cocaine discriminative stimulus and are not appreciably self-administered in rhesus monkeys. These compounds are generally more potent than cocaine as dopamine uptake inhibitors, *in vitro,* although their actions *in vivo* are not consistent with this action. These observations suggest that differing binding profiles at the serotonin and norepinephrine transporter as well as at muscarinic receptors might have significant impact on the pharmacological actions of these compounds. In addition, by varying the structures of the parent compounds and thereby modifying their physical properties, pharmacokinetics as well as pharmacodynamics will be directly affected. Therefore, in an attempt to systematically evaluate the impact of chemical modification on these actions, a series of N-substituted (H, CH3, allyl, benzyl, propylphenyl and butylphenyl) analogs of 3'-chloro-, 4'-chloro- and 4,4"-dichloro-BZT were synthesized. These compounds were evaluated for displacement, in rat tissue, of [3H]WIN 35,428 from DAT, [3H]citalopram from the serotonin transporter, [3H]nisoxetine from the norepinephrine transporter and [3H]pirenzepine from muscarinic m1 receptors. These studies provide binding profile data that can now be used to correlate with future behavioral analyses of these compounds and may provide insight into the kind of structural/binding profile that might be targeted as a potential treatment for cocaine abuse. Newman, A.H., Robarge, M.J., Howard, I.M., Wittkopp, S.L., George, C., Kopajtic, T., Izenwasser, S., and Katz, J.L. Journal of Medicinal Chemistry, 44, pp. 633-640, 2001.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Program Activities

New NIDA PAs and RFAs

On February 6, 2001, NIDA issued a Program Announcement entitled **Cutting-Edge Basic Research Awards (CEBRA) (PAR-01-047).** The CEBRA is a new mechanism designed by NIDA to foster novel research approaches. It is specifically designed to support research that is high-risk and potentially high-impact and that is underrepresented or not included in NIDA's current portfolio. There are two stages to the award: an early R21 exploratory phase, and a subsequent R01 development phase. Both will be reviewed on an expedited basis by NIDA, and innovation will be an important consideration.

On February 12, 2001, NIDA issued a Program Announcement entitled **Prescription Drug Abuse (PA-01-048).** This PA encourages research aimed at reducing prescription drug abuse while supporting appropriate medical use of therapeutic agents with abuse liability. To promote the Nation's health, research is needed to understand the factors contributing to prescription drug abuse, to characterize the adverse medical and social consequences associated with this abuse, and to develop effective prevention and service delivery approaches and behavioral and pharmacological treatments. Applications to address this issue are encouraged across a broad range of experimental approaches including basic, clinical, and epidemiological studies.

On February 2, 2001, NIDA issued an RFA entitled **Therapeutic Community Research (DA-01-015).** This RFA encourages new directions in behavioral treatment and services research in Therapeutic Communities (TCs) that provide treatment for drug abuse and addiction. Specifically, this RFA encourages research aimed at improving the therapeutic efficacy and efficiency of TCs. Research on therapeutic approaches that include behavioral treatments, alone or in combination with pharmacotherapies is encouraged. In addition, this RFA encourages studies on TC treatment processes; research to integrate new research-based interventions into TC treatment; and research on TC organizational and managerial processes. Letter of Intent Receipt Date for this RFA: March 19, 2001; Application Receipt Date: April 19, 2001.

PAs and RFAs Issued With Other NIH Components/Agencies

On January 25, 2001, NIDA, in conjunction with a number of other NIH Institutes and other agencies, issued a Program Announcement entitled **Research on Emergency Medical Services for Children (PA-01-044).** This multi-agency announcement is designed to improve the quality and quantity of research related to emergency medical services for children (EMSC). The types of research included under the term EMSC are: prevention research to reduce the need for emergency care; clinical research to ensure that children receive high quality and appropriate medical, nursing and mental health care in an emergency; health systems research, from pre-hospital care, to the emergency department, to inpatient care and return to the community; cost-effectiveness analyses; and methodological studies to improve the quality of research conducted.

On February 28, 2001, NIDA, in conjunction with a number of other NIH Institutes and other agencies, issued a Program Announcement entitled **Research on Child Neglect (PA-01-060).** This PA is a follow-up to the NIH Consortium RFA on Child Neglect. It is complemented by PA-99-133 Career Development Awards: Child Abuse and Neglect Research issued August 5, 1999, and a Notice concerning supplements to expand current studies to include child neglect issues and additional data analyses.

On March 19, 2001, NIDA, together with numerous other NIH Institutes issued a Program Announcement entitled **Development of Zebrafish Mutagenesis and Screening Tools (PA-01-070).** This PA is intended to encourage investigator-initiated applications for research designed to exploit the power of mutagenesis screening in zebrafish in order to detect and characterize genes, pathways, and phenotypes of interest in development and aging, organ formation, behavior, and disease processes.

On March 20, 2001, NIDA, the National Institute of Mental Health (NIMH), and the National Institute of Neurological Disorders and Stroke (NINDS) issued a joint Program Announcement entitled **HIV-1 Infection of the Central Nervous System (PA-01-072).** The objective of this cooperative effort is to foster investigations that will provide the foundation for the rapid development of therapeutic interventions to prevent and treat the effects of HIV-1 on the central nervous system (CNS). Application ranging from basic research to clinical diagnosis and treatment are of interest.

On March 20, 2001, NIDA, the National Institute of Mental Health (NIMH), and the National Institute of Alcohol Abuse and Alcoholism (NIAAA) issued a Program Announcement entitled **HIV Treatment Adherence Research (PA-01-073).** This PA identifies gaps in the understanding of antiretroviral medication therapies (ART) adherence, and encourages studies to address the role of adherence through all phases of treatment and illness, the need to broaden the scope of intervention to enhance treatment adherence, and the importance of tailoring methodological and intervention advances to the special needs and context of affected populations. Emphasis is on the development of innovative approaches to adherence and behavior change, especially models of interventions to improve adherence.

On April 3, 2001, NIDA, in conjunction with numerous other NIH Institutes issued a Program Announcement entitled **Novel Approaches to Enhance Animal Stem Cell Research (PA-01-076).** The purpose of this PA is to encourage research to enhance stem cells as a model biological system. Research to isolate, characterize, and identify totipotent and multipotent stem cells from nonhuman biomedical research animal models, as well as to generate reagents and techniques to characterize and separate those stem cells from other cell types is encouraged.

On April 3, 2001, NIDA, in conjunction with a number of other NIH components issued a Program Announcement entitled **Strategies for Germ-Line Modification in the Rat (PAR-01-077).** This PA invites applications for the purpose of establishing methods for the efficient production of rat models that contain germ-line mutations that will facilitate the transfer of biological concepts to human health problems. Development of rat embryonic stem cell (ESC) technology by modification of current techniques or development of new approaches will meet the needs of researchers using the rat to study human health and disease.

On February 13, 2001, NIDA, in conjunction with a number of other NIH components issued an RFA entitled **International Clinical, Operational and Health Services Research and Training Award (ICOHRTA) (TW-01-003).** This RFA will support training to facilitate collaborative, multidisciplinary, international clinical, operational, health services and prevention sciences research between U.S. institutions and those in developing countries, as well as emerging democracies of Eastern Europe, Russia and the Newly Independent States (NIS). The ICOHRTA will address global health problems by extending and enhancing the research of the collaborating U.S. and foreign scientists while increasing the clinical, operational, health services and prevention research capacity of the collaborating scientists and their institutions. Letter of Intent Receipt Date for this RFA: March 15, 2001; Application Receipt Date: April 27, 2001.

On February 28, 2001, NIDA, the National Institute of Mental Health (NIMH), and the National Institute of Nursing Research (NINR) issued an RFA entitled **Community Implementation of HIV Prevention Interventions (MH-01-006).** This RFA invites research grant applications that target research on the translation and adoption of empirically tested and proven Human Immunodeficiency Virus (HIV) research-based prevention interventions into community-based public health settings. This initiative is intended to foster partnerships among researchers and community-based organizations in the process of adapting and adopting proven interventions. Letter of Intent Receipt Date for this RFA: April 13, 2001; Application Receipt Date: May 11, 2001.

On April 19, 2001, NIDA, the National Institute of Mental Health (NIMH), and the National Institute of Neurological Disorders and Stroke (NINDS) issued a joint RFA entitled **Institutional Research Training Programs: Increasing Diversity (MH-01-009).** The purpose of this RFA is to encourage National Research Service Award (NRSA) institutional research training grant (T32) applications designed to recruit, train, and retain minority individuals in doctoral and/or postdoctoral programs in research areas encompassed by the missions of one or more of the three sponsoring institutes. Letter of Intent Receipt Date: July 10, 2001; Application Receipt Date: August 10, 2001.

Other Program Activities

NIDA/VACSP #1018 Buprenorphine Best Practices Trial

Enrollment for the study closed on December 31, 2000 with a total of 583 patients being enrolled. 33.3% of the patients enrolled were female. The mean age at baseline was 36.8 years (38.0 median) with a range of 16 to 66. Patients can participate up to one year from the date of their enrollment. As of March 12, 2001, 379 patients were still following the protocol. The main reasons for dropout were failure to return to clinic (57%) followed by the patient's request to discontinue (9%).

As of March 12, 2001, 56.8% the adverse events (AEs) reported, were considered mild, 37.5% were moderate, and 5.7% severe. Of the 583 patients participating, 46.3% reported no adverse events while 53.7% reported one or more AEs. There were 43 serious adverse events (SAEs) reported of which only 3 were considered possibly study drug related. The remaining SAEs were considered to be unrelated to study drug by the study physicians.

Annual reviews were held with the Perry Point VA Human Rights Committee and the NIDA/VA Data and Safety Monitoring Board. Both committees have approved the study to continue.

Clinical Trials Network (CTN) Update

Three additional awards were made in January to increase the number of nodes from 11 to 14. The new nodes are located at: University of Washington, Duke University, and New York State Psychiatric Institute.

The CTN began enrolling patients in January 2001 at multiple sites across the United States in its first study, Buprenorphine/Naloxone vs. Clonidine for Outpatient Detoxification. A total of 360 patients at 7 different sites in 6 states are being recruited.

In March 2001, the CTN began enrolling patients at multiple sites for its second study, Buprenorphine/Naloxone vs. Clonidine for Inpatient Detoxification. A total of 360 patients at 6 different sites in 5 states are being recruited.

In April 2001, the CTN began enrolling pilot patients in 4 additional behavioral studies. Motivational Enhancement Therapy is conducted at 6 sites; Motivational Interviewing is carried out at 5 sites; and Motivational Incentives is at 7 methadone clinic sites and at 7 drug free clinic sites. The sites are located throughout the 14 nodes including the new nodes awarded in January 2001.

Seventeen new protocol concepts were submitted March 20, 2001 for review and consideration for further development into new protocols.

NIDA's New and Competing Grants Awarded Since February 2001

Agar, Michael H. -- Friends Research Institute
Trend Theory In Community Context

Ahmed, Mahmoud S. -- University of Missouri
Medications Development for the Pregnant Opiate Addict

Beaudoin, Alison O. -- Yale University
Disulfiram for Cocaine Abuse In Methadone Patients

Bell, Jeanne E. -- University of Edinburgh
Neurodegeneration In HIV Infected Drug Users

Bentler, Peter M. -- University of California
New Psychometric Methods for Substance Abuse Research

Berridge, Craig W. -- University of Wisconsin
Amphetamine-Like Stimulants: Norepinephrine & Behavior

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

Buhusi, Catalin V. -- Duke University
Dopaminergic Mechanisms of Interval Timing & Drug Abuse

Cabeza De Vaca, Soledad -- New York University School of Medicine

Regulation of Drug Addiction By Feeding-Related Peptides

Carlezon, William A. -- McLean Hospital
Biobehavioral Mechanisms of Drug Reward and Addiction

Carroll, Marilyn E. -- University of Minnesota
A Primate Model of Drug Abuse: Intervention Strategies

Casada, John H. -- University of Texas Health Sciences Center at San Antonio
Emotional Control of Sedative Self-Medication In PTSD

Catley, Delwyn -- University of Kansas Medical Center
Role of Controllability In Scheduled Smoking Reduction

Chandra, Siddharth -- University of Pittsburgh
Opium Addiction: A Behavioral/Economic Analysis

Colwill, Ruth M. -- Brown University
Murine Model of Marijuana-Induced Executive Dysfunction

Cunningham, Kathryn A. -- University of Texas
Neuropsychopharmacology of MDMA: Monoaminergic Mechanisms

Cunningham, Kathryn A. -- University of Texas
Neuropsychopharmacological Interactions - Cocaine & Serotonin

Deadwyler, Samuel A. -- Wake Forest University School of Medicine
Electrophysiological Assessment of Cannabinoid Receptors

Devane, Carl L. -- Medical University of South Carolina
Pharmacogenetics of Methadone

D'Souza, D. Cyril -- Yale University
Altered Cannabinoid Sensitivity In Schizophrenia

Eisenstein, Toby K. -- Temple University School of Medicine
Opioid Dependence, Immunity and Infection

El-Bassel, Nabila -- New York University
Preventing HIV and Other STDs Among Drug-Involved Women

Epstein, Joel -- University of Missouri
Analysis of Differing Drug Abuse Education Technologies

Evins, Anne E. -- Massachusetts General Hospital
Nicotine and Smoking Cessation In Schizophrenia

Fillmore, Mark T. -- University of Kentucky
Cognitive Processes In Cocaine and Polydrug Abuse

Finn, Kristin V. -- Research Institute on Addictions
Alcohol and Marijuana Use In School Settings

Flanagan, Constance A. -- Pennsylvania State University
Prevention As A Civic Issue

Frederick, Blaise D. -- McLean Hospital
fMRI Technique Development for Substance Abuse Research

Galanter, Marc -- Nathan S. Kline Institute
Methadone Anonymous: Behavioral Therapy Development

Galli, Aurelio A. -- University of Texas Health Sciences Center
Amphetamine Regulation of Dopamine Transport

Gascoigne, Nicholas R. -- Scripps Research Institute

Cannabinoid Receptor Dynamics In T Cell Activation

Gauda, Estelle B. -- Johns Hopkins University
Nicotine Induced Neuroplasticity In the Carotid Body

George, Tony P. -- Yale University
Nicotinic Receptors and Cognitive Function In Schizophrenia

Goeders, Nicholas E. -- Louisiana State University Health Sciences Center
Role for the HPA Axis In Methamphetamine Reinforcement

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

Greengard, Paul -- Rockefeller University
Drugs of Abuse -- Role of Protein Phosphorylation

Grobe, James E. -- University of Kansas
Smoking Controllability/Moderation of Tobacco Effects

Grodzicker, Terri I. -- Cold Spring Harbor Laboratory
Cellular Biology of Addiction

Henderson, Leslie P. -- Dartmouth Medical School
Steroid Regulation of Ion Channels

Hersh, Louis B. -- University of Kentucky
Degradation of Opioid Peptides

Hien, Denise A. -- St. Luke's Roosevelt Hospital
Cocaine, Self-Regulation, and Maternal/Child Aggression

Honda, Christopher N. -- University of Minnesota
Opioid Receptors and Spinal Nociception

Howell, Leonard L. -- Emory University
Neuropharmacology of Cocaine

Hurt, Hallam -- Albert Einstein Healthcare Network
In Utero Cocaine Exposure: Child Neurocognitive Outcome

Itzhak, Yossef -- University of Miami
Substituted Amphetamines: No-Dependent Mechanisms

Johanson, Chris-Ellyn -- Wayne State University
Brain Imaging of Tobacco Craving Using fMRI

Kandel, Denise B. -- Columbia University
Substance Dependence/Abuse In the U.S.Population

Kellar, Kenneth -- Georgetown University
Nicotinic Receptors Autonomic Ganglia and Adrenal Gland

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

Knuepfer, Mark M. -- Saint Louis University
Sympathetic Regulation of Endotoxemia In Drug Abuse

Kornetsky, Conan -- Boston University School of Medicine
Drugs of Abuse and Brain-Stimulation Reward In the Mouse

Kumar, Mahendra -- University of Miami
HIV-1 + IDUs: Endocrine Consequences & Medical Outcomes

Labar, Kevin S. -- Duke University

Spatiotemporal Dynamics of Emotional Memory Networks

Leslie, Frances M. -- University of California, Irvine
Nicotine Regulation of Developing Brain Catecholamines

Lewis, David E. -- University of Wisconsin
An Abef Synthon for Norditerpenoid Alkaloids

Lewis, Deborah L. -- Medical College of Georgia
Brain Cannabinoid Receptor Signaling and Pharmacology

Lewis, John W. -- University of Bath
Discovery of New Treatments for Drug Abuse

Liddle, Howard A. -- University of Miami
Economic Evaluation of Adolescent Drug Services

Lombardi, Emilia L. -- University of California, Los Angeles
Substance Use and Treatment Within a Transgender Sample

Madden, John J. -- Emory University
8th Conference: Drug Abuse, Immunomodulation and AIDS

Maier, Steven F. -- University of Colorado
Stressor Controllability, Drugs of Abuse, and Serotonin

Makriyannis, Alexandros -- University of Connecticut
Endocannabinoid Active Sites As Therapeutic Targets

Maragos, William F. -- University of Kentucky Medical Center
Methamphetamine and HIV Protein-Induced Neurotoxicity

Mccance-Katz, Elinore F. -- Albert Einstein College of Medicine
Enhancing Health Care of Drug Users With HIV

Mccance-Katz, Elinore F. -- Albert Einstein College of Medicine
Cocaethylene-Cocaine Agonist Therapy/Tolerance Induction

McCarty, Dennis -- Oregon Health Sciences University
Client and Counselor Attitudes Toward Medication

McKay, James R. -- University of Pennsylvania
Effectiveness and Costs of Enhanced Cocaine Treatments

Meisel, Robert L. -- Purdue University
Dopamine Sensitization By Motivated Behaviors

Melega, William P. -- University of California, Los Angeles
Brain and Behavioral Alterations After Methamphetamine

Mello, Nancy K. -- McLean Hospital
Buprenorphine: A Behavioral Analysis

Micevych, Paul E. -- University of California, Los Angeles
Sex Steroid Activation of Opioid Circuits In the CNS

Michael, Adrian C. -- University of Pittsburgh
Extracellular Neurochemistry and Substance Abuse

Middaugh, Lawrence D. -- Medical University of South Carolina
Cocaine Self Administration And Relapse In Mice

Milby, Jesse B. -- University of Alabama at Birmingham
Cost Effective Treatment for Dually Diagnosed Homeless

Morgan, Drake -- Wake Forest University School of Medicine

Vulnerability To the Reinforcing Effects of Opioids

Nair, Madhavan P. -- SUNY at Buffalo
Heroin-AIDS Encephalopathy: Neuropathogenesis Mechanisms

Nation, Jack R. -- Texas A & M University
Heavy Metals and Polydrug Self-Administration

Neisewander, Janet L. -- Arizona State University
Neural Mechanisms of Drug-Seeking Behavior

Nishith, Pallavi -- University of Missouri
Substance Use and Dissociation As Risk Factors for PTSD

Ondersma, Steven J. -- Wayne State University
Brief Intervention In At-Risk First-Time Mothers

Pan, Zhizhong Z. -- University of California, San Francisco
Opioid Receptors In the Mechanisms of Opioid Tolerance

Pasternak, Gavril W. -- Sloan Kettering Institute-Cancer Research Center
Biochemical Characterization of Opioid Binding Sites

Paulus, Martin P. -- University of California, San Diego
MDMA & Amphetamine: Behavioral Organization In Mice

Paulus, Martin P. -- University of California, San Diego
Neuroimaging of Decision Making In Stimulant Addiction

Pelham, William E. -- University of New York
Development of Drug Use and Abuse In ADHD Adolescents

Porreca, Frank -- University of Arizonia
Opioid and Non-Opioid Actions of Dynorphin In Pain

Rayport, Stephen G. -- Columbia University
Glutaminase Knockouts and Drug Dependence

Reilly, Mark P. -- Arizona State University
Toward a General Theory of Drug Behavior Dynamics

Reti, Irving M. -- Johns Hopkins University
NARP Expression and Drugs of Abuse

Rhee, Soo H. -- University of Colorado
Causes of Comorbidity:Substance Use Disorder, ADHD & CD

Richards, Jerry B. -- University of Buffalo
Models of Impulsive Behavior In Mice

Roberts, David C. -- Wake Forest University School of Medicine
A Novel Animal Model of Cocaine Addiction

Roberts, David C. -- Wake Forest University School of Medicine
GABA Modulation of Cocaine & Heroin Self-Administration

Rogers, Thomas J. -- Temple University School of Medicine
Opioid & Chemokine Receptor Interactions Relative To HIV

Rohsenow, Damaris J. -- Brown University
Motivating Substance Abusers To Quit Smoking

Samuolis, Jessica -- Fordham University
Autonomy/Relatedness In Families of Drug Abusing Teens

Schoffelmeer, Anton N. -- Free University

Gene Expression Patterns During Heroin Seeking Behavior

Siegal, Harvey A. -- Wright State University
Crack & Health Service Use: A Natural History Approach

Simon, Eric J. -- New York University School of Medicine
32nd International Narcotics Research Conference (INRC)

Singer, Lynn T. -- Case Western Reserve University
Cocaine Exposed Infants and Their Mothers -- Follow-Up

Smith, James B. -- Mercer University
Behavioral Influences on Drug Tolerance

Snow, Diane M. -- University of Kentucky Medical Center
Maternal Cocaine Use and Neurite Outgrowth

Sorkin, Alexander D. -- University of Colorado Health Sciences Center
Dopamine Transporter Regulation By Endocytosis

Spealman, Roger D. -- Harvard Medical School
Nonhuman Primate Model of Cocaine Relapse and Treatment

Steketee, Jeffery D. -- Louisiana State University
The Medial Prefrontal Cortex and Cocaine Sensitization

Stitzer, Maxine L. -- Johns Hopkins University School of Medicine
Recovery Housing and Drug Abuse Treatment Outcomes

Stout, Julie C. -- Indiana University
Cognitive Modeling of Risky Decisions In Substance Users

Strathdee, Steffanie A. -- Johns Hopkins University
Baltimore Needle Exchange Program Evaluation

Tsuang, Ming T. -- Massachusetts Mental Health Research Corporation
Molecular Genetics of Heroin Dependence

Van Bockstaele, Elisabeth J. -- Jefferson Medical College
Opioid Modulation of the Coeruleo-Cortical Pathway

Van De Kar, Louis D. -- Loyola University, Chicago
Treatment of Cocaine-Induced 5-HT Dysfunction

Villanueva, Miguel -- University of New Mexico
Zuni Pueblo Veteran Project

Vlahov, David -- New York Academy of Medicine
Expanded Syringe Access Program: New York Evaluation

Ware, Norma C. -- Harvard Medical School
Social Course of Adherence To HAART In Active Drug Users

Weisner, Constance M. -- University of California, San Francisco
Integrated Drug and Medical Care-Cost and Effectiveness

White, Francis J. -- Finch University of Health Sciences
Mouse Behavior Models of Cocaine Addiction

Wills, Thomas A. -- Albert Einstein College of Medicine
Young Children's Vulnerability To Substance Use

Wills, Thomas A. -- Albert Einstein College of Medicine
Vulnerability and Protective Factors For Early Onset

Wood, Ruth I. -- University of Southern California

Neurobiology of Androgen Reward

Woods, James H. -- University of Michigan
Evaluation of Protein Based Medications Against Cocaine

Yoburn, Byron C. -- St. John's University
Protein Kinase In Opioid Receptor Regulation & Tolerance

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Extramural Policy and Review Activities

Review Meetings

For this Council cycle, the Office of Extramural Affairs arranged and managed 12 committees for the review of grant applications and 14 for contract proposal reviews. In addition, one contract concept was reviewed.

The reviews for NIDA's chartered committees were held, which include NIDA-E (Treatment Review Committee), NIDA-F (Health Services Review Committee), NIDA-L (Medications Development Committee), and NIDA-K (Training Committee). One Special Emphasis Panel was held to review applications in conflict with the chartered committees. Six Special Emphasis Panels were constituted for reviews of specific mechanisms: centers, program projects (two meetings), institutional development programs, B/STARTs, and conference grants.

One meeting was held for reviews of the RFA entitled **Services Research on the National Drug Abuse Treatment Clinical Trials Network.**

The Contracts Review Branch managed the following reviews of proposals:

N43DA-1-5509 Topic 36	**Develop Materials for Gathering Data and Completing Social Network Analysis in Drug Abuse Prevention**
N43DA-1-7716 Topic 38	**High-throughput Screening of Functional Activity of Proteins Using Biosensor-Based Technology**
N43DA-1-7719 Topic 40	**Fluorescent Probes**
N43DA-1-7720 Topic 8	**Drug Supply Services Support<**/TD>
N01DA-1-1102	**Policy Planning Support Services**
N43DA-1-5507 Topic 34	**Develop New Technologies for Abuse Prevention Delivery**
N01DA-1-8816	**In Vitro Receptor Activity Determinations for Medications Development**
N01DA-1-8814	**Technical and Conference Support**
N01DA-1-7725	**Antinociception Physical Dependence and Abuse Liability Testing**
N44DA-1-8803 Phase II SBIR	**HIV Risk Assessment for Women in a Health Care Setting**
N44DA-1-5503 Phase II SBIR	**Telemedicine**
N44DA-1-7705 Phase II	**Transdermal THC**

SBIR	
N44DA-1-7708 Phase II SBIR	**Development of Placebo Marijuana Cigarettes**
N01DA-1-8813	**Development and Manufacture of Pharmaceutical Products for Addiction Treatment**

In addition, a concept for N01DA-1-5514 **State and Local Epidemiologic Planning and Information Development** was reviewed.

Consumer members participated in the review meetings for the NIDA-E (Treatment) and NIDA-F (Health Services) study sections in February and March 2001. The initial experience was positive in terms of contributions made by the new members and their interactions with the rest of the committee. OEA is evaluating this process.

Staff Training and Policy Development

The OEA Symposium Series continued its monthly meetings for staff development. In January 2001, Dr. Ron Geller, Director, Office of Extramural Programs, NIH, spoke on developing Program Announcements and Requests for Applications. Dr. Rita Liu, Associate Director for Grants Activities, OEA, presented on reviews of Centers in February 2001. In March 2001, Dr. George Stone, Chief, Extramural Inventions and Technology Resources Branch, NIH, and Mr. John Salzman, IEdison User Support Specialist, NIH, led a presentation of intellectual property and the rights and responsibilities of grantees, contract recipients, and NIH staff. April 2001's session was a question and answer forum with NIDA's Director, Dr. Alan Leshner. The OEA Symposium Series is organized by Dr. William C. Grace, Deputy Director, OEA.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Congressional Affairs

(Prepared April 11, 2001)

FISCAL 2002 BUDGET

Before Congress adjourned for its 2-week Spring recess on April 7, 2001, the House passed its FY 2002 budget resolution (H. Con. Res. 83). The Senate, in a series of votes on the measure, added billions for higher spending. On a key vote prior to passage, the Senate shifted $450 billion from the budget resolution's tax-cut allocation to education and debt reduction. For health, the budget resolution assumes $41 billion for discretionary health, which is $2.2 billion above last year's spending level. At the same time, the budget includes a $2.8 billion increase for NIH.

President Bush released his detailed budget proposal on Monday, April 9, 2001. The $1.96 trillion budget for fiscal 2002 would hold discretionary spending to a 4 percent increase overall. The President's top domestic priorities, education and defense, would get the biggest boosts. Those increases would be offset by reductions in other areas, including environmental and natural resources programs, agriculture and transportation. The Administration has indicated that the President may veto appropriations bills exceeding his 4 percent target.

The President's budget reflects the Administration's commitment to continue the five-year plan to double the NIH budget by FY 2003, with FY 2002 representing the fourth installment of this plan. NIH would get the biggest discretionary spending increase ever, with a boost of $2.8 billion to a total of $23.1 billion - a 13.5% increase over FY 2001. Of that amount, $12.5 billion, a 12.6% increase, would be spent on research project grants to fund 9,158 new and competing grants. Support for AIDS research would increase by $258 million, or 11.5%. NIDA would receive $907,369,000 in FY 2002, for a 16.2% increase over 2001.

MEETINGS/BRIEFINGS

January 29, 2001 - At the request of staff of the Senate Judiciary Committee, Dr. Alan I. Leshner, briefed a bipartisan group of Committee staff. The focus of the meeting was on research relating to drug abuse treatment programs in the criminal justice system and aftercare components. Mary Mayhew and Keith Van Wagner, OSPC, accompanied Dr. Leshner.

March 15, 2001 - Dr. Alan I. Leshner briefed Rep. Ralph Regula (R-OH), Chairman, House Appropriations Subcommittee on Labor HHS/Education, and his staff on the current state of drug abuse treatment and prevention research. Of particular interest to the Chairman was the development of the Clinical Trials Network. Mary Mayhew, OSPC, accompanied Dr. Leshner.

March 21, 2001 - At the request of Rep. C.W. 'Bill' Young (R-FL), Chairman, House Appropriations Committee, Dr. Alan I. Leshner, briefed the Chairman and his staff on a wide-range of drug abuse issues. Specifically, Dr. Leshner discussed the Clinical Trials Network, emerging drug trends in Florida, and prescription drug abuse among the elderly. Mary Mayhew, OSPC, accompanied Dr. Leshner.

March 22, 2001 - At the request of Senator Orrin Hatch (R-UT), Chairman of the Senate Judiciary Committee, Dr. Alan Leshner met with the Committee's Majority Staff Director to follow-up on key issues related to the March 14, 2001, Senate Judiciary Committee hearing on "Treatment, Education and Prevention: Adding to the Arsenal in the War on Drugs". Mary Mayhew, OSPC, accompanied Dr. Leshner.

HEARINGS

Senate Judiciary Committee Hearing - March 14, 2001

Dr. Leshner was invited to testify before the Senate Judiciary Committee at a hearing on "Treatment, Education, and Prevention: Adding to the Arsenal in the War on Drugs." The hearing focused on the need for a comprehensive strategy to combat the national problem of addiction. Witnesses included representatives from the Drug Enforcement Administration, the U.S. Attorney's office, as well as state organizations, advocacy groups and private citizens.

In his statement before the Committee, Dr. Leshner stressed the importance of drug treatment and prevention research. He pointed out that numerous studies have shown that addiction treatments are just as effective as those for other illnesses. For example, one very important analysis recently published in the *Journal of the American Medical Association* (JAMA, October 4, 2000) clearly shows that addiction treatments work just as well as treatments for other chronic, relapsing illnesses such as asthma, hypertension, and diabetes. He testified that scientific discoveries are fueling the development of more successful strategies to deal with addicted criminal offenders. The core phenomenon is that untreated addicted offenders have extremely high rates of post-release recidivism both to drug use and to criminality. However, providing science-based treatments while offenders are under criminal justice control can dramatically reduce recidivism, again both to drug use and to later crime. He went on to say that, understanding addiction as a treatable, chronic illness has beneficial ramifications for our national drug control efforts. In answering questions about jail-based substance abuse treatment, Dr. Leshner said it is important that we not settle for "just anything called treatment," but rather focus on programs that are comprehensive and science-based.

Senate Caucus on International Narcotics Control Hearing - March 21, 2001

The Senate Caucus on International Narcotics Control, co-chaired by Sen. Charles Grassley (R-IA) and Sen. Joseph Biden (D-DE), held a hearing on "America at Risk: The Ecstasy Threat". In their opening statements, the co-chairmen spoke of the importance of educating America's youth on MDMA. Sen. Grassley complimented the work of NIDA in trying to further our understanding of the drug, while Sen. Graham (D-FL) touched upon expanding research that explains how Ecstasy disrupts serotonin levels in the brain. During the hearing the Senators explored with the witnesses methods by which to control MDMA's use and educate potential users as to its dangers. Testifying at the hearing were representatives from the Office of National Drug Control Policy, the Drug Enforcement Administration, U.S. Customs and state and local law enforcement agencies.

House Government Reform Subcommittee on Criminal Justice, Drug Policy and Human Resources Hearing - March 27, 2001

The House Government Reform Subcommittee on Criminal Justice, Drug Policy and Human Resources held a hearing on "'Medical' Marijuana, Federal Drug Law and the Constitution's Supremacy Clause". The Subcommittee, chaired by Rep. Mark Souder (R-IN), heard testimony from groups for the legalization of marijuana for medicinal purposes, and those opposed. In addition, witnesses from the Drug Enforcement Administration and the Institute of Medicine testified.

House Appropriations Subcommittee on Labor/HHS/Ed will hold NIH hearings May 16, 2001

The Committee on Appropriations, Subcommittee on Labor, HHS, and Education will hold the "NIH Budget Overview" hearing on May 16, 2001. Dr. Ruth Kirschstein, Acting Director, will testify. Dr. Alan I. Leshner, Director, NIDA, and other Institute/Center Directors will accompany Dr. Kirschstein.

BILLS OF INTEREST

S. 89 - Drug-Free America Act of 2001 - Sen. Charles Grassley (R-IA) introduced S. 89 on January 22, 2001, a bill that primarily is designed to enhance the illegal narcotics control activities of the US, including provisions relating to enhancing inspection and drug interdiction capabilities of the Customs Service and the National Guard. The bill also authorizes NIDA's Clinical Trials Network to conduct its large-scale treatment studies in community settings. Under the proposed legislation, the authorization would be through Fiscal Year 2007. The bill also includes a 'sense of the Senate' section that encourages NIH to work with experts from private industry to promote research regarding

pharmacological options that may be employed to support drug treatment efforts. The bill would also increase the number of residential drug abuse treatment units in Federal prisons and compel the Secretary of HHS to award grants in establishing adolescent therapeutic community treatment programs. In addition, it would have grants made by ONDCP to establish the National Community Anti-Drug Coalition, funding up to two million dollars in Fiscal Year 2002. S. 89 was referred to the Senate Judiciary Committee.

S. 160 - Drug Abuse Treatment on Demand Assistance Act - Sen. Barbara Boxer (D-CA) introduced S. 160 on January 23, 2001. The bill would authorize appropriations for grants for the purpose of increasing the maximum number of individuals to whom public and nonprofit private entities are capable of providing effective treatment for substance abuse, with the goal of ensuring that substance abuse treatment is available for all who seek it. It would set up state grant programs to support: the construction of treatment facilities; payments to treatment centers; drug testing; and counseling, including mental health services. Among the programs proposed under the bill, several would provide substance abuse treatment to convicted criminals. S. 160 would authorize $600 million annually from Fiscal Year 2002 through 2006. States would be required to match the money with non-federal contributions. S. 160 was referred to the Senate Health, Education, Labor and Pensions Committee.

S. 304 - Drug Abuse Education, Prevention and Treatment Act of 2001 - Citing the need for a more balanced approach to the war on drugs, a bipartisan group of senators introduced S. 304 on February 13, 2001. Sen. Orrin Hatch (R-UT) and four co-sponsors (2 Republican, 2 Democrat) introduced the bill to reduce illegal drug use and trafficking and to help provide appropriate drug education, prevention, and treatment programs. Along with provisions that would increase penalties for drug-related offenses involving juveniles and reestablish drug courts, S. 304 allows for drug-free prison incentive grants for the creation and expansion of substance abuse treatment programs in correctional settings. Included in the bill is language that encourages an aftercare component in the treatment of prisoners for drug abuse and addiction. Section 308 calls for the expansion of drug abuse prevention and treatment research at NIDA and authorizes an appropriation of $76.4 million for that purpose. The bill also provides for the development of additional school and community-based drug education and prevention programs that are 'researched-based'. In addition, S. 304 contains a section that would include religious organizations as Non-Governmental Organizations that should be considered to provide assistance on the same basis as other such organizations. Upon its introduction, S. 304 was referred to the Senate Committee on the Judiciary.

S. 595 - Fairness in Treatment: The Drug and Alcohol Addiction Recovery Act of 2001 - A bill to amend the PHS Act, Employee Retirement Income Security Act of 1974, and the IRS Code of 1986 to provide for nondiscriminatory coverage for substance abuse treatment services under private group and individual health coverage was introduced by Sen. Paul Wellstone (D-MN) on March 22, 2001. S. 595 was referred to the Committee on Health, Education, Labor and Pensions.

Amendment Number 186 to H.C. Res. 83 - On April 4, 2001, the Senate passed the Specter-Harkin amendment to H.C. Res. 83 by a vote of 96 to 4. This legislation amends the FY 2002 budget resolution to increase the assumption for NIH within the function 550 total by $700 million. This would put NIH on the doubling track in 5 years, with a $3.5 billion increase in FY 2002. H.C. Res. 83 originally assumed a $2.8 billion increase for NIH, consistent with the President's request. The amendment was co-sponsored by Senators Mikulski (D-MD), Collins (R-ME), Landrieu (D-LA), Kerry (D-MA), Wellstone (D-MN), Murray (D-WA), DeWine (R-OH), Sarbanes (D-MD), and Snowe (R-ME).

S. 723 - Stem Cell Research Act of 2001 - On April 5, 2001, Sen. Arlen Specter (R-PA) Chairman, Appropriations Subcommittee on Labor, HHS, Education, introduced S. 723, a bill to amend the PHS Act to provide for human embryonic stem cell generation (derivation) and research. The bill had 12 cosponsors. S. 723 was referred to the Committee on Health, Education, Labor and Pensions.

H.R. 162 - Mental Health and Substance Abuse Parity Amendments of 2001 - Introduced by Rep. Marge Roukema (R-NJ) on January 3, 2001, H.R. 162 is identical to legislation sponsored in the 106th Congress by the Representative. The bill would amend the Public Health Service Act, Employee Retirement Income Security Act of 1974, and the Internal Revenue Code of 1986 to prohibit group and individual health plans from imposing treatment limitations or financial requirements on the coverage of mental health benefits and on the coverage of substance abuse and chemical dependency benefits if similar limitations or requirements are not imposed on medical and surgical benefits. H.R. 162 has been referred to the House Education and the Workforce, the House Energy and Commerce, and the House Ways and Means committees. It currently has 91 co-sponsors (79 Democrats, 11 Republicans, and 1 Independent).

H.R. 1167 - Comprehensive Tuberculosis Elimination Act of 2001 - A bill to amend the Public Health Service Act with respect to making progress toward the goal of eliminating tuberculosis, was introduced by Rep. Sherrod Brown (D-OH). H.R. 1167 was referred to the Committee on Energy and Commerce.

H.R. 1185 - Global Access to HIV/AIDS Medicines Act of 2001 - A bill to prohibit the revocation or revision of any intellectual property or competition law or policy of a developing country that regulates HIV/AIDS pharmaceuticals or medical technologies. Introduced March 22, 2001 by Rep. Barbara Lee (D-CA), H.R. 1185 was referred to Energy and Commerce and Judiciary Committees.

H.R. 1194 - Harold Hughes-Bill Emerson Substance Abuse Treatment Parity Act of 2001 - Introduced March 22, 2001 by Rep. Ramstad (R-MN). A bill to amend the Employee Retirement Income Security Act of 1974, Public Health Service Act, and the Internal Revenue Code of 1986 to provide parity with respect to substance abuse treatment benefits under group health plans and health insurance coverage. H.R. 1194 was referred to the Committee on Education and the Workforce, House Energy and Commerce, House Ways and Means.

H.R. 1260 - Ban on Human Cloning Act - On March 28, 2001, Rep. Kerns (R-IN) introduced H.R. 1260, which was referred to the Judiciary Committee.

H.R. 1340 - Biomedical Research Assistance Voluntary Option Act - On April 3, 2001, Rep. Bilirakis (R-FL) introduced H.R. 1340, a bill to amend the IRS Code of 1986 to allow taxpayers to designate that part or all of any income tax refund be paid over for use in biomedical research conducted through NIH. H.R. 1340 was referred to the Committees on Ways and Means and Energy and Commerce.

H.R. 1454 - A bill to prohibit the importation of bidi cigarettes - On April 4, 2001, Rep. Gallegly (R-CA) introduced H.R. 1454. The bill cites the economic and health related reasons for the legislation. For example, it states that 430,000 people die every year from tobacco use; medical expenses from treating smoking-related diseases cost the U.S. economy $89,000,000,000 annually; studies indicate that bidi cigarettes manufactured with flavors, such as strawberry, chocolate, and mandarin orange, are more likely to induce children to smoke; and that bidi cigarettes are more likely to be sold illegally to youth and without required warning labels; because of similar appearance to marijuana cigarettes, bidi cigarettes are considered to be a more likely "gateway drug", and could lead to more children using illegal drugs; and bidi cigarettes generally deliver 3 to 8 times more nicotine, 3 times more carbon monoxide and 5 times more tar, as well as higher levels of phenol, ammonia, nitrosamines, and hydrogen cyanide, than conventional U.S. filtered cigarettes. H.R. 1454 was referred to the Committee on Ways and Means.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

International Activities

NIDA sponsored a seminar on **Development of Drug Abuse Research Infrastructure in Latin America** February 17, 2001, during the American Association for the Advancement of Science (AAAS) Annual Meeting in San Francisco. Speakers included NIDA Director Dr. Alan I. Leshner; Dr. Steven W. Gust, Acting Director, International Program; Dr. Ivan D. Montoya, Clinical Trials Network Branch, DTR&D, discussing Colombia; Dr. Flavio Pechansky, Federal State University of Rio Grande du Sol, Brazil; Dr. Maria Elena Medina-Mora, Mexican Institute of Psychiatry; and Dr. Diana Rossi, Intercambios of Argentina. The panel members discussed how U.S. researchers and policymakers could learn from the new developments, re-emerging situations, and evolving research infrastructures in Latin America. Presenters also summarized local and regional needs for capacity building and additional international collaborative research on drug abuse.

Dr. Hem Raj Pal, India, and Dr. Fernando Wagner, Mexico, have been selected as the **2001 WHO/NIDA/CPDD International Traveling Fellows.** The awards will support the researchers' collaborative visits with U.S. scientists and participation in two June 2001 scientific meetings, the NIDA-sponsored *Building International Research on Drug Abuse: Children and Youth at Risk,* and the College on Problems of Drug Dependence (CPDD) Annual Scientific Meeting. NIDA, the World Health Organization (WHO), and CPDD support the competitive International Traveling Fellowships. Dr. Pal will visit Dr. Thomas F. Babor, University of Connecticut Health Center, to discuss developing low-cost and low-intensity intervention programs. Dr. Wagner will work with Drs. Arthur Alterman and Thomas McLellan, University of Pennsylvania, on cross-national collaboration to evaluate and enhance the validity of the Addiction Severity Index for use in Mexico and other countries.

The **2000-2001 INVEST Research Fellows visited NIDA in February 2001** to learn how the Institute administers its research programs and meet with Institute staff. On March 1, 2001, Dr. Henrik Druid, Sweden, and Dr. Chuang Liu, China, met with scientists at the Intramural Research Program (IRP) in Baltimore, including Dr. Steven Goldberg, Preclinical Pharmacology Section; Dr. Marilyn Huestis, Clinical Pharmacology Branch; Dr. Alane Kimes, Neuroimaging Research Branch; Dr. Amy Newman, Medicinal Chemistry Section; and Dr. Kenzie Preston, Treatment Research Branch. At NIDA headquarters in Bethesda, Dr. Druid met with Dr. Harold Gordon, Clinical Neurobiology Branch, DTR&D, and Dr. Liu met with Dr. Steven Grant, Clinical Neurobiology Branch, DTR&D. The INVEST Fellows were joined by the 2000-2001 Hubert H. Humphrey Drug Abuse Research Fellows for a seminar on the U.S. National Institutes of Health grant application process presented by the following NIDA staff members: Dr. Steven Gust, International Program, OSPC; Dr. Mark Swieter, Office of Extramural Affairs; and Dr. Cindy Miner, Science Policy Branch, OSPC. Dr. Sharon Hrynkow, Deputy Director, NIH Fogarty International Center, also presented during the seminar.

The **2001 NIDA Distinguished International Scientists** have begun their international collaborations. Dr. Christian SchŸtz, Ludwig-Maximilians University, Germany, is working with Dr. John Krystal, Yale School of Medicine, to prepare a research grant proposal for a pilot study of the effects of the opioid antagonist naloxone on a challenge with the NMDA antagonist memantine. Dr. Tibor Wenger, Semmelweis University, Hungary, is collaborating with Dr. Billy Martin, Virginia Commonwealth University, using immunohistochemistry to determine the anatomical relationship between cannabinoid and dopamine systems. Dr. Anton Bespalov, Pavlov Medical University, Russia, is working with Dr. Athina Markou, The Scripps Research Institute, to study the intravenous self-administration of nicotine in nicotine-dependent mice.

Two NIDA grantees and their Russian colleagues began work in April 2001 on collaborations supported by the **International Competitive Design Awards for Innovative Drug Abuse and HIV/AIDS Prevention Efforts**

awarded by NIDA for participants in the 1999 *U.S. - Russia Binational Workshop: Drug Abuse and Infectious Disease Prevention Strategies.* Dr. Holly Hagan, Seattle-King County Health Department, is working on two projects; one with Dr. Natalia Doljanskaya, Ministry of Health Research Institute on Addiction, the other with Dr. Arman Karapetian, Pavlov Medical University. Dr. Kevin Haggarty, University of Washington, is collaborating with Dr. Grigory Latyshev, St. Petersburg Drug Abuse Prevention Center.

Three **new brochures describe NIDA international fellowship and professional development programs.** The brochures describe the program components, eligibility requirements, application procedures, deadlines, and award notification dates for INVEST Research Fellowships, NIDA Hubert H. Humphrey Drug Abuse Research Fellowships, and NIDA Distinguished International Scientist Collaboration Program Awards. INVEST Research Fellowships provide one year of U.S. training for scientists from any other country who have at least two years of postdoctoral research experience. The NIDA Humphrey Fellowships offer academic course work and professional affiliations for mid-career professionals from eligible countries who hold a doctoral or master's degree and have substantial professional or research experience in drug abuse. The Distinguished Scientist Awards support collaborative efforts by veteran drug abuse researchers from any other country.

Mr. Richard A. Millstein, Deputy Director, NIDA, hosted a meeting of Andrea Muccioli, President, and Dr. Gian-Paolo Brusini, Scientific Director, San Patrignano Community, Rimini, Italy, with NIDA treatment research, services research, HIV/AIDS research, and international staff on potential collaborations, March 21, 2001, Rockville, MD.

Dr. Steven Gust led a NIDA briefing for a delegation from the Norwegian government on April 4, 2001. NIDA staff, including Dr. Eve Reider and Susan David, Prevention Research Branch, DESPR, Drs. Richard Hawks, Jack Blaine, and Steven Grant, DTR&D, and Dr. James Colliver, DESPR made presentations on NIDA's programs. The visiting delegation included Guri Ingebrigtesen, Minister of Social Affairs; Eva Jupskas, Political Advisor; Ingelin Killengreen, National Police Commissioner; Ellen Seip, Director General; Jostein Soldal, Chief of Information; and Dag Rekve, Advisor.

On February 21, 2001, Dr. Elizabeth Robertson, Prevention Research Branch, DESPR, met with Tomas Hallberg, Director, European Cities Against Drug Use to discuss similarities and differences in prevention approaches between the U.S. and Europe.

Drs. Eve Reider and Elizabeth Robertson, Prevention Research Branch, DESPR, met on April 2, 2001, with Maricel Fuentes and Carlos Valdivieso, Director, Fundacion Paz Ciudadana of Chile to discuss drug abuse and violence prevention programs in the U.S. and Chile. Chile has adopted the Life Skills Training program, primarily through the advocacy of the Fundacion.

Dr. Henry Francis, CAMCODA, and Dr. Jack Blaine, DTR&D, attended a national Chinese medical officers meeting on AIDS and drug use in Kunming, China on March 5-10, 2001 sponsored by the World AIDS Foundation. Dr. Francis gave a lecture, reviewing for the 100 participants from all the provinces in China, the medical consequences of drug use and the epidemiology of HIV, Hepatitis B and C spread associated with intravenous drug use. Dr. Blaine gave a review of all the pharmacotherapies and behavioral therapies used in substance abuse treatment and how they may be used to prevent HIV transmission or at least minimize high risk behavior for HIV infection. He also discussed the methodologies which may be most useful in medical and addiction treatment facilities. After the meetings, Drs. Francis and Blaine talked with several Chinese drug use investigators interested in applying for NIDA grants.

Dr. Eve Reider, Prevention Research Branch, DESPR, represented NIDA and presented at a conference in South Africa on March 21-22, 2001. The meeting, *Youth Risk Reduction in South Africa: A Working Conference,* is part of an initiative by NIDA-funded prevention researchers from Pennsylvania State University and researchers from eight universities in South Africa. The initiative involves developing a collaborative research agenda to address the issue of reducing sexual- and drug-related risk behaviors of South African youth using the prevention methodology of the NIDA-funded grants as a starting point for discussion.

Dr. Jag H. Khalsa, CAMCODA, in collaboration with Drs. Jonathan Kagan and Karin Klingman, Division of Therapeutics, National Institute on Allergy and Infectious Diseases (NIAID), presented NIDA research efforts in the area of drug-drug interactions at the *2nd International Workshop on HIV Pharmacotherapy,* Noordwijk, the Netherlands, April 2-4, 2001. The meeting was sponsored by Virology Education, the Netherlands, and co-sponsored by the pharmaceutical industry. About 160 clinicians and scientists attended the meeting, which featured presentations on various aspects of pharmacokinetic/pharmacodynamics of interactions among the various classes of antiretroviral drugs. The organizers welcomed the NIH participation and will add a new section on interactions among drugs of abuse and medications used in the treatment of drug addiction (such as methadone, LAAM, or buprenorphine) and co-occurring infections (such as HIV) at the next international workshop, scheduled for April 2002 in the United States, probably either in Baltimore or Washington, DC.

Dr. Jean Lud Cadet gave a presentation entitled "Free Radicals, Neuronal Apoptosis, and Activation of Multiple Transduction Pathways" at the Pucon Neurotoxicity meeting held in Chile, March 15-19, 2001.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Meetings/Conferences

NIDA, with The National Center on Addiction and Substance Abuse at Columbia University (CASA) and NIMH, sponsored a conference entitled **Food for Thought: Substance Abuse and Eating Disorders,** on January 23, 2001, in New York, NY. The conference brought together top experts and researchers from around the country to explore the science of how and why these disorders develop, the role of our culture and the media, and prevention and treatment. Dr. Alan I. Leshner delivered the keynote address.

The **Fifth Annual PRISM Awards** were held on April 4, 2001, in Los Angeles, CA. NIDA sponsored the event with the Entertainment Industries Council and the Robert Wood Johnson Foundation. These awards are bestowed yearly to members of the entertainment community who have accurately depicted drug, alcohol and tobacco abuse and addiction in their television and motion picture productions. Dr. Alan I. Leshner, Director, NIDA; Dr. Timothy P. Condon, Associate Director, NIDA; Dr. Jack Stein, Deputy Director, OSPC; and Ms. Beverly Jackson, Chief, Public Information and Liaison Branch, OSPC represented NIDA. Winning productions included the feature film "Traffic" and TV series "Cosby: Raising Paranoia" (CBS), "Sex and the City: Quitting Smoking" (HBO), "Third Watch: Know Thyself (NBC), "E.R.: Carter's Addiction" (NBC), and "Days of Our Lives: Fetal Alcohol Syndrome" (NBC). Coverage of this event appeared in *The Associated Press, The Hollywood Reporter, The Washington Post, United Press International, LA Times, City News Service, Daily Variety,* and *Join Together Online.*

NIDA launched its prescription drug abuse initiative at a press conference, **Prescription Drugs: Misuse, Abuse, and Addiction,** on April 10, 2001. Partners in the initiative are AARP, the American Academy of Family Physicians, the American Pharmaceutical Association, the National Association of Chain Drug Stores, the National Community Pharmacists Association, the National Council on Patient Information and Education, and the Pharmaceutical Research and Manufacturers of America. After the press conference, NIDA sponsored a scientific meeting to present research updates on Prescription Drugs: Misuse, Abuse, and Addiction. At this event, NIDA released a new research report to answer questions about the consequences of abusing commonly prescribed medications. Coverage of this event appeared in *Associated Press, WebMD, CBS Healthwatch, The Washington Times, USA Today, Reuters Health, Detroit News, Pittsburgh Post-Gazette, Chicago Tribune, Scripps Howard News Service,* and *United Press International.*

As part of this year's **Brain Awareness Week** activities, NIDA sponsored, **Who Wants to Be a NIDA Neuroscientist,** on March 14-15, 2001 and attended by 400 middle school children. Intended to teach children about their brains and generate interest in brain research, this event was held at the National Museum of Health and Medicine and was cosponsored by the Dana Alliance for Brain Initiatives and NIH. Participating NIDA staff included Drs. Cathrine Sasek, Cindy Miner, Nancy Pilotte, Suman Rao, Angela Martinelli, and Marina Volkov.

On January 11-12, 2001, NIDA and NIDDK co-sponsored the **1st Annual Meeting of RFA-funded Microarray Researchers** to discuss the challenges presented by microarray research and to find approaches to overcome these difficulties and facilitate data sharing. The meeting was held in Rockville, MD, and was co-chaired by Dr. Rebekah Rasooly, DNBR. Nearly 30 researchers funded through DA-00-003 and DK-00-002 attended, along with numerous staff from many NIH Institutes. The first day was a joint meeting that focused on issues in experimental design, methodology, analysis and data storage that are pre-requisites for eventual data sharing. On the second day, the NIDA and NIDDK grantees met separately and developed specific data-sharing steps unique to their specialized research interests.

On April 19, 2001 NIDA sponsored a day-long Symposium entitled **The Challenge of Psychostimulant Addiction: Both Reward Circuitry and Inhibitory Deficits May Help Explain Why It's So Difficult for Our Patients to**

Say No, at the American Society of Addiction Medicine's annual Medical-Scientific Conference at the Century Plaza Hotel in Los Angeles, CA. The symposium presented state-of-the-art information on the brain reward circuitry important in psychostimulant addiction, and its modulation by stress, and by frontal inhibitory circuits. Deficits in these inhibitory circuits have been documented in stimulant users, and may help explain not only the ongoing vulnerability to relapse, but also the initial vulnerability to addiction. Dr. Frank Vocci, Director, DTR&D, and Dr. Anna Rose Childress, University of Pennsylvania, co-chaired the symposium and discussed the implications of this research for the development of better pharmacological and behavioral treatments for drug addiction. Drs. Steven Grant, Clinical Neurobiology Branch, DTR&D, and Yavin Shaham, Behavioral Neuroscience Branch, Intramural Research Program, also participated as presenters. The Symposium organizers were Drs. Anna Rose Childress, Frank Vocci, and Dorynne Czechowicz.

On April 17-18, 2001, DTR&D's Behavioral Treatment Development Branch sponsored a workshop for currently funded Stage I translational behavioral treatment development researchers. Council member Steven Hayes and BTDB Branch Chief Lisa Onken co-chaired the workshop, designed to facilitate the progress and promote the success of grantees doing this type of novel research.

A CTN National Steering Committee Meeting was held January 8-10, 2001, in Tampa, Florida. The members met to discuss participation of 8 new nodes in the current protocols; select additional members for the Operations Committee from the new nodes; establish a Design and Analysis Work Group; and set up new work groups for developing research agendas which focus on women and gender issues and HIV/AIDS.

The first **meeting of the CTN Dissemination Subcommittee** was held February 1-2, 2001, in Bethesda, MD. The Subcommittee established definitions, a common language, and discussed guidelines for dissemination activities for the CTN. Presentations were given by NIDA's Office of Science Policy and Communications and CSAT/ATTC representatives.

The **Focused Aftercare Protocol Team** held a two-day meeting in Los Angeles, CA, on February 8-9, 2001. The participants discussed the new protocol and how to implement it at the community treatment sites.

A **CTN Quality Assurance Subcommittee Meeting** was held February 26-27, 2001, in Bethesda, MD. The members reviewed quality assurance plans for the current protocols and drafted guidelines for quality assurance monitoring for CTN protocols.

The **CTN Data Management Subcommittee** met in New Orleans, LA, on March 1-2, 2001. The meeting focused on data management issues with the current protocols and how to standardize the flow of data through the system. Members from thirteen of the fourteen nodes attended.

The **CTN Data and Safety Monitoring Board** met March 19, 2001, in Bethesda, Maryland. The members reviewed the protocol entitled Buprenorphine/Naloxone: Comparison of Three Taper Schedules for Opiate Detoxification, discussed recruitment and retention reports, and reviewed adverse events.

A **CTN National Steering Committee Meeting** was held April 2-4, 2001, in Bethesda, Maryland. The meeting focused on the status of the ongoing protocols, updates of the project teams, reports from the various subcommittees, approval of a conflict of interest policy, and creation of work groups to address CTP protocol participation and peer progress review. A representative from one of the National Cancer Institute's clinical trials network gave a presentation on how their network is organized and run.

The **CTN Training Subcommittee** held a two day meeting April 30-May 1, 2001, in Gaithersburg, Maryland.

The **CTN Training Subcommittee** held a training session on Good Research Practice (GRP) on May 2, 2001, in Gaithersburg, Maryland, to train protocol on site personnel in GRP standards.

A two-day training meeting on the inpatient protocol for buprenorphine naloxone vs. clonidine for detoxification was held April 23-24, 2001, in Los Angeles, California.

The CTN co-sponsored a meeting with NIDA on women and gender research issues May 14-15, 2001, in Bethesda, Maryland.

NIDA's Special Populations Office convened the **African American Researchers and Scholars and the Asian/Pacific Islander Work Groups** on March 29-30, 2001 at the Neuroscience Center in Rockville, Maryland.

NIDA's Special Populations office held the first planning meeting of the September 24-26 national conference on minority research on February 21-22, 2001 in Rockville, Maryland. Members of the planning group include NIDA staff and members of NIDA's four racial/ethnic work groups and other constituent groups.

NIDA's Women and Gender Research Group sponsored a seminar by Dr. Wendee Wechsberg entitled **Gender Differences, Women Drug Abusers, and HIV Risk: Lessons Learned and Future Prospects,** February 5, 2001. The seminar was organized by Dr. Dionne Jones, CAMCODA.

On February 16, 2001 the Prevention Research Branch hosted a presentation by Dr. David Hawkins, Richard Catalano and Michael Arthur from the Social Development Group at the University of Washington. The title of the presentation was: Prevention Science in Communities: From Research to Practice.

Mr. Richard A. Millstein, Deputy Director, NIDA, participated in the Expert Panel Group to the University of Illinois at Chicago on its Impact Teen State Drug Abuse Project, February 15, 2000, Arlington, VA.

Mr. Millstein presented at the New York State Association of Drug Treatment Court Professionals on "Addiction and Treatment: What Does the Science Say?", March 8, 2001, Saratoga Springs, NY.

Mr. Millstein spoke with the Asian-American/Pacific Islander Work Group on NIDA initiatives, March 29, 2001, Rockville, MD.

Mr. Millstein spoke with the African-American Researchers and Scholars Work Group on NIDA initiatives, March 29, 2001, Rockville, MD.

Mr. Millstein was a presenter at the opening session of the Lonnie B. Mitchell Historically Black Colleges and Universities Substance Abuse Conference, April 4, 2001, Baltimore, MD.

Mr. Millstein was the keynote speaker at the Hispanic/Latino Family in the New Millennium Conference: Strategies to Prevent and Treat Substance Abuse Among Hispanic/Latino Children and Adolescents on May 10, 2001 in San Juan, Puerto Rico. He spoke on "Science-Based Views of Drug Abuse and Addiction: Where We Are and Where We're Going".

Dr. Timothy P. Condon, Associate Director, NIDA, presented an "Update on NIDA's Research/Practice Blending Activities" at the Robert Wood Johnson Foundation in Princeton, NJ on February 5, 2001.

Dr. Timothy P. Condon presented "The NIDA National Clinical Trials Network" at the AACAP K12 Annual Retreat at Seabrook Island, SC on March 9, 2001. He was joined by two CTN investigators, Drs. Kathleen Brady and Paula Riggs who provided perspectives from different CTN nodes.

Dr. Timothy P. Condon presented "National Institute on Drug Abuse: Treatment Principles and the National Clinical Trials Network" at the Join Together - Demand Treatment! Partners Institute at Jupiter Beach, FL on March 13, 2001.

Dr. Timothy P. Condon gave two presentations, "Advances in Drug Addiction Research: Implications for Research and Practice" and "Science Advances in the Emerging Drug Problem: What We Have Learned", and led a discussion during a half day symposium entitled "The Brain and Addiction: Scientific Advances" in Honolulu, HI on April 16, 2001.

Dr. Timothy P. Condon presented "Nicotine and the Brain" and co-moderated a workshop on "New Dimensions in Tobacco Cessation" at the Seeing Through the Smoke: 2001 Tobacco Control Conference in Honolulu, HI on April 17, 2001.

Dr. Timothy P. Condon presented an "Update on Club Drugs" at the American Academy of Pediatrics Committee on Substance Abuse in Washington, DC on April 23, 2001.

Dr. Jack Stein, Deputy Director, OSPC, conducted a workshop, "Update on Drug Addiction Research" at the Commonwealth Prevention Alliance 2001: Leading the Challenge, in State College, PA on April 6, 2001.

Dr. Jack Stein conducted a workshop, "Drugs and the Brain" at the Maryland D.A.R.E. 2001 In-Service Training, in Ocean City, MD on April 11, 2001.

Dr. Jack Stein presented a luncheon keynote, "Putting Drug Addiction Research to Use" at the 35th Annual Spring Conference of the Wisconsin Association on Alcohol and Other Drug Abuse in Madison, WI on May 15, 2001.

Beverly Jackson, Chief, Public Information and Liaison Branch, OSPC, led a workshop, "Maximizing News Coverage from Scientific Findings" at the Association of American Medical Colleges Group on Institutional Advancement National Professional Development Conference in Savannah, GA on March 9, 2001.

Dr. Frank Vocci, Director, DTR&D, presented "Rationales for Immunologic and Metabolic Approaches to Smoking Cessation" at the SNRT meeting held in Seattle, WA, March 23, 2001.

At the American Society of Addiction Medicine (ASAM) meeting on April 22, 2001, Dr. Vocci presented "Why Buprenorphine, Why Now, and the Political and Regulatory Environments" at an ASAM training symposium on buprenorphine.

Dr. Frank Vocci, Director, DTR&D, presented "Approaches and Promises in the Development of Pharmacotherapies for Cocaine Dependence" at Psychiatry Grand Rounds, University of Texas at San Antonio, April 24, 2001.

Dr. Frank Vocci, Director, DTR&D, gave a lecture entitled "Perspective in Drug Abuse Research" at the Georgetown University Medical School, April 30, 2001.

Dr. Joseph Frascella, DTR&D, gave a talk entitled "The Mechanisms of Addiction" in the workshop "The Dynamics of Addiction" at the Lonnie E. Mitchell National HBCU Substance Abuse Conference, Baltimore, Maryland, April 4-6, 2001.

Dr. Joseph Frascella participated in the Eighth Annual Undergraduate and Graduate Science Research Symposium at Morgan State University in Baltimore, Maryland, April 19, 2001.

Dr. Betty Tai, DTR&D, gave a presentation on the CTN at the annual American Society of Addiction Medicine (ASAM) Meeting on April 19-22, 2001, in Los Angeles, California.

Robert Walsh, DTR&D, presented an update on the status of the NIDA/VACSP #1018 Buprenorphine Best Practices Trial at the National Association of State Controlled Substance Authorities (NASCSA)/Center for Substance Abuse Treatment, SAMHSA sponsored meeting held on March 19, 2001. The purpose of this meeting was to discuss and address Federal and State issues of concern that relate to the new Federal legislation (the Drug Abuse Treatment Act, "DATA") and new narcotic medications.

Robert Walsh, DTR&D participated in the Social Sciences Forum entitled "Integrating Primary Care and Substance Abuse Treatment: Lessons from Scotland" held at the University of Maryland, BaltimoreCounty on April 4, 2001.

On February 22-25, 2001, Dr. Dorynne Czechowicz, Behavioral Treatment Development Branch, DTR&D, represented NIDA on the Workshop Planning Committee of the American Methadone Treatment Association, which met in St. Louis, MO.

Dr. Jane B. Acri, DTR&D, participated in a Drug Awareness Mock Courtroom Trial and presented the long-term effects of drug abuse for the Alpha Chi Omega Foundation and the Beta Rho Chapter at American University on February 11, 2001.

Dr. Jane B. Acri provided a guest lecture in the Psychopharmacology course at the Uniformed Services University of the Health Sciences' Department of Medical and Clinical Psychology entitled "Cocaine Abuse and Medication Development," on April 9, 2001.

Dr. Teresa Levitin, Director, OEA, served as the NIDA representative to the NIH Working Group on the R21 Mechanism, a group examining NIH mechanisms for stimulating and reviewing exploratory and developmental grant applications.

Dr. Kay Nimit, Clinical, Epidemiolgical and Applied Sciences Review Branch, OEA, organized a scientific presentation, "Monitoring Drug Use with Alternative Matrices," by Dr. Marilyn Huestis of the Division of Intramural Research, in conjunction with the NIDA-E (Treatment Research) meeting in February 2001.

Dr. William C. Grace, Deputy Director, OEA, served as a reviewer for HIV proposals for the National Institute of Allergy and Infectious Diseases Prevention Science Review Committee in March 2001.

Dr. Levitin co-chaired the committee to organize the NIDA program at the Society for Research on Child Development (SRCD) April 19-22, 2001 in Minneapolis, MN. She also presented information at the discussion hour on child and adolescent research support at NIDA. At SRCD, Dr. Levitin co-chaired a symposium, "Building Bridges between Child Development and Substance Abuse Research: Challenges and Opportunities" and participated in other activities at SRCD to highlight NIDA's interest in child research.

Dr. Mark Swieter, Basic Sciences Review Branch, OEA, served as a judge for the Fairfax High School Science Fair on February 6, 2001.

Dr. Marina Volkov, Clinical, Epidemiological, and Applied Sciences Review Branch, OEA, co-organized with Dr. Minda Lynch, Division of Neurobiology and Basic Research, a seminar at Macalester College for faculty members of non-research intensive colleges and universities in Minnesota. The seminar, which took place on April 18, 2001, covered

NIDA programmatic interests and the NIH grant application process.

Dr. Swieter participated in the African American Researchers and Scholars Group (AARSG) meeting held at NIDA March 29-30, 2001 and answered questions about the review process.

Dr. Lula Beatty, Chief, Special Populations Office, attended the governance meetings of the American Psychological Association in Crystal City, Virginia on March 22-25, 2001. She was selected Vice-Chair of the Committee on Women in Psychology for 2002.

Dr. Lula Beatty presented an overview of NIDA to participants in NIH's Extramural Research Associates Program on January 30, 2001.

Dr. Lula Beatty presented a seminar on March 27, 2001 at Howard University entitled Drug Abuse in African American Women.

Dr. Lula Beatty attended the Lonnie Mitchell HBCU Substance Abuse Conference in Baltimore, Maryland on April 4-6, 2001. She co-chaired the student program which consisted of six sessions including a student poster session which featured work accomplished by students working with NIDA's intramural scientists, a session featuring minority supplement recipients, and a presentation by NIDA staff members, Drs. Joseph Frascella and Eric Moolchan.

Ana Anders, Senior Advisor on Special Populations, met with the newly formed National Hispanic Science Network on Drug Abuse (NHSN) Steering Committee at the University of Miami in Miami, Florida on January 17-19, 2001.

Ana Anders chaired the Latino Behavioral Health Institute annual conference planning committee meeting held on February 16, 2001.

Ana Anders chaired a meeting of NIDA's internal Asian American and Pacific Islander Workgroup on February 1, 2001 in Rockville, Maryland.

Ana Anders, as a member of the HHS/Hispanic Employee Organization, planned for a HHS-wide meeting that was held on March 23, 200l in Bethesda, Maryland.

Ana Anders attended and participated in the National Hispanic Medical Association Annual Conference on March 23, 2001.

Dr. David Shurtleff, Deputy Director, DNBR, represented and described NIDA's mission and funding opportunities at an Eastern Psychological Association (EPA) sponsored symposium on funding opportunities from Federal agencies at the Annual EPA meeting held on April 20-22, 2001 in Washington, D.C.

Dr. Cora Lee Wetherington, DNBR and NIDA's Women and Gender Research Coordinator, gave an invited talk, "How Does Gender Matter in CTN Research?" at the CTN Steering Committee meeting, January 8-10, 2001, Clearwater, FL.

Dr. Minda Lynch, BCSRB, DNBR, participated in a Spring Research Festival at the State University of New York at Buffalo in May 2001. Her presentation was entitled "Career Funding Mechanisms at NIH".

Dr. Cora Lee Wetherington, DNBR and NIDA's Women and Gender Research Coordinator, along with Dr. Debbie Henken, NICHD, made a luncheon presentation at the American University in Washington, DC on NIH funding opportunities, March 19, 2001. The event was sponsored by the American University Office of Sponsored Research.

Dr. Cora Lee Wetherington, chaired the session, "Sex Hormones and Neurotransmitter Functioning" at the Society for Research on Nicotine and Tobacco meeting, March 23-25, 2001, Seattle, WA. The session was co-organized by Drs. Sharon Allen (University of Minnesota), Dorothy Hatsukami (University of Minnesota), and Dr. Wetherington. The speakers were Drs. Allen, Hatsukami, Neal Benowitz (University of California San Francisco), Imad Damaj (Medical College of Virginia), Rosemarie Booze (University of Kentucky), Eric Donny (Johns Hopkins Bayview Medical Center), and C. Oncken (University of Connecticut Health Center).

Dr. Peter Hartsock, CAMCODA, represented the Department at the annual Seniors Meeting of the federal Interagency Arctic Research Policy Committee (IARPC), National Science Foundation, April 10, 2001. IARPC coordinates all federal research related to the Arctic and is chaired by the Director of the National Science Foundation.

Dr. Elizabeth Robertson, PRB, DESPR, was a delegate to the Enhancing Prevention in America's Communities think tank meeting at the Palo Alto Center, Stanford University, on April 5 and 6, 2001. This is a jointly funded project by NIDA, RWJF and other organizations to develop a consensus statement of prevention actions to improve living conditions for youth in the U.S.

Dr. Elizabeth Robertson, PRB, DESPR, presented on the topic of "Prevention Science: Moving into the Future" at Grand Rounds, Washington University, St. Louis on April 24 and 25, 2001.

On May 14 and 15, 2001, Dr. Elizabeth Robertson, PRB, DESPR, was guest lecturer at the University of Alabama, Tuscaloosa, on the topic of "Prevention Science: Taking a Life Course Perspective."

Drs. James Colliver, Elizabeth Robertson, Jacques Normand, and Nick Kozel of DESPR and Dr. Cindy Miner of OSPC met with Matt Magio, Philip Ponzurick, and John Nolan of the National Drug Intelligence Center (NDIC), Department of Justice, to discuss use of NIDA-generated information in NDIC reports, NIDA's need for information from NDIC, and procedures for cooperating with NDIC in generation and review of their documents.

Dr. James Colliver, DESPR, is NIDA's representative to the Department of Health and Human Services Data Council Youth Substance Use Workgroup, which meets monthly. This workgroup is examining ways of improving the coordination between the Department's three main surveys that collect data on drug and alcohol use among youth -- Monitoring the Future, the Youth Risk Behavior Survey, and the National Household Survey on Drug Abuse.

Dr. Jacques Normand, DESPR, presented at a NICHD Workshop on Bias in Intervention Research, Bethesda, MD, February 21, 2001.

Dr. Jerry Flanzer, DESPR, presented a grantmanship workshop along with Dr. Peter Delany, Acting Deputy Director, DESPR, at the Annual Meeting of the Society on Social Work Research, Atlanta, January 19-21, 2001.

Dr. Flanzer met with the executive council of the National Association of Social Workers, to discuss future involvement in drug abuse research activities, March 23, 2001.

Dr. Thomas Hilton, DESPR, represented NIDA at the Center for Therapeutic Research Scientific Advisory Board meeting at the National Drug Abuse Research Institute in New York, February 12, 2001.

Dr. Jean Lud Cadet, IRP, presented "Research Opportunities for Physicians" at Hunter College in New York, January 16-17, 2001.

Dr. Jonathan Katz, IRP, chaired a Symposium in Honor of W. H. Morse at the Forty-fifth Annual Meeting of the Behavioral Pharmacology Society, Orlando, Florida, May 2001.

Dr. Jonathan Katz presented a paper entitled "Behavioral Studies of Heterogeneity of Actions of Dopamine Uptake Inhibitors". The paper was an invited presentation at the 2001 Annual Meeting of the American Society for Pharmacology and Experimental Therapeutics, April 2001.

Dr. Amy Newman, IRP, presented an invited lecture entitled "Novel Probes for the Dopamine Transporter" to the Department of Medicinal Chemistry, Virginia Commonwealth University, Richmond, Virginia, November 2000.

Dr. Amy Newman presented a paper entitled "Tropane-based Irreversible Ligands for the Dopamine Transporter". This was an invited presentation for the Symposium on Synthesis and SAR Studies of New Targets for the Dopamine Transporter at the Joint 52nd Southeast/56th Southwest Regional Meeting of the American Chemical Society, New Orleans, LA, December 2000.

Dr. Amy Newman presented an invited lecture entitled "Novel Probes for the Dopamine Transporter" to the Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, Baltimore, MD, February 2001.

Dr. Stephen Heishman, IRP, presented an invited lecture entitled "Tobacco, Nicotine, and Human Cognition" at the Maryland Psychiatric Research Center, Catonsville, MD, December 2000.

Dr. Stephen Heishman presented an invited lecture entitled "Pharmacology of Cannabis and Detection of Marijuana Intoxication" at the annual meeting of the American Academy of Forensic Sciences, Seattle, WA, February 2001.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Media and Education Activities

Awards

Several of NIDA's products won awards in the first **NIH Plain Language Awards.** *Walking a Good Path,* a 2001 calendar and artcard promoting it, won superior plain language product (Sheryl Massaro, OSPC). *NIDA NOTES 15(5)* (David Anderson, OSPC), *Mind Over Matter* (teacher's guide, magazine, posters, and web site) (Dr. Cathrine Sasek, OSPC) and the *Office of Extramural Affairs Frequently Asked Questions pages on the NIDA website* (Dr. Teresa Levitin, OEA and Dr. William C. Grace, OEA) won honorable mentions.

The NIDA web site was selected for the **National Science Teachers Association sciLINKS,** and the web address will be included in textbooks.

The NIDA web site received the **Recognized by 4therapy.com Award** for providing useful mental health content.

Press Releases

January 2001 - **NIDA News*Scan***

- Teen Marijuana Use Can Lead to Anxiety, Depression, or Aggression
- New Treatment Approach for Marijuana Dependence
- Blocking Morphine Receptor Prevents Tolerance-But Not Dependence-From Developing in Mice
- Neonatal Stress in Rats Increases Vulnerability to Cocaine Use Later in Life

As a result of News*Scan* promotion, coverage appeared in *Alcoholism & Drug Abuse Weekly.*

January 17, 2001 - **New Research Expands Understanding of Treatment for ADHD.** Although methylphenidate (Ritalin) is the most frequently prescribed drug for treating attention deficit hyperactivity disorder (ADHD), its mechanism of action and its effects on the human brain have been poorly understood. In an article in the January 12, 2001, online issue of the *Journal of Neuroscience,* researchers have for the first time assessed the effects of therapeutic doses of oral Ritalin on the levels of dopamine in the human brain. Dopamine imbalances appear to be closely related to ADHD symptoms. Coverage of this publication appeared in *Newsday* (New York, NY), and *The Hindu* (India's national newspaper).

January 30, 2001 - **African American Teens at Greater Risk of Tobacco Addiction.** For African American teens who smoke, culturally-appropriate evaluation of nicotine dependence is an important part of cessation treatment, according to a study published in the December 2000 issue of the *Journal of the National Medical Association.* This study clarifies some of the distinguishing characteristics of tobacco addiction among adolescent African Americans. Coverage of this publication appeared in *Alcoholism & Drug Abuse Weekly, Join Together Online,* and *Reuters Health.*

January 31, 2001 - **Research Shows TV PSAs Effective in Reducing Teen Marijuana Use.** Researchers have demonstrated that television public service announcements (PSAs) designed for and targeted to specific teen personality-types can significantly reduce their marijuana use. In a study published in the February 2001 issue of the *American Journal of Public Health,* researchers report that PSAs with an anti-marijuana use message resulted in at least a 26.7 percent drop in the use of that drug among the targeted teen population. Coverage of this publication

appeared in *Join Together Online,* and *Alcoholism & Drug Abuse Weekly.*

February 1, 2001 - **Dopamine Receptors Implicated in Obesity.** A deficiency of dopamine in the brain may explain why some individuals engage in pathological overeating, resulting in severe obesity, according to a study published in the February 3, 2001, *Lancet.* Dopamine is a neurotransmitter that acts in the brain and helps regulate feelings of pleasure and modulates the rewarding properties of food. Coverage of this publication appeared in *US News & World Report, Time, Newsday, The Chicago Sun-Times, The Pittsburgh Post-Gazette, The Washington Times, The Denver Post* and other media outlets.

March 1, 2001 - **Methamphetamine Abuse Leads to Long-Lasting Changes in the Human Brain that are Linked to Impaired Coordination and Memory.** Methamphetamine, a highly addictive stimulant drug, whose abuse has reached epidemic proportions in many parts of the United States, causes long-term changes in the human brain that are associated with impaired memory and motor coordination, according to a study published in the March 2001 issue of the *American Journal of Psychiatry.* Researchers found that these effects are seen even in methamphetamine addicts who have been off the drug for 10 months or more. A second study by the same research group reveals additional long-lasting brain changes caused by the drug, including an unexpected increase in cellular activity in certain areas of the brain. Coverage of this publication appeared in *Reuters Health, CBS HealthWatch, HealthScout, WebMD, CNN.com, MSNBC.com, The New York Times, USA Today, The Seattle Times, Investor's Business Daily* and other media outlets.

March 2001-NIDA **News*Scan***

- Incentive to Work Helps to Keep Addicts Drug Free
- NIDA Premieres New Web Site
- NIDA Announces RFA for Tools to Generate Genetically-Altered Mice
- Upcoming Events

As a result of *NewsScan* promotion, coverage appeared in *Join Together Online* and *Substance Abuse Funding News.*

March 7, 2001 - **Study Confirms Gender Differences in Progression from HIV to AIDS. *Despite Differences in "Viral Load," Men and Women Develop AIDS at the Same Rate.*** (Joint press release with NIAID.) During the first years of HIV infection, women have significantly lower amounts of the virus in their blood than do men, according to one of the largest studies ever to examine gender-specific differences of HIV infection. Despite their lower initial viral levels, women suffer the loss of immune cells and develop AIDS just as swiftly as men. The findings, reported in the March 8, 2001, issue of *The New England Journal of Medicine,* lend further support to recent changes in the criteria used to help doctors tailor anti-HIV drug therapy to delay the onset of AIDS. Coverage of this publication appeared in *The Associated Press, Reuters Health, The Washington Times, The Boston Globe,* and other media outlets.

March 14, 2001 - **Scientists Identify Process That Plays Key Role in Brain Changes Involved in Cocaine Addiction.** Researchers supported by NIDA identified a process in the brain that may underlie addiction to cocaine and other drugs of abuse. Their research indicates that repeated exposure to cocaine causes a change at the level of gene expression that leads to altered levels of a specific brain protein called cyclin-dependent kinase 5 (Cdk5). The Cdk5-related process leads to changes in brain cells that are thought to play a role in cocaine addiction. The March 15, 2001, issue of *Nature* reports the findings. Coverage of this publication appeared in *Join Together Online* and *Alcoholism & Drug Abuse Weekly.*

March 19, 2001 - **NIDA News*Scan***

- Study Finds That Methamphetamine Use Can Increase Stroke-Related Brain Damage
- Study Examines Link Between Dopamine Receptor and Curtailing Cue-induced Craving for Cocaine
- Nicotine Causes Degeneration in Brain's "Weak Link" for Addictive Drugs
- Brain Hormone That Helps Regulate Food Intake May Dampen Drug Craving: Finding Exploits Possible Relationship Between Addiction and Eating Disorders
- NIDA Joins in Recognizing National Inhalants and Poisons Awareness Week in March
- Upcoming Events

April 10, 2001 - **NIDA and Partners Announce National Initiative on Prescription Drug Misuse and Abuse.** NIDA and several national organizations announced a public health initiative to raise awareness about recent trends in the misuse and abuse of prescription drugs in the United States. The initiative seeks to inform the public,

physicians, pharmacists, and others about the misuse and abuse of medications and promote additional research on the subject. Joining with NIDA are AARP, the American Academy of Family Physicians, the American Pharmaceutical Association, the National Council on Patient Information and Education, and the Pharmaceutical Research and Manufacturers of America. Coverage of this event appeared in *Associated Press, WebMD, CBS Healthwatch, The Washington Times, USA Today, Reuters Health, Detroit News, Pittsburgh Post-Gazette, Chicago Tribune, Scripps Howard News Service,* and *United Press International.*

Opinion Pieces

February 2001, - Article by Alan I. Leshner, Ph.D.-"Addiction Results from Biochemical Process"

Articles of Interest

December 30, 2000, *The Associated Press*-Interview of Frank Vocci, Ph.D.-"Heroin Addiction Rising Amid Too Little Treatment"

January 2, 2001, *The Washington Post*-Interview of Alan I. Leshner, Ph.D.-"To Get Healthier, Learn From a Drug Addict"

January 3, 2001, *The Philadelphia Inquirer*-Interview of Charles Sharp, Ph.D.-"Laughing Gas Use and Deaths Are on the Rise"

January 10, 2001, *CBS HealthWatch*-Interview with Jerry Frankenheim, Ph.D.- "'Party Drug' Has Deadly Effects Even Without Alcohol"

January 16, 2001, *NewsDay.com*-Interview of Alan I. Leshner, Ph.D.-"How Ecstasy Works" (3-part series on ecstasy)

January 21, 2001, *The New York Times Magazine*-Interview of Alan I. Leshner, Ph.D.-"The Pursuit of Ecstasy"

January 23, 2001, *The New York Times*-Interview of Alan I. Leshner, Ph.D.-"Doctors Don't Always Address Drug Abuse" (this Associated Press article also appeared in *The Record [Bergen County, NJ], Join Together Online, The Philadelphia Inquirer*)

January 24, 2001, *Sacramento Bee*-Interview of Jean Lud Cadet, M.D.-"Meth More Dangerous Than Expected, Study Says"

February 2001, *Current Health 2*-Interview of Jack Stein, Ph.D.-"Stimulants: Fast Track to Disaster"

February 5, 2001, *US News & World Report*-Interview of Alan I. Leshner, Ph.D.-"Cracking Down on Ecstasy"

February 7, 2001, *MSNBC.com*-Interview of Timothy P. Condon, Ph.D.-"Beating an Addiction to Meth" (Part of an online series "Meth's Deadly Buzz: America's Home-Grown Drug Epidemic")

February 9, 2001, *HealthScout*-Interview with Jerry Frankenheim, Ph.D.-"Kicking Club Drug is No Kick"

February 11, 2001, *The New York Times Magazine*-Letter to the Editor by Alan I. Leshner, Ph.D.-"Experiencing Ecstasy"

February 12, 2001, *NewsWeek*-Interview of Alan I. Leshner, Ph.D.-"Fighting Addiction: Special Report"

February 21, 2001, *University Wire*-Interview of Roy Wise, Ph.D.-"Genes May Determine Addiction"

February 28, 2001, *The Wall Street Journal*-Interview of Alan I. Leshner, Ph.D.-"Would Marijuana Be OK by Prescription If You Didn't Get High?"

March 7, 2001, *JAMA*-Interview of Alan I. Leshner, Ph.D.-"Talking with Alan I. Leshner, Ph.D., National Institute on Drug Abuse Director"

March 9, 2001, *Reuters Health*-Interview of Alan I. Leshner, Ph.D.-"Substance Abuse Number One Health Problem in US"

March 13, 2001, *The New York Times*-Interview of Alan I. Leshner, Ph.D.-"Scientists Test Hallucinogens for Mental

Ills"

March 15, 2001, *The Washington Post*-Interview of Alan I. Leshner, Ph.D.-"In Senate Debate on Drugs, 'Traffic' Moves Minds"

March 15, 2001, *The Deseret News (Salt Lake City, UT)*-Interview of Glen Hanson, Ph.D.-"Utah Center Seeks Answers on How to Treat Addictions"

March 19, 2001, *Time*-Interview of Alan I. Leshner, Ph.D.-"Who's Feeling No Pain? *The Latest Trendy Drugs Are Old-Fashioned Painkillers. They're Chic, Mellowing and Way Addictive*"

March 19, 2001, *The Associated Press*-Interview of Wallace B. Pickworth, Ph.D.-"Study: Bidis as Addictive as Regular Cigarettes"

March 27, 2001, *The Associated Press*-Interview of Alan I. Leshner, Ph.D.-"Study Fights 'Crack Baby' Perception" (NIDA-funded research; coverage also appeared in *HealthScout, The Washington Post, The Boston Herald, The Philadelphia Inquirer, Newsday* and other media outlets)

March 30, 2001, *Washington City Paper*-Interview of Alan I. Leshner, Ph.D.-"The Habit of Perfection: *The Partnership of the Entertainment Industries Council, Inc. and the National Institute on Drug Abuse Helps Hollywood Get Its Depictions of Drug Use Exactly Right*"

April 4, 2001, *MSNBC Investigates*-Interview of Alan I. Leshner, Ph.D.-Story about ecstasy

April 6, 2001, *NBC Today Show*-Interview of Alan I. Leshner, Ph.D.-Story about ecstasy

April 7, 2001 (premiere), and April 21, 2001 (repeated nationwide), *In the Mix: A National PBS Weekly Series for Teens*-Interview of Alan I. Leshner, Ph.D.-"Ecstasy"

April 9, 2001, *Newsweek*-Interview of Alan I. Leshner, Ph.D.-"Painkillers *Vicodin and OxyContin: Hot Drugs That Offer Relief-And Danger*" (cover story)

NIDA Exhibits Program

Meetings where NIDA exhibited publications and program announcements over the past several months are as follows:

February 15-20, 2001	American Association for the Advancement of Science
March 8-11, 2001	47th Annual Council on Social Work Education
March 22-25, 2001	49th Annual National Science Teachers Association
March 22-25, 2001	American Society for Adolescent Psychiatry
March 23-25, 2001	7th Annual Society for Research on Nicotine and Tobacco with the 22nd Annual Meeting of the Society of Behavioral Medicine
March 25-27, 2001	Cognitive Neuroscience Society
March 31-April 4, 2001	Experimental Biology
April 3-5, 2001	PRISM Awards
April 4-6, 2001	The Lonnie E. Mitchell National HBCU Substance Abuse Conference
April 10, 2001	Prescription Drugs: Misuse, Abuse, and Addiction
April 19-22, 2001	Society for Research in Child Development
April 19-22, 2001	American Society of Addiction Medicine
May 5-10, 2001	American Psychiatric Association
May 16-18, 2001	National Council on Patient Information and Education

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

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

The National Institute on Drug Abuse (NIDA) is part of the National Institutes of Health

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Planned Meetings

NIDA will sponsor a workshop on May 29, 2001 entitled **Bridging Neurobiological, Behavioral, and Prevention Sciences (2)** at the Hyatt Regency-Capitol Hill, Washington, DC. NIDA is sponsoring this workshop for early career scientists who may be at the intersection of these disciplines relevant to their career development and research interests. This workshop, co-organized by Drs. Bill Bukoski, OD, DESPR and Minda Lynch, BCSRB, DNBR is being conducted in conjunction with the 2001 Annual Meeting of the Society for Prevention Research (SPR) in Washington, D.C.

Drs. Susan Volman and Minda Lynch, BCSRB, DNBR are the organizers of a symposium planned for this year's Society for the Study of Ingestive Behavior meeting at the University of Pennsylvania in June 2001. The session, entitled **Like Drugs for Chocolate: Separate Rewards Modulated by Common Mechanisms?** will include presentations from Dr. Marci Pelchat (Monell Chemical Senses Ctr.) on "Of Human Bondage: Craving, Obsession, Compulsion and Addiction", Dr. Regina Carelli (UNC) on "Neurophysiological Analysis of Cocaine Self-Administration Vs. Natural Reinforcement", Dr. Ann Kelley (University of Wisconsin-Madison) on "Opioid Modulation of Taste Hedonics within the Ventral Striatum", and Dr. Kenneth Carr (NY School of Medicine) on "Augmentation of Drug Reward by Chronic Food Restriction: Behavioral Evidence and Underlying Mechanisms". Dr. Patricia Sue Grigson from Hershey Medical Center is also a co-organizer for this meeting and will be serving as discussant for the panel.

Drs. Cindy Miner and Angela Martinelli of OSPC's Science Policy Branch are organizing a workshop, **NIDA Tutorials** to be held prior to this year's CPDD meeting in Scottsdale, Arizona in June. This workshop is designed to provide junior investigators with fundamental information from a variety of disciplines representing the breadth of drug abuse and addiction research. Speakers include James C. Anthony, Ph.D., Johns Hopkins University, William Boggan, Ph.D. and Kathleen Brady, M.D., Ph.D. of Medical University of South Carolina, Kathryn Cunningham, Ph.D. of University of Texas and Charles Inturrisi, Ph.D. of Cornell University Medical Center.

Drs. Cindy Miner and Angela Martinelli of OSPC's Science Policy Branch are organizing a grant writing workshop designed for junior investigators at the Annual CPDD meeting in Scottsdale, Arizona in June 2001. Drs. Mark Swieter, OEA, and David Shurtleff, DNBR, are also participating to educate young investigators about the grant review and funding processes at NIH and NIDA.

Dr. Bill Bukoski, OD, DESPR; Dr. Minda Lynch, Acting Chief, BCSRB, DNBR; and Dr. David Shurtleff, Deputy Director for Program, DNBR, are coordinating a NIDA sponsored scientific workshop as part of the June 2001 annual meeting of the College on Problems of Drug Dependence (CPDD), Scottsdale, Arizona. The workshop is titled: **Adolescence and Drug Prevention: Translational Perspectives.** Three seminal presentations by senior scientists will address newly emerging basic research findings on child and adolescent development (cognitive, neurobiological, endocrine, psychosocial, etc.) and assess their implications for the design of prevention and treatment interventions for drug abuse and co-morbid disorders.

The Regulatory Affairs Branch, DTR&D, will be holding a workshop at the annual College on Problems of Drug Dependence (CPDD) on Monday, June 18, 2001 entitled **Regulatory and Human Protections Issues for Running Clinical Trials in Drug Dependent Populations.** Robert Walsh, RAC and Frank Vocci, Ph.D. will co-chair the workshop which is intended to help PIs become more familiar with recent views and regulations regarding Human Protections, Investigational New Drug (IND) submissions, and the use of Data and Safety Monitoring Boards in clinical trials. Robert Walsh will discuss New NIH Regulations That Affect The Way We Do Our Clinical Studies. Michael Carome, M.D., of the newly formed Office of Human Research Protections will present Clinical Trials in Drug

Dependent Populations: Important Considerations for the IRB. Techniques for Preparing A Successful IND Submission, will be presented, by Juris Mezinskis, Ph.D., of the Cincinnati VAMC. Dr. Celia Jaffe Winchell, from the Food and Drug Administration (FDA), will discuss Successful Interactions with FDA During the IND Review Process.

On July 19-20, 2001, NIDA will hold a symposium entitled **MDMA/Ecstasy Research: Advances, Challenges, and Future Directions** at the William H. Natcher Conference Center, NIH Campus, Bethesda, MD. This symposium will focus on the scientific research on methylenedioxymethamphetamine (MDMA), including MDMA neuropharmacology, addiction liability, neuropathology and its long-term behavioral consequences, ontogenetic effects, other toxicology, drug interactions, patterns of abuse, perceptions of risk, prevention research, and the toxicology of amphetamines sometimes replacing MDMA (such as PMA and PMMA). This conference is being planned by Drs. Jerry Frankenheim (chair), DNBR, Dorynne Czechowicz, DTR&D, Joseph Frascella, DTR&D, Steven Grant, DTR&D, Glen Hanson, DNBR, Elizabeth Lambert, CAMCODA, Rita Liu, OEA, Minda Lynch, DNBR, Dorota Majewska, DTR&D, Angela Martinelli, OSPC, Cindy Miner, OSPC, Ro Nemeth, DTR&D, Moira O'Brien, DESPR, and Eve Reider, DESPR.

On August 9-10, 2001, NIDA will hold its **2nd National Conference on Drug Abuse Prevention Research: A Progress Update** at the Omni-Shoreham Hotel, Washington, DC. Top drug abuse prevention scientists will share research findings from the past five years with community leaders, educators, and other practitioners. Family, school, media, and multi-context prevention projects will be presented. Determining effective practices and interventions for particular communities and groups will be a major focus. Emerging trends in drug abuse prevention will be highlighted.

Drs. David Shurtleff and Minda Lynch (DNBR) are organizing a symposium for the American Psychological Association's annual meeting to be held in August 2001 in San Francisco. The symposium, entitled **Impulsivity and Drug Abuse,** will feature presentations by Dr. Jane Taylor (Yale University) on "Cortico-Limbic-Striatal Dysfunction after Stimulant Administration: Evidence for Impulsivity from Animal Models", from Dr. Peter Finn (Indiana University) on "Signal Salience and Working Memory in Impulsivity: Implications for Substance Abuse", from Dr. Suzanne Mitchell (University of New Hampshire) on "Correlates of Heightened Impulsivity in College Students", and from Dr. Joel T. Nigg (Michigan State University) on "Unitary Versus Multiple Inhibition Processes: A Developmental Perspective".

Dr. Minda Lynch, BCSRB, DNBR is serving as the NIDA representative on a planning committee for a fall meeting on **Stigma,** sponsored by the Fogerty Institute and several other NIH institutes. This trans-NIH meeting is scheduled for September 5-7, 2001 and will be held at Pooks Hill Marriott, Bethesda, MD. Thematic areas to be addressed in a presentation and break-out group format include epidemiology, theoretical perspectives, methodology, interventions, ethical and legal aspects, and discussion around exemplars of disease-associated stigma.

National **CTN Steering Committee Meetings** are planned for the follow dates and locations: July 16-18, 2001, in Denver, CO; and October 22-24, 2001, in Bethesda, MD.

The **CTN Data and Safety Monitoring Board** will meet June 25-26, 2001, and September 17-18, 2001, in Bethesda, Maryland.

The **CTN Annual Kick Off Meeting** is scheduled for September 10-11, 2001, in Washington, D.C.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Publications

The Problems of Drug Dependence, 2000: Proceedings of the 62nd Annual Scientific Meeting of the College on Problems of Drug Dependence
NIH Pub. No. 01-4918

This publication is more than just a "proceedings" from a meeting-as the most comprehensive gathering of scientific information on all aspects of substance abuse this document is invaluable to researchers and other scientists.

Research Report Series: Hallucinogens and Dissociative Drugs
NIH Pub No. 01-4209

This publication summarizes current knowledge about rates of use, methods of action, effects, and acute and long-term dangers of two important classes of drugs of abuse. Hallucinogenic drugs, which include LSD and mescaline, act on the serotonin system to produce profound distortions of the user's sense of reality. The dissociative drugs include the anesthetic agents PCP and ketamine and the cough suppressant dextromethorphan, all of which cause feelings of separation from the body. Ketamine use has increased in recent years; in addition to its conscious abuse, it has also been given to unsuspecting victims to incapacitate them for sexual assaults.

Research Report Series: Prescription Drugs-Abuse and Addiction
NIH Pub. No. 01-4881

This publication provides concise but detailed research findings of national interest regarding the increasing trend in abuse of prescription drugs and why they are prescribed, how they work in the brain and body, and what happens with improper use. It covers interactions of prescription drugs with other drugs and alcohol, abuse rates among various populations, as well as what is known about diagnosing and treating prescription drug abuse. This publication is geared to the educated lay public-particularly the elderly. In addition, this publication includes a list of references and resources for further information.

Research Report Series: Inhalant Abuse (Spanish)
NIH Pub. No. 01-3818(S)

This publication provides information based on research on the use and prevalence of inhalants, presents information on the types of inhalants, the consequences of use, who abuses inhalants, and where to get help.

Principles of Drug Addiction Treatment: A Research-Based Guide (Spanish)
NIH Pub. No. 01-4180(S)

This publication provides research-based information about addiction, drug treatment, and recovery for new patients undergoing treatment for addiction, and for their friends and families. The publication helps guide new patients in getting the most from their treatment and warns about possible difficulties during treatment and recovery.

NIDA NOTES

NIDA NOTES, Volume 16, Number 1

The lead story in this issue reports on research indicating that maternal smoking during pregnancy is associated with toddler negativity and with early smoking experimentation by children. Researchers queried mothers about their smoking habits before, during, and after pregnancy and on their children's behavior. In the Director's Column, Dr. Leshner details the health disparities that exist among minority populations in relationship to drug abuse treatment and what NIDA is doing to address this issue. Another research article discusses how an alcohol-treatment medication, disulfiram, is being used to reduce cocaine abuse among heroin treatment patients, with a sidebar about a large clinical study on disulfiram's effects on cocaine use. Other stories discuss the nicotine patch as a treatment for smokeless tobacco use, the extent of smokeless tobacco use by women, release of a high school curriculum supplement on addiction, and NIDA's participation in meetings and programs about methamphetamine abuse in Southeast Asia. The Tearoff provides information about the NIDA Community-Based Outreach Model: A Manual To Reduce the Risk of HIV and Other Blood-Borne Infections Among Drug Users. The Bulletin Board announces the receipt of a prestigious Federal service award by a senior NIDA administrator.

NIDA NOTES, Volume 16, Number 2

The lead story in this issue reports on brain imaging studies that indicate that the same brain sites are involved in cue-induced cocaine craving and normal rewards. In a Director's Column titled "Reducing Drug Abuse and Addiction is Not a Multiple Choice Test," Dr. Leshner explains why thinking about drug abuse and addiction in simple either/or categories, such as "brain disease" versus "personal choice," "treatment" versus "holding the addict responsible," and "inhibiting supply" versus "reducing demand" oversimplifies the dynamic complexity of the problem. To make progress, he says, we will need to use comprehensive approaches that blend public health and public safety components. Other articles report on the annual Monitoring the Future survey, the increased risk of adolescents, women, and whites to becoming nicotine dependent, and the equal effectiveness of three types of opioid treatment medications. Other stories highlight a NIDA-sponsored conference on the club drug GHB, and drug abuse-related products developed by small businesses with NIDA support. The Tearoff provides information on LSD and related drugs. The Bulletin Board presents information on three new members of NIDA's National Advisory Council.

CTN Publications

The third news report for the CTN was approved on April 19, 2001. The newsletter was distributed to all CTN nodes and posted on the CTN web page.

Several protocol brochures for patients were translated into Spanish this period. The CTN brochure entitled "What Are Clinical Trials?" was also translated into Spanish.

Fourteen editions of the CTN Bulletin Board were distributed this period. The Bulletin Board is a weekly electronic report on the activities of the various protocol teams and subcommittees of the CTN.

Other Publications

Glantz, M.D., and Leshner, A.I. Drug Abuse and Developmental Psychopathology. Development and Psychopathology, 12, pp. 795-814, 2000. This article discusses the application of principles of developmental psychopathology to understanding recent drug abuse research findings and to identifying critical directions for future research. Among the issues discussed and viewed from this perspective are: antecedent and co-occurring psychopathological conditions and other problem behaviors; the diversity of the nature of, paths to, and processes and outcomes related to drug abuse; the role of intermediary influences; the interaction of individual and environmental predisposing and protective factors; directions for prevention research; the role of families and other social institutions in intervention; and, developmental stage characteristics.

In the May issue of Nature Biotechnology, Dr. Rebekah Rasooly co-authored a short report describing a meeting of microarray researchers funded through NIDA's microarray initiative, DA-00-003. The report describes the plans formulated by the investigators to facilitate progress in this field through improved methods for data standardization and sharing. This arrangement may serve as a model for other national/international microarray data curation/storage efforts.

Robarge, M.J., Agoston, G.E., Izenwasser, S., Kopajtic, T., George, C. and Newman, A.H. Highly Selective Chiral N-Substituted 3_-[bis(4'-fluorophenyl)methoxy]tropane Analogues for the Dopamine Transporter: Synthesis and Comparative Molecular Field Analysis. Journal of Medicinal Chemistry, 43, pp. 1085-1093, 2000.

Newman, A.H. Novel Pharmacotherapies for Cocaine Abuse 1997-2000. Expert Opinion on Therapeutic Patents, 10, pp. 1095-1122, 2000. *Invited review.*

Hoffman, B.T., Kopajtic, T., Katz, J.L., and Newman, A.H. 2D QSAR Modeling of Dopamine Transporter Inhibitor Affinity Using Genetic Algorithm Variable Selection of Molconn Z Descriptors. Journal of Medicinal Chemistry, 43, pp. 4151-4159, 2000.

Katz, J.L. and Alling, K.L. Discriminative Stimulus Effects of Putative D3 Dopamine Receptor Agonists in Rats. Behavioural Pharmacology, 11, pp. 483-493, 2000.

Bergman, J., Koek, W., Holtzman, S.G., Stephens, D.N., Katz, J.L., Balster, R.L. and France, C.P. Agonist Efficacy, Drug Dependence, and Medications Development. Psychopharmacology, 153, pp. 67-84, 2000.

Newman, A.H., Robarge, M.J., Howard, I.M., Wittkopp, S.L., George, C., Kopajtic, T., Izenwasser, S., and Katz, J.L. Structure-Activity Relationships at the Monoamine Transporters and Muscarinic Receptors for N-substituted-3_-[3'-Cl-, 4'-Cl-, 4',4"-diCl-substituted)diphenyl] methoxytropanes. Journal of Medicinal Chemistry, 44, pp. 633-640, 2001.

Katz, J.L., Agoston, G.E., Alling, K.L., Kline, R.H., Forster, M.J., Woolverton, W.L., Kopajtic, T.A. and Newman, A.H. Dopamine Transporter Binding without Cocaine-like Behavioral Effects: Synthesis and Evaluation of Benztropine Analogs Alone and In Combination with Cocaine. Psychopharmacology, 154, pp. 362-374, 2001.

Woolverton W.L., Hecht G.S., Agoston G.E., Katz, J.L. and Newman, A.H. Further Studies of the Reinforcing Effects of Benztropine Analogs in Rhesus Monkeys. Psychopharmacology, 154, pp. 375-382, 2001.

Hayashi, T., Hirata, H., Asanuma, M., Ladenheim, B., Tsao, L.I., Cadet, J.L. and Su, T.P. Delta Opioid Peptide [D-Ala2, D-Leu5]Enkephalin Causes a Near Complete Blockade of the Neuronal Damage Caused by a Single High Dose of Methamphetamine: Examining the Role of p53. Synapse, 39(4), pp. 305-312, 2001.

Imam, S.Z., Newport, G.D., Itzhak, Y., Cadet, J.L., Islam, F., Slikker, W. and Ali, S.F. Peroxynitrite Plays a Role in Methamphetamine-induced Dopaminergic Neurotoxicity: Evidence from Mice Lacking Neuronal Nitric Oxide Synthase Gene or Overexpressing Copper-Zinc Superoxide Dismutase. J. Neurochem., 76(3), pp. 745-749, 2001.

Moolchan, E.T., Berlin, I., Robinson, M.L., and Cadet, J.L. African-American Teen Smokers: Issues to Consider for Cessation Treatment. J Natl Med Assoc., 92(12), pp. 558-562, 2000.

Frost, D.O. and Cadet, J.L. Effects of Methamphetamine-induced Neurotoxicity on the Development of Neural Circuitry: A Hypothesis. Brain Res Rev 34(3), pp. 103-118, 2000.

Huestis, M.A., Gorelick, D.A., Heishman, S.J., Preston, K.L., Nelson, R.A., Moolchan, E.T. and Frank, R.A. Blockade of Smoked Marijuana Effects in Humans by the Oral CB1-Selective Cannabinoid Receptor Antagonist SR141716. Archives of General Psychiatry, 58, pp. 322-328, 2001.

Woods, A.S. and Huestis, M.A. A Study of Peptide-Peptide Interaction by MALDI. Journal of Mass Spectrometry, 12, pp. 88-96, 2001.

Huestis, M.A., Cone, E.J., Wong, C.J., Umbricht, A. and Preston, K.L. Monitoring Opiate Use in Substance Abuse Treatment Patients by Sweat and Urine Testing. Journal of Analytical Toxicology, 24, pp. 509-521, 2000.

Moolchan, E.T., Cone, E.J., Wtsadik, A., Huestis, M.A., and Preston, K.L. Cocaine and Metabolite Elimination Patterns in Chronic Cocaine Users During Cessation: Plasma and Saliva Analysis. Journal of Analytical Toxicology, 24, pp. 458-466, 2000.

Wang, Y., Hayashi, T., Chang, C.F., Chiang, Y.H., Tsao, L.I., Su, T.P., Borlongan, C.V., and Lin, S.Z. Methamphetamine Potentiates Ischemia/Reperfusion Insults after Transient Middle Cerebral Artery Ligation in Mice. Stroke, 32, pp. 775-782, 2001.

Hayakawa, T., Chang, M.C.J., Rapoport, S.I. and Appel, N.M. Selective Dopamine Receptor Stimulation Differentially Affects [3H]arachidonic acid Incorporation, a Surrogate Marker for Phospholipase A2-mediated Neurotransmitter Signal Transduction, in a Rodent Model of Parkinson's Disease. J. Pharmacol. Exp. Ther., 296, pp. 1074-1084, 2001.

Myers, C.S., Contreras, M.A., Chang, M.C.J., Rapoport, S.I. and Appel, N.M. Haloperidol Downregulates Phospholipase A2 Signaling in Rat Basal Ganglia Circuits. Brain Res., 896, pp. 96-101, 2001.

Acri, J.B., Thompson, A.C., and Shippenberg T.S. Modulation of Pre and Postsynaptic Dopamine D2 Receptor Function

by the Selective Kappa-Opioid Receptor Agonist U69593. Synapse, 39, pp. 343-350, 2001.

Miller, D.K., Crooks, P.A., Teng, L-H, Witkin, J.M., Munzar, P., Goldberg, S.R., Acri, J.B., and Dwoskin, L.P. Lobeline Inhibits the Neurochemical and Behavioral Effects of Amphetamine. Journal of Pharmacology and Experimental Therapeutics, 296, pp. 1023-1034, 2001.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Staff Highlights

Honors and Awards

Alan I. Leshner, Ph.D., NIDA Director, received the 2000 GEICO Public Service Award for outstanding contributions in the field of Substance Abuse Prevention and Treatment.

Length of Service Awards

The following NIDA Intramural Research Program (IRP) staff members were presented with Length of Service Awards at an IRP All Hands Meeting held on April 17, 2001.

20 Years of Service
Dr. Steven Goldberg

10 Years of Service
Dr. Jean Lud Cadet
Dr. Carlo Contoreggi
Patricia Jemellaro
Leslie Johnson
Theresa Kopajtic
Rosemary Perrot
Carol Sneeringer
Eric Thorndike

Staff Changes

Blair Gately joined OSPC in March 2001 as the Deputy Press Officer in the Public Information and Liaison Branch. Ms. Gately has a Bachelor of Science degree in Journalism from the University of Maryland, a certificate in Public Relations from the University of Virginia, and has taken Science Writing courses at The Johns Hopkins University Graduate School of Arts and Sciences. Prior to joining OSPC, she worked at Voice of America and at NIH as a writer/editor for "The NIH Record" and as a Public Affairs specialist at the National Heart, Lung and Blood Institute.

Dr. Melissa Racioppo joined the Behavioral Treatment Development Branch, DTR&D, as a new Program Officer on February 26, 2001. Prior to coming to NIDA, Dr. Racioppo was working as a post-doctoral fellow at the University of Pennsylvania School of Medicine. Dr. Racioppo will be leading programs of research in the adolescent, family/couples therapy, group therapy, and criminal justice system areas.

Elaine Solano joined DESPR's Epidemiology Research Branch as a Secretary on March 25, 2001. Ms. Solano was formerly employed by the U.S. Department of Agriculture for ten years.

Robert Walsh, R.A.C. was promoted to Chief of the Regulatory Affairs Branch, Division of Treatment Research and Development, in January 2001. He has been with NIDA since 1987 when he joined the Research Technology Branch in the Division of Preclinical Research. Mr. Walsh ran the NIDA Drug Supply Program and was one of the founding members of NIDA's Medications Development Division. His current duties include insuring that the division's clinical trials are in compliance with applicable laws and regulations from NIH, DEA, FDA, OHRP and other governmental

agencies. He is also currently the Study Director for the NIDA/VACSP #1018 Best Practices Trial exploring the use of buprenorphine in non-traditional settings.

Dr. Elizabeth Rahdert retired on March 30, 2001, after 15 years of working for the federal government. Dr Rahdert was responsible for leading a program of research on the treatment of adolescents.

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

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

Director's Report to the National Advisory Council on Drug Abuse
May, 2001

Grantee Honors

Dr. Kathleen Brady, Principal Investigator for the CTN's South Carolina Node, was selected as South Carolina Woman of Achievement Award recipient by Governor Jim Hodges of South Carolina. The Governor's Commission on Women hosted an awards ceremony on May 14, 2001, at the Governor's Mansion in South Carolina.

Dr. Ivy Carroll of Research Triangle Institute (RTI) in North Carolina will receive the 2001 Charles H. Herty Award, bestowed annually by the Georgia Section of the American Chemical Society, in recognition of his significant contributions in organic and medicinal chemistry. The most widely recognized contribution on which Dr. Carroll's award is based is the development of the 3-phenyltropane class of compounds as potential treatment agents for cocaine abuse.

Dr. Linda B. Cottler, Associate Professor of Epidemiology in Psychiatry, Department of Psychiatry, Washington University, received the Washington University School of Medicine Academic Women's Network Mentoring Award for Outstanding Mentoring. Dr. Cottler is the principal investigator for a NIDA funded Institutional Training Program in Drug Abuse Comorbidity and Statistics.

Dr. Murray Goodman, Professor of Chemistry and Biochemistry at the University of California at San Diego, was awarded an Arthur C. Cope Scholar Award for 2001 by the American Chemical Society. The award is for advances made in the area of the synthesis of neuropeptides and peptidomimetics, including the use of constrained amino acids, in order to better understand opiate receptor conformations.

Dr. Michael L. Hecht, Department of Speech Communication, Pennsylvania State University, and his research team received the ITVA (International Television Video Association) Awards, Arizona Chapter, for Student Productions: Lavantate, Leave, The Ride, and Rechaza. These were four videos produced for a NIDA grant by South Mountain High School students.

Dr. S. Michael Owens, Professor of Pharmacology and Toxicology at the University of Arkansas for Medical Sciences' (UAMS) College of Medicine has been named to the University's *Wilbur D. Mills Endowed Chair in Alcoholism and Drug Abuse Prevention* for his extraordinary leadership in research, teaching and service. The endowed chair is the highest academic honor bestowed by UAMS in recognition of distinguished accomplishment and exemplary service. Dr. Owens' research program has been continuously funded by NIDA since 1986. The investiture ceremony will be held on May 24, 2001 in Little Rock, AR.

[Office of the Director][Report Index]