National Institute on Drug Abuse

Director's Report

to the

National Advisory Council on Drug Abuse

May, 2000

Index

[Office of Director] [First Report Section]

National Institute on Drug Abuse

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

May, 2000

Research Findings

Basic Research

Repeated Exposure to Psychostimulants and Opiates Produces Morphological Changes in Dendrites of Nucleus Accumbens and Prefrontal Cortex

Changes in behavior and brain function that outlast the pharmacological actions of drugs are hallmarks of repeated drug use. Most studies of long-lasting drug effects have focused on changes in the biochemical or neurophysiological properties of neurons. Dr. Terry Robinson and Dr. Bryan Kolb have been investigating morphological changes in dendrites as another marker of long-lasting alterations of synaptic function in response to drug treatment. Repeated injections in rats of either amphetamine or cocaine produced an increased number of dendritic branches and a higher density of dendritic spines on medium spiny neurons in the shell of the nucleus accumbens and on apical dendrites of layer V pyramidal cells in the prefrontal cortex, measured 25 days after drug exposure. Both of these neuron types are targets of dopaminergic input from the VTA. Interestingly, a similar study with repeated doses of morphine showed changes in dendritic morphology in the opposite direction: the complexity of dendritic branching and the number of dendritic spines was reduced. These morphological changes are likely to alter the patterns of synaptic connectivity in NAc and prefrontal cortex and may account for some of the persistent neurobehavioral consequences of repeated exposure to psychostimulant and opioid drugs. The opposite results from the two classes of drugs may underlie some of the differences in their long-term consequences, such as differential effects on cognitive processes mediated by the prefrontal cortex. Robinson, T.E. and Kolb, B. Alterations in the Morphology of Dendrites and Dendritic Spines in the Nucleus Accumbens and Prefrontal Cortex Following Repeated Treatment with Amphetamine or Cocaine. European Journal of Neuroscience, 11, pp. 1598-604, 1999; Robinson, T.E. and Kolb, B. Morphine Alters the Structure of Neurons in the Nucleus Accumbens and Neocortex of Rats. Synapse, 33, pp. 160-162, 1999.

Cellular Machinery for the Endocytosis of the AMPA Receptor Plays an Important Role in Synaptic Plasticity

Glutamate is the major excitatory neurotransmitter in the central nervous system. One important class of glutamate receptors is the ionotropic receptors or AMPA receptors. This class of receptors has been shown to be important in synaptic plasticity and has been shown to be regulated by chronic treatment with either cocaine or morphine. Potential mechanisms by which the responsiveness to glutamate can be altered at a synapse is by modifying the number of receptors, the sensitivity of each receptor, or the distribution of the receptors. The number of receptors at a synapse can be changed by increasing synthesis and the rate of insertion of the receptor, or decreasing the rate in which the receptors are removed from the membrane and degraded. The removal of the AMPA receptor from the membrane takes place via endocytosis. Another mechanism by which sensitivity can be changed is by altering the distribution of receptors so that receptor concentration can be more or less concentrated at a synapse. Work by NIDA grantees, Drs. Robert Malenka at Stanford University, Roger Nicoll, and Mark Von Zastrow at UCSF, have shown that the removal of the AMPA receptor from the postsynaptic membrane of a neuron by endocytosis is induced by glutamate attaching or binding to the AMPA receptor. They demonstrate that this form of endocytosis is mediated by a dynamin-dependent process. In a subsequent paper, they show that post synaptic blockade of endocytosis

enhances the amplitudes of the AMPA receptor response and blocks long term depression, a special form of synaptic plasticity. This result shows that the composition of the post synaptic membrane like the presynaptic membrane is dynamically regulated by endocytosis and that the cellular machinery for the endocytosis of the AMPA receptor plays an important role in synaptic plasticity. Luscher, C., Xia, H., Beattie, E.C., Carroll, R.C., von Zastrow, M., Malenka, R.C., and Nicoll, R.A. Role of AMPA Receptor Cycling in Synaptic Transmission and Plasticity. Neuron, 24(3), pp. 649-58, 1999. Carroll, R.C., Beattie, E.C., Xia, H., Luscher, C., Altschuler, Y., Nicoll, R.A., Malenka, R.C., and von Zastrow, M. Dynamin-dependent Endocytosis of Ionotropic Glutamate Receptors. Proc. Natl. Acad. Sci. U.S.A., 96(24), pp. 14112-14117, 1999.

Cannabinoid/Dopamine Agonist Combinations

A recent study by Drs. Bertha Madras and Allyn Howlett has indicated that intramuscular injection of a synthetic THC derivative, levonantradol, at a non-sedating dose of 0.03mg/kg in monkeys, followed by a course of successive injections of increasing concentrations of the D2 dopamine agonist pergolide, produced a significant decrease in locomotor activity and an increase in eyelid closure (sedation), rather than the expected promotion of hyperactivity. The same trend was found to a lesser extent for the selective D2 agonist quinelorane, but not for the D1 agonist SKF81297. The choice of the agents used was based on data showing that levonantradol by itself can produce sedation and reduced activity in monkeys, pergolide is of interest in potentially treating cocaine addiction, and quinelorane is an agent for use in improving activity in animal models of Parkinson's disease. If these results are found to extend further to other cannabinoids and THC itself interacting with dopamine agonists, they may have implications in the management of neuropsychiatric diseases and in the co-administration of cocaine or amphetamines, together with marijuana. J. Pharmacology and Experimental Therapeutics, 292, pp. 952-959, 2000.

Regulation of Immune Responses by the Cannabinoid Receptor

The regulation of immune responses by a cytokine (IL2) has been modulated through the administration of cannabinoids. This was shown to occur through the regulation of transcription processes in the same immune-type cell. A strong interaction between the cannabinoid and cytokine systems was displayed and it was also revealed that the immune system can use the cannabinoid system to regulate host susceptibility. NIDA-supported investigators previously reported that immunosuppressive cannabinoids inhibited interleukin (IL)-2 steady-state mRNA expression and secretion by phorbol-12-myristate-13-acetate plus ionomycin-activated mouse splenocytes and EL4 murine T-cells. In this study these researchers show that inhibition of IL-2 production by cannabinol, a modest central nervous system-active cannabinoid, is mediated through the inhibition of IL-2 gene transcription. Moreover, electrophoretic mobility shift assays demonstrated that cannabinol markedly inhibited the DNA binding activity of nuclear factor of activated T-cells (NF-AT) and activator protein-1 (AP-1) in a time- and concentration-dependent manner in activated EL4 cells. The inhibitory effects produced by cannabinol on AP-1 DNA binding were quite transient, showing partial recovery by 240 min after cell activation and no effect on the activity of a reporter gene under the control of AP-1. Conversely, cannabinol-mediated inhibition of NF-AT was robust and sustained as demonstrated by an NF-AT-regulated reporter gene. Collectively, these results suggest that decreased IL-2 production by cannabinol in EL4 cells is due to the inhibition of transcriptional activation of the IL-2 gene and is mediated, at least in part, through a transient inhibition of AP-1 and a sustained inhibition of NF-AT. Yea, S.S., Yang, K.H., and Kaminski, N.E. Role of Nuclear Factor of Activated T-Cells and activator Protein-1 in the Inhibition of Interleukin-2 Gene Transcription by Cannabinol in EL4 T-cells. J. Pharm. Exper. Ther., 292, pp. 597-605, 2000.

Neuroimmune Regulation by Cannabinoids

Two different cannabinoid receptors have been cloned, CB1 and CB2. CB1 is more common to the central nervous system and CB2 to the peripheral systems such as lymphocytes. The cannabinoid modulation of glia, the macrophages of the brain, was studied by Puffenbarger, Boothe, and Cabral. Little is known about cannabinoid's action on glial cell function. Using several cannabinoid agonists and antagonists, they found that neither CB1 nor CB2 receptors were involved in glial cell regulation. The usual cannabinoid antagonists were not functioning as antagonists. These results suggest the possibility of the involvement of other systems and/or the functioning of unique heretofore unrecognized properties of one of the two known cannabinoid receptors in these cells. In this study the effect of cannabinoids on the induction of cytokine mRNA by rat microglial cells was examined. Exposure of neonatal rat cortical microglial cells to the exogenous cannabinoid delta(9)-tetrahydrocannabinol (THC) resulted in reduced amounts of lipopolysaccharide (LPS)-induced mRNAs for IL-1-alpha, IL-1 beta, IL-6, and TNF-alpha. Of these cytokine mRNAs, the response of that for IL-6 was exquisitely sensitive to THC. Similarly, exposure of microglial cells to the putative endogenous cannabinoid anandamide before LPS treatment resulted in a decrease in cytokine mRNA levels, but not to the same extent as that caused by THC; however, when methanandamide, the nonhydrolyzable analog of anandamide was tested, its ability to inhibit cytokine mRNA expression was comparable to that of THC. Exposure of microglial cells to either of the paired enantiomers CP55,940 or CP56,667 resulted in similar inhibition of

LPS-induced cytokine mRNA expression. A comparable inhibitory outcome was obtained when the paired enantiomers levonantradol and dextronantradol were employed. Neither the CB1-selective antagonist SR141716A nor the CB2-selective antagonist SR144528 was able to reverse the inhibition of cytokine mRNA expression by levonantradol. The CB2 antagonist, however, when administered alone, augmented the production of cytokine mRNAs. Collectively, these studies demonstrate that cannabinoids can modulate levels of cytokine mRNA in rat microglial cells; however, the inhibition of cytokine mRNA expression is apparently not mediated through either of the CB1 or CB2 cannabinoid receptors. Puffenbarger, R.A., Boothe, A.C., and Cabral, G.A. Cannabinoids Inhibit LPS-Inducible Cytokine mRNA Expression in Rat Microglial Cells GLIA, 29, pp. 58-65, 2000.

Opioids and Cell Division in Embryonic Brain

Recently Dr. Kurt Hauser and his collaborators designed experiments to assess whether opioids can modulate cell proliferation in the embryonic brain through the endogenous opioid systems of the embryonic and maternal organisms. Their findings demonstrated that the endogenous embryonic and maternal opioid systems are involved in the regulation of cell division in the ventricular zone of the embryonic cortex. Their data also showed that small numbers of neural precursors in the neocortical germinal zone possessed mu, delta and kappa opioid receptor immunoreactivity in embryonic day 16 of the mouse. Furthermore, an acute exposure of mouse embryos to opioid agonist or antagonists modified labeled thymidine incorporation in the cells. In their view, these findings support the notion that endogenous opioids participate in prenatal cortical development. Reznikoz, K., Hauser, K. F., et al. Opioids Modulate Cell Division in the Germinal Zone of the Late Embryonic Neocortex. European J. Neuroscience, 11, pp. 2711-2719, 1999.

Dynorphin A and Neurodegeneration

Dynorphin A is an endogenous opioid peptide that preferentially activates kappa opioid receptors and is antinociceptive at physiological concentrations. However, growing evidence suggests that exposure to high concentrations of dynorphin can induce hyperalgesia and allodynia and may contribute to neural damage. A recent study undertaken by Dr. Kurt Hauser and his team to assess the role of dynorphin in neurodegeneration showed that dynorphin A could have paradoxical effects on neuronal viability through both opioid and non-opioid (glutamatergic) receptor mediated actions. These studies were carried out using isolated populations of neurons enriched in both kappa-opioid and NMDA receptors from embryonic mouse spinal cord. The researchers observed that at micromolar concentrations, dynorphin A elevated intracellular calcium levels and caused a significant loss of neurons. These excitotoxic effects were completely blocked by the NMDA antagonist MK-801, suggesting that dynorphin A was acting through NMDA receptors. In contrast, opioid antagonists exacerbated the toxic effects of dynorphin. These findings led the investigators to suggest that toxic effects of dynorphin are mediated by glutamatergic receptors and override the potential beneficial actions of opioid receptors. Hauser, K.F., Foldes, J.F., and Turbek, C.S. Dynorphin D (1-13) Neurotoxicity in Vitro: Opioid and Non-Opioid Mechanisms in Mouse Spinal Cord Neurons. Experimental Neurology, 106, pp. 361-375, 1999.

POMC and Leptin Regulation

The mechanisms by which leptin influences energy homeostasis are not yet understood. Several observations indicate that proopiomelanocortin (POMC) is involved in the regulation of food intake and may be a mediator of leptin action. A recent study undertaken by Dr. Wardlaw and her team to assess this interaction in obese leptin receptor-deficient rats showed significant decreases in POMC gene expression and peptide levels in the medial basal hypothalamus (MBH) of obese as compared to lean rats. They also observed an acute increase in the levels of POMC primary transcript in the medial basal hypothalamus of non-obese animals after a single intracerebro-ventricular injection of leptin, which supports their notion that leptin plays a role in the regulation of POMC gene transcription. These findings led the investigators to conclude that POMC is an important mediator of the effects of leptin on food intake and energy expenditure. These findings may have applications for drug abuse and AIDS-associated complications such as weight loss and anorexia, and may have implications for understanding and managing opiates and withdrawal. Korner, J., Chua, S.C., Williams, J.A., Leibel, R.L. and Wardlaw, S.L. Regulation of Hypothalamic Proopiomelanocortin by Leptin in Lean and Obese Rats. Neuroendocrinology, 70, pp. 377-383, 1999.

Fundamental Mechanisms of Dopamine Neurotransmission

Amphetamines can dramatically stimulate locomotor activity by increasing dopamine release and by inhibiting its reuptake. Dr. David Sulzer of Columbia University, in collaboration with colleagues from Genentech, Univ. of California San Francisco, Stanford University, and the Universidad de Valencia, produced genetically altered mice lacking the alpha-synuclein protein and studied the response of the knockout mice to amphetamine. The mutant mice displayed a decreased locomotor response to amphetamines. In addition, the mutant mice had reduced levels of total

striatal dopamine and the neurons exhibited increased dopamine release in response to paired electrical stimuli. The researchers concluded that alpha-synuclein is an essential presynaptic, activity-dependent negative regulator of dopamine neurotransmission; they attributed the attenuated response to amphetamine to either the altered pattern of dopamine neurotransmission or the reduced dopamine content. This finding is significant for basic neurobiology as well as for understanding why alpha-synuclein is associated with the etiology of Parkinson's Disease and Alzheimer's Disease. Abeliovich, A., Schmitz, Y., et al. Mice Lacking Alpha-Synuclein Display Functional Deficits in the Nigrostriatal Dopamine System. Neuron, 25, pp. 239-252, 2000.

Making the Connection Between Synaptic Vesicle Recycling and Cytoskeletal Organization

Drugs of abuse effect both synaptic transmission and synaptic plasticity, the growth of new synaptic connections. Synaptic vesicle recycling, an integral part of synaptic transmission, takes place via endocytosis. Actin-mediated cytoskeletal reorganization is an important component of neural plasticity and is required to guide axons to their target. Regis Kelly and Britta Qualmann at the University of California San Francisco determined that isoforms of the protein syndapin play a role in both endocytosis and actin dynamics. Syndapins localize to sites of high actin turnover in neuron-like cells and co-localizes with dynamin, a part of the endocytosis machinery, in neuroendocrine cells. Overexpression of full-length syndapin had a strong effect on cortical actin organization and induced extensions of the axon called filopodia, while overexpression of a portion of the syndapin protein inhibited endocytosis in vivo. The researchers concluded that syndapin isoforms link endocytosis and cytoskeletal dynamics in mature nerve terminals and other cell types. Thus this protein links two cellular functions, synaptic transmission and synaptic plasticity, that are affected by drugs of abuse. Qualmann, B. and Kelly, R.B. Syndapin Isoforms Participate in Receptor-Mediated Endocytosis and Actin Organization. J. Cell Biol., 148, pp. 1047-1061, 2000.

Region-Specific mRNA Processing of MOR-1 and MOR-1C in Rat Brain

Using rabbit antisera generated against the C-terminal peptide sequences of the mu opioid receptor splice variant MOR-1C, Dr. Pasternak and his team immunohistochemically examined the regional distribution of MOR-1C and compared it with MOR-1. They found that, overall, the distribution of MOR-1C-like immunoreactivity (-LI) differed from MOR-1-LI. Both MOR-1C-LI and MOR-1-LI were prominent in a few central nervous system regions, including the lateral parabrachial nucleus, the periaqueductal gray, and laminae I-II of the spinal trigeminal nuclei and the spinal cord. In the striatum, hippocampal formation, presubiculum and parasubiculum, amygdaloid nuclei, thalamic nuclei, locus coeruleus, and nucleus ambiguous MOR-1-LI predominated, whereas MOR-1C-LI was absent or sparse. Conversely, MOR-1C-LI exceeded MOR-1-LI in the lateral septum, the deep laminae of the spinal cord, and most hypothalamic nuclei such as the median eminence, periventricular, suprachiasmatic, supraoptic, arcuate, paraventricular, ventromedial, and dorsomedial nuclei. Double-labeling studies showed colocalization of the two receptors in neurons of the lateral septum, but not in the median eminence or in the arcuate nucleus, even though both MOR-1 isoforms were expressed. Because both MOR-1 and MOR-1C are derived from the same gene, these differences in regional distribution represent region-specific mRNA processing. Abbadie, C., Pan, Y.X., and Pasternak, G.W. Differential Distribution in Rat Brain of Mu Opioid Receptor Carboxy Terminal Splice Variants MOR-1C-Like and MOR-1-Like Immunoreactivity: Evidence for Region-Specific Processing. J. Comp. Neurol., 419, pp. 244-256, 2000.

Role of D1 Receptor in Cocaine- and Amphetamine-Induced Behavioral Changes

Cocaine and amphetamine can induce both short-term and long-term behavioral changes in rodents. The major target for these psychostimulants is thought to be the brain dopamine system. After cocaine and amphetamine treatments, Dr. Xu and his colleagues at the University of Cincinnati tested both the locomotor and stereotyped behaviors in mutant mice lacking the dopamine D1 receptor and wild-type control mice to determine whether the dopamine D1 receptor plays a crucial role in the behavioral effects of psychostimulants. They observed that the overall locomotor responses of D1 receptor mutant mice to repeated cocaine administration were significantly reduced compared to those of the wild-type mice. The responses of the D1 receptor mutant mice to cocaine injections were not significantly different from their responses to saline injections. D1 receptor mutant mice were less sensitive than the wild-type mice to acute amphetamine stimulation over a dose range although they exhibited similar behavioral responses to their wild-type cohorts. Immunostaining experiments indicated that there was no detectable neurotoxicity in the nucleus accumbens in both D1 receptor mutant and wild-type mice after repeated amphetamine administration. These data suggest that the D1 receptor plays an essential role in mediating cocaine- and amphetamine-induced behavioral changes in mice. Xu, M., Guo, Y., Vorhees, C.V., and Zhang, J. Behavioral Responses to Cocaine and Amphetamine Administration in Mice Lacking the Dopamine D1 Receptor. Brain Research, 852, pp. 198-207, 2000.

Pharmacogenetic Variability in Neuronal Nicotinic Receptor-Mediated Antinociception

The ability to predict inter-individual differences in drug efficacy or toxicity, based on genetic factors that influence drug disposition or drug action, is fast becoming a realistic goal. Dr. Christopher Flores of the University of Texas Health Science Center at San Antonio investigated epibatidine, a prototypical nicotinic analgesic drug, to see if it exhibits pharmacogenetic variability in antinociceptive activity. All strains of mice tested exhibited significant antinociception that peaked between 10 and 20 minutes following systemic injection of epibatidine. However, there was fourfold-variability in the magnitude of peak effect between mouse strains, with DBA/2 and A strains showing much greater sensitivity than all others tested. All mouse strains returned to baseline nociceptive threshold 30 minutes post-injection except for the A strain. In contrast, these mice exhibited significant antinociception for at least 3 hours following epibatidine administration. Thus, expressing the data as area under the time-latency curve to take into account both the magnitude and duration of effect, epibatidine displayed approximately 20-fold higher antinociceptive potency in the A strain as compared with the C3H/He strain. The effects of epibatidine in both the A and C3H/He strains were dose-dependent and sensitive to antagonism by the selective neuronal nicotinic channel blocker mecamylamine. Taken together, these data demonstrate the existence of pharmacogenetic variability in neuronal nicotinic receptor-mediated antinociception between inbred strains of mice and presage the potential for similar variability in analgesic response to nicotinic-based analgesics in humans. Future studies will seek to identify the chromosomal loci underlying the variability. Flores, C.M., Wilson, S.G., and Mogil, J.S. Pharmacogenetic Variability in Neuronal Nicotinic Receptor-Mediated Antinociception. Pharmacogenetics, 9, pp. 619-625, 1999.

Direct Protein-Protein Coupling Enables Cross-Talk Between Dopamine D5 and Gamma-aminobutyric Acid A Receptors

GABAA (gamma-aminobutyric-acid A) and dopamine D1 and D5 receptors represent two structurally and functionally divergent families of neurotransmitter receptors. The former comprises a class of multi-subunit ligand-gated channels mediating fast interneuronal synaptic transmission, whereas the latter belongs to the seven-transmembrane-domain single-polypeptide superfamily of receptors that exert their biological effects, including the modulation of GABAA receptor function, through the activation of second-messenger signaling cascades by G proteins. NIDA grantee Dr. Niznik and his coworkers at the University of Toronto show that GABAA-ligand-gated channels selectively form a complex with D5 receptors through the direct binding of the D5 carboxyl-terminal domain with the second intracellular loop of the GABAA gamma2(short) receptor subunit. This physical association enables mutually inhibitory functional interactions between these receptor systems. For the first time it also shows a mechanistic basis allowing for the functional differentiation of D1 and D5 receptors. The data highlight a previously unknown signal transduction mechanism whereby subtype-selective G-protein-coupled receptors dynamically regulate synaptic strength independently of classically defined second-messenger systems, and provide a heuristic framework in which to view these receptor systems in the maintenance of psychomotor disease states. Liu, F., Wan, Q., Pristupa, Z.B., YU, X-M, Wang, Y.T., and Niznik, H.B. Nature, 403, pp. 274-280, 2000.

Prefrontal Cortex is Necessary for the Induction, but not the Expression of Cocaine Sensitization

Behavioral sensitization is considered a useful animal model for studying the development of craving in humans. In collaborative studies, the laboratories of Drs. Marina Wolf and Frank White at the Chicago Medical School have been investigating the role of prefrontal cortex and its glutamatergic inputs to the VTA in cocaine sensitization. Previously, they found that behavioral sensitization to repeated doses of cocaine could be prevented by lesions of prefrontal cortex and by blockade of either the NMDA or AMPA classes of glutamate receptors. These treatments also prevented the changes in dopamine receptor sensitivity in the VTA and NAc that are likely cellular correlates of behavioral sensitization. A more recent study showed that sensitization was expressed with no decrement when these same treatments - prefrontal lesions or NMDA-receptor blockade - were carried out only on the day of testing for sensitization. These results are consistent with a model of sensitization that requires NMDA receptor activation in the VTA via glutamate release from axons originating in the prefrontal cortex. An implication of this model is that inputs to the prefrontal cortex from other events associated with drug taking could increase or decrease a drug's ability to modify midbrain function. Conversely, since neither prefrontal cortex nor NMDA-receptor activation is necessary for the expression of sensitization, it may not be possible to reverse some drug effects by engaging the cognitive and executive functions of prefrontal cortex. Li, Y., Hu, X.T., Berney, T.G., Vartanian, A.J., Stine, C.D., Wolf, M.E., and White, F.J. Both Glutamate Receptor Antagonists and Prefrontal Cortex Lesions Prevent Induction of Cocaine Sensitization and Associated Neuroadaptations. Synapse, 34, pp. 169-180, 1999; Li, Y., Wolf, M.E., White, F.J. The Expression of Cocaine Sensitization is not Prevented by MK-801 or Ibotenic Acid Lesions of the Medial Prefrontal Cortex. Behavioral Brain Research, 104, pp. 119-125 1999.

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

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Research Findings

Behavioral Research

A New Rapid Assessment Method for Dopamine Receptor Agonists

Recent studies suggest that dopamine D1-like and D2-like receptor agonists have differing profiles of cocaine-related actions. Dr. Barak Caine and his colleagues at the McLean Hospital-Harvard Medical School sought to develop a procedure for comparing the effects of D-1- and D-2-like agonists on cocaine self-administration in rhesus monkeys using a rapid pre-treatment dose-comparison procedure. Complete inverted U-shaped dose-effect functions for cocaine self-administration were obtained in all monkeys trained with the rapid assessment procedure. Levels of responding, moreover, were associated with the unit dose of cocaine. Pretreatment with D1-like agonists produced downward shifts in the cocaine dose-effect function at doses that also markedly decreased food-maintained responding. In contrast, pretreatment with D2-like agonists shifted the cocaine dose-effect function to the left. D2-like agonists also increased responding maintained by the cocaine-associated cue lights alone, and moderately decreased food-maintained responding. The authors conclude that D1- and D2-like agonists produce qualitatively different effects on cocaine self-administration that may influence their usefulness for the treatment of cocaine abuse and dependence. Caine, S.B., Negus, S.S., and Mello, N.K. Effects of Dopamine D(1-like) and D(2-like) Agonists on Cocaine Self-Administration in Rhesus Monkeys: Rapid Assessment of Cocaine Dose-Effect Functions. Psychopharmacology, 148, pp. 41-51, 2000.

Drug Discrimination: Training Dose Influences Subjective Drug Effects

Drug discrimination studies have found that animals trained with lower doses of a training drug are more sensitive to detecting the subjective Ôcue' properties of that drug on subsequent discrimination tests. These animals are also more sensitive to the subjective, interoceptive cue effects of other drugs as well, when tested with compounds that show generalization to the training drug. Few studies have assessed the effects of training dose on discrimination profiles in human subjects. Kollins and Rush examined the effects of training dose of d-amphetamine (10 mg or 20 mg) in human subjects performing a drug discrimination task. The dose-response curve for detecting amphetamine was shifted to the left in subjects trained with the lower dose of d-amphetamine. Subjects trained with the lower dose also reported greater subjective effects on scales of "like the drug", "stimulated", and "feel like socializing," while other self-reported effects of d-amphetamine, such as "anxious" and "bad effects" did not vary with training dose. The authors conclude that prior experience with the lower dose rendered these subjects more sensitive to the interoceptive cue properties of d-amphetamine and also to some of the positive subjective effects of this drug. These observations are important because detecting interoceptive drug cues may contribute to relapse. Kollins, S.H. and Rush, C.R. Effects of Training Dose on the Relationship Between Discriminative Stimulus and Self-Reported Drug Effects of d-Amphetamine in Humans. Pharmacol. Biochem. Behav., 64, pp. 319-326, 1999.

Dopaminergic Substrates for the Subjective Effects of Caffeine

At low doses, the methylxanthine caffeine acts as a behavioral stimulant in human subjects and induces locomotor activation in the rat. However, higher doses (>300 mg in humans) produce agitation and anxiety on self-report

measures and induce a suppression of animal behavior. Recent evidence suggests that the low dose activation may occur, in part, *via* the same central dopaminergic system that serves as the critical substrate for behavioral effects of other psychostimulants (e.g., amphetamine or cocaine). Little is known about dopaminergic involvement in subjective effects of caffeine. Drs. Powell, Koppelman and Holtzman from Emory University found that D1 and D2 dopamine receptor antagonists completely block the discriminative stimulus effects of low, but not high, caffeine doses in the rat. Animals trained to discriminate a low dose of caffeine from saline did not show generalization to higher doses of caffeine, suggesting that low and high doses induce qualitatively different subjective effects. These findings mimic self-report measures from human subjects and suggest that increasing doses of this stimulant may recruit different transmitter systems or induce behavioral effects through different neurochemical mechanisms. Powell, K.R., Koppelman, L.F. and Holtzman, S.G. Differential Involvement of Dopamine in Mediating the Discriminative Stimulus Effects of Low and High Doses of Caffeine in Rats. Behav. Pharmacol., 10, pp. 707-716, 1999.

d,l-Fenfluramine Decreases Aggressive and Impulsive Responding in Adult Males with a History of Conduct Disorder

The effects of acute doses of *d,l*-fenfluramine (0.2, 0.4, and 0.8 mg/kg) on aggression and impulsivity were examined in ten male subjects with a history of conduct disorder and criminal behavior. Aggression was assessed with a laboratory-based point subtraction aggression procedure that provides subjects with aggressive, escape, or monetary response options. Impulsivity was assessed in a delay of gratification task in which subjects chose between a small reward after a short delay and a larger reward after a longer delay. Impulsivity was measured as frequent choice of the short delayed reward. In the aggression procedure, *d,l*-fenfluramine produced a dose-related decrease in aggressive responding, but did not alter escape responding, and slightly increased monetary responding. *d,l*-fenfluramine releases serotonin and the finding that *d,l*-fenfluramine decreases aggression is consistent with a body of literature relating aggression and serotonin. *d,l*-fenfluramine also dose-dependently decreased impulsive responding, a finding consistent with published animal data showing a reduction in impulsivity following *d,l*-fenfluramine administration. Cherek, D.R., and Lane, S.D. Effects of *d,l*-Fenfluramine on Aggressive and Impulsive Responding in Adult Males with a History of Conduct Disorder. Psychopharmacology, 146, pp. 473-481, 1999.

Methodological Issues: Cumulative Dosing, Progressive Ratio, and Inferential Statistics

Dr. Marc Branch, University of Florida, recently published new data concerning the use of various methodologies in drug abuse research. He found that repeated use of the cumulative dosing procedure produced dose-response curves that were not as reliable as those produced by non-cumulative dosing procedures. He argued for the action of Pavlovian factors in producing the less reliable curves under the cumulative dosing procedure (Walker, D.J. and Branch, M.N. Response Suppression During Cumulative Dosing: A Role for Pavlovian Conditioning. Behavioural Pharmacology, 9, pp. 255-271, 1998). Branch and his colleagues also examined the role of step size in the progressive ratio procedure, a procedure commonly used to assess the reinforcement strength of drugs. Results indicated that step size did not affect the break point, but was inversely related to the average number of completed ratios in a manner well fit by a power function (Stafford, D., and Branch, M.N. Effects of Step Size and Break-Point Criterion on Progressive Ratio Performance. Journal of the Experimental Analysis of Behavior, 70, pp. 123-138, 1998). In a more recent paper, Branch described two things that statistical significance testing does not do: 1) provide a quantitative estimate of the reliability of a result and 2) estimate the probability that the results were due to chance. He argues that significance testing frequently: reduces scientific responsibility; is employed in a poor manner to test theory; emphasizes population parameters over behavior; limits the reasons for doing experiments; and discounts reliability in effects in some types of research. Branch, M.N. Statistical Inference in Behavior Analysis: Some Things Significance Testing Does and Does Not Do. The Behavior Analyst, 22, pp., 87-92, 1999.

Menstrual Cycle Phase Affects the Subjective Effect of *d*-Amphetamine

Research from the laboratory of Dr. Harriet de Wit at the University of Chicago shows that menstrual cycle phase is a factor in the subjective response to acute *d*-amphetamine. Sixteen healthy women received oral d-amphetamine during the follicular and mid-luteal phases of the menstrual cycle. Under *d*-amphetamine, subjective effects were greater during the follicular phase than the luteal. Subjects reported a greater feeling of "high," euphoria (ARCI MBG), and energy and intellectual efficiency (ARCI BG) during the follicular than the luteal phase, and more liking and wanting of the drug. During the follicular phase (when estrogen levels are high and progesterone levels are low), higher estrogen levels were associated with feeling energetic and intellectually efficient. During the luteal phase, when levels of both estrogen and progesterone are relatively high, the response to *d*-amphetamine was unrelated to estrogen level. Justice, A.J.H. and de Wit, H. Acute Effects of *d*-Amphetamine During the Follicular and Luteal Phases of the Menstrual Cycle in Women. Psychopharmacology, 145, pp. 67-75, 1999.

Menstrual Cycle Phase Affects Smoking Withdrawal Symptoms and Depressive Symptomatology

Dr. Kenneth Perkins and colleagues at the University of Pittsburgh found that in women who attempt to quit, phase of the menstrual cycle affects withdrawal symptoms. In a study of 78 women enrolled in a smoking cessation trial, women who quit during the luteal phase of their cycle had significantly more withdrawal symptoms and more depressive symptomatology during the week after quitting than women who quit during their follicular phase. These data suggest that women seeking to quit smoking may reduce the adverse effects of cessation by choosing to quit during the follicular phase. Perkins, K.A., Levine, M., and Marcus, M. Tobacco Withdrawal in Women and Menstrual Cycle Phase. Journal of Consulting and Clinical Psychology, 68, pp. 176-180, 2000.

Clonidine Blocks Immunosuppressive Effects of Morphine Withdrawal

It is known that morphine depresses immune system function. Changes in immune function during opiate withdrawal are not well understood. Drs. West, Dykstra and Lysle at the University of North Carolina Chapel Hill pretreated rats undergoing opiate detoxification with the drug clonidine, an alpha-2 adrenergic agonist used to alleviate opiate withdrawal symptoms during detoxification. Pretreatment with clonidine prevented opiate withdrawal associated decreases in concanavalin A, toxic shock syndrome toxin, splenic conA-stimulated interferon-gamma production, and splenic natural killer cell activity. Thus, clonidine treatment may be efficacious not only for attenuating withdrawal symptoms during opiate detoxification but may also be protective against withdrawal-induced immunosuppression. West, J.P., Dykstra, L.A. and Lysle, D.T. Immunomodulatory Effects of Morphine Withdrawal in the Rat are Time-Dependent and Reversible by Clonidine. Psychopharmacology, 146, pp. 320-327, 1999.

Role of Glutamatergic NMDA Receptor in Opiate Tolerance Depends on Degree of Tolerance

Recent experimental evidence has implicated central glutamatergic systems in opiate tolerance. The involvement of central glutamatergic NMDA receptors in tolerance has been demonstrated for morphine but not for other opiates with a high intrinsic efficacy, such as fentenyl. Drs. Allen and Dykstra suggest this may indicate that NMDA receptors are involved in only the milder forms of opiate tolerance. They found that rats receiving an NMDA antagonist during chronic opiate treatment showed a blockade of tolerance to antinociceptive effects when the morphine dose was 10 mg/kg, but only an attenuation when the daily dose was 20 or 40 mg/kg. Since the NMDA antagonist had no effect on analgesia in non-dependent rats, and did not affect the acute analgesic effects of morphine, it appears that NMDA receptor systems participate in the development of tolerance rather than in its expression. Their results suggest that different biochemical mechanisms may be involved in the development of tolerance with opiates of varying intrinsic efficacy. Allen, R.M. and Dykstra, L.A. The Role of Morphine Maintenance Dose in the Development of Tolerance and its Attenuation by an NMDA Receptor Antagonist. Psychopharmacology, 148, pp. 59-65, 2000.

Subjective Effects of Nicotine-Containing and De-Nicotinized Cigarettes

Researchers at the University of Vermont compared smokers' preference for nicotine-containing and de-nicotinized cigarettes. In one phase of the experiment, under separate conditions, smokers were given the opportunity to "purchase" cigarette puffs from a nicotine-containing cigarette or a de-nicotinized cigarette. In a second phase of the experiment, both cigarette types were available simultaneously and smokers could choose between a nicotine-containing cigarette and a de-nicotinized cigarette. The researchers found that when the de-nicotinized cigarette was the only cigarette available, the number of puffs taken and the self-reported measure of enjoyment were not different from those measures obtained when the nicotine-containing cigarette was the only cigarette available. When both cigarette types were available simultaneously, however, consumption of the nicotine-containing cigarette was significantly greater. These results suggest that smoking-related factors other than the direct effects of nicotine contribute to smoking and can, in fact, maintain smoking. However, if given a choice, smokers prefer nicotine-containing cigarettes, indicating that the combined effects of nicotine and other smoking-related factors is clearly the preferred option. Shahan, T.A., et al. Comparing the Reinforcing Efficacy of Nicotine and De-Nicotinized Cigarettes: A Behavioral Economic Analysis. Psychopharmacology, 147, pp. 210-216, 1999.

Tolerance to Nitrous Oxide's Hypothermic Effects

Hypothermia is an adverse effect of the abused drug nitrous oxide. Dr. Doug Ramsey at the University of Washington sought to determine whether tolerance to nitrous oxide hypothermia could develop within a single administration of this analgesic gas. Using a rodent model, he found that only a few animals demonstrated evidence of acute hypothermic tolerance over a 120-minute gas administration period. Over the next ten days, the experimental rats received five additional 30-minute exposures to 60 percent nitrous oxide and five 30-minute exposures to placebo, while the control rats received only placebo gas exposures. Chronic tolerance developed to nitrous oxide induced

hypothermia over repeated administrations. A test for Pavlovian drug conditioning found no evidence that conditioned temperature effects contributed to chronic tolerance development. In a second experiment, naive rats were given a 380-minute exposure to 60 percent nitrous oxide and a 380-minute exposure to placebo gas in a counterbalanced order. Acute tolerance did develop to nitrous oxide hypothermia, with the recovery of temperature beginning after a mean of 141 minutes of gas administration. Hence, both acute and chronic tolerance developed to nitrous oxide's hypothermic effects in rats. Ramsay, D.S., Omachi, K., Leroux, B.G., Seeley, R.J., Prall, C.W., and Woods, S.C. Nitrous Oxide-Induced Hypothermia in the Rat: Acute and Chronic Tolerance. Pharmacol. Biochem. Behav., 62, pp. 189-196, 1999.

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

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

National Institute on Drug Abuse

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

May, 2000

Research Findings

Treatment Research and Development

A Clinical Profile of Women with PTSD and Substance Dependence

This paper compared the clinical characteristics of two groups of women (those with Post Traumatic Stress Disorder (PTSD) and Substance Use Disorder (SUD) and those with PTSD only) to better understand why some women with PTSD also develop SUD, while others do not. The dual diagnosis women consistently had a more severe clinical profile, including worse life conditions, greater criminal behavior, higher number of lifetime suicide attempts, etc. One discrepant finding, however, was their lower rate of major depression. Interestingly, the two groups did not differ in number or type of lifetime traumas, PTSD onset or severity, family history of substance use, coping style, functioning level, psychiatric symptoms, or sociodemographic characteristics. Najavits, L.M., Weiss, R.D., and Shaw, S.R. Psychology of Addictive Behaviors, 13, pp. 98-104, 1999.

Associations Between Tobacco Smoking and Illicit Drug Use Among Methadone Maintained Opiate Dependent Individuals

Researchers at the University of California at, Los Angeles examined the relationship between levels of cigarette smoking and levels of illicit drug use in 32 patients enrolled in a heroin treatment program. The participants included heavy smokers (20-40 cigarettes per day), nonsmokers, and "chippers" who smoke fewer than 5 cigarettes per day. Breath and urine samples were evaluated over a 7-day period. The findings showed that the amount of cocaine and heroin use was directly related to the level of tobacco use in a stepwise fashion from nonsmokers, to chipper, to heavy smokers. This supports existing evidence suggesting associations between tobacco and opiate and cocaine use, and strongly suggest that smoking cessation should be offered to all methadone maintained individuals. Frosch, D.L., Shoptaw, S., Nahom, D., and Jarvik, M.E. Experimental and Clinical Psychopharmacology, 8, pp. 1-7, 2000.

The Relationship Between Anxiety Levels and Outcome of Cocaine Abuse Treatment

Investigators at Brown University examined how self-reported anxiety levels were related to cocaine use variables and patterns over the course of treatment and at 3 months post-treatment. Patients were 108 cocaine abusers receiving cognitive-behavioral coping skills treatment for their cocaine abuse. Results showed that state anxiety scores significantly declined for all participants from pre- to post-treatment and then remained stable into the follow-up period, regardless of relapse status. Trait anxiety was positively correlated with negative consequences due to cocaine use and negatively correlated with days in treatment. Findings suggest that elevated anxiety scores at pre-treatment subside with time, do not require clinical management of associated anxiety symptoms, and may be a temporary byproduct of experiencing negative consequences due to recent cocaine use. O'Leary, T.A., Rohsenow, D.J., Martin, R., Colby, S.M., Eaton, C.A., and Monti, P.M. American Journal of Drug and Alcohol Abuse, 26, pp. 179-194, 2000.

A Within-Subject Comparison of Three Different Schedules of Reinforcement of Drug Abstinence Using Cigarette Smoking as an Exemplar

In this study, investigators examined three schedules of reinforcement for promoting and sustaining short-term drug abstinence, using cigarette smoking as an exemplar of drug self-administration. The schedules studied were: 1) fixed magnitude of reinforcement for abstinence, 2) progressive increase in magnitude of reinforcement for abstinence with a reset contingency for drug use, and 3) progressive increase in magnitude of reinforcement for abstinence without a reset contingency. Eighteen subjects participated in all three schedules in a counterbalanced order. Each schedule was in effect for five consecutive days. The total amount of reinforcement available was the same during each condition. Findings indicate that the progressive magnitude with a reset schedule was more effective than the other two schedules in sustaining an initial period of abstinence. This study extends and provides further support for results that have been demonstrated in previous studies. Roll, J.M. and Higgins, S.T. Drug and Alcohol Dependence, 58, pp. 103-109, 2000.

A Brief Abstinence Test: Voucher-based Reinforcement of Cocaine Abstinence

Drs. Stitzer, Bigelow, Silverman and colleagues at the Johns Hopkins University School of Medicine and Dr. Cone, NIDA Intramural Research Program, conducted a study to assess the effectiveness of a brief abstinence reinforcement procedure for initiating cocaine abstinence in methadone maintenance patients. On the Monday of test week, 72 cocaine-abusing methadone patients were offered a $100 voucher if urine samples collected on Wednesday indicated they had abstained from cocaine across that 2-day period. A patient was considered abstinent and the voucher delivered if the urine benzoylecgonine concentration decreased by 50% from Monday to Wednesday or the concentration of Wednesday's urine sample was <300 ng/ml. Results indicate 79% of the patients showed urinalysis evidence of abstention from cocaine, Monday to Wednesday of test week. In a sub-sample (n=50), results indicate significantly more patients abstained from cocaine during the test week (84%) than during the same period the week before (36%) or the week after (32%) test week. Robles, E., Silverman, K, Preston, K.L., Cone, E.J., Katz, E., Bigelow, G.E., and Stitzer, M.L. Drug & Alcohol Dependence, 58, pp. 205-212, 2000.

Contingency Management for Accurate Predictions of Urinalysis Test Results and Lack of Correspondence with Self-Reported Drug Use Among Polydrug Abusers

Dr. Schuster and colleagues, Wayne State University School of Medicine, conducted a pilot study to assess the effectiveness of a contingency management procedure to enhance the validity of self-reports of drug use among 63 older (mean age 40.6 years) opiate-dependent poly-drug abusers enrolled in a drug treatment program. Participants in the reinforced prediction condition received vouchers worth $2.50 if their self-report predictions were accurate whereas participants in the non-reinforced prediction condition did not receive anything for accurate predictions. Preliminary results indicate both reinforced and non-reinforced patients were highly accurate in making urine drug screen (UDS) predictions, with predictions being equally accurate for heroin and cocaine but more accurate for positive than for negative UDS results. Although more research is needed to confirm these findings, results suggest poly-drug abusers' predictions of urine screen results might be sufficiently valid such that a program might save UDS costs by testing only those specimens obtained from patients reporting drug-free urines. Downey, K.K., Helmus, T.C. and Schuster, C.R. Psychology of Addictive Behaviors, 14(1), pp. 69-72, 2000.

Gender Differences in Hostility of Opioid-Dependent Outpatients: Role in Early Treatment Termination

In this study, Dr. Nancy Petry and Dr. Warren Bickel evaluated gender differences in hostility and the role of hostility in predicting early treatment termination of opioid-dependent patients. Subjects were 104 patients (68 males and 36 females) in a buprenorphine- maintenance treatment program. Opioid-dependent females scored significantly higher on the Buss-Durkee Hostility Scale, compared to males. Early treatment termination was defined as remaining in treatment less than 30 days, and 13% of males and 25% of females were classified as early terminators. Severity of legal and employment problems and the interaction between hostility and gender were predictors of early treatment termination. Patients with less severe legal problems and patients with greater employment problems were more likely to terminate early from treatment. Higher levels of hostility predicted early treatment termination of female patients, but hostility levels were not associated with treatment termination in male patients. Results from this study show that female heroin addicts have high levels of hostility and suggest that hostility may be an important predictor of premature termination of treatment, especially among opioid-dependent women. These data suggest that hostility should be assessed early in treatment and that increased effort may be needed to enhance participation of hostile women in treatment programs. Petry, N. and Bickel, W. Drug and Alcohol Dependence, 58, pp. 27-33, 2000.

Longer Term Methadone Maintenance, Combined with Some Psychosocial Counseling, is More Effective Than 180-Day Psychosocially Enriched Detoxification Treatment of Opioid

Dependence

Investigators from the University of California, San Francisco, compared outcomes of 179 opioid-dependent patients randomly assigned to either a methadone maintenance treatment group or a psychosocially enriched 180-day methadone detoxification group. The methadone maintenance group was eligible for 14 months of methadone maintenance, followed by a 2-month detoxification. Participants in this group were required to attend substance abuse group therapy 1 hour per week for the first 6 months of maintenance, and 1 hour per month of individual therapy. Patients in the detoxification group received methadone only for the first 180 days of their treatment. During this time, they attended 2 hours per week of group therapy; 1 hour per week of cocaine group therapy if they had tested positive for cocaine upon admission to the study; a series of 14 one-hour weekly substance abuse education classes; and 4 weekly individual therapy sessions. This group also received 6 months of aftercare services that included weekly individual and group therapy and liaison services with the criminal justice system, medical clinics, and social service agencies, but no additional methadone after the first 180 days of treatment. Study results showed that more patients in the MMT group remained in treatment for longer periods of time (438.5 days vs. 174 days) and had lower heroin use rates than did shorter-term methadone detoxification patients. Of the MMT group, 77 out of 91 patients were still in the study at the 12-month mark, while only 57 of 88 methadone detoxification patients were still in the study. MMT also resulted in a lower rate of drug use-related HIV-risk behaviors and a lower level of criminal activity. Sees, K.L., Delucchi, K.L., Masson, C., Rosen, A., Clark, H.W., Robillard, H., Banys, P., and Hall, S.M. JAMA, 283, pp. 1303-1310, 2000.

A Comprehensive Guide to the Application of Contingency Management Procedures in Clinical Settings: A Review

Controlled clinical trials have demonstrated the efficacy of contingency management procedures in treating substance use disorders. This paper reviews the rationale of contingency management interventions and provides a review of scientific studies in this area. Research-based guidelines are provided for clinicians and researchers to use when designing and administering contingency management interventions in community-based clinical settings. Petry, N.M. Drug and Alcohol Dependence, 58, pp. 9-25, 2000.

Effects of Cocaine Alone or Cocaine plus GBR 12909 on the Cardiovascular Hemodynamic and Electrophysiology

A safety assessment of the cardiovascular effects of cocaine, GBR12909, and the combination of the two compounds was conducted in animals. The study revealed that 10 mg/kg GBR 12909 given orally had no effect on the cardiovascular effects that were produced by cocaine, when given either before or after the administration of cocaine. The study by M. Smith, J. Ludens, L. Hulesbos, G. Schafer, P. Newton, N. Olivier and J. Terrill was presented as a poster entitled "Effects of Cocaine Alone or Cocaine plus GBR 12909 on the Cardiovascular Hemodynamic and Electrophysiology Parameters in Conscious Unrestrained Beagle Dogs" was presented at the annual meeting of the Society of Toxicology, March 2000.

Long-Term Neurotoxicity Associated with Methamphetamine Abuse

Dr. Thomas Ernst and colleagues at the Harbor-UCLA Medical Center studied long-term changes in brain neurochemistry in abstinent methamphetamine abusers. Using the brain imaging technique, proton magnetic resonance spectroscopy (1H MRS), cerebral metabolite concentrations were measured in the basal ganglia, frontal white matter, and frontal cortex. Twenty-six abstinent methamphetamine abusers (median recency of last methamphetamine use, 4.25 months) with a history of methamphetamine dependence (median total cumulative lifetime exposure, 3.64 kg) were compared to 24 healthy subjects with no history of drug abuse. Results showed that the concentration of N-acetyl-aspartate (NA), a neuronal marker, was reduced in the basal ganglia and frontal white matter in methamphetamine abusers compared to controls. The frontal white matter NA concentration correlated inversely with lifetime methamphetamine use. These methamphetamine users showed significantly reduced total creatine in the basal ganglia, and increased choline-containing compounds and myo-inositol, a glial marker, in the frontal gray matter. These results provide important evidence for long-term neuronal damage and glial abnormalities in abstinent (some up to 21 months) methamphetamine abusers. Ernst, T., et al., Evidence for Long-term Neurotoxicity Associated with Methamphetamine Abuse: A 1H MRS Study. Neurology, 54, pp. 1344-1349, 2000.

Marijuana Users Have Attenuated Activity in the Cerebellum

Dr. Robert Block and associates at the University of Iowa Medical School used PET to measure regional cerebral blood flow in frequent marijuana users. PET scans were acquired after at least 25 hours of monitored abstinence. During

the PET scan subjects rested quietly with eyes closed and refrained from speaking. Compared to control subjects, the marijuana users exhibited substantially lower blood flow (18%) in a large region of the posterior cerebellum relative to the rest of the brain. A small relative reduction in blood flow (<2 %) was also observed in the ventral prefrontal cortex (area 11). In contrast, marijuana users exhibited slightly higher blood flow (<2%) in the right anterior cingulate. A reduction in basal cerebellar function may underlie marijuana-induced impairments in motor co-ordination and alterations in the sense of time. Block, R.I., et al., Neuroreport, 11(4), pp. 1-5, 2000.

Effects of Marijuana Use on Brain Volume

Dr. Robert Block and associates at the University of Iowa Medical School used structural MRI to determine whether frequent marijuana use produces lasting alterations in brain anatomy. Automated image analysis procedures were used to measure global and regional brain volumes. Separate measures were taken for gray and white matter. There were no qualitative or quantitative evidence for cerebral atrophy or clinically significant abnormalities in the frequent marijuana users. Nor were there any quantitative differences between controls and frequent marijuana users in any of the volumetric measures. The investigators did find reliable gender differences in volumetric measures, suggesting that the methods were sensitive enough to detect clinically relevant differences in brain volume. Block, R.I., et al., Neuroreport, 11(3), pp. 1-6, 2000.

Functional Deficits in Basal Ganglia of Children with ADHD

Drs. Perry Renshaw and Martin Teicher of Harvard Medical School employed a novel fMRI procedure, T2 relaxometry, to measure steady state blood flow and indirectly assess blood volume in the striatum (caudate and putamen) and to test for medication effects in boys (6-12 years old) with attention deficit/hyperactivity disorder (ADHD). Boys with ADHD had higher T2 relaxation time measures in the putamen bilaterally than healthy control subjects. These relaxation times strongly correlated with the child's capacity to sit still and with his accuracy in accomplishing an attention task. Daily treatment with methylphenidate significantly changed the T2 relaxation times in the putamen of children with ADHD, although the magnitude and direction of the effect was strongly dependent on the child's un-medicated activity state. These results show that methylphenidate exerted different effects on the putamen--presumably increasing perfusion in the more hyperactive children but decreasing it in ADHD children with normal activity. Behavioral results indicated that methylphenidate substantially decreased the activity of ADHD children who were objectively hyperactive, but exerted little effect on ADHD children not objectively hyperactive. Importantly, these results demonstrate that methylphenidate can exert differential effects that may vary with the biological/behavioral state of the subject and that ADHD symptoms may be closely associated with the functional abnormalities in the putamen, which is a structure mainly involved in the regulation of motor behavior. Anderson, C.M., et al., Functional Deficits in Basal Ganglia of Children with Attention-Deficit/Hyperactivity Disorder Shown with Functional Magnetic Resonance Imaging Relaxometry. Nature Medicine, 6(4), pp. 470 - 473, 2000.

Mendelian Genetic Model for Smoking Behavior Supported in an Analysis of Three Generation Families

Dr. Gary Swan of SRI International conducted complex segregation analysis in three generation-families to determine the best model for transmission of smoking behavior. This is the first study to date to use three generations for this determination. It was found that the best-fitting model was that of a dominant major gene with low estimated frequency and residual familial correlations. These correlations demonstrate strong influence of mothers (negative) and spouses (positive) toward smoking behavior. However, it should be noted that the sample was selected from those participating in a longitudinal study of aging and health and not selected for smoking behavior per se. Therefore, it is presumed that these results underestimate genetic transmission because heavy-smoking individuals are less likely to volunteer for the study, and many more smokers in the registry may have already died. Nevertheless, these results encourage future linkage studies. Cheng, L.S., Swan, G.E., and Carmelli, D.A. Genetic Analysis of Smoking Behavior in Family Members of Older Adult Males. Addiction, 95(3), pp. 427-435, March 2000.

Opiates Have a Differential Modulating Role in the Hypothalamic-Pituitary-Adrenal Response Depending on the Presence of Stress

Dr. Yan Zhou in the laboratory of Dr. Mary Jeanne Kreek at the Rockefeller University assessed corticosterone (CORT), ACTH, and pro-opioimelanocortin (POMC) mRNA levels following administration of morphine or saline, and with or without access to water. Morphine (with free access to water) increased ACTH, CORT, and POMC in the hypothalamus while water restriction (and saline administration) increased only ACTH and POMC in the anterior pituitary. However, with morphine and restricted access to water, there were no changes in any of these parameters. Thus, it was concluded that the effects of morphine on HPA activation or POMC mRNA expression depend on the

presence of stresses that may reflect a counter-regulatory role of opiates on the stress response and on opioid gene expression. Zhou,Y., Spangler, R., Maggos, C.E., Wang, X.M., Han, J.S., Ho, A. and Kreek, M.J. Hypothalamic-Pituitary-Adrenal Activity and Pro-opiomelanocortin mRNA Levels in the Hypothalamus and Pituitary of the Rat are Differentially Modulated by Acute Intermittent Morphine with or without Water Restriction Stress. Journal of Endocrinology, 163, pp. 261-267, 1999.

Continued Studies in Both Acute and Chronic "Binge" Administration of Cocaine or Morphine in Rats Demonstrate Changes in mRNA Levels and the Need for DARPP-32

Among the most recent findings in drug administration in rats by Dr. Mary Jeanne Kreek's Laboratory of the Biology of Addictive Diseases (Rockefeller University) was an increase in mRNA for _-opioid receptors in the frontal cortex, nucleus accumbens, and amygdala following acute (3 times in one day) "binge" administration of cocaine. Similar acute injections of morphine increased levels of m RNA for preprodynorphin and kappa opioid receptors. Following chronic cocaine administration (3 times a day for 14 days) the expected increases in either plasma ACTH or corticosterone were not seen in mice deficient in the DARRPP-32 gene. This suggests that this gene plays a role in mediating the stimulatory effects of cocaine on the HPA axis. Yuferov, V., Zhou, Y., Spangler, R., Maggos, C.E., Ho, A. and Kreek, M.J. Acute "Binge" Cocaine Increases mu-opioid Receptor mRNA Levels in Areas of the Rat Mesolimbic Mesocortical Dopamine System. Brain Research Bulletin, 48(1), 109-112, 1999; Wang, X.M., Zhou, Y., Spangler, R., Ho, A., Han, J.S. and Kreek, M.J. Acute Intermittent Morphine Increases Preprodynorphin and Kappa Opioid Receptor mRNA Levels in the Rat Brain. Molecular Brain Research, 66, pp. 184-187, 1999; Zhou, Y., Schlussman, S.D., Ho, A., Spangler, R., Fienberg, A.A., Greengard, P. and Kreek, M.J. Effects of Chronic "Binge" Cocaine Administration on Plasma ACTH and Corticosterone Levels in Mice Deficient in DARPP-32. Neuroendocrinology, 70, pp. 196-199, 1999.

Hormone Fluctuations Appear to Affect Cocaine Metabolism and Behavioral Response in Rat

In the Biology of Addictive Disease Laboratory (Rockefeller University) of Dr. Mary Jeanne Kreek, "binge" administration of cocaine increased plasma levels of the cocaine metabolite, benzoylecgonine, more during metestrus-diestrus than during estrus and proestrus. Stereotypic behavior and locomotion were also greater during the same period. Qui–ones-Jenab, V., Ho, A., Schlussman, S.D., Franck, J. and Kreek, M.J. Estrous Cycle Differences in Cocaine-Induced Stereotypic and Locomotor Behaviors in Fischer Rats. Behavioural Brain Research, 101, pp. 15-20, 1999.

A Synthetic Fragment of the Endogenous Peptide, Dynorphin, Could Possibly Be Utilized to Manage Cocaine Addiction and Enhance Pain Relief from Opiate Treatment

Dynorphin A1-13 was administered to healthy non-drug-abusing subjects by Dr. Mary Jeanne Kreek and her colleagues at the Rockefeller University to determine if it affects opioid receptors. Increased levels of prolactin, indicating reduced dopaminergic tone, followed different doses of dynorphin. Pretreatment with antagonists demonstrated the effect was likely due to _-opioid receptors and possibly _-opioid receptors. Another study showed this compound was well tolerated and produced modest, but transient, subjective responses. Finally, when administered to patients with chronic pain in conjunction with reduced opiate medication, some pain relief was noted. Kreek, M.J., Schluger, J., Borg, L., Gunduz, M. and Ho, A. Dynorphin A1-13 Causes Elevation of Serum Levels of Prolactin through an Opioid Receptor Mechanism in Humans: Gender Differences and Implications for Modulation of Dopaminergic Tone in the Treatment of Addictions. Journal of Pharmacology and Experimental Therapeutics, 288(1), pp. 260-269, 1999; King, A.D., Ho, A., Schluger, J., Borg, L., and Kreek, M.J. Acute Subjective Effects of Dynorphin A(1-13) Infusion in Normal Healthy Subjects. Drug and Alcohol Dependence, 54, pp. 87-90, 1999; Portenoy, R.K., Caraceni, A., Cherny, N.I., Goldblum, R., Ingham, J., Inturrisi, C.E., Johnson, J.H., Lapin, J., Tiseo, P.J. and Kreek, M.J. Dynorphin A(1-13) Analgesia in Opioid-Treated Patients with Chronic Pain: A Controlled Study. Clinical Pharmacodynamics, 17(1), pp. 33-42, 1999.

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

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

National Institute on Drug Abuse

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

May, 2000

Research Findings

Research on AIDS and Other Medical Consequences of Drug Abuse

Obesity and Immune Function

Baum and her colleagues (Shor-Posner, et al.) report that mild to moderate obesity in HIV-infected chronic drug users does not impair immune function and is associated with better HIV-1-related survival. The investigators collected nutritional and immunological data, prior to protease inhibitor administration, in 125 HIV-1 seropositive participants (82 men and 43 women, mean age 42±6 years) and 148 HIV-1-seronegative controls from the Miami HIV-1-Infected Drug Abusers Study cohort at a community clinic from 1992 to 1996. Based on the body mass index (BMI) measurements, 18% of the HIV-1+ group was obese (BMI>27) in comparison to 29% of the seronegative group. Over an 18-month period, 60.5% of the non-obese HIV-1+ patients exhibited a 25% decline in CD4 cell count, compared with 18% of the obese patients ($p < 0.004$). During the follow-up period, 38% of the lean and 13% of the non-obese study subjects died of HIV-1 related causes. Measurements of BMI were inversely associated with progression to death, independent of CD4 cell count <200 cells/mm3 ($p<0.02$). These data suggest that mild-to moderate obesity in HIV-infected drug users has no significant effect on their immune function and is associated with better survival. Further research is underway to determine the long-term impact of obesity on disease progression in HIV-infected drug abusers. Shor-Posner, G., Campa, A., Zhang, G., Persaud, N., Maria-Jose Miguez-Burbano., and Baum, M. When Obesity Is Desirable: A Longitudinal Study of the Miami HIV-1-Infected Drug Abusers (MIDAS) Cohort. Journal of Acquired Immune Deficiency Syndrome, 23(1), pp. 81-88, 2000.

Elicitation Study Focuses on the Sexual Risk Practices of African American Crack Users

A descriptive elicitation research study was conducted in Washington, D.C. to better understand the attitudes, beliefs, and barriers that affect the adoption and maintenance of condom use to prevent sexual transmission of HIV. An ethnographer recruited 64 adults for participation in the study. Participants were interviewed using semi-structured interview guides that were developed as cognitive maps for interviewing, rather than as questionnaires. The data were coded and analyzed according to condom use outcome expectancies, normative beliefs about condom use, and contextual facilitators and barriers of condom use. Participants described few positive condom use outcome expectancies, while detailing several negative expectations. Participants described few contextual barriers to condom use, although situational barriers, including crack addiction, were identified. Unlike other studies, this project did not find that cultural or social factors inhibited women from introducing condoms into sexual relationships, other than those related to intimate sexual relationships or to the special situation of sex and crack. Culturally determined sexual scripts may be important in determining condom use: Normative beliefs were weakly related to condom use with casual partners, but strongly influenced condom use with intimate partners. Williams, M., Bowen, A., Elwood, W., McCoy, C., McCoy, V., et al. Determinants of Condom Use Among African Americans Who Smoke Crack Cocaine. Culture, Health, and Sexuality. 2(1), pp. 15-32, 2000.

Cocaine Regulation of the Chemokine and their Receptors

Chemokine receptors are important for the entry of human immunodeficiency virus (HIV) into most cells. Nair and his

colleagues (SUNY at Buffalo) have shown an effect of cocaine on these chemokine systems. They have identified a cellular action for the known stimulation of HIV growth by cocaine. Earlier studies supported a significant role for cocaine in the susceptibility to and the progression of HIV-1 infection. Recently, several unique HIV-1 entry coreceptors (e.g., CCR5 and CCR3) and a trio of HIV-1-specific suppressor chemokines, namely, RANTES (regulated-upon-activation T expressed and secreted), macrophage inflammatory protein 1 alpha (MIP-1 alpha) and MIP-1 beta, were identified. Although cocaine has been linked to the immunopathogenesis of HIV-1 infection, the corresponding cellular and molecular mechanism(s) have not been well defined. We hypothesize that cocaine mediates these pathologic effects through the down-regulation of HIV-1-suppressing chemokines and/or up-regulating HIV-1 entry coreceptors in HIV-1-infected subjects, resulting in disease progression to AIDS. Our results show that cocaine selectively down-regulates endogenous MIP-1 beta secretion by normal peripheral blood mononuclear cells (PBMC), while cocaine did not affect the MIP-1 beta production by PBMC from AIDS patients. Cocaine also selectively suppresses lipopolysaccharide-induced MIP-1 beta production by PBMC from HIV-infected patients. Further, cocaine significantly down-regulates endogenous MIP-1 beta gene expression, while it up-regulates HIV-1 entry coreceptor CCR5 by normal PBMC, These studies suggests a role for cocaine as a cofactor in the pathogenesis of HIV infection and support the premise that cocaine increases susceptibility to and progression of HIV-1 infection by inhibiting the synthesis of HIV-I protective chemokines and/or up-regulating the HIV-1 entry coreceptor, CCR5. Nair, M.P.N., Chadha, K.C., Hewitt, R.G. Mahajan, S., Sweet, A. and Schwartz, S.A. Cocaine Differentially Modulates Chemokine Production by Mononuclear Cells from Normal Donors and Human Immunodeficiency Virus Type 1-Infected Patients. Clinical and Diagnostic Laboratory Immunology, 7(1), pp. 96-100, Jan 2000.

Gastrointestinal Infections and Opiates

Patients infected with HIV suffer from increased incidence and severity of a number of opportunistic infections of the gastrointestinal tract, including *Salmonella typhimurium,* and others such as cryptosporidium. The present studies showing that MU opioid agonists increase susceptibility to oral infection with Salmonella suggest that use of heroin type drugs may be a cofactor in increased incidence of infection with this organism in HIV infected patients. The studies showing that morphine inhibits intestinal IgA and IgG antibody responses to a microbial toxin could provide a mechanism to account for these chronic gastrointestinal infections and the enhanced severity of these infections in HIV infected individuals who abuse opioids. To assess whether morphine potentiated Salmonella replication, a strain of Salmonella containing a temperature sensitive plasmid, was used. These grow at the permissive temperature of 30'C, but not at 37'C, that is, in the body. When the organisms are inoculated orally into mice, the plasmid in the Salmonella cannot replicate. Thus, when the bacteria are recultured from inoculated animal tissue using agar, with and without antibiotic, the number of plasmid--free (antibiotic sensitive) and plasmid-bearing (antibiotic resistant) bacteria can be enumerated. It was found that >95% of the organisms retrieved from the morphine--treated mice were plasmid-free, whereas in the original inoculum approximately 80% of the organisms contained the plasmid. These results show that in the morphine-treated mouse the wild type Salmonella replicated vigorously in the gastrointestinal tract, producing plasmid-free progeny, and that morphine potentiates Salmonella replication. In contrast, the other types of opiates, U50,488H (kappa), DPDPE (delta-1), or deltorphin (delta-2) produced no detectable Salmonella in any of the tissues. These results suggest that a predominantly mu agonist (morphine) has a greater effect than the delta1, delta2 or k agonists in potentiating gastrointestinal opportunistic infections such as Salmonella. MacFarlane, A.S., Peng, X., Meissler, J.J. Jr., Rogers, T.J., Geller, E.B., Adler, M. W. and Eisenstein, T.K. Morphine Increases Susceptibility to Oral *Salmonella typhimuriu*m Infection. J. Infect. Dis., 181(4), pp. 1350-1358, April 2000.

Perceptions of Tuberculosis and Treatment Adherence for Adolescents and Adults with HIV

HIV-infected individuals are a population at very high risk for and often among the least able to afford health care resources. In this study of adolescents and adults infected with HIV, interviews were completed to assess perceptions of tuberculosis (TB) infection rates and physician TB behavior, and patient knowledge of TB transmission and treatment adherence. The sample consisted of HIV-infected youth (N = 199) from adolescent clinical care sites in three cities and HIV-infected adults (N = 133) in New York. Adolescents reported they were significantly less likely to be tested for TB; however, testing rates were high for both samples. Results indicated that approximately 9% of both samples reported infection with TB; the majority reported receiving medication (97%), and consistent medication adherence (93%). The overall mean knowledge score regarding TB was 66% and there were significant age differences, with adolescents less knowledgeable than adults, and young males tending to be less knowledgeable than young females. Age, gender and experience with TB (self-perception of TB, testing history and clinic choice) significantly predicted accuracy of knowledge about TB. Results suggest that education and support from their community health care sources may substantially reduce chances of contracting and spreading TB. Murphy, D.A., Rotheram-Borus, M.J., and Joshi, V. HIV-Infected Adolescent and Adult Perceptions of Tuberculosis Testing, Knowledge and Medication Adherence in the USA. AIDS Care-Psychological and Socio-Medical Aspects of AIDS/HIV,

12(1), pp. 59-63, 2000.

Amphetamine Use in Youths Living with HIV (YLH)

In this study amphetamine use and its correlates were examined among 337 youths living with HIV (YLH) to determine whether its use is associated with increased transmission acts and poor health. One third of YLH engaged in amphetamine use in their lifetime, and 21% reported current use (last 3 months). Results showed that compared with those who never used (never-users), users initiated other drug use at younger ages, used more types of drugs, reported more emotional distress, employed escape coping significantly more frequently, had more sexual partners and more sexual encounters. Although users and never-users did not differ on physical symptoms or whether they have been diagnosed with AIDS, users reported significantly higher T-cell counts than never-users. Despite poor psychosocial functioning, amphetamine users have higher T-cell counts than other YLH. The continued high-risk profile of transmission acts among users suggests that preventive interventions must target specific drugs used by YLH. Rotheram-Borus, M.J., Mann, T., and Chabon, B. Amphetamine Use and Its Correlates Among Youths Living with HIV. AIDS Education and Prevention, 11(3), pp. 232-242, 1999.

Correlates of Perceived Compliance with AZT Dosing Among African American Drug Users

A pilot study was conducted in Washington, DC, to explore the associations between sociodemographic, drug use, and health belief factors and perceived compliance with zidovudine (AZT). The sample for this data analysis focused on 47 African American current drug injectors or crack cocaine smokers who were also HIV seropositive and receiving treatment for HIV infection. Participants were interviewed using a questionnaire developed for the study. Compliance was measured as perceived compliance; perception of compliance was measured by asking how often participants believed that they missed taking a specified medication, using a 5-point, Likert-type scale. The analyses demonstrated that HIV positive drug users are not a homogenous group in terms of compliance. Approximately a third of the drug users perceived that they were always compliant with AZT dosing and by implication, with other medications, including protease inhibitors. Perceived compliance was found negatively correlated with age, homelessness, number of injections in the previous 30 days, trading sex for drugs, and the perception that AIDS is no longer a serious disease since the development of new antiretroviral medications. Intensity of feelings of joy, fear, and the belief that taking more anti-HIV medications would result in better health were found to be positively correlated. Stability of lifestyle is an important factor in determining the level of compliance with HIV antiretroviral drugs, suggesting that factors associated with a stable lifestyle (not being homeless, trading sex for drugs, or injecting drugs, and having more social resources and peer and social supports) are key for interventions aimed at increasing compliance with antiretroviral medications among racial/ethnic minority drug users receiving treatment for HIV infection. Williams, M., Bowen, A., Ross, M., Freeman, R., and Elwood, W. Perceived Compliance with AZT Dosing Among a Sample of African-American Drug Users. International J. STD and AIDS, 11, pp. 57-63, 2000.

Patterns of Methamphetamine Use Among High Risk Men Are Complex and Variable

An ethnographic study was conducted in the Pacific Northwest to characterize the patterns of methamphetamine use among high risk men who use drugs and have sex with men (DUMSM). Data collection involved contextual, unobtrusive community observations; focus group interviews with service providers and community leaders; and semi-structured interviews with 103 men who currently used methamphetamine. Most of the men identified themselves as gay; and 20% were non-White (Native American, Latino, African American), reflecting the ethnic/racial background of the Seattle King County AIDS caseload. Almost all of the sample were HIV positive or had an AIDS diagnosis. The data indicate that there are complex and possibly overlapping social and cultural ecologies among injection drug-using men who have sex with men in the Seattle area. Most of the participants reported extensive histories of intermittent or ongoing drug use, including cocaine, MDMA (ecstasy), marijuana, heroin, and alcohol. All reported that, when they tried methamphetamine, they became "hooked." In fact, some participants said it was easier to stop using heroin than methamphetamine. Nearly half of the interviewees reported injection as their primary method of drug use. Study participants reported widely variable strategies for having safer sex in their intimate encounters, with some saying they used condoms more with casual partners than with intimate partners. Many of the participants reported that they were less likely to discuss their HIV status with potential sex partners if they were high on methamphetamine. Gorman, E.M. and Carroll, R.T. Substance Abuse and HIV: Considerations with Regard to Methamphetamine and Other Recreational Drugs for Nursing Practice and Research. J Assoc. Nurses in AIDS Care, 11(2), pp. 51-62, 2000.

Determinants of the Quantity of Hepatitis C Virus RNA

The quantity of hepatitis C virus (HCV) RNA was assessed in 969 persons who acquired HCV through injection drug use. Serum HCV RNA levels covered the linear range of the assay (from 200,000 to >120million equivalents/mL). The

mean log10 HCV RNA level was significantly higher in 468 HIV-infected IDUs vs. 501 HIV-uninfected IDUs (P<.001). Among the HIV-uninfected IDUs, lower HCV RNA was independently associated with younger age (P<.001), ongoing hepatitis B infection (P=.005), and the absence of needle sharing (P=.020). However, more than 90% of the variability of HCV RNA levels was not explained by these sociodemographic, environmental and virologic factors, indicating the need for further research to determine what factors are responsible for the level of HCV RNA in the blood. Thomas, D.L., Astemborski, J., Vlahov, D., et al., JID, 181, pp. 844-851, 2000.

A Prospective Study of HIV Disease Progression in Female and Male Drug Users

Disease progression and mortality was assessed in a cohort of drug users attending a methadone maintenance program with on-site primary care. CD4 cell decline and distribution of AIDS-defining illnesses were studied in a cohort of 222 HIV-infected women and 302 HIV-infected men. Rates of CD4 cell decline, the distribution of first AIDS-defining illnesses, and the time to clinical AIDS did not differ by sex. Mortality rates for women and men were similar (8.71/100 person yrs. vs. 9.85/100 person yrs). However, CD4 cell count, two or more HIV-related symptoms, and crack-cocaine use were associated with an AIDS outcome. Webber, M.P., Schoenbaum, E.E., Gourevitch, M.N. et al., AIDS, 13, pp. 257-262, 1999.

Study Finds HIV Moving Into Younger, Impoverished, and Rural Populations in Brazil

Researchers examined the nature of the HIV/AIDS epidemic among marginalized drug users in Rio de Janeiro, with a specific focus on differential infection rates in economically distinct communities. Indigenous outreach workers recruited 1,544 cocaine users from a variety of "shantytown" and rural target areas or *favelos* that are clustered on the hills and mountainsides of Rio and from "asphalt" areas or districts of the city that contain basic infrastructure (i.e., downtown and residential areas). Researchers found that the HIV infection was introduced early into the upper and middle classes of Rio, but now appears to be penetrating into younger, more impoverished, and more rural populations concurrently with the rise in injection drug-related and heterosexually acquired cases of AIDS. They point out that, as the epidemiology of HIV changes, increasing numbers of people who were not targets of early information and prevention campaigns are at significant risk of infection. The findings indicate that it is feasible to access impoverished communities using indigenous outreach workers, and that residents of impoverished areas are willing to participate in AIDS education/prevention programs. The lower HIV prevalence in the impoverished communities in Rio appears to be a function of two factors: (1) the initial introduction of HIV to Brazil seems to have occurred primarily in upper and middle classes, and (2) even though favela residents have high risks for HIV, their social networks are isolated and excluded from the mainstream. The isolation may have been somewhat protective up to now, but with the infection beginning to appear among younger, high risk, impoverished, and rural populations at this time, the need is urgent for a renewed HIV information and prevention campaign-one that targets highly marginalized persons not reached when the campaigns were initially launched. Surratt, H., Indigence, Marginalization, and HIV Infection Among Brazilian Cocaine Users. Drug and Alcohol Dependence, 58, pp. 267-274, 2000.

Hepatitis B Infection among Young Injection Drug Users

This study compares the demographic characteristics and risk behaviors for hepatitis B infection among injection drug users younger than 30 years with those aged 30 or older to evaluate participants' knowledge, attitudes, and experiences of infection, screening, and vaccination against hepatitis B virus. A systematic sample of injection drug users not currently in a treatment program were recruited and interviewed at needle exchange programs and community sites. Participants were 135 injection drug users younger than 30 years and 96 injection drug users aged 30 or older. Injection drug users younger than 30 were found to be twice as likely as drug users aged 30 or older to report having shared needles in the past 30 days (36/135 [27%] vs 12/96 [13%]). Injection drug users younger than 30 were also twice as likely to report having had more than two sexual partners in the past 6 months (80/135 [53%] vs 29/96 [30%]). Although 88 of 135 (68%) young injection drug users reported having had contact with medical providers within the past 6 months, only 13 of 135 (10%) had completed the hepatitis B vaccine series and only 16 of (13%) perceived themselves as being at high risk of becoming infected with the virus. The authors concluded that young injection drug users have been immunized even though they have more frequent contact with medical providers and are at a higher risk for new hepatitis B infection than older drug users. Clinicians caring for young injection drug users and others at high risk of infection should provide education, screening, and vaccination to reduce an important source of hepatitis B infection. Seal, K.H., Edlin, B.R., Ochoa, K.C., Tulsky, J.P., Moss, A.R., Hahn, J.A. Risk of Hepatitis B Infection among Young Injection Drug Users in San Francisco: Opportunities for Intervention. Western Journal of Medicine, 172(1), pp. 16-20, 2000.

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

National Institute on Drug Abuse

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

May, 2000

Research Findings

Epidemiology, Etiology and Prevention Research

Monitoring the Future (MTF) Study

Results from the 1999 MTF were released on December 17, 1999. The major findings are summarized below. For more information, go to http://www.nida.nih.gov. The study findings are also available in a NIDA-published report: Johnston, L.D., O'Malley, P.M., & Bachman, J.G. (2000). *Monitoring the Future National Results on Adolescent Drug Use: Overview of Key Findings, 1999.* NIH publication 00-4690. Rockville, MD: National Institute on Drug Abuse. This report is available on the internet at http://monitoringthefuture.org/.

Results from the 1999 MTF suggest that, with a few exceptions, use of marijuana and most other illicit drugs remained unchanged from 1998 to 1999 among 8th, 10th, and 12th graders. There were however, notable increases in the use of MDMA (ecstasy) among 12th graders and steroids among 8th and 10th graders. With a few exceptions, use of alcohol, and cigarettes also generally remained unchanged. In addition, for a third year in a row, attitudes toward use of illicit drugs, alcohol, and cigarettes generally remained unchanged or improved in all three grades, although attitudes about steroid use eroded somewhat among high school seniors.

Illicit Drug Use

- Data from the 1999 MTF indicate the rates of illicit drug use remained largely unchanged in 1998 and 1999. Illicit drug use had increased between 1991 and 1996, and slowed between 1996 and 1997. Many differences between 1998 and 1999 were not statistically significant. However, there were notable increases in MDMA and steroids.
- Lifetime, past year, and past month use of **any illicit drug** did not change from 1998 to 1999 in any of the three grades. However, among 8th graders the 1999 past month rate of 12.2 percent, represented a statistically significant decrease from the high mark of 14.6 percent reached in 1996. Similar results were found for lifetime and past year **any illicit** use statistics between 1996 and 1999.
- Lifetime, past year, and past month use of **marijuana/hashish** did not change in any grade between 1998 and 1999. In 1999, lifetime rates of **marijuana/hashish** were 49.7, 40.9, and 22.0 percent for 12th, 10th, and 8th graders respectively.
- In 1998, lifetime and past year use of **crack** increased among 8th graders to its highest levels since 1991, the first year data were available for students in this grade. In 1999, past year use of **crack** declined to 1.8 percent (down from 2.1 percent in 1998). When examining subgroups, declines in past year use occurred among 8th graders residing in the South and West census regions (2.5% and 2.6% in 1998 to 1.9% and 1.8% in 1999 respectively).
- There were no statistically significant differences in **inhalant** use between 1998 and 1999. During the 9 years for which data are available for 8th graders, lifetime, past year, and past month inhalant use appears to have peaked in 1995. Inhalant use continues to be generally more prevalent among 8th graders than the two higher grades.

- Increases in the use of **MDMA (ecstasy)** were observed for the first time since 1996, when collection of data on this drug was initiated. Lifetime, past year, and past month use increased between 1998 and 1999 among 12th graders. Lifetime: from 5.8 percent to 8.0 percent; past year: from 3.6 percent to 5.6 percent; past month: from 1.5 percent to 2.5 percent. The increase in past year use among 12th graders occurred among females (2.7% to 5.6%), those residing in the Northeast (3.7% to 9.4%), and those residing in large metropolitan statistical areas (MSAs) (3.2% to 6.1%).
- Past year use among 10th graders also increased (from 3.3 percent in 1998 to 4.4 percent in 1999). The increase in past year use among 10th graders occurred among females (2.9% to 4.2%), those residing in the Northeast (3.8% to 7.0%), and those residing in large metropolitan statistical areas (2.5% to 5.2%).
- Past year use of **Rohypnol** among 8th graders decreased from 0.8 percent in 1998 to 0.5 percent in 1999. A survey question about Rohypnol, sometimes referred to as the "date rape" drug, was first asked in 1996. While a statistically significant change occurred for 8th graders, it should be kept in mind that these rates are quite small. The 1999 rate for both 10th and 12th graders was 1.0 percent, which was not a statistically significant change from the 1998 rates.
- Use of **ice (crystal methamphetamine)** in the past year decreased to 1.9 percent among 12th graders in 1999 (it was 3.0 percent in 1998).
- Past year, and past month use of use of **steroids** increased among 8th and 10th graders. Past year use increased from 1.2 percent in 1998 to 1.7 percent in 1999 for both 8th and 10th graders. Past month use remains under one percent in 8th and 10th grades in spite of increases in 1999 (e.g., 0.5 percent in 1998 to 0.7 percent in 1999 among 8th graders). Also, lifetime use of **steroids** increased among 10th graders (from 2.0 percent in 1998 to 2.7 percent in 1999). Increases in past year **steroid** use among 8th graders occurred among males (1.6% to 2.5%) and whites (1.1% to 1.5%). The increase in past year use among 10th graders occurred among males (1.9% to 2.8%).
- Use of **marijuana, cocaine, other cocaine, inhalants, heroin, other narcotics, hallucinogens, LSD, PCP, amphetamines, barbiturates, and tranquilizers** remained stable for all three grades and all recency-of-use categories (lifetime, past year, past month, and daily use where measured).

Alcohol Use

- **Alcohol** use has generally remained stable in the past few years among 8th and 10th graders, and more recently among 12th graders, though at levels which most people would find unacceptably high.
- Daily **alcohol** use decreased for 12th graders. Use among these students decreased from 3.9 percent in 1998 to 3.4 percent in 1999.
- After decreasing to 38.3 percent in 1998, the proportion of 10th graders reporting having **been drunk** sometime during the past year increased to 40.9 percent in 1999.
- Also more 8th graders in 1999 had **5 or more drinks in a row** during the past two weeks (from 13.7 percent in 1998 to 15.2 percent in 1999). An increase also occurred among males (from 14.4% to 16.4%).

Cigarettes and Smokeless Tobacco

- Use of **cigarettes** during the past month among 8th graders decreased 1.6 percentage points to 17.5 percent in 1999.
- Between 1997 and 1998, 10th graders' lifetime, past month, and daily use of **cigarettes** in the past month decreased from 60.2%, 29.8%, and 18.0% in 1997 to 57.7%, 27.6%, and 15.8% in 1998 respectively. Between 1998 and 1999, these rates did not change statistically (the 1999 rates were 57.6%, 25.7%, and 15.9%). However, past month use, decreased among 8th graders (from 19.1% in 1998 to 17.5% in 1999).
- In 1997, daily cigarette use in the past month among seniors was at its highest level since 1979 (24.6% in 1997 vs. 25.4% in 1979). In 1998, seniors' **daily smoking** decreased to 22.4% and smoking a **half-pack or more cigarettes per day** decreased from 14.3% to 12.6%. In 1999 seniors' rate of smoking did not change statistically (daily smoking=23.1% and 1/2 pack +/day=13.2%).
- African American students continue to have the lowest rates of **smoking**. Past month smoking among 8th, 10th, and 12th grade whites and Hispanics is around double or more the rate among their African American peers. For

example, in 1999, 14.9 percent of African American seniors report current smoking compared to 40.1 percent of white and 27.3 percent of Hispanic seniors.

Perceived Harm, Disapproval, and Perceived Availability

- Among 8th and 10th graders, there were several changes in the perceived risk and disapproval that were in the favorable direction. Notable changes in perceived availability among 12th graders were found, all favorable. The one notable exception was steroids.
- The perceived harm in trying **crack** once or twice decreased among 12th graders, declining to 48.2 percent in 1999 from 52.2 percent in 1998.
- Disapproval of using **smokeless tobacco** regularly increased among 8th and 10th graders. Perceived availability of **cigarettes** decreased among 8th graders.
- Perceived harmfulness of taking **steroids** decreased 6 percentage points among 12th graders to 62.1 percent in 1999 (down from 68.1 in 1998). This drop marks the largest attitudinal change ever observed in the MTF.
- In the 1999 survey, more 8th and 10th graders reported personal disapproval of people taking **inhalants** once or twice. (8th graders: from 83.0 to 85.2 percent; 10th graders: from 85.6 to 88.4 percent).
- Perceived availability of several drugs decreased among seniors; perception of "fairly easy" or "very easy" access decreased for **cocaine, LSD, PCP, other psychedelics, amyl/butyl nitrites, heroin, and tranquilizers**. The only increase in perceived availability occurred for steroids among 10th graders (from 33.0 percent in 1998 to 35.9 percent in 1999).

Trends (1991-1999)

- For many drugs, there have been significant increases between 1991 and 1997. The most dramatic case was the change in **marijuana** use from 1991 to 1997. For 8th graders, past year use of this substance has nearly tripled, from 6.2% in 1991 to 17.7% in 1997. However, between 1996 and 1999, use rates declined for students in this grade. Among sophomores, past year use has more than doubled from 15.2 percent in 1992 to 34.8 percent in 1997, with a statistically significant decrease occurring in 1998 (31.1 percent) and remaining unchanged in 1999. Past year use among seniors has almost doubled from 21.9 percent in 1992 to 38.5 percent in 1997, and remained unchanged in 1998 and 1999 at 37.5 percent and 37.8 percent respectively.
- Between 1991 and 1996, all three grade levels reported increased use of **cigarettes**. So far, the high mark for cigarette use (lifetime, past month, daily, and _ pack or more per day) appears to have occurred in 1996 for 8th and 10th graders only. Between 1997 and 1998, statistically significant decreases were observed for 10th graders and 12th graders, while estimates among 8th graders did not change. In 1999, past month use decreases among 8th graders (from 19.1 percent in 1998 to 17.5 percent in 1999). All other differences were not statistically significant.

Long-Term Trends (seniors only)

- After more than a decade of declining use (1980-1992), **marijuana** use rose from 1993 to 1995, remained level from 1995 to 1996, increased again from 1996 to 1997, and remained unchanged in 1998 and 1999. For past year prevalence, self-reported marijuana use by seniors peaked at 50.8 percent in 1979 and then declined to a low of 21.9 percent in 1992. Past year **marijuana** use then increased steadily to 38.5 percent in 1997 with no change in the 1998 and 1999 rate (37.5 percent in 1998, 37.8 percent in 1999).
- Among seniors in the class of 1997, daily **cigarette** smoking reached 24.6 percent, its highest level since 1979, when 25.4 percent of seniors reported daily cigarette use. Daily smoking decreased between 1979 and 1980 (21.3 percent) and then remained basically level for many years. During the early 1990's increases were observed, followed by a decrease in 1998 to 22.4 percent. In 1999 the daily rate was 23.1 percent, which is statistically unchanged from the 1998 rate.

Methodological Note: In 1998, Monitoring the Future questionnaires were changed from confidential (i.e., with some identifying information being gathered) to anonymous for half of the 8th and 10th grade samples. Assuming higher rates of self-reporting of drug use when questionnaires are anonymous, this change may have resulted in some overestimation of increases and underestimation of decreases. For example, results from the matched half-sample of 8th graders receiving the anonymous questionnaires in both 1998 and 1999, showed a 1.4 percentage point decline in past year marijuana use while the full sample showed a decline of 0.4 percentage points. However, the change was

not statistically significant in either case

The 47th biannual meeting of the **Community Epidemiology Work Group (CEWG),** was held in Los Angeles, California on December 14-17, 1999. The CEWG is composed of researchers from 21 metropolitan areas of the United States who meet semiannually to report on patterns and trends of drug abuse in their respective areas; emerging drugs of abuse; vulnerable populations and factors that may place people at risk of drug use and abuse; and, negative health and social consequences. Reports are based on drug abuse indicator data, such as morbidity and mortality information, treatment data and local and State law enforcement data. Additional sources of information include criminal justice, correctional, medical and community health data, local and State survey information and research findings from ethnographic studies. The following are highlights from the meeting:

IN THE PAST 6 MONTHS...

Following several reporting periods of stable or declining trends, some indicators of cocaine abuse show slight rebounds in many cities; increases among younger age groups in some indicators warrant watching. Some indicators, however, continue to suggest declining or stable trends.

Heroin indicators are mixed. Younger populations continue to initiate use in several cities, and some are shifting from snorting to injecting.

Marijuana indicators suggest generally stable or increasing trends in most CEWG sites.

Declines in **methamphetamine** consequences are reported in most CEWG sites, especially as reflected in ED data.

"Club drugs," especially **GHB, GBL,** and **MDMA,** continue to spread across the country.

Cocaine - Following several reporting periods of stable or declining cocaine trends, mortality, emergency department (ED), and female arrestee urinalysis indicators suggest slight increases in many cities. Based on partial-1999 data, cocaine-related mortality(i) appears to be increasing in three cities (Philadelphia, Phoenix and Seattle) and declining or stable in four (Honolulu, Miami, Minneapolis/St. Paul and San Diego). Cocaine ED mentions(ii) increased significantly in five cities (Dallas, Los Angeles, Philadelphia, Phoenix, and Washington, DC), with the largest shift a 45-percent increase in Dallas. Nonsignificant ED increases were reported in the majority of the other cities; no significant declines were noted. Disturbingly, cocaine ED mentions per 100,000 population in the 12-17 age group increased sharply in four cities (Baltimore, Boston, Dallas, and Denver). By contrast, treatment admission figures(3) show generally declining or stable trends. Generally declining or stable trends were also found in cocaine-positive urinalysis percentages(4) among adult male arrestees, except in Miami and Washington, DC, where levels increased; the drug is now surpassed by marijuana in all but six cities. By contrast, among female arrestees, cocaine is still the most commonly detected drug in all but one city (San Diego); levels increased in six cities (Dallas, Detroit, Minneapolis, Philadelphia, Phoenix, and San Diego) and declined only in Los Angeles. Crack injection continues to be reported in some cities, including Boston, New York, and Washington, DC. Increased availability of cocaine hydrochloride (HCl) is reported in some cities, including Boston, Dallas, Denver, Philadelphia, and Phoenix.

Heroin - Heroin indicators show mixed trends. Mortality figures(1) declined slightly in 5 cities (Honolulu, Minneapolis/St. Paul, Philadelphia, San Diego, and Seattle) and increased only in Phoenix. Heroin ED mentions(2) declined significantly in only one city (San Francisco) and increased significantly in four (Miami, New Orleans, Newark, and Washington, D.C.). Heroin is the predominant drug of choice among treatment admissions(3) (excluding alcohol-only, but including alcohol-in-combination) in 6 of 18 reporting sites. Opiate-positive urinalysis levels(4) among adult males remained relatively low and stable in most cities, excluding Washington, D.C., where opiate-positive levels among adult males more than doubled. Similarly, among adult females, opiate-positive levels remained relatively stable, except in Chicago (where they declined notably) and in Minneapolis and New Orleans (where levels more than doubled). Heroin purity(5) remained stable or declined in most cities; prices fluctuated. Purity declines were particularly steep in three western cities (Denver, Los Angeles, and San Francisco); conversely, purity more than doubled in Miami. Younger populations are increasingly initiating heroin use in many CEWG cities, including Atlanta, Baltimore (especially among suburbanites), Boston (where ethnographic sources report high school students snorting heroin), Denver (where ethnographic sources report college students increasingly using heroin and street youth switching from methamphetamine to heroin use), Philadelphia (where new users are often adolescents), St. Louis, San Diego, San Francisco, and Seattle (where young injectors are increasing). In Atlanta, Baltimore, Chicago, Denver, and New York, the proportion of treatment clients who snort is increasing; conversely, in Newark and Seattle (among younger users), injecting is on an upward trend. In Boston and Miami, new and younger users are reportedly progressing from snorting to injecting. On Chicago's South Side, reports of heroin/cocaine combinations ("speedballs" or "John Belushi") increased, and the proportion of treatment admissions who reported

snorting rose dramatically. In Washington, DC, a variant of heroin, nicknamed "bag delight," dissolves without heat.

Marijuana - Marijuana ED mentions(2) increased significantly in 3 cities (Dallas, Philadelphia, and San Diego) and nonsignificantly in 10 others; they remained level in 4 cities; and they declined significantly in only 1 city (New Orleans) and nonsignificantly in 2 cities. Marijuana is the predominant primary drug treatment problem3 in four cities (Denver, Minneapolis/St. Paul, New Orleans, and Seattle). Treatment percentages increased (5-9 percentage points) in three cities (Denver, Philadelphia, and San Diego) and remained relatively stable elsewhere. Among adult male arrestees(4), marijuana has now surpassed cocaine as the most commonly detected drug in the majority of CEWG cities; positive findings increased sharply in four cities (Atlanta, Los Angeles, Miami, and Washington, DC) and remained relatively stable elsewhere. Levels also remained relatively stable among female arrestees, except for notable increases in four cities (Chicago, Denver, Minneapolis, and New Orleans) and a decline in Seattle. Juvenile arrestee levels also remained relatively stable, but they exceeded adult marijuana-positive levels at all four sites where juveniles were tested. In some cities, such as Denver, increased potency resulting from genetic plant manipulation may have contributed to increased consequences, especially among older users who had started smoking marijuana in their teens and have recently resumed use. Marijuana is increasingly used as a delivery medium for other psychoactive drugs. For example, in Chicago, blunts are often laced with either crack or PCP ("3750s"). Marijuana/crack combinations are also reported in Boston, Minneapolis/St. Paul ("fireweed"), and parts of Texas; and marijuana/PCP combinations are also reported in Minneapolis/St. Paul ("happy stick"), Philadelphia ("loveboat" or "wet"), and New York. In Philadelphia, blunts are also laced with cocaine HCl ("turbo"). Marijuana/embalming fluid combinations are reported in Minneapolis/St. Paul ("wets" or "amp"), New York ("duck foot," which also includes the pesticide DDT), and parts of Texas (where this combination also includes PCP). In Texas, joints are also dipped in codeine cough syrup.

Stimulants - Methamphetamine ("crystal meth, "ice") remains concentrated in the West and, to a lesser extent, in some rural areas elsewhere. In the West, recent indicators suggest declines, possibly related to national and community prevention programs, stricter precursor laws, increased clandestine lab seizures, and declining methamphetamine potency. In the East, methamphetamine indicators remain low, but ethnographic and law enforcement evidence indicates a slight increase in availability, especially in rural areas and among whites. Mortality figures(1) show methamphetamine-related deaths remained relatively stable, except in Minneapolis/St. Paul and San Diego where they declined, and in Honolulu and Phoenix where they increased. Methamphetamine ED mentions(2) declined in six cities (Denver, Los Angeles, Phoenix, San Diego, San Francisco, and Seattle) and increased significantly only in Dallas. Methamphetamine remains the number-one primary drug problem among treatment admissions in Honolulu and San Diego(3), although in San Diego most methamphetamine indicators declined. Methamphetamine-positive percentages among adult male arrestees(4) increased notably in only two cities (San Diego and Seattle); percentages among adult female arrestees decreased notably in Phoenix. Methamphetamine users are heterogeneous, consisting of many small subgroups, as suggested by ethnographic data in Atlanta, where methamphetamine indicators appeared for the first time among arrestees. In Minneapolis/St. Paul, "snow," methamphetamine that allegedly contains extra lithium and produces hallucinations, is available. In Phoenix, where lab seizures recently increased dramatically, 2-phenethylamine is present in seizures, and ephedra, an herb, is used as a precursor.

Methylenedioxymethamphetamine (MDMA) ("ecstasy," "E," "Florida dove," "Mitsubishi," "red devils," "white dove," "XTC"), used primarily as a club drug at raves, dance clubs, and college scenes, seems to be increasing in Boston, Miami, New Orleans, New York, and parts of Texas; it is also reportedly available in Atlanta, Chicago, Minneapolis/St. Paul, New Jersey, Phoenix, St. Louis, Seattle, and Washington, DC. In Boston, it seems to be spreading outside the club scene. In Minneapolis/St. Paul, respirator masks rubbed with menthol-based cold ointments are worn after taking MDMA, a practice believed to heighten the drug's effect. In Atlanta, the content of what is sold as MDMA may vary widely. In Miami, Washington, DC, and parts of Texas, LSD and MDMA are combined in a pill form called "nexus," and in Chicago, homemade MDMA is sold as "wigits." Methylphenidate (Ritalin) is abused by young adults in Minneapolis/St. Paul and in middle- and upper-class communities in Boston; African-Americans in Chicago sometimes inject it with heroin or heroin and cocaine. White IDUs in Chicago inject Phenmetrazine (Preludin).

Depressants - Problems associated with "rave" and "club drugs" have dramatically risen in 1999. Gamma-hydroxybutyrate (GHB, a central nervous system depressant) and two of its precursors, gamma butyrolactone (GBL) and 1,4 butanediol (1,4 BDL, also called tetramethylene) have been increasingly involved in poisonings, overdoses, drug rapes, other criminal behaviors, and fatalities in nearly every CEWG city and their surrounding suburban and rural areas. These products, obtainable over the Internet and sometimes still sold in health food stores, are also available at gyms, nightclubs, raves, gay male party venues, on college campuses, or on the street. They are commonly mixed with alcohol, have a short duration of action, and are not easily detectible on routine hospital toxicology screens. GBL is available in commercial products such as Blue Nitro, Renew-Trient, and Revivarent G, while

1,4 butanediol is sold in products such as Enliven, Weight Belt Cleaner, and Revitalize Plus. New esters and analogs continue to appear as Federal and State laws remove the sale of these drugs. The tranquilizer ketamine ("Special K" or "vitamin K"), also common in the club, rave, and party scene, is reported in numerous cities, including Baltimore (where users are predominantly suburban white youth from middle- and upper-socioeconomic backgrounds), Boston (where some white middle-class youth inject it, it is also used as a heroin adulterant, and it may have been involved in some overdose deaths), Minneapolis/St. Paul (where small amounts appear in crime labs), New York (where it is available on the street, it is either snorted or injected, and it is sometimes mistaken for cocaine HCl), Newark, and Phoenix. Clonazepam (Klonopin or Rivotril) and alprazolam (Xanax, or "sticks") use, in various combinations and with alcohol, has recently increased in Boston, where diverted prescription drug seizures have increased sharply after a recent rash of pharmacy break-ins. Those two drugs have replaced flunitrazepam (Rohypnol) among adolescents in Miami; similarly, in parts of Texas, clonazepam continues to replace flunitrazepam, especially in combination with beer. Flunitrazepam continues to be a problem among treatment admissions in Texas, particularly among young Hispanic males along the Mexican border, and it has been involved in numerous poison control calls. Seizures of that drug have increased during the past year in New Orleans, where it remains common among white upper-class high school and college students. It is also widely available in Atlanta, where it arrives via couriers from Mexico or by mail through Florida from South America. Diazepam remains the most readily available and frequently used pharmaceutical depressant in Chicago; in New York, however, it is now second to alprazolam as the leading psychoactive prescription drug. Recent deaths in Seattle have involved concomitant injection of heroin and a depressant, typically diazepam.

Hallucinogens - Despite relatively low numbers in traditional data sources, qualitative data suggest that hallucinogen use is not uncommon among adolescents and young adults. Emergency department mentions generally declined for both lysergic acid diethylamide (LSD) (significantly in Baltimore, New Orleans, and San Francisco) and phencyclidine (PCP) (significantly in seven cities: Denver, Detroit, Miami, Minneapolis/St. Paul, New York, San Francisco, and Washington, DC); however, PCP mentions increased significantly in Dallas and New Orleans. Among arrestees, PCP-positive findings remained generally stable, except for a slight increase in Dallas and, following a decade of marked decline, a marked upturn in Washington, DC. The recent increases in the Dallas PCP indicators may reflect the use of marijuana cigarettes dipped in embalming fluid containing PCP. PCP is often smoked with marijuana, as continues to be reported in Chicago ("wicky stick" or "donk"), New York, and St. Louis. Some medical emergencies in south Florida have involved LSD abused with "rolls" (MDMA and cocaine). In parts of Texas, LSD is sometimes mixed with other drugs such as MDMA, diazepam, and Demenex (a diet pill from Mexico), and it is sometimes sold with methamphetamine. LSD in Dallas is becoming more available in the young adult nightclub scene. In Seattle, LSD and mushrooms turn up frequently at local concerts or raves. Psilocybin mushrooms ("shrooms") and mescaline are common among adolescents and young adults in Boston. In New York, the term "eaters" refers to teenagers and young adults who use locally grown mushrooms, which are sometimes dipped in or treated with PCP, LSD, or methamphetamine. Peyote is readily available in Phoenix.

Other drugs-A substance with mild hallucinogenic effects, called "red rock opium," "red run," and "red stuff," is smoked in Baltimore in combination with marijuana. It contains dracorhodin, a compound found in the plant Daemonorops draco ("dragon's blood"), used in varnishes and stains, as an herbal medicine, and to make incense. Teenagers in south Florida occasionally abuse two local anticholinergic plants, "devil's trumpet" and "angel's trumpet," by various routes (orally or via smoking), for their hallucinogenic properties. The plants' toxic effects have led to at least three medical emergencies. Jimson weed was involved in one recent death and several poison center calls per month in Phoenix. Cough medicines with dextromethorphan (DXM) are commonly abused by teens in Boston and Minneapolis/St. Paul ("robo tripping"). "Huffing" of toluene and other solvents continues among youth in Philadelphia. Three of four recent inhalant deaths in Phoenix involved toluene. Inhalant deaths also continue to be reported in Texas. Sildenafil citrate (Viagra) is reportedly used as a recreational drug in Boston. Needle exchange personnel in areas surrounding Boston report steroid injection among young male body builders. In Atlanta, law enforcement sources note the potential for abuse of the anabolic steroid clenbuterol (Spiropent) by weight lifters.

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(1) Mortality figures are for 1998 versus 1999 projections (based on first-half-year 1999 data) and were available in six reporting areas.

(2) Emergency department mentions are for 20 CEWG cities in the Drug Abuse Warning Network (DAWN) of SAMHSA's Office of Applied Studies; comparisons are for 1997 versus 1998 estimates, except for age group comparisons, which are for 1996 versus 1998; changes are noted only when statistically significant at pÐ0.05.

(3) Treatment admission figures are primary drug of abuse as a percentage of total admissions; total admissions exclude alcohol-only but include alcohol-in-combination. Comparisons generally are for first-half-1998 versus first-half-1999 data.

(4) Arrestee urinalysis data are for the 18 CEWG cities in the National Institute of Justice's Arrestee Drug Abuse Monitoring (ADAM) program; comparisons are for 1998 versus first-half-1999; first-half-1999 data are preliminary; changes are noted only when they are _5 percentage points.

(5) Heroin price and purity information are for 19 CEWG cities in the Drug Enforcement Administration (DEA) Domestic Monitor Program (DMP); comparisons are for 1998 versus first-half-1998.

Effects of Adolescent Substance Use on Autonomy, Positive Activity Involvement, and Perceived Competence in Young Adulthood

Researchers at Arizona State University used data from a longitudinal study of a children of alcoholics and demographically matched controls to test the relationship between adolescent alcohol and drug use and later young adult autonomy, positive activity involvement, and perceived competence. Participants were assessed in three annual interviews in adolescence (mean age: 12.7 years at Time 1) and then again 5-7 years later, in young adulthood (median age: 20 years). Path analyses and latent growth curve models were used to test the effects of adolescent substance use on both self-reported and collateral-reported outcomes, controlling for correlated risk factors (parental alcoholism, adolescent psychopathology, and parental support), preexisting levels of the outcome, and concurrent young adult substance use. Results showed that adolescent drug and alcohol use were associated with lowered levels of young adult autonomy, positive action, and competence, and that these effects remained significant after controlling for a variety of adolescent risk factors, concurrent young adult drug use, and preexisting levels of youth adult outcome variables. Alcohol use effects were more complex. Adolescent heavy drinking was associated with less positive adult outcomes, but more in collateral reports than in self- reported outcomes. Moreover. young adult heavy drinking was either uncorrelated with or positively correlated with higher levels of perceived competence, suggesting different developmental significance of alcohol use in adolescence than in young adulthood. These findings suggest that prevention of drug abuse in adolescents can not only have proximal benefits such as reductions in impaired driving but also improve psychosocial outcomes such as autonomy and competence. Chassin, L., Pitts, S.C., and DeLucia, C. The Relation of Adolescent Substance Use to Young Adult Autonomy, Positive Activity Involvement, and Perceived Competence. Development and Psychopathology, 11(4), pp. 915-932, 1999.

Competence Skills Help Deter Smoking Among Inner City Adolescents

This study tested whether higher levels of general competence are linked to more frequent use of refusal assertiveness, that is in turn related to less subsequent smoking among inner city adolescents. It was based on a longitudinal study conducted during a 3-year middle school or junior high school period. A sample of 1459 students attending 22 middle (ages 11-14 years) and junior high (ages 12-15 years) schools in New York City participated. Students completed surveys at baseline, one year follow up, and two year follow up. The students self reported smoking, decision making skills, personal efficacy, and refusal assertiveness. Teams of three to five data collectors administered the questionnaire following a standardized protocol. These data were collected in school during a regular 40 minute class period. Results from structural equation modeling showed that decision making and personal efficacy (that is, general competence) predicted higher refusal assertiveness and this greater assertiveness predicted less smoking at the two year follow up. The tested model had a good fit and was parsimonious and consistent with theory. The authors concluded that smoking prevention programs often teach refusal skills in order to help youth resist peer pressure to smoke. The present findings suggest that teaching general competence skills may help to reduce smoking because youth with better personal efficacy and decision making skills are better able to implement smoking refusal strategies. Epstein, J.A., Griffin, K.W., Botvin, G.J. Competence Skills Help Deter Smoking Among Inner City Adolescents. Tobacco Control, 9(1), pp. 33-39, 2000.

The Dynamics of Alcohol and Marijuana Initiation: Patterns and Predictors of First Use in Adolescence

This study, guided by the social development model, examined the dynamic patterns and predictors of alcohol and marijuana use onset. Survival analysis and complementary log-log regression were used to model hazard rates and etiology of initiation with time-varying covariates. The sample was derived from a longitudinal study of 808 youth interviewed annually from 10 to 16 years of age and at 18 years of age. Alcohol initiation rose steeply up to the age of 13 years and then increased more gradually; most participants had initiated by 13 years of age. Marijuana initiation showed a different pattern, with more participants initiating after the age of 13 years. This study showed that: (1) the risk of initiation spans the entire course of adolescent development; (2) young people exposed to others who use substances are at higher risk for early initiation; (3) proactive parents can help delay initiation; and (4) clear

family standards and proactive family management are important in delaying alcohol and marijuana use, regardless of how closely bonded a child is to his or her mother. Kosterman, R., Hawkins, J.D., Guo, J., Catalano, R.F., and Abbott, R.D. The Dynamics of Alcohol and Marijuana Initiation: Patterns and Predictors of First Use in Adolescence. American Journal of Public Health, 90(3), pp. 360-366, 2000.

Developmental Associations between Substance Use and Violence

In a study of the developmental associations between substance use and violence, investigators focused on the trends in each behavior throughout adolescence, how the behaviors covaried over time, and the symmetry of associations taking into account frequency and severity of each behavior. They also examined whether changes in one behavior affected changes in the other behavior over time. Six years of annual data were analyzed for 506 boys who were in the 7th grade at the first assessment. Concurrent associations between frequency of substance use and violence were relatively strong throughout adolescence and were somewhat stronger for marijuana than alcohol, especially in early adolescence. Type or severity of violence was not related to concurrent alcohol or marijuana frequency, but severity of drug use was related to concurrent violence frequency. Depending, to some degree, on the age of the subjects, the longitudinal relationships between substance use and violence were reciprocal during adolescence and slightly stronger for alcohol and violence than for marijuana and violence. Further, increases in alcohol use were related to increases in violence; however, when early alcohol use was controlled, increases in marijuana use were not related to increases in violence. Only in early adolescence was the longitudinal relationship between marijuana use and later violence especially strong. The strength of the longitudinal associations between violence and substance use did not change when common risk factors for violence and substance use were controlled. Overall, the data lend more support for a reciprocal than for a unidirectional association between substance use and violence. Prevention efforts should be directed at aggressive males who are multiple-substance users in early adolescence. White, H.R., Loeber, R., Stouthamer-Loeber, M., Farrington, D.P. Developmental Associations between Substance Use and Violence. Development and Psychopathology, 11(4), pp. 785-803, 1999.

Tobacco Smoking and Depressed Mood in Late Childhood and Early Adolescence

Building on previous observations about a suspected causal association linking tobacco smoking with depression, investigators at Johns Hopkins University used prospective data to study the temporal sequencing of tobacco smoking and depressed mood in late childhood and early adolescence. The sample consisted of 1731 youths (aged 8-9 to 13-14 years) attending public schools in a mid-Atlantic metropolitan area; they were assessed at least twice from 1989 to 1994. Survival analysis was used to examine the temporal relationship from antecedent tobacco smoking to subsequent onset of depressed mood, as well as from antecedent depressed mood to subsequent initiation of tobacco use. Tobacco smoking signaled a modestly increased risk for the subsequent onset of depressed mood but antecedent depressed mood was not associated with a later risk of starting to smoke tobacco cigarettes. This evidence is consistent with a possible causal link from tobacco smoking to later depressed mood in late childhood and early adolescence, but not vice versa. Wu, L.T. and Anthony, J.C. Tobacco Smoking and Depressed Mood in Late Childhood and Early Adolescence. American Journal of Public Health, 89(12), pp. 1837-1840, 1999.

Tobacco Smoking and Other Suspected Antecedents of Nonmedical Psychostimulant Use in the United States, 1995

This study investigates the extent to which tobacco smoking is associated with the nonmedical use of psychostimulants and the temporal order of the age of first use for tobacco and psychostimulants within a nationally representative sample of United States household residents. At the same time, alcohol use and other suspected determinants of psychostimulant use are investigated and held constant, using multiple regression models. Data were taken from public use files of the 1995 National Household Survey on Drug Abuse. Conditional logistic regression analyses were performed to derive estimated relative odds of using stimulants for tobacco smokers versus nonsmokers, holding constant other potentially distorting influences. The study found an independent association between tobacco smoking and nonmedical use of stimulant drugs, with and without adjustment for suspected confounding variables. Additional variables identified as being associated with lifetime stimulant use included lifetime alcohol use, being male, being 18-24 years of age, and not being married. This study provides recent evidence on tobacco smoking as one of the potentially malleable risk factors for the nonmedical use of stimulant drugs. Wu, L.T. and Anthony, J.C. Tobacco Smoking and Other Suspected Antecedents of Nonmedical Psychostimulant Use in the United States, 1995. Substance Use & Misuse, 34(9), pp. 1243-1259, 1999.

Male Twin Study of Substance Use and Disorders

This study used data from personal interviews of 1198 male-male twin pairs from a population-based registry to investigate sources of individual differences in risk. Models were fit to the data to assess the relative contributions of

genetic and familial-environmental factors to use, heavy use, abuse and dependence of several categories of substances. Findings suggest that the use of any drug, cannabis and hallucinogens are influenced by both genetic and environmental factors, while twin resemblance for use of sedatives, stimulants, cocaine, and opiates, and heavy use, abuse, and dependence of most substances, resulted from only genetic factors. Heritability of risk ranged between 60 and 80 percent. A number of potential limitations and biases were considered and discussed. This study adds importantly to the growing body of data supporting genetic factors as powerful predictors of drug use disorder liability, and has important implications for prevention and treatment. Kendler, K.S., Karkowski, L.M., Neale, M.C., and Prescott, C.A. Illicit Psychoactive Substance Use, Heavy Use, Abuse, and Dependence in a US Population-Based Sample of Male Twins. Archives of General Psychiatry, 57, pp. 261-269, 2000.

Drug Problems and Psychological Distress Among a Community Sample of Adults

Although the comorbidity of drug abuse and psychological distress is well established in adult treatment samples, the directionality of this association is in question. There is less evidence that this relationship exists among community samples of adults. The prospective relationships between psychological distress and drug problems (e.g., alcohol, marijuana, and cocaine) were examined in a community sample of 470 adults. Results addressed three theories -- self-medication/self-derogation, impaired functioning and general deviance -- to explain the relationship between drug use and psychological distress. Although the latent construct of polydrug problems was largely unaffected by psychological distress and generally had no effect on psychological distress, several specific effects emerged. Providing support for the impaired-functioning theory, adults who abused drugs early on experienced later impaired functioning, anxiety, suicidal ideation, psychoticism, hostility, and decreased purpose in life four years later, providing support for both the self-medication and self-derogation theories. Those who experienced aspects of psychological distress (e.g., dysphoria, suicidal ideation) reported drug problems four years later. Moderate cross-sectional support was also found for the general deviance theory in that social conformity reduced or eliminated the associations between polydrug problems and the measures of psychological distress. Implications of these findings are discussed. Newcomb, M.D., Vargas-Carmona, J., and Galaif, E.R. Drug Problems and Psychological Distress Among a Community Sample of Adults: Predictors, Consequences, or Confound? Journal of Community Psychology, 27(4), pp. 405-429, 1999.

Childhood Peer Rejection and Aggression Predicting Delinquency in Adolescence

In this study sociometric surveys were completed at third grade for a predominantly low-socioeconomic status, urban sample of African American boys and girls, and youth reports of delinquency were gathered at grades 6, 8, and 10. Results showed that patterns of association between childhood peer rejection and aggression and delinquency severity varied by gender. For boys, the additive effect of childhood peer rejection and aggression was a strong predictor of more serious delinquency, whereas for girls only aggression predicted more serious delinquency. For boys, the combination of peer rejection and aggression was associated with felony assaults, and aggression was associated with a wide variety of offenses during adolescence, whereas for girls only peer rejection predicted involvement in minor assault. Results of the study were discussed in terms of the early starter pathway of antisocial behavior as it relates to peer rejection and aggression for boys, differing predictive patterns for girls, and implications for intervention with children with emotional and behavioral disorders. Miller-Johnson, S., Coie, J.D., Maumary-Gremaud, A., Lochman, J., and Terry, R. Relationship Between Childhood Peer Rejection and Aggression and Adolescent Delinquency Severity and Type Among African American Youth. Journal of Emotional and Behavioral Disorders, 7 (3), pp. 137-146, 1999.

Outcomes of Universal Family-Focused Preventive Interventions: One- and Two-Year Follow-ups of a Controlled Study

This article summarizes the literature on alcohol initiation outcomes of universal family interventions and examines the long-term effects of the Iowa Strengthening Families Program (ISFP), a drug abuse prevention program. The ISFP was a longitudinal, controlled efficacy study with 446 families from 22 rural school districts. Alcohol initiation has been shown to be a precursor to drug initiation. In this study, a four-item index of alcohol initiation was used (Alcohol Initiation Index - AII), with low scores representing a lower level of initiation. Higher- and lower-dosage intervention groups were compared on individual initiation behaviors. AII scores were significantly lower among intervention group adolescents than among control group adolescents (e.g., onset of drinking without parental permission, onset of drunkenness) ranged from approximately 30% to 60% lower) at one- and two-year follow-up assessments. Intervention dosage-related initiation differences were evident only at the one-year follow-up. Spoth, R., Redmond, C., & Lepper, H. Alcohol Initiation Outcomes of Universal Family-Focused Preventive Interventions: One- and Two-Year Follow-ups of a Controlled Study. Journal of Studies on Alcohol, (Suppl. 13), pp. 103-111, 1999.

Predicting Violent Behavior

Data from the Seattle Social Development Project (SSDP), a prospective study involving a panel of youths followed since 1985 were used to replicate and extend findings on risk factors for youth. Data on potential risk factors for violence at age 18 years were measured at ages 10, 14, and 16 years. Changes in the strength of prediction over time were examined in the individual, family, school, peer and community domains. Attention was also given to the additive strength of increasing numbers of risk factors in the prediction of violence at age 18 years and the correct classification of youth having committed a violent act. At each age, risk factors strongly related to later violence were distributed among the five domain areas. Ten of 15, 20 of 25, and 19 of 21, risk factors measures at ages 10, 14, and 16, respectively were predictive of violent acts at age 18. Several risk factors were important across time, for example hyperactivity, low academic performance, peer delinquency, and availability of drugs in the neighborhood predicted violence at ages 10, 14, and 16 years. Analyses of the additive effects of risk factors revealed that youths exposed to multiple risks were more likely than others to engage in later violence. Compared to youth exposed to fewer than 2 risk factors, those exposed to 5 or more were 7 times more likely to have been violent at age 20 and 10 times more likely to have been violent at ages 14 and 16. The overall accuracy of predicting youths that would go on to commit violent acts was limited. Herrenkohl, T.I., Maguin, E., Hill, K.G., Hawkins, J.D., Abbott, R.D., and Catalano, R.F. Developmental Risk Factors for Youth Violence. Journal of Adolescent Health, 26(3), pp. 176-186, 2000.

Predictors of Youth Violence

Adolescents are more likely to perpetrate and be victimized by interpersonal violence than any other age group. Researchers from the University of Washington and the Research Institute on Addictions, Buffalo, NY have examined the risk factors in the individual, family, school, peer and community domains that predict youth violence at age 18. In a prospective study from the Seattle Social Development Project, data on risk factors were collected at ages 10, 14, and 16 and used to predict violent behavior at age 18. Of the eleven constructs measured at all three ages, four consistently predicted later violence: hyperactivity (parent rating), low academic performance, peer delinquency, and availability of drugs. Risk factors for violence at age 18 were identified as early as age 10, but the strength of the associations between risk factors and violence at age 18 years generally increased at ages 14 and 16 years. Paralleling findings from research on delinquency, mental health disorders, and substance use, youths exposed to multiple risks at each developmental point were more likely to engage in violence at age 18. Taken together these findings provide strong justification for directing preventive interventions to populations exposed to high numbers of risks. Herrenkohl, T.I., Maguin, E., Hill, K.G., Hawkins, J.D., Abbott, R.D., and Catalano, R.F. Developmental Risk Factors for Youth Violence. J. of Adolescent Health, 25(1), pp. 1-11, 1999.

Effects of Confidential Versus Anonymous Survey Procedures on Reporting of Drug Use and Related Attitudes and Beliefs

This study examines the question, "If young people are asked to report their use of drugs, what survey procedures are most likely to produce truthful responses?" This issue was particularly salient because the Monitoring the Future Study was changing from a confidential to a fully anonymous procedure for 8th and 10th grade students. Nationally representative samples of 8th and 10th grade students were surveyed, some in anonymous conditions and some in confidential conditions. Sample sizes were 18,667 8th graders (49.8 percent in anonymous) and 15,419 10th graders (48.9 percent in anonymous). Results show that 10th grade students surveyed with the confidential procedures were just as willing to report their drug-using behaviors as were those surveyed using anonymous procedures. Among 8th graders, results show that at most there was only a very modest mode of administration effect and quite possibly no effect at all. These findings are reassuring for school-based surveys that use confidential conditions to research student drug use and related attitudes and beliefs. O'Malley, P.M., Johnston, L.D., Bachman, J.G., and Schulenberg, J. A Comparison of Confidential Versus Anonymous Survey Procedures: Effects on Reporting of Drug Use and Related Attitudes and Beliefs in a National Study of Students. Journal of Drug Issues 30(1), pp. 35-54, 2000.

Initial Positive Impact of Using Fast Track with A High Risk Child Sample

Fast Track is a multisite, multicomponent preventive intervention for young children at high risk for long-term antisocial behavior. Based on a comprehensive developmental model, the intervention included a universal-level classroom program plus social skills training, academic tutoring, parent training, and home visiting to improve competencies and reduce problems in a high-risk group of children selected in kindergarten. Results at the end of first grade showed moderate positive effects on children's social, emotional, and academic skills, peer interactions and social status, and conduct problems and special-education use. Parents reported less use of physical discipline, greater ease and/or satisfaction in parenting, more positive involvement with their children, and increased school involvement. There was minimal evidence of differential intervention effects across child gender, race, site, and

cohort. Bierman, K.L., Coie, J.D., Dodge, K.A., Greenberg, M.T., Lochman, J.E., McMahon, R.J., and Pinderhughes, E.E. Initial Impact of the Fast Track Prevention Trial for Conduct Problems: I. The High-Risk Sample. Journal of Consulting and Clinical Psychology, 67 (5), pp. 631-647, 1999.

Effectiveness of the PATHS Curriculum and Teacher Consultation in the Fast Track Prevention Model

In this study the authors examined the effectiveness of the universal component of the Fast Track prevention model: the PATHS (Promoting Alternative Thinking Strategies) curriculum and teacher consultation. They used a randomized clinical trial involving 198 intervention and 180 comparison classrooms from neighborhoods with greater than average crime in 4 U.S. locations. In the intervention schools, first grade teachers delivered a 57-lesson social competence intervention focused on self-control, emotional awareness, peer relations, and problem solving. Findings indicated significant effects on peer ratings of aggression and hyperactive-disruptive behavior and observer ratings of classroom atmosphere. Quality of implementation predicted variation in assessments of classroom functioning. Bierman, K.L., Coie, J.D., Dodge, K.A., Greenberg, M.T., Lochman, J.E., McMahon, R.J., Pinderhughes, E.E. Initial Impact of the Fast Track Prevention Trial for Conduct Problems: II. Classroom Effects. Journal of Consulting and Clinical Psychology, 67 (5), pp. 648-657, 1999.

Dynamics of Alcohol and Marijuana Initiation

The Seattle Social Development Project has followed the initiation of alcohol and marijuana prospectively in 808 subjects beginning in fifth grade (10 _ years old) and continuing through age 18. A large portion of the participants were from low-income households; half of the subjects participated in the school free-lunch program. The sample was gender balanced and the ethnic composition was 46% Caucasian, 24% African American, 21% Asian American, and 3% from other ethnic groups. The social development model provided the framework for examining etiology, and this analysis focused on individual, family, and peer constructs. At age 10 _, 25% of the sample had tried alcohol and 3% had tried marijuana. Alcohol initiation rose relatively quickly to about age 13, by which time the cumulative initiation rate was 64%. From age 13 to 18 the rate of initiation slowed. In contrast, marijuana initiation remained relatively flat through age 13, and then the rate of initiation increased over the next 5 years until by age 18, 50% of the sample had initiated marijuana use. Asian American ethnicity reduced the likelihood of alcohol use, as did strong parental norms about teen alcohol use, while alcohol use by peers and associates increased the likelihood of initiation. For marijuana, African Americans and Native Americans were more likely to initiate use and Asian Americans were less likely to initiate use than Caucasians. Males were more likely to initiate use, as were those who had previously initiated alcohol use. Parents' proactive family management inhibited initiation as did teens' own norms against marijuana use, but marijuana use by acquaintances and siblings was a strong predictor of initiation. This study suggests that prevention efforts should span the entire adolescent period, with alcohol prevention efforts directed toward preteen years and marijuana prevention efforts focused on later teen years. Prevention efforts should encourage clear family standards and proactive management as well as address the influence of peers, siblings, and other acquaintances who use drugs and alcohol. Kosterman, R., Hawkins, J.D., Guo, J., Catalano R.F., and Abbott, R.D. The Dynamics of Alcohol and Marijuana Initiation: Patterns and Predictors of First Use in Adolescence. American Journal of Public Health, 90, pp. 360-366, 2000.

Protective Effect of Social-Environmental Factors on Future Drug Use

This research focuses on the interrelation of the parent-child attachment, unconventionality, friends' drug use, and the young adult's use of drugs. Data were collected from participants at 4 points in time: early adolescence, late adolescence, early 20s, and late 20s. Data were collected from mothers at the 3 points in time that corresponded with the first 3 collections of data from their children. Both the youths and their mothers were individually interviewed. The findings indicated that the effect of parent-child mutual attachment was mediated through early adolescent personality attributes of greater responsibility, less rebelliousness, and intolerance of deviance. These non-drug-prone personality and behavioral attitudes, in turn, insulated the young adult from affiliating with drug-using peers, and these attitudes were related to less drug use in the early 20s and ultimately in the late 20s. The results suggest that interventions focused on enhancing parent-child mutual attachment should result in a reduction of the risk factors conducive to drug use during the late 20s. The fact that these findings cover a decade and a half, from early adolescence to the late 20s, underscores the significance of placing drug use in a perspective that includes familial and behavioral aspects. Brook, J.S., Whiteman, M., Finch, S., and Cohen, P. Longitudinally Foretelling Drug Use in the Late Twenties: Adolescent Personality and Social-Environmental Antecedents. J. Genet. Psychol., 161(1), pp. 37-51, 2000.

The Course of Well-Being and Substance Use During the Transition to Young Adulthood

This study examines the impact of social roles and contexts on health and well-being between the senior year of high school (age 18) and 4 years post-high school (age 22) using multicohort national panel data drawn from the Monitoring the Future study. The project has surveyed nationally representative samples of about 17,000 high school seniors each year in the United States since 1975 using questionnaires administered in classrooms. About 2,400 individuals are randomly selected from each senior year cohort for follow-up. The panel sample used in this study consisted of 17 consecutive cohorts of respondents who were surveyed as high school seniors from 1976 through 1992 and who participated in the first two biennial follow-up surveys. The purpose was to determine the extent to which the individual-level courses of well-being and substance use during the transition from adolescence to young adulthood varied as a function of cohort, gender, and life paths. Results showed that during this transition, well-being increased significantly (i.e., self-esteem, self-efficacy, and social support increased; self-derogation, fatalism, and loneliness decreased) as did substance use (i.e., cigarette, alcohol, and marijuana use; binge drinking). However, self-efficacy did not increase as much in the more recent cohorts compared with the earlier ones. Over time, absolute levels of well-being have changed little, and the same is true for gender and life-path differences in well-being. Substance use was higher in the earlier cohorts than in the later, generally representing period effects. For nearly all measures, men reported higher levels of well-being and substance use compared with women. Among the life paths, there were many overall differences in both well-being as well as substance use. Schulenberg, J., O'Malley, P.M., Bachman, J.G., and Johnston, L.D. "Spread Your Wings and Fly": The Course of Well-Being and Substance Use During the Transition to Young Adulthood. In L. J. Crockett & R. K. Silbereisen (Eds.), *Negotiating Adolescence in Times of Social Change.* New York: Cambridge University Press, pp. 224-255, 2000.

Predicting Boys' Externalizing Behavior and Risk of Developing Substance Use Disorder

Applying an ontogenetic framework for understanding the development of substance use disorders (SUD), researchers at the Pennsylvania State University and the University of Pittsburgh examined individual traits in family context to identify processes that account for the relationship between fathers' substance use (SUD+ or SUD-) status and sons' externalizing behaviors. Results obtained from SUD+ (n = 89) and SUD- (n = 139) families show that fathers' abusive propensities toward their sons mediated the relationship between fathers' SUD+ status and sons' externalizing behavior scale (EBS) scores 2 years later. Thus, fathers' abusive propensities toward their sons may reflect a process in which SUD liability is transmitted, in part, through a harsh, unnurturing family. Individual traits, family contextual variables, and deviant peer affiliations accounted for 58 percent of the variance on sons' EBS scores. The authors speculate that children reared in harsh, controlling family contexts may develop callous traits such as lack of empathy for others, and such traits in children have been associated with greater levels of conduct problems. They conclude that family-based prevention programs that take account of members' temperament traits and the abusive propensities of parents toward offspring may help to reduce children's liability to Conduct Disorder and Substance Use Disorder outcomes. Blackson, T.C., Butler, T., Belsky, J., Ammerman, R.T., Shaw, D.S., and Tarter, R.E. Individual Traits and Family Contexts Predict Sons' Externalizing Behavior and Preliminary Relative Risk Ratios for Conduct Disorder and Substance Use Disorder Outcomes. Drug and Alcohol Dependence, 56(2), pp. 115-131, 1999.

Hormonal and Behavioral Homeostasis in Boys at Risk for Substance Abuse

A study at the Center for Education and Drug Abuse Research (CEDAR) at the University of Pittsburgh examined the influences of cortisol reactivity, androgens, age-corrected pubertal status, parental personality, and family and peer dysfunction on behavioral self-regulation (BSR) in boys at high average risk (HAR) and low average risk (LAR) for substance abuse. Differences between risk groups in cortisol and androgen concentrations, and cortisol reactivity were also examined. Subjects were 10-12-year-old sons of substance abusing fathers (HAR; n = 150) and normal controls (LAR; n = 147). A multidimensional construct of BSR was developed based on multiple measures and multiple informants. Boys reported on family dysfunction and deviant behavior among their peers. Parents reported on their propensity to physically abuse their sons, and their own number of DSM-III-R Antisocial Personality Disorder symptoms. Endocrine measures included plasma testosterone, dihydrotestosterone, and salivary cortisol. HAR boys, compared to LAR boys, had lower mean concentrations for testosterone, dihydrotestosterone, salivary cortisol prior to evoked related potential testing, and lower cortisol reactivity. The number of maternal Antisocial Personality Disorder symptoms, parental potential for physical abuse, degree of family dysfunction, and peer delinquency were significantly associated with BSR. Parental aggression, antisocial personality symptoms, and parental physical abuse potential are likely to influence sons' behavioral dysregulation and homeostatic stress reactivity. These key components of liability are posited to increase the likelihood of developing suprathreshold Psychoactive Substance Use Disorder (PSUD). The authors suggest that interventions to prevent exacerbation of poor behavioral self regulation should address family dysfunction and deviant peer affiliation as well as the severity of current BSR impairment. Dawes, M.A., Dorn, L.D., Moss, H.B., Yao, J.K., Kirisci, L., Ammerman, R.T., and Tarter, R.E. Hormonal and Behavioral Homeostasis in Boys at Risk for Substance Abuse. Drug and Alcohol Dependence, 55(1-2), pp. 165-

176, 1999.

Deprivation and Deviance

Using multivariate logistic regression, this study estimated models showing that negative self-feelings, induced by perception of relative economic deprivation, motivate adoption of deviant behavior patterns including property crimes, violence, and drug use. Stiles, B.L., Liu, X., and Kaplan, H.B. Relative Deprivation and Deviant Adaptations: The Mediating Effects of Negative Self-Feeling. Journal of Research in Crime and Delinquency, 37, pp. 64-90, 2000.

Predictors of Polydrug Use Among Four Ethnic Groups: A 12-Year Longitudinal Study

Adolescent risk and protective constructs associated with adult polydrug use among four ethnic groups were examined. Both mean and relational differences among the constructs were examined by ethnic group. Teenage polydrug use was a significant predictor of adult polydrug use for Caucasians, African-Americans, and Latinos. Although this relationship was not evident for Asians, teenage alcohol use increased adult cigarette use, and early religiosity increased adult alcohol use. Early parental support/bonding predicted less adult polydrug use for Caucasians. For Latinos, general social conformity and low liberalism decreased cigarette use as an adult. In general, the implications of the results are that prevention strategies should emphasize the reduction of teenage drug use to decrease adult polydrug use among Caucasians, Latinos, and African-Americans. Future research should examine other possible risk and protective conditions related to adult polydrug use among diverse populations. Galaif, E.R. and Newcomb, M.D. Predictors of Polydrug Use Among Four Ethnic Groups: A 12-Year Longitudinal Study. Addictive Behaviors, 24(5) pp. 607-631, 1999.

The Association of Current Stimulant Use with Demographic, Substance Use, Violence-related, Social and Intrapersonal Variables Among High Risk Youth

This article reports the association of current stimulant use with demographic, other substance use, violence-related, social and intrapersonal variables among a large sample of high risk adolescents. A total of 21.4% of the sample reported using stimulants in the last 30 days. In a final, multivariable model, nonredundant concurrent predictors of current stimulant use were reports that friends use stimulants, reports that stimulants were likely to be used again in the next 12 months, use of alcohol, hallucinogens, or cocaine in the last 30 days, use of alcohol or other drugs to feel more safe, and reports of depression in the last week. Being above the median on none to all seven of these correlates predicted from 0% to 85% of those who were above the median on current stimulant use. One may speculate that programming for these stimulant-using youth should include treatment of multiple substances, depression, and correction of social-cognitive misperceptions. Sussman, S., Dent, C.W., and Stacy, A.W. The Association of Current Stimulant Use with Demographic, Substance Use, Violence-related, Social and Intrapersonal Variables Among High Risk Youth. J Addictive Behavior, 24(6), pp. 741-748, 1999.

The Association of Group Self-identification and Adolescent Drug Use in Three Samples Varying in Risk

This study provides a cross-sectional analysis of the relations between group self-identification and adolescent drug use in three samples of youth: comprehensive high-school, continuation high school, and runaway/street youth. Youth identified with discrete groups in all three samples, and similar general groups were formed. In most comparisons, a high-risk group showed greater levels of drug use than did other groups. This is the first study to demonstrate that group self-identification (a) is a generalizable construct across different types of adolescent samples, (b) is related to use of drugs other than tobacco, and (c) remains a significant correlate of drug use controlling for its relations with demographic variables and several other psychosocial variables. Sussman, S., Simon, T.R., Stacy, A.W., Dent, C.W., Ritt, A., Kipke, M.D., Montgomery, S.B., Burton, D. and Flay, B.R. The Association of Group Self-identification and Adolescent Drug Use in Three Samples Varying in Risk. J Applied Sociology Psychology, 29 (8), pp. 1555-1581, 1999.

Parent-Child Conversations About Tobacco Use

In this study parents engaged their 6th- and 8th-grade daughters in a conversation about tobacco, using a pamphlet designed to encourage effective family communication about tobacco. Results indicated that parent-daughter conversations about tobacco use were successfully carried out in a nonaversive manner. The conversations were perceived to have gone well, with very little conflict reported. The daughters reported that the parental advice was helpful and they did not resist receiving such advice. The pamphlet topics most frequently discussed included: consequences of smoking as experienced by friends and relatives, difficulty of quitting, promotional tactics of tobacco companies, making rules about tobacco use, and deciding on the consequences of rules adherence or violation. Ary,

D.V., James, L., and Biglan, A. Parent-Daughter Discussions to Discourage Tobacco Use: Feasibility and Content. Adolescence, 34 (134), pp. 275-282, 1999.

Relationship Between Group Self-Identification Adolescent Drug Use

This study examined the relationship between group self-identification and adolescent drug use in three samples of youth: comprehensive high-school, continuation high-school, and runaway/street youth. Youth identified with discrete and generally similar groups in all three samples. A high-risk group in each of the samples showed greater levels of drug use than did other groups in most comparisons. This is the first study to demonstrate that group self-identification is a generalizable construct across different types of adolescent samples, is related to use of drugs other than tobacco, and remains a significant correlate of drug use controlling for its relations with demographic variables and several other psychosocial variables. Sussman, S., Simon, T.T., Stacy, A.W., Dent, C.W., Ritt, A., Kipke, M.D., Montogomery, S.B., Burton, D., and Flay, B.R. The Association Group Self-identification and Adolescent Drug Use in Three Samples Varying in Risk. Journal of Applied Social Psychology, 29(8), pp. 1555-1581, 1999.

After-School Self-Care and Adolescent Smoking

This study examined the independent contributions of the setting and the intensity of after-school self-care to the cigarette smoking behaviors of 2,352 ninth graders. The authors found that the intensity of the self-care experience was significantly associated with adolescent smoking behavior irrespective of the typical setting of the adolescents' after-school activities. The findings indicated that a nonpermissive parenting style, family rule-setting about cigarettes, and in absentia parental monitoring may reduce the likelihood of cigarette smoking among both latchkey and nonlatchkey adolescents. Targeting these aspects of the home lives of all adolescents has the potential to reduce smoking behaviors among latchkey as well as nonlatchkey children. Mott, J.A., Crowe, P.A., Richardson, J., and Flay, B. After-School Supervision and Adolescent Cigarette Smoking: Contributions of the Setting and Intensity of After-School Self-Care. Journal of Behavioral Medicine, 22(1), pp. 35-58, 1999.

A Social Stress Model for Substance Abuse in Immigrant Hispanic Women

The authors used cross-sectional interview-administered surveys of 60 low-income predominantly Mexican-American women to examine the independent variables of stress, social support and influences, personal competencies and community resource utilization patterns in relation to the outcome variable of alcohol and drug use (alcohol, cigarettes, marijuana, cocaine and opiates). Their findings suggested that the levels of drug use in this study sample were lower than in the general USA population regardless of pregnancy status. Results of bivariate correlations indicated that women with higher drug use indices had more lenient attitudes regarding drug use and were more likely to have family and friends that used alcohol and drugs. Women who used alcohol themselves and whose partners used alcohol and drugs reported significantly higher levels of stress, weaker social support and lower levels of self-esteem. Lindenberg, C.S., Strickland, O., Solorzano, R., Galvis, C., Dreher, M., and Darrow, V.C. Correlates of Alcohol and Drug use Among Low-Income Hispanic Immigrant Childbearing Women Living in the USA. International Journal of Nursing Studies, 36 (1), pp. 3-11, 1999.

Cultural Sensitivity in Prevention Research

This article raises several issues commonly encountered in preventive intervention research in the US--from key conceptual issues surrounding the construct of race, ethnicity, culture, and minority status, to the conceptualization, design, recruitment, measurement, delivery, data analysis, interpretation, and dissemination of an intervention project--and suggests possible solutions aimed at fostering genuine cultural sensitivity while satisfying the demands of rigorous scientific inquiry. The article is an attempt to stimulate discussion in the area of cultural sensitivity, which should be of concern to all psychologists interested in applied and preventive intervention. Dumas, J.E., Rollock, D, Prinz, R.J., Hops, H., and Blechman, E.A. Cultural Sensitivity: Problems and Solutions in Applied and Preventive Intervention. Applied & Preventive Psychology, 8, pp. 175-196, 1999.

Long-term Outcomes of Two Universal Parenting Prevention Interventions

The present investigation extends prior work that reported findings on two universal family-focused preventive intervention programs. At posttest, each had direct effects on one proximal parenting outcome (intervention-targeted parenting behavior) and indirect effects on two global/distal outcomes (parent-child affective quality and general child management). A replication of the previously tested parenting outcome model was conducted with one-year follow-up data using procedures identical to those in the earlier study. Results of the present study (N = 404 families) indicate that statistically significant effects on parenting behaviors were sustained at the one-year period following the posttest. Redmond, C., Spoth, R., Shin, C., and Lepper, H. Modeling Long-Term Parent Outcomes of Two Universal

Family-Focused Preventive Interventions: One-Year Follow-up Results. Journal of Consulting and Clinical Psychology, 67(6), pp. 975-984, 1999.

Drug Use and Personality Factors Affect Parent-Child Attachment Relationship

In this longitudinal study, data were collected during early adulthood in 1992 and in 1996/1997 via a structured questionnaire. The researchers assessed the extent to which participants' personality attributes, substance use, and relationships with their mothers predicted the quality of the parent-child bond. Participants with certain personality attributes (e.g., high sensitivity), less frequent marijuana use, or a close relationship with their mothers were found to have a greater likelihood of having a close parent-child attachment relationship with their own children at a later time. Results also showed that the risk of earlier substance use on the parent-child relationship was offset by protective factors in the parents' personality domain. In addition, protective factors in the various parental domains synergistically interacted with a low frequency of marijuana use, relating to a closer parent-child attachment relationship. The findings suggest that certain parenting styles are transmitted across generations and interventions in the personality and drug use domains can help increase the likelihood that parents will form close attachment relationships with their own children. Brook, J.S., Richter, L., and Whiteman, M. Effects of Parent Personality, Upbringing, and Marijuana Use on the Parent-Child Attachment Relationship. J. Am. Acad. Child. Adolesc. Psychiatry, 39(2), pp. 240-248, 2000.

Family Structure and Educational Attainment

This study used structural equation modeling to account for the relationship between family structure during adolescence and educational attainment in adulthood. The investigators found that intact family of origin was associated with better financial situation in the parental home and a positive school experience, which in turn were associated with later entry into adult work and marriage roles, and finally to continuing educational attainment beyond high school. Chen, Z. and Kaplan, H.B. Explaining the Impact of Family Structure During Adolescence on Adult Educational Attainment: A Longitudinal Study. Applied Behavioral Science Review, 7, pp. 23-40, 1999.

Survival Sex Among Runaway and Homeless Youth

Investigators at Research Triangle Institute analyzed data on 12-21-year-olds from a nationally representative sample of shelter youths and a multi-city sample of street youths to determine the prevalence and correlates of survival sex. "Survival sex" refers to the selling of sex to meet subsistence needs, including sex to get drugs or money to get drugs. Results indicated that approximately 28 percent of street youths and 10 percent of shelter youths reported having participated in survival sex, which was associated with age, days away from home, victimization, criminal behaviors, substance use, suicide attempts, sexually transmitted disease, and pregnancy. These findings highlight the need to develop services that provide alternatives to the sex trade as a means of meeting economic needs for runaway and homeless youth. It was concluded that intensive and ongoing services are needed to provide resources and residential assistance for these youth. Green, J.M., Ennett, S.T., and Ringwalt, C.L. Prevalence and Correlates of Survival Sex Among Runaway and Homeless Youth. American Journal of Public Health, 89, pp. 1406-1409, 1999.

Psychosocial Predictors of Current Drug Use, Drug Problems, and Physical Drug Dependence in Homeless Women

Risk and protective factors associated with three qualitatively different drug use constructs describing a continuum of drug use were studied among a sample of 1,179 homeless women. Relationships among positive and negative sources of social support, positive and negative coping strategies, depression, and the drug constructs of current drug use, drug problems, and physical drug dependence were assessed using structural equation models with latent variables. Current drug use was predicted by more negative social support (from drug-using family/friends), depression, and less positive coping. Drug problems were predicted by more negative coping, depression, and less positive coping. Physical drug dependence was predicted by more negative social support and depression and less positive social support. Results highlighted the importance of investigating both the positive and negative dimensions of psychosocial functioning, while suggesting that empowering homeless women and offering tangible resources for coping with the stress of being homeless may be beneficial to them. Galaif, E.R., Nyamathi, A.M., and Stein, J.A. Psychosocial Predictors of Current Drug Use, Drug Problems, and Physical Drug Dependence in Homeless Women. Addictive Behaviors, 24(6), pp. 801-814, 1999.

Parentification and its Impact on Adolescent Children of Parents with AIDS

Parentification refers to children or adolescents assuming adult roles before they are emotionally or developmentally

ready to manage those roles successfully. An assessment of the predictors and outcomes of parentification was made among adolescent children of Parents with AIDS (PWAs) in two phases. In Phase 1, relationships among parental AIDS-related illness, parent drug use, parent and adolescent demographics, and parentification indicators (parental, spousal, or adult role-taking) were assessed among 183 adolescent-parent pairs (adolescents: 11 to 18 years, M = 14.8 years, 54 percent female; parents: 80 percent female). Adult role-taking was associated with maternal PWAs, female adolescents, and greater parent drug use. Greater parental AIDS-related illness predicted more spousal and parental role-taking. Parent drug use predicted more parental role-taking. In Phase 2, the impact of parentification on later adolescent psychological adjustment was examined (N = 152 adolescents). Adult role-taking predicted more internalized emotional distress; parental role-taking predicted externalized problem behaviors, sexual behavior, alcohol and marijuana use, and conduct problems. Given these dysfunctional outcomes, interventions to mitigate parentification among children of PWAs are discussed. Stein, J.A., Riedel, M., Rotheram-Borus, M.J. Parentification and Its Impact on Adolescent Children of Parents with AIDS. Family Process, 38(2), pp. 193-208, 1999.

Multivariate Applications in Substance Use Research

Researchers at Indiana University and Arizona State University collaborated in editing a new book that introduces the latest advances in quantitative methods and illustrates how to apply these methods to address important questions in substance use research. The book brings together methodologists developing innovative quantitative methods with researchers who have collected data capable of addressing significant substance abuse issues. The book examines the use of state-of-the-art longitudinal techniques to assess change over time. Researchers studying the etiology, treatment, and prevention of substance use and abuse will find this volume useful in illustrating the application of current statistical techniques to enable them to make optimal use of their data. Indiana University's 20-year Smoking Project formed the basis of several of the chapters, in which authors studied the processes of initiation and progression of smoking and how they are relate to psychosocial development. With chapters by a number of well known substance abuse researchers, the volume covers use of latent curve methods for describing individual trajectories of adolescent substance use over time; methods for analyzing longitudinal data for individuals nested within groups such as families, classrooms, and treatment groups; how different patterns of missing data influence the interpretation of results; recent advances in longitudinal growth modeling; methods of studying mediation when there are multiple mediating pathways underlying an intervention effect; methods of identifying moderating relations in structural equation models; use of structural equation models to evaluate a preventive intervention; epidemic modeling techniques for understanding the spread of substance use in society; use of latent transition analysis to model substance use as a series of stages; and logistic regression methods of prospectively predicting smoking cessation. Rose, J.S., Chassin, L., Presson, C.C., and Sherman, S.J. (eds.) Multivariate Applications in Substance Use Research: New Methods for New Questions. Mahwah, NJ: Lawrence Erlbaum Associates, 2000.

The Impact of Interviewer Characteristics on Drug Use Reporting by Male Juvenile Arrestees

The impact of interviewer and subject effects on cocaine and marijuana use disclosure was evaluated in a sample of over 3,000 male juvenile arrestees. Analyses evaluated the viability of Social Attribution and Conditional Social Attribution models of interviewer effects. The viability of alternative models was investigated in the context of comparative analyses excluding and including statistical adjustments for the clustering of responses by interviewers. Interviewer effects were more salient in models predicting marijuana disclosure than in models predicting cocaine disclosure. Logistic regression analyses provided support for Social Attribution and Conditional Social Attribution models of interviewer effects. Models suggested large interviewer cluster effects. Cluster adjustment altered interpretation of effects for both cocaine and marijuana. Subject race/ethnicity effects were salient in models predicting disclosure for both drugs, but were especially large in models predicting cocaine disclosure. Fendrich, M., Johnson, T., Shaligram, C., and Wislar, J.S. The Impact of Interviewer Characteristics on Drug Use Reporting by Male Juvenile Arrestees. Journal of Drug Issues, 29(1) pp. 37-58, 1999.

Continued Smoking Over 25 Years

This study tested the hypothesis that high daily cigarette consumption and addiction to smoking are risk factors for the long-term continuation of smoking. Using longitudinal data from 986 male smokers, the investigators entered cigarettes per day, psychological addiction, age, and education into a survival analysis as predictors of continued smoking over a 25-year period. Younger men and those who smoked more cigarettes per day were more likely to remain smokers in the long term. Addiction and education level were not significant predictors of continued smoking. Heavier smokers are more at risk than lighter smokers for long-term smoking. It is therefore very important to provide smoking cessation treatments for heavy smokers as early as possible after the initiation of smoking. Nordstrom, B.L., Kinnunen, T., Utman, C.H., Krall, E.A., Vokonas, P.S., Garvey, A.J. Predictors of Continued Smoking Over 25 Years of Follow-Up in the Normative Aging Study. American Journal of Public Health, 90(3), pp. 404-406,

2000.

Prevention of Post-Rape Psychopathology

The authors developed an acute time-frame hospital-based video intervention to minimize anxiety during forensic rape exams, and prevent post-rape posttraumatic stress disorder (PTSD), panic, and anxiety. Results of preliminary data indicated that psychological distress at the time of the exam was strongly related to PTSD symptomatology 6 weeks post-rape, and the video intervention successfully reduced distress during forensic exams. Resnick, H., Acierno, R., Holmes, M., Kilpatrick, D.G., and Jager, N. Prevention of Post-Rape Psychopathology: Preliminary Findings of a Controlled Acute Rape Treatment Study. Journal of Anxiety Disorders, 13 (4), pp. 359-370, 1999.

Limited Prosocial Information Exchange And Substance Use

This study assessed attitudes, drug use, and mental health status in pregnant, inner-city residents. Structured interviews revealed that the 38 substance users were more likely to report favorable attitudes toward drugs and polysubstance use, disengagement coping, depressive symptoms, negative affect, and antisocial behavior than were 45 nonusers. During videotaped interviews, trained observers coded less warmth and less prosocial information exchange (e.g., self-disclosure, question asking) among users. Factor analysis of measures of coping and its concomitants yielded a three-factor (prosocial, antisocial, asocial) solution, with substance users more likely to use asocial and antisocial coping. These results suggest that coping has emotional, social, and cognitive elements. This study is the first to demonstrate an association between a substance-using lifestyle and limited prosocial information exchange. Blechman, E.A., Lowell, E.S., Garrett, J. Prosocial Coping and Substance Use During Pregnancy. Addictive Behaviors, 24, pp. 99-109, 1999.

The Minnesota DARE PLUS Project:

Creating Community Partnerships to Prevent Drug Use and Violence The Minnesota DARE PLUS Project is a randomized trial of 24 schools and communities. Students in eight schools receive the usual junior high Drug Abuse Resistance Education (DARE) curriculum in the 7th grade; eight schools receive the curriculum with the addition of parent involvement, peer leadership, and community components in the 7th and 8th grades; eight schools serve as controls. This article describes the background and conceptualization, the curriculum, the added intervention components, and the evaluation strategy for the DARE PLUS Project. Perry, C.L., Komro, K.A., Veblen-Mortenson, S., Bosma, L., Munson, K, Stigler, M., Lytle, L.A., Forster, J.L., and Welles, S.L. The Minnesota DARE PLUS Project: Creating Community Partnerships to Prevent Drug Use and Violence. J. School Health. 70(3), pp. 84-88, 2000.

Perceived Invulnerability and Cigarette Smoking Among Adolescents

Adolescent perceptions of invulnerability toward smoking and nonsmoking-related health risks were examined among 432 continuation high school students. Smokers were less likely than nonsmokers to report feeling invulnerable to both smoking and nonsmoking-related health risks. Among the smokers, those who reported feeling invulnerable to smoking related health risks, compared to those who reported feeling vulnerable, smoked fewer cigarettes, were less addicted, were less likely to intend to smoke more in the future, attempted to quit fewer times in the past, valued their health more, and reported higher public body awareness. In a multiple logistic regression model, only high public body awareness, fewer previous attempts to quit, and being in the action stage of change (compared to being in the precontemplation stage of change) remained significant independent concurrent predictors of being in the invulnerable group. These results suggest, contrary to some previous work, that perceived invulnerability may be predictive of quitting tobacco use and may reflect relative invulnerability; that is, lighter use of tobacco. Milam, J.E., Sussman, S., Ritt-Olson, A., and Dent, C.W. Perceived Invulnerability and Cigarette Smoking Among Adolescents. J. Addictive Behaviors, 25 (1), pp. 71-80, 2000.

Examining Ethnic-Group Differences in the Predictors of Substance Use

The authors describe some approaches to studying ethnic-group differences in the predictors of substance use. They include probing for mediators, multisample analyses of structural models and an experimental trial of a preventive intervention. In their studies they found some ethnic-group differences as well as many similarities in the structure of constructs and the relationships between variables. It was noted that the challenge for researchers is using appropriate research methods for studying ethnicity, uncovering the basis for ethnic-group differences when they occur, knowing when statistical differences are meaningful, and acknowledging when developmental models are comparable. Barrera, M., Castro, F.G., and Biglan, A. Ethnicity, Substance Use, and Development: Exemplars for Exploring Group Differences and Similarities. Development and Psychopathology, 11 (4), pp. 805-822, 1999.

Health Correlates of Sexual Violence in Homeless Women

Researchers at RAND and UCLA documented the association of rape with specific health and substance use/abuse characteristics in a probability sample of 974 homeless women in Los Angeles County. Structured interviews were administered to women aged 15-44 who had spent at least one of the past 30 nights in non-traditional housing. Thirteen percent of the women reported being raped in the past year, and half of these women had been raped at least twice in the past year. Women reporting recent rape fared worse on every physical and mental health measure and were more likely to have a lifetime history of drug abuse or dependence and reports of recent drug use than other homeless women. These data indicate that sexual violence is a major problem confronting homeless women and that all homeless women who present with serious mental, physical, or substance abuse problems should be screened for violent experiences. Wenzel, S.L., Leake, B.D., and Gelberg, L., Health of Homeless women with Recent Experience of Rape. Journal of General Internal Medicine 15(4), 2000.

Women Who Use Crack Cocaine

FAST (Female Atlanta Study, N=149 women), a 4-year ethnographic study to develop a clearer understanding of the lives of female crack cocaine users, is presented in a way that captures how these women arrived at their use; how they survive under their current circumstances, such as the constant threat of HIV/AIDS and violence; how they develop and maintain intimate relationships; how they combine the multiple social roles of mother and drug user; and how--as they share their aspirations and expectations for the future--their stories underscore the effects of poverty, sexism, and racism on their lives. Many of the women recognize their own responsibility for ensuring positive change. Dr. Sterk includes an argument for a harm reduction approach and reminds the reader that the strength and courage of these women may be futile without social policies that are realistic and appropriate for women. Sterk, C. Women Who Use Crack Cocaine. Philadelphia, PA: Temple University Press, pp. 242, 1999.

Safety First: A Reality-Based Approach to Teens, Drugs, and Drug Education

This monograph reviews findings from research on the epidemiology and etiology and of drug abuse among young people and drug abuse prevention programs. It presents the information in terms appropriate for policy makers, program designers and evaluators, and laymen to rethink approaches to prevention of drug abuse. She concludes there are fundamental problems with drug education because the foundations of conventional school-based drug education are fundamentally flawed. Many programs are based on the conviction that any use of illegal drugs is inherently pathological, an indication that something is wrong, whereas alternative explanations acknowledge the importance of culture. As a sociologist, she notes that American people and their children are bombarded with messages that encourage them to imbibe and medicate with a variety of substances, including alcohol, tobacco, caffeine, and prescription drugs. Fifty-one percent of Americans use alcohol regularly and one-third have tried marijuana at some time. Teenage drug use appears to mirror American proclivities. Dr. Rosenbaum's review of the literature arrives at a reality-based alternative: safety-first drug education. The first assumption of safety-first drug education is that teenagers can make responsible decisions if given honest, science-based drug education (students were motivated to quit using marijuana for health reasons or negative drug effects they themselves experienced or learned about from sources they trust). The second assumption of safety first is that total abstinence may not be a realistic alternative for all teenagers. Proclaiming a drug-free American culture by some arbitrary date is not deemed realistic, but reduction of drug use and drug problems is realistic and a key measure of success. A third assumption of safety-first drug education is to differentiate between use, abuse, and dependency. The youthful user must know he/she is not trapped and has a choice and can reduce use and influence the outcome. Dr. Rosenbaum's book provides scientific support for these positions and some guidelines for developing safety-first drug education to equip students with information they can trust and use as a the basis for making responsible decisions. Rosenbaum, M. Safety First: A Reality-Based Approach to Teens, Drugs, and Drug Education. San Francisco, CA: The Lindesmith Center, pp. 1-12, 1999.

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

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

National Institute on Drug Abuse

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

May, 2000

Research Findings

Services Research

Contingency Management in Outpatient Methadone Treatment: A Meta-Analysis

A meta-analysis was conducted on contingency management interventions in outpatient methadone treatment settings. The outcome was drug use during treatment, as detected through urinalysis. Significant moderators of outcomes included type of reinforcement provided, time to reinforcement delivery, the drug targeted for behavioral change, number of urine specimens collected per week, and type of subject assignment. These factors represent important considerations for the utilization of contingency management techniques for the reduction of drug use during treatment related to reduced risk behaviors. Griffith, J.D., Rowan-Szal, G.A., Roark, R.R., and Simpson, D.D. Drug and Alcohol Dependence, 58, pp. 55-66, 2000.

Office-based Methadone Prescribing: Acceptance by Inner-city Practitioners in New York

In preparation for a study of office-based methadone treatment in New York City, 71 providers from 11 sites were surveyed about their willingness to prescribe methadone in their office-based practices. In the U.S., methadone maintenance is restricted by federal and state regulations to specialized clinics that serve fewer than 20% of the heroin-dependent population. In Europe, Canada, and Australia, primary health care providers are used widely to prescribe methadone. Eighty-five percent of the respondents had methadone-maintained patients who came to their practice for other care. One-third felt knowledgeable enough to prescribe methadone, and 66% said they would if given proper training and support (88% among AIDS care providers). Half expressed concern that they might be unable to meet the multiple needs of these patients. Forty-seven respondents were willing to become methadone providers with additional training and ancillary support. These providers could serve, at 10-20 patients each, 470-940 patients, a population the size of 3 to 5 average methadone clinics. McNeely, J., Drucker, E., Hartel, D., and Tuchman, E. Journal of Urban Health-Bulletin of the New York Academy of Medicine, 77(1), pp. 96-102, 2000.

Drug Treatment and 12-Step Program Participation: The Additive Effects of Integrated Recovery Activities

This study examined the separate and combined effects of 12-step programs and drug treatment on recovery. Treatment participants with pretreatment 12-step involvement stayed in treatment longer and were more likely to complete the 24-week treatment program. Both pretreatment 12-step involvement and duration of participation in drug treatment were associated with subsequent 12-step involvement. Importantly, an additive effect was found for these recovery activities -- those who participated concurrently in both drug treatment and 12-step programs had higher rates of abstinence than those who participated only in treatment or in 12-step programs. The researchers suggest that rather than being used as recovery alternatives, drug treatment and 12-step programs are utilized by the patient as integrated recovery activities. Fiorentine, R., Hillhouse, M.P. Journal of Substance Abuse Treatment, 18, pp. 65-74, 2000.

Drug Abuse Treatment Outcome Study of Adolescents: A Comparison of Client

Characteristics and Pretreatment Behaviors in Three Treatment Modalities

The sample was 3382 adolescent subjects who presented for treatment from 1993 to 1995 in 37 programs in Pittsburgh, Pennsylvania; Miami, Florida; Minneapolis, Minnesota; Chicago, Illinois; Portland, Maine; and New York City, New York. Interviewers queried subjects about their background, including education and employment; physical and mental health; use of tobacco, alcohol, and other drugs; sexual experiences; legal problems: religious beliefs; and treatment experience. The findings indicate that the long-term residential treatment modality was the least gender balanced and had the most African-American and Hispanic clients. This modality was also distinguished by the proportion of clients who were referred to treatment by the juvenile or criminal justice system. Compared with other modalities, short-term inpatient clients were more likely to be female and white and to report more indicators of psychiatric impairment. Outpatient clients were slightly younger than clients in the other modalities, had higher levels of school attendance at the time of admission to treatment, had the least criminally involved lifestyles, and the lowest rates of (regular daily or weekly) drug use were also the lowest of the three modalities for all drugs assessed, and they had the least drug treatment experience. The findings suggest that there is a need for more community-based adolescent substance abuse treatment programs and more training in substance abuse treatment programs to serve the specific needs of incarcerated youth and youth under criminal justice supervision. Finally, the researchers recommended that programs be designed to address such specialized issues as comorbid substance abuse and psychiatric problems, family dysfunction, physical and sexual abuse, gender and ethnic differences, and academic performance. Rounds-Bryant, J.L., Kristiansen, P.L., and Hubbard, R.L. Am J Drug Alcohol Abuse, 25(4), pp. 573-591, 1999.

Substance Abuse Treatment Cost Offsets Vary with Gender, Age, and Abstinence

Likelihood The cost-offset effect has been promoted as a way for substance abuse treatment to pay for itself by generating reductions in health care utilization in other areas. Clients (n = 5,434) that were abstinent for 24 months following substance abuse treatment had lower post-treatment utilization than clients that had relapsed. An examination of cost offsets revealed a complex interplay between gender, age, and type of utilization (medical versus psychiatric). Cost offsets were larger for women over 40 years old. Zywiak, W.H., Hoffmann, N.G., Stout, R.L., Hagberg, S., Floyd, A.S., and DeHart, S.S. J Health Care Finance, 26(1), pp. 33-39, 1999.

Client Engagement in Drug Treatment

This study investigates why some clients are more likely to engage in treatment. Findings indicate that the predictors of treatment engagement are generally confined to current treatment experiences. For both women and men, the perceived utility of treatment, ancillary services, and the client-counselor relationship are the strongest predictors of client engagement in treatment. Client characteristics are generally not strong predictors of treatment engagement. Concerning the client-counselor relationship, the findings suggest that women may respond more favorably to an empathic counseling style, whereas men may respond to a more utilitarian style. The findings contradict popular stereotypes about the treatment-receptive client, identify possible directions for treatment improvement, and highlight the need for more research examining the treatment experience of the client. Fiorentine, R., Nakashima, J., and Anglin, M.D. Journal of Substance Abuse Treatment, 17(3), pp. 199-206, 1999.

Psychiatric Comorbidity and the 16-month Trajectory of Substance-Abusing and Substance-Dependent Juvenile Offenders

This study examines correlates of internalizing and externalizing disorders among substance-abusing and substance-dependent juvenile offenders to determine the association between psychiatric comorbidity and psychosocial functioning of the youths 16 months later. Participants were 118 juvenile offenders meeting DSM-III-R criteria for substance abuse or dependence and their families. Comorbidity for externalizing disorders was associated with high rates of antisocial behavior and predicted worse 16-month outcomes than substance abuse alone or substance abuse with comorbid internalizing disorders. For criminal activity and drug use, the presence of internalizing disorders buffered the deleterious effect of externalizing disorders on substance-abusing and substance-dependent juvenile offenders. Even in substance-abusing delinquents, a population already extreme in antisocial behavior, the presence of externalizing disorders indicates high risk for deterioration. Randall, J., Henggeler S.W., Pickrel S.G., and Brondino M.J. J. Am. Acad. Child Adolesc. Psychiatry, 38(9), pp. 1118-1124, 1999.

Victims as Victimizers: Physical Aggression by Persons with a History of Childhood Abuse

Substance abuse has been called the dominant characteristic of families involved in child abuse cases, but the frequency with which childhood victims become adult victimizers is uncertain. This study examines whether a history of childhood sexual or physical abuse is associated with becoming a victimizer (i.e., abusing or assaulting others) as

an adult. Interview data from 439 intravenous drug users found a history of sexual or physical abuse before 16 years of age was reported by 51% of women and 31% of men. Seventeen percent of the subjects reported being victimizers. Among childhood victims of physical or sexual abuse, 28% victimized others; among those who denied childhood abuse, 10% victimized others. Two thirds of victimizers reported being under the influence while assaulting others. Controlling for gender, having children, education, race, and history of incarceration, childhood abuse was significantly associated with becoming a victimizer (odds ratio, 3.6). This study confirms a high rate of childhood abuse among intravenous drug users suggesting that treatment programs should both assess and program for treating the adult for past abuse and preventing future victimization. Clarke, J., Stein, M.D., Sobota, M., Marisi, M., and Hanna, L. Arch Intern Med, 159(16), pp. 1920-1924, 1999.

Drug Treatment Effectiveness and Client-Counselor Empathy. Exploring the Effects of Gender and Ethnic Congruency

This study examined the effects of gender and ethnic congruency between patients and counselors on perceived counselor empathy, client engagement in treatment, and abstinence during and after outpatient drug treatment. The findings indicate that client-counselor gender and ethnic congruence were significantly associated with higher levels of perceived counselor empathy for all gender, ethnic, and age groups. However, client-counselor gender and ethnic congruence were not consistently associated with higher levels of treatment engagement and abstinence for all gender, ethnic, and age groups. The findings support a recommendation of paying closer attention to matching clients to counselors. This may be especially important for women, Latinos, and clients 35 years or older. With some female patients it may also be important to match with respect to ethnicity. Also with Latino clients, routinely matching a client to an empathic counselor regardless of gender or ethnicity of the counselor would lead to more favorable treatment outcomes than matching clients solely to gender and ethnically-congruent counselors. Fiorentine, R., Hillhouse, M.P. Journal of Drug Issues, 29(1), pp. 59-74, 1999.

Integrative Modeling of Client Engagement and Outcomes during the First 6 Months of Methadone Treatment

Integrative models containing client and treatment components were tested in a sample of 396 daily opioid users from three methadone maintenance treatment sites. Measures included client motivation at intake as well as repeated assessments of therapeutic engagement (relationships between clients and their counselors, session attendance, and results of urine testing) during the first 6 months of treatment. There was a positive effect of pretreatment motivation on engagement and a reciprocal positive relationship between components of engagement and their effects on lowering drug use throughout treatment. Further analyses addressed differential effects of group versus individual counseling and showed that group session attendance was associated with higher rates of drug-negative urines. Joe, G.W., Simpson, D.D., Greener, J.M., and Rowan-Szal, G.A. Addictive Behaviors, 24(5), 1999.

Biopsychosocial Characteristics and Treatment Outcomes of Pregnant Cocaine-dependent Women in Residential and Outpatient Substance Abuse Treatment

This study compared treatment outcomes of pregnant cocaine-dependent women and their infants enrolled in residential (N=32) and outpatient (N=32) treatments. No significant differences between treatment programs were found in retention or infant birth outcomes, but abstinence and patterns of attrition showed differences favoring residential treatment. Comfort, M., Kaltenbach, K.A. J. Psychoactive Drugs, 31(3), pp. 279-289, 1999.

New Directions in Alcohol and Drug Treatment under Managed Care

Studies on managed care and substance abuse were reviewed to explore potential effects of the introduction and expansion of managed care on the financing and organization of public and private alcohol and drug abuse treatment systems. Managed care will continue to have major effects on the organization of service delivery, the workforce, and the provision of services, especially in its impact on links between treatment agencies and the medical community, and other health and social service agencies. The impact of a new emphasis on treatment accountability through the mechanisms of outcomes monitoring and performance indicators has yet to be determined. Weisner, C., McCarty, D., Schmidt, L. Am. J. Manag. Care, 5 Spec No, SP 57-69, 1999.

Prison-based Substance Abuse Treatment, Residential Aftercare and Recidivism

The impact of residential aftercare on recidivism following prison-based treatment was examined. Data were collected from male inmates (293 treated, 103 untreated) in a 9-month in-prison therapeutic community (ITC) and several community-based transitional therapeutic communities (TTCs). Post-release recidivism was based on state criminal history records. ITC treatment, especially when followed by residential aftercare, was effective for reducing post-

release recidivism rates, supporting a recommendation for a continuum of care model (from institution to community) with high quality programs and services. Hiller, M.L., Knight, K., and Simpson, D.D. Addiction, 94(6), pp. 833-842, 1999.

The Effect of Copayments on Drug and Alcohol Treatment following Inpatient Detoxification under Managed Care

The study examined the rates and duration of outpatient substance abuse treatment following inpatient detoxification under managed care. Seven years of claims data from a large behavioral health care carve-out plan were used to identify patients. Seventy-nine percent of the detoxification patients received formal substance abuse treatment, the majority within the week following discharge. Formal follow-up care lasted an average of ten weeks, with visits occurring on average about once a week. When other variables likely to influence participation in substance abuse treatment were controlled for, the level of outpatient copayments significantly affected the rate of participation in treatment. The results suggest that reducing copayment levels is one mechanism for increasing the likelihood that individuals with severe drug and alcohol problems will receive subsequent treatment. Stein, B., Orlando, M., Sturm, R. Psychiatric Services, 51(2), pp. 195-198, 2000.

"I Already Stopped": Abstinence Prior To Treatment

Pre-treatment abstinence and its relation to subsequent outcome was investigated using data collected for a randomized experimental design immediately after assessment for publicly funded substance abuse treatment at the King County Assessment Center (KCAC) in Seattle. Participants (N = 565), who had illicit drug use in the 90 days prior to KCAC referral to treatment, waited a median of 12 days (range = 0-108 days) until either treatment entry or waiting list dropout. Forty-five percent of participants reported abstinence from initial assessment to when they entered or failed to enter treatment. Higher rates of abstinence were associated with shorter waiting periods, less substance use prior to initial assessment, and higher readiness to change. Pre-treatment abstinence was not associated with either treatment entry or completion. Findings suggest that individuals can become abstinent prior to treatment, but this is not a good predictor of treatment entry, completion, or outcome. Rosengren, D.B., Downey, L., Donovan, D.M. Addiction, 95(1), pp. 65-76, 2000.

Effectiveness of Comprehensive Services for Crack-Dependent Mothers with Newborns and Young Children

The Family Rehabilitation Program (FRP) is a network of community-based programs providing comprehensive services to families, including prenatally cocaine-exposed newborns, with drug-dependent parents in New York City. An admission sample of 173 mothers in 17 FRP sites was studied for one year. Average retention was 10 months; half the clients were still active in the program at follow-up. Mothers completing or still active in FRP had higher rates of abstinence and substantially lower average levels of cocaine use (by hair analysis) at follow-up than those exiting prematurely. The percent of families with children removed from homes did not increase significantly between admission and follow-up, and completing or remaining active in the program were associated with less out-of-home placement at follow-up. Magura, S., Laudet, A., Kang, S.Y., Whitney, S.A. Journal of Psychoactive Drugs, 31(4), pp. 321-338, 1999.

The Addiction Severity Index: A Field Study of Internal Consistency and Validity

The validity and internal consistency of the Addiction Severity Index (ASI) was tested in a network of inner-city alcohol and drug abuse clinics. A sample of 8,984 ASI scores was collected over a 34-month period. Construct validity was examined by computing the internal consistency of all subscales. Convergent and divergent validity of composite scores and of severity ratings were evaluated using correlation matrices. ASI scores were found to be internally consistent and valid under non-ideal conditions, even though the recommended administration protocol may not always have been followed as faithfully as might be desirable. This robustness bodes well for the use of the ASI in on-line clinical environments. Leonhard, C., Mulvey, K., Gastfriend, D.R., and Schwartz, M. Journal of Substance Abuse Treatment, 18(2), pp. 129-135, 2000.

Exploring the Additive Effects of Drug Misuse Treatment and 12-Step Involvement: Does 12-Step Ideology Matter?

This study examines the effects of 12-Step ideology on 12-Step program participation and abstinence from drug use. Acceptance of 12-Step ideology, particularly strong agreement with the need for frequent, lifelong attendance at 12-Step meetings, and the need to surrender to a "higher power" were found to be significant predictors of weekly or

more frequent attendance at 12-Step meetings independent of other mediating variables. Acceptance of the notion that controlled or nonproblematic drug use is not possible predicted abstinence independent from 12-Step participation and other potentially mediating variables. These findings have implications for group process and recovery from drug misuse. Fiorentine, R., Hillhouse, M.P. Subst. Use Misuse, 35(3), pp. 367-397, 2000.

Crack-Cocaine Users as Victims of Physical Attack

A retrospective and prospective natural history design was used to study correlates of physical attack among 440 not-in-treatment crack-cocaine users in Dayton, Ohio. Physical attack was found to be widespread among these crack cocaine users. Between baseline and 12-month follow-up, the odds of men being attacked were significantly less than those for women. The findings did not vary by ethnicity. Injuries often resulted in the need for medical care. These findings point to the need for accessible and effective drug abuse treatment to diminish harm to this population. Siegal, H.A., Falck, R.S., Wang, J., and Carlson, R. J National Medical Association, 92, pp. 76-82, 2000.

Lifetime Severity Index for Cocaine Use Disorder (LSI-Cocaine): A Predictor of Treatment Outcomes

The validity of a lifetime severity index for cocaine use disorder was developed and tested for its ability to predict post treatment outcome using data from the national Drug Abuse Treatment Outcome Study. The index, based on 28 items, considered frequency of use, recency, dependency, and attempt to quit. A higher value of the index, indicating greater severity, predicted a greater likelihood of relapse. The odds ratios were 5.7 for high severity and 4.4 for medium severity, relative to low severity and shorter time to relapse. Similarly, the polytomous logistic analysis indicated that the index predicted levels of post treatment cocaine use. Odds ratios of daily use were 47.8 for the high severity and 18.8 for medium severity; the corresponding odds ratios of weekly use were 6.75 and 5.10 and for less-than-weekly use were 3.35 and 3.57. The index can be a useful measure for both clinical and research purposes. Hser, Y., Shen, H., Grella, C., and Anglin, M.D. J. Nerv. Ment. Dis., 187(12), pp. 742-750, 2000.

Shorter Hospital Stays and More Rapid Improvement Among Patients With Schizophrenia and Substance Abuse

Length of stay and treatment response of inpatients with acute schizophrenia were examined to determine whether differences existed between those with and without comorbid substance-related problems. In a sample of 608 patients with a diagnosis of schizophrenia or schizoaffective disorder and substance abuse treated on hospital units with integrated dual diagnosis treatment researchers found that dually diagnosed patients were found to have improved markedly faster compared with patients without a dual diagnosis (30 percent shorter stays on both voluntary and involuntary units). They also showed somewhat greater symptomatic improvement and no increase in 18-month readmission rates. Dually diagnosed patients with schizophrenia appear to stabilize faster during acute hospitalization than those without a dual diagnosis. The authors hypothesize that substance abuse may temporarily amplify symptoms or that these patients may have a higher prevalence of better-prognosis schizophrenia. The availability of integrated dual-focus inpatient treatment and a well-developed outpatient system may also have helped these patients recover more rapidly. Ries, R.K., Russo, J., Wingerson, D., Snowden, M., Comtois, K.A., Srebnik, D., and Roy-Byrne, R. Psychiatric Services, 51, pp. 210-215, 2000.

Episodes Of Mental Health and Substance Abuse Treatment Under a Managed Behavioral Health Care Carve-Out

A growing number of payers of mental health and substance abuse services, including private employers and state governments, have adopted managed behavioral health care "carve-out" programs. Such payers seek to control rising metal health services and substance abuse (MHSA) benefit costs and to address adverse selection, while insuring needed services. The study found that adoption of a carve-out for Massachusetts state employees was associated with a dramatic drop in total MHSA costs per episode (particularly for individuals with severe MHSA conditions). The carve-out also was associated with a shift away from the use of facility care toward the use of outpatient care for enrollees with a diagnosis of unipolar depression. Huskamp, H. Inquiry, 36, pp. 147-161, 1999.

Impacts of Insurance on the Demand and Utilization of Drug Abuse Treatment: Implications for Insurance Mandates

The demand for, utilization of, and utilization costs for drug abuse treatment were estimated using an insurance claims database from self-insured employers. Approximately three-quarters of the increase in in-patient usage attributable to fractional co-insurance was due to increased usage per person (the other one-quarter was from to

increased numbers of users). About half of the increase in outpatient usage was due to increased usage per person. These estimates may provide useful measurements of the potential impacts of improved drug abuse treatment coverage. Although the potential induced in-patient expenditures and dead-weight losses are substantial compared to co-insurance rates of 0.5, losses can be trimmed by adjusting co-insurance, even at rates of approximately 0.1. Goodman, A.C., Hanken, J.R., Nishura, E., and Sloan, J.J. International Journal of the Economics of Business, 6(3), pp. 331-348, 1999.

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

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

National Institute on Drug Abuse

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

May, 2000

Research Findings

Intramural Research

Treatment Section, Clinical Pharmacology and Therapeutics Research Branch

Methadone Dose Increase and Abstinence Reinforcement for Treatment of Continued Heroin Use in Patients Maintained on Methadone

Although methadone maintenance is an effective therapy for heroin dependence, some patients continue to use heroin and may benefit from therapeutic modifications. This study evaluated a behavioral intervention, a pharmacological intervention, and a combination of both. All patients received daily methadone maintenance (initially 50 mg/day PO) and weekly counseling throughout the study. Following baseline treatment patients who continued to use heroin were randomly assigned to one of four interventions: 1) contingent vouchers for opiate-negative urine specimens (N=29); 2) dose increase to 70 mg/day (N=31); 3) combined contingent vouchers and dose increase (N=32); 4) neither intervention (comparison standard; N=28). Methadone dose increases were double blind. Vouchers had monetary value and were exchangeable for goods and services. Groups not receiving contingent vouchers received matching vouchers independent of urine test results. Primary outcome measure was opiate-negative urine specimens (thrice weekly urinalysis). Contingent vouchers and a methadone dose increase each significantly increased the percentage of opiate-negative urines during the intervention phase. Contingent vouchers, with or without a dose increase, increased the duration of sustained abstinence as assessed by urine screens. Dose increase, with or without contingent vouchers, reduced self-reported frequency of use and self-reported craving. In methadone-maintained patients who continued to use heroin, abstinence reinforcement and a methadone dose increase were each effective in reducing use. When combined, they did not dramatically enhance each other's effects on any one outcome measure, but they did appear to have complementary benefits. Preston, K.L., Umbricht, A., and Epstein, D.H. Archives of General Psychiatry, 57, pp. 395-404, 2000.

Chemistry & Drug Metabolism Section, Clinical Pharmacology and Therapeutics Branch

Tobacco Craving is Associated with Craving for Other Drugs of Abuse

Two experiments were conducted to determine whether active imagery would elicit tobacco craving in smokers with histories of drug abuse who were not interested in quitting smoking. In Experiment 1, researchers used scripts that contained positive, negative, or neutral affective content with and without descriptions of smoking urge. Scripts with urge content and negative affect scripts increased subjective reports of tobacco craving. An interaction between affective manipulation and urge content was observed on self-reported mood. In Experiment 2, positive affect scripts that varied in amount of urge content produced an orderly increase in tobacco craving as a function of urge intensity, suggesting that changes were specific to the imagery manipulation. In both experiments, increases in tobacco craving were positively correlated with craving for drug of choice, suggesting that stimuli that engender smoking urges may occasion craving for other drugs of abuse. Taylor, R.C., Harris, N.A., Singleton, E.G., Moolchan, E.T., and Heishman, S.J. Tobacco Craving: Intensity-Related Effects of Imagery Scripts in Drug Abusers. Experimental and Clinical

Psychopharmacology, 8, pp. 75-87, 2000.

Cellular Neurophysiology Section, Cellular Neurobiology Research Branch

Cellular Expression of the Immediate Transcription Factor Nurr1 Suggest a Gene Regulatory Role in Specific Dopaminergic Neurons

Nurr1, an orphan receptor of the nuclear receptor superfamily, is widely expressed in the central nervous system (CNS) including brain regions where dopaminergic neurons are abundant. Recent analyses of Nurr1 null mutant mice, have shown that Nurr1 is essential for the development and survival of midbrain dopaminergic neurons. However, other dopaminergic neuronal populations do not seem to be affected by ablation of the Nurr1 gene. The purpose of the present study was to investigate the degree of co-existence of Nurr1 mRNA and tyrosine hydroxylase (TH) immunoreactivity in the brain of adult mice to better characterize the selective effects of Nurr1 on catecholaminergic neurons. Results indicate that the majority of TH immunoreactive neurons in the substantia nigra (SN; 96%), ventral tegmental area (VTA; 95%), retrorubral field (91%), olfactory bulb (85%), linear nucleus raphe (91%) and central grey (61%) express Nurr1. In contrast, dopaminergic cells of the paraventricular and periventricular hypothalamic nucleus showed only a few Nurr1/TH double labeled neurons, while TH immunoreactive neurons in the arcuate nucleus and zona incerta did not express Nurr1 mRNA. Nurr1 expression was also excluded from (nor)adrenergic neurons of the brain stem. In conclusion, Nurr1 transcripts were not found in all CNS catecholaminergic neurons. Nurr1 expression was confined to periglomerular and midbrain dopaminergic neurons. These results suggest that within the adult mouse brain, Nurr1 may participate in dopaminergic functions of the olfactory bulb and midbrain. Manipulation of Nurr-1 expression may allow modulation of dopaminergic circuits critical for substance abuse and addiction. BŠckman, C., Perlmann, T., Wallen, A., Hoffer, B.J., and Morales, M. Brain Research, 851, pp. 125-132, 1999.

Molecular Neuropsychiatry Section, Cellular Neurobiology Research Branch

Chronic Exposure to Antibodies Directed Against Anti-Opiate Peptides Alters Delta-Opioid Receptor Levels

The development of addictive states in response to chronic opioid use may be regulated partially by the release of endogenous peptides. These anti-opiate peptides (AOP) are secreted or released into the CNS and produce diverse actions that counterbalance the effects of prolonged opiate exposure. Though the mechanism(s) by which these peptides exert their physiological properties remain largely unknown, there is some indication that AOP's modulate opioid receptor levels. In this study, IRP researchers investigated the effects of chronically infused alpha-melanocyte stimulating hormone (alpha-MSH), dynorphin(1-8) (DYN(1-8)), dynorphin A (DYNA), and NPFF antibodies on delta-opioid receptor expression in rat brains. Quantitative autoradiographic experiments revealed that antibodies directed against alpha-MSH and DYNA produced significant increases in delta receptor levels in the caudate, claustrum, and cingulate cortex of the rat brain. Conversely, NPFF monoclonal antibodies caused significant decreases in the caudate, nucleus accumbens, olfactory tubercle, and cingulate cortex. These results suggest that the density of delta-opioid receptors is affected by changes in the levels of the anti-opioid peptides in the extracelluar fluid in the rat brain. Goodman, C.B., Heyliger, S., Emilien, B., Partilla, J.S., Yang, H.Y., Lee, C.H., Cadet, J.L. and Rothman, R.B. Peptides, 20(12), pp. 1419-24, 1999.

Caffeine Withdrawal Increases Cerebral Blood Flow Velocity and Alters Quantitative Electroencephalography (EEG)

Cessation of daily caffeine consumption produces a withdrawal syndrome comprised of subjective symptoms and functional impairment. Few controlled studies have examined the physiological effects of caffeine withdrawal. The present study examined the effect of caffeine withdrawal on cerebral blood flow velocity and quantitative EEG. Ten volunteers reporting moderate caffeine intake (mean 333 mg/day) participated in this double-blind study. Subjects completed several tests when maintaining their normal diet (baseline period) and during two 1-day periods during which they consumed caffeine-free diets and received capsules containing placebo (placebo test session) or caffeine (caffeine test session) in amounts equal to their baseline daily caffeine consumption. Blood flow velocity was determined for four arteries: right and left middle (MCA), and right and left anterior (ACA) cerebral arteries using pulsed transcranial Doppler sonography. EEG was recorded for 3 min from eight scalp sites while subjects sat, with eyes closed, in a sound-attenuated electronically shielded chamber. Subjective effects were assessed with questionnaires. Results showed an effect of the placebo (21-h withdrawal) condition compared to the caffeine condition. Placebo significantly increased the mean velocity, systolic velocity and diastolic velocity (cm/s) in all four cerebral arteries. In the MCA, the pulsatility index was significantly decreased following placebo. Placebo significantly increased EEG theta power. Placebo also produces subjective effect changes, including increases in heavy feelings in

arms and legs and decreases in ability to concentrate. The caffeine and baseline conditions produced similar results on both the physiological and subjective measures. Cessation of daily caffeine consumption produced changes in cerebral blood flow velocity and quantitative EEG. These changes may be related to classic caffeine withdrawal symptoms of headache, drowsiness and decreased alertness. Jones, H.E., Herning, R.I., Cadet, J.L., Griffiths, R.R., Psychopharmacology (Berl) 147(4), pp. 371-377, 2000.

The Regulation of Cerebral Blood Flow During Intravenous Cocaine Administration in Cocaine Abusers

Cocaine abuse is associated with heightened risk of life-threatening neurological complications such as strokes, seizures, and transient ischemic attacks. We used transcranial Doppler (TCD) sonography, a continuous measure of cerebral blood flow velocity, to better understand the changes in cerebral hemodynamics produced by cocaine administration, which may lead to an increased risk for stroke in cocaine abusers. Heart rate and blood pressure were also measured. Blood flow velocity of seven cocaine abusers was studied during placebo, 10-, 25-, and 50-mg intravenous (i.v.) injections of cocaine. A significant increase in mean and systolic velocity that lasted for about two minutes was observed with all doses of cocaine, with no change in the placebo condition. This increase in systolic velocity indicates that cocaine produces an immediate and brief period of vasoconstriction in large arteries of the brain. The present results elucidate the time course of cocaine's acute cerebrovascular effects and provide a better understanding of the etiology of cocaine-related stroke and transient ischemic attacks. Herning, R.I., Better, W., Nelson, R., Gorelick, D., and Cadet, J.L. Ann N Y Acad. Sci., 890, pp. 489-494, >

Methamphetamine Administration Causes Overexpression of nNOS in the Mouse Striatum

The accumulated evidence suggests that the overproduction of nitric oxide (NO) is involved in methamphetamine (METH)-induced neurotoxicity. Using NADPH-diaphorase histochemistry, neuronal nitric oxide synthase (nNOS) and inducible nitric oxide synthase (iNOS) antibody immunohistochemistry, the possible overexpression of nNOS and iNOS was investigated in the brains of mice treated with METH. The number of positive cells or the density of positive fibers was assessed at 1 h, 24 h and 1 week after METH injections. There were no clear positive iNOS cells and fibers demonstrated in the brains of mice after METH treatment. In contrast, METH caused marked increases in nNOS in the striatum and hippocampus at 1 and 24 h post-treatment. The nNOS expression normalized by 1 week. There were no statistical changes in nNOS expression in the frontal cortex, the cerebellar cortex, nor in the substantia nigra. These results provide further support for the idea that NO is involved in the neurotoxic effects of METH. Deng, X. and Cadet, J.L. Brain Res. 851(1-2), pp 254-257, 1999.

Null Mutation of c-fos Causes Exacerbation of Methamphetamine-Induced Neurotoxicity

Methamphetamine neurotoxicity has been demonstrated in rodents and nonhuman primates. These neurotoxic effects may be associated with mechanisms involved in oxidative stress and the activation of immediate early genes (IEG). It is not clear, however, whether these IEG responses are involved in a methamphetamine-induced toxic cascade or in protective mechanisms against the deleterious effects of the drug. As a first step toward clarifying this issue further, the present study was thus undertaken to assess the toxic effects of methamphetamine in heterozygous and homozygous c-fos knock-out as well as wild-type mice. Administration of methamphetamine caused significant reduction in [(125)I]RTI-121-labeled dopamine uptake sites, dopamine transporter protein, and tyrosine hydroxylase-like immunohistochemistry in the striata of wild-type mice. These decreases were significantly exacerbated in heterozygous and homozygous c-fos knock-out mice, with the homozygous showing greater loss of striatal dopaminergic markers. Moreover, in comparison with wild-type animals, both genotypes of c-fos knock-out mice showed more DNA fragmentation, measured by the number of terminal deoxynucleotidyl transferase-mediated dUTP nick-end-labeled nondopaminergic cells in their cortices and striata. In contrast, wild-type mice treated with methamphetamine demonstrated a greater number of glial fibrillary acidic protein-positive cells than did c-fos knock-out mice. These data suggest that c-fos induction in response to toxic doses of methamphetamine might be involved in protective mechanisms against this drug-induced neurotoxicity. Deng, X., Ladenheim, B., Tsao, L. and Cadet, J.L. J. Neurosci. 19(22), pp. 10107-10115, 1999.

Brain Imaging Section, Neuroimaging Research Branch

In Vivo Labeling nAChRs with 6-[F-18]Fluoro-A85380

A new tracer for positron emission tomography (PET), 6-[F-18]fluoro-3-(2(S)-azetidinylmethoxy)-pyridine (6-[F-18]fluoro-A-85380 or 6-[F-18]FA), was synthesized by no-carrier-added [F-18]fluorination of 6-iodo-3-((1-tert-butoxycarbonyl-2(S)-azetidinyl)methoxy)pyridine followed by acidic deprotection. Radioactivity as 6-[F-18]fluoro-A-85380 reflects the regional densities of brain nAChRs reported in the literature. Evidence of binding to nAChRs and high specificity of the binding in vivo was demonstrated by inhibition with nAChR selective ligands, as well as with

unlabeled 6-fluoro-A-85380. A preliminary toxicology study of the 6-fluoro-A-85380 showed a relatively low biological effect. Scheffel, U., Horti, A.G., Koren, A.O., Ravert, H.T., Banta, J.P., Finley, P.A., London, E.D. and Dannals, R.F. Nuclear Medicine and Biology, 27, pp. 51-56, 2000.

Kinetic Modeling Study with PET and [C-11]Iomazenil

Quantification of the PET benzodiazepine receptors using the antagonist, [C-11]Iomazenil, at low specific activity was previously described. The current study presents quantitative benzodiazepine receptor binding in human subjects using PET imaging and high specific activity [C-11]Iomazenil. Values for the kinetic rate constants and measures of benzodiazepine receptor binding, including binding potential and volume of distribution, were similar to results obtained with the single photon emission computed tomography (SPECT) radioligand [I-123]Iomazenil, and the prior report with low specific activity [C-11]Iomazenil. Kinetic modeling using the three compartment model with PET and high specific activity [C-11]Iomazenil provides a reliable measure of benzodiazepine receptor binding. Bremner, J.D., Horti, A., Staib, L.H. Zea-Ponce, Y., Soufer, R., Charney, D.S. and Baldwin, R. Synapse, 35, pp. 68-77, 2000.

5-Iodo-A-85380, an Alpha4 Beta2 Subtype-Selective Ligand for Nicotinic Acetylcholine Receptors

In an effort to develop selective radioligands for in vivo imaging of neuronal nAChRs, we synthesized 5-iodo-3-(2(S)-azetidinylmethoxy)pyridine (5-iodo-A-85380) and labeled it with I-125 and I-123. The affinity of 5-iodo-A-85380 for alpha4 beta2 nAChRs in rat and human brain is defined by Kd values of 10 and 12 pM, respectively, similar to that of epibatidine (8 pM). In contrast to epibatidine, however, 5-iodo-A-85380 is more selective in binding to the alpha4 beta2 subtype than to other nAChR subtypes. In rat adrenal glands, 5-iodo-A-85380 binds to nAChRs containing alpha3 and beta4 subunits with 1/1000th the affinity of epibatidine, and exhibits affinities of 1/60th and 1/190th those of epibatidine for alpha7 and muscle-type nAChRs, respectively. Moreover, in contrast to epibatidine and cytisine, 5-iodo-A-85380 exhibits no binding to brain regions in mice homozygous for a deletion mutation of the beta2 subunit of nAChRs. Binding of 5-iodo-A-85380 in rat brain is reversible, and is characterized by high specificity and a slow rate of dissociation of the receptor-ligand complex (t1/2 for dissociation ca. 2 h). These properties, along with other features observed previously in vivo (low toxicity, rapid penetration of the blood-brain barrier, and a high ratio of specific to nonspecific binding), suggest that this compound, labeled with I-125 or I-123 is superior to other radioligands available for in vitro and in vivo studies of alpha4 beta2 nAChRs, respectively. Mukhin, A.G., GŸndisch, D., Horti, A.G., Koren, A.O., Tamagnan, G., Kimes, A.S., Chambers, J., Vaupel, D.B., King, S.L., Picciotto, M.R., Innis, R.B. and London, E.D. Molecular Pharmacology, 57, pp. 642-649, 2000.

Orbitofrontal Cortex and Drug Abuse

The orbitofrontal cortex (OFC) plays a central role in human behavior. Anatomically connected with association areas of all sensory modalities, limbic structures, prefrontal cortical regions that mediate executive function, and subcortical nuclei, this brain region can serve to integrate the physical and emotional attributes of a stimulus-object and to establish a motivational value based on estimation of potential reward. To the extent that addictive disorders reflect a dysregulation of the ability to evaluate potential reward against harm from drug self-administration, it would be anticipated that substance abuse disorders might reflect dysfunction of the OFC. With the application of brain imaging techniques to the study of human substance abuse, evidence has been obtained that activity in the OFC and its connections plays a role in several components of the maladaptive behavior of substance abuse, including expectancy, craving, and impaired decision-making. London, E.D., Ernst, M., Grant, S., Bonson, K., and Weinstein, A. Cerebral Cortex, 10, pp. 334-342, 2000.

Preclinical Pharmacology Section, Behavioral Neuroscience Research Laboratory

Alteration of the Behavioral Response to Nicotine by Caffeine Exposure

Nicotine and caffeine are among the most widely used licit drugs and their consumption is often characterized by concurrent use. Some epidemiological reports suggest that smokers consume caffeine to enhance the effects of nicotine. In a series of recent experiments on rats, the effects of chronic exposure to caffeine in the drinking water on behavioral responses to nicotine or other psychomotor stimulants were assessed. Using a two-lever drug-discrimination procedure in rats, there was a significant increase in the speed of acquisition of the nicotine discrimination at the lowest caffeine concentration, while at the highest concentration there was a tendency for caffeine to retard acquisition of the nicotine discrimination. Interestingly, the dopamine component of the discriminative stimulus effects of nicotine was not present in caffeine-drinking rats at the high concentration, but it appeared to be enhanced at the lowest concentration (as evidenced by shifts to the left in the dose-response curves for generalization to amphetamine and cocaine). In rats exposed to the above oral caffeine regimens, caffeine dose dependently facilitated the increase of dopamine release in the nucleus accumbens shell after injection of nicotine

using in-vivo microdialysis procedures. These studies provide evidence that the behavioral propeties of nicotine and other psychomotor stimulants can be modified by chronic caffeine exposure. The pharmacological basis for any putative interaction between these drugs remains to be established. Goldberg, S.R., Jaszyna, M., Gasior, M., Tanda, G., Poster, 2000. Society for Research on Nicotine and Tobacco Annual Meeting, Arlington, VA, February 18-20, 2000.

Behavioral Neuroscience Section, Behavioral Neuroscience Research Laboratory

Role of Noradrenaline in Stress-Induced Relapse to Heroin Seeking

Using a reinstatement procedure, it has been shown that intermittent footshock stress reliably reinstates extinguished drug-taking behavior in rats. Here we studied the role of noradrenaline (NE), one of the main brain neurotransmitters involved in responses to stress, in reinstatement of heroin seeking. We first determined the effect of clonidine, an alpha-2 adrenergic receptor agonist that decreases NE cell firing and release, on stress-induced reinstatement of heroin seeking. Rats were trained to self-administer heroin (0.1 mg/kg/infusion, IV, three 3-h sessions/day) for 9-10 days. Extinction sessions were given for up to 11 days during which saline was substituted for the drug. Tests for reinstatement were then conducted after exposure to intermittent footshock (5, 15 and 30 min, 0.5 mA). During testing, clonidine was injected systemically (0.01-0.04 mg/kg, IP) or directly into the lateral or fourth ventricles (0.001-0.003 mg/rat). Clonidine (0.001-0.002 mg/site) or its charged analogue, ST-91 (0.0005-0.001 mg/site), was also injected bilaterally into the locus coeruleus (LC), the main noradrenergic cell group in the brain. Clonidine blocked stress-induced reinstatement of drug seeking when injected systemically or into the cerebral ventricles. In contrast, neither clonidine nor ST-91 consistently altered stress-induced reinstatement when injected into the locus coeruleus. We, therefore, studied the effect of lesions of the lateral tegmental NE neurons on stress-induced reinstatement. 6-Hydroxydopamine lesions performed after training for heroin self-administration had no effect on extinction of heroin-taking behavior, but significantly attenuated reinstatement induced by intermittent footshock. These data suggest that (1) clonidine prevents stress-induced relapse to heroin seeking by its action on neurons other than those of the locus coeruleus, and (2) that activation of the lateral tegmental NE neurons contributes to stress-induced reinstatement of heroin seeking. Shaham, Y., Highfield, D., Delfs, J., Leung, S., and Stewart, J. Clonidine Blocks Stress-Induced Reinstatement of Heroin Seeking in Rats: An Effect Independent of the Locus Coeruleus Noradrenergic Neurons. European Journal of Neuroscience, 12, pp. 292-302, 2000.

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

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

National Institute on Drug Abuse

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

May, 2000

Program Activities

New PAs/RFAs

NIDA PAs

On January 19, 2000, NIDA issued a Program Announcement entitled **Neurobiological and Behavioral Research on Nicotine and Tobacco Components (PA-00-45).** The purpose of this PA is to expand the basic science knowledge base on the neurobiological and behavioral effects of nicotine and associated tobacco chemicals, as part of continuing efforts to explain and prevent their use and to develop effective treatments for nicotine addiction. This PA encourages research on any aspect of the effects of nicotine and other tobacco components, using neurobiological, behavioral, or other methods in humans, animals, or in vitro systems, that seeks to explain nicotine use, addiction, or other effects in humans.

On February 10, 2000, NIDA issued a Supplement Announcement entitled **Supplements for the Study of Drug Abuse and HIV/AIDS (PAS-00-058).** With this Supplement Announcement, NIDA plans to continue to develop a strong multidisciplinary research program in response to the complex challenges of drug abuse and HIV/AIDS. The Supplement Program is designed to encourage and enhance interactive, multidisciplinary collaborative projects involving researchers with primary foci both within and outside the area of drug abuse.

On February 10, 2000, NIDA issued a Program Announcement entitled **NIDA Small Grants Program (PAR-00-059).** This PA updates and replaces PAR-97-038, published in the NIH Guide for Contracts and Grants Vol. 26, No. 6, February 21, 1997. The small grants program accepts applications that fall within any of the scientific program interests of NIDA. This includes a wide variety of biomedical, behavioral, clinical, health services, epidemiological, behavioral and prevention research areas relevant to the study of drug abuse or addiction processes.

PAs With Other NIH Components

On January 19, 2000, NIDA, in conjunction with a number of other NIH Institutes, issued a Program Announcement entitled **Biobehavioral Research for Effective Sleep (PA-00-046).** The goal of this PA is to stimulate clinical and applied research on behavioral, psychosocial, and physiological consequences of acute and chronic partial sleep deprivation in either chronically ill or healthy individuals and to develop environmental, clinical management, and other interventions with the potential to reduce sleep disturbances and significantly improve the health of large numbers of people.

On February 22, 2000, NIDA, in conjunction with a number of other NIH Institutes, issued a Program Announcement entitled **Mechanisms in HIV Dementia and Other CNS Diseases (PAS-00-065).** This PA invites investigator-initiated grant proposals to study potential common immunological and inflammatory mechanisms involved in the etiology of HIV-1 associated dementia (HAD) and neurodegenerative and/or autoimmune diseases of the nervous system such as Alzheimer's, Parkinson's disease and multiple sclerosis. One intent of this PA is to encourage basic and clinical scientists who have been working in the previously disparate areas of infectious, autoimmune and neurodegenerative disease to develop multidisciplinary collaborations to search for common factors in the causation

of these and other related diseases.

On March 13, 2000, NIDA, in conjunction with the National Institute of Mental Health (NIMH) issued a Program Announcement entitled **Interventions for Suicidal Youth (PA-00-077).** The purpose of this PA is to support efforts to develop and test interventions that build on risk and protective factors for suicidal behaviors in youth. This PA identifies the need to test the effectiveness of interventions for reducing suicidal behavior from a number of approaches, ranging from broad-based community or school-based prevention efforts, to more targeted approaches that reduce suicidal behavior in youth with identified mental or substance abuse disorders.

On April 6, 2000, NIDA, in conjunction with numerous other NIH Institutes, issued a Program Announcement entitled **Earth-Based Research Relevant to the Space Environment (PA-00-088).** The purpose of this PA is to stimulate ground-based research on basic, applied and clinical biomedical and behavioral problems that are relevant to human space flight or that could use the space environment as a laboratory. Although none of the research supported under this initiative would be conducted is space, it is anticipated that it would form a basis for future competitively reviewed studies which could be conducted on the International Space Station, or other space flight opportunities, by skilled on-board specialists.

RFAs With Other NIH Components

On February 14, 2000, NIDA, in conjunction with several other NIH Institutes, issued an RFA entitled **Adolescent Medicine Trials Network for HIV/AIDS Interventions (HD-00-002).** The purpose of this RFA is to support a research network infrastructure with the capacity for behavioral, microbicidal, prophylactic, therapeutic, and vaccine trials to take full advantage of the results of the detailed observational and laboratory-intensive studies of the Adolescent Medicine HIV/AIDS Research Network.

On February 16, 2000, NIDA, in conjunction with numerous other NIH Institutes, issued an RFA entitled **Mutagenesis Screens/Phenotyping Tools for Zebrafish (HD-00-004).** The purpose of this RFA is to encourage 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, behavior, organ formation, and disease processes. Applications that propose to advance the technologies associated with such phenotyping are also welcome.

Other Program Activities

National Drug Abuse Treatment Clinical Trials Network

Nineteen applications were received for NIDA's re-issuance of the "National Drug Abuse Treatment Clinical Trials Network" RFA on March 16, 2000. This RFA is the second issue with the intention to develop a geographically diverse and encompassing network. Five to six new awards will be made in September 2000 and will double the size of the Clinical Trials Network. In February 2000, a sixth node, New York, was awarded. The PI is Dr. John Rotrosen who is affiliated with New York University.

MATTT Meeting

The Methamphetamine Addiction Treatment Think Tank (MATTT) meeting was held on January 12, 2000 to review the existing science and to brainstorm on treatment strategies. This is the first step following the NIDA Director's initiative to establish a methamphetamine dependence pharmacotherapy program.

Clinical Research Efficacy Screening Trial (CREST-I) Study Completion

Each NIDA/VA Medications Development Research Unit has completed recruiting 60 subjects each in their CREST studies (three medications each and an unmatched placebo). The data are being analyzed and were presented for consultant's review on April 26, 2000.

GBR 12909

The study report from the Phase I (healthy volunteer) study is complete and will be reviewed in May 2000 in planning for the next cocaine interaction study. The study showed 30-40% dopamine transporter occupancy at the 100mg dose level. Based on primate data this may be clinically meaningful in cocaine treatment.

Methylphenidate in Cocaine Dependant Individuals with ADD

This open label feasibility study showed promising effect of methylphenidate in decreasing cocaine use in this co-morbid subgroup. NIDA has awarded a grant for Dr. Frances Levin to further study methylphenidate in this subgroup in a large double blind study.

New Clinical Trials Operations (CTO) Contract Protocol Reviews

Tolcapone, Ondansteron, Modafinil, and Metyrapone were all peer reviewed for studies through the CTO mechanism. All drugs were approved for studies at different phases, and protocols are being submitted to IRBs for review.

Update on Selegiline

In the immediate release study the last few subjects are finishing the study. The protocol for the Selegiline Transdermal System study is in review at the level of the VA Cooperative Studies Program review committee.

Strategic Planning for Medications Development

On April 5, 2000 the Medications Development Program of the Division of Treatment Research and Development presented a comprehensive description of its current mission and focus, capabilities, portfolio development, asset deployment, and future directions and plans to members of the National Advisory Council on Drug Abuse and other invited consultants. Presentations by all branches and programs involved in medications discovery and development occurred throughout the day, with active question and answer sessions. An executive session of the reviewers occurred on April 6, 2000 with the goal of presenting recommendations to NIDA Director, Dr. Alan Leshner.

Desipramine in Cocaine Dependence

Several past studies have suggested that desipramine might potentially be effective in the treatment of cocaine dependence, but the results were equivocal and inconsistent. Therefore, NIDA supported additional studies with desipramine under better- controlled trial conditions and in selected populations of cocaine addicts. These studies have been recently completed. On March 10, 2000, DTR&D/NIDA held a symposium to evaluate the results of these trials. The opinions of independent NIDA consultants were solicited as to whether the data warranted initiation of phase III trials with desipramine as potential therapy for cocaine dependence.

Dr. Thomas Kosten presented results of a trial with desipramine in treating methadone or buprenorphine maintained cocaine addicts. Dr. Edward Nunes presented a trial that tested the efficacy of desipramine in treating depressed cocaine addicts. Dr. Jane Campbell compared the efficacy of desipramine in cocaine- addicted men versus cocaine-addicted women. Dr. Ivan Montoya presented the results of a trial conducted at the Addiction Recent Center. Drs. Frank Gawin and Elena Stark presented the results of their study comparing the effects of desipramine with flupenthixol (a neuroleptic) and a study evaluating the concept of a specific therapeutic window that may be critically determinative for demonstrating efficacy of desipramine. Globally, the results of these studies showed either no effect or marginal effect only in selected populations of patients. However, Dr. Gawin's data suggested that there might be a therapeutic window for desipramine effects (plasma concentrations of 30 - 80 ng/ml), and that concentrations below or above this window are ineffective. Such window could have a theoretical merit. Because desipramine is a pro-dopaminergic and pro-noradrenergic drug, optimal concentrations in blood could potentially compensate for an apparent dopaminergic and noradrenergic deficiency in addicts, while doses above this optimum could mimic cocaine euphorigenic effects and induce craving.

The collective opinion of consultants was that these data do not warrant NIDA's engagement in a phase III trial with desipramine, but that NIDA should further evaluate the concept of a desipramine therapeutic window in a phase II studies, using independent contract investigators. The Clinical Trials Branch, DTR&D is preparing to undertake such a trial with desipramine.

Review of Progress, Potential Anti-Cocaine Vaccine

On March 24, DTR&D/NIDA attended a meeting with Drs. Thomas Kosten, Dr. Marian Fishman and representatives of the British company Cantab (which holds the rights to this particular vaccine), discussing future clinical studies with anti-cocaine antibodies. Dr. Kosten is the Principal Investigator of a Strategic Program for Innovative Research on Cocaine (and other Psychomotor Stimulants) Addiction Pharmacotherapy (SPIRCAP) grant which was awarded to

further research and development of an anti-cocaine vaccine. Dr. Kosten has already completed a Phase I safety study of the vaccine, and he and Dr. Fischman are planning additional studies.

Summer Internship Program/Summer Research Fellowship Program

The NIH Summer Internship Program (for students in high school through graduate school) and the Summer Research Fellowship Program (for medical and dental students) accepted electronic applications from Nov. 15, 1999 to March 1, 2000. NIDA IRP received over 200 applications from students interested in a summer internship experience in one of the intramural labs. Students are currently being selected. It is anticipated that about 15 students will be accepted into the program. Dr. Stephen Heishman coordinates the program and can be contacted at sheish@intra.nida.nih.gov.

Minority Recruitment & Training Program

The Minority Recruitment & Training Program has been accepting applications for its Summer 2000 Program. The NIDA, IRP Minority Recruitment & Training Program (MRTP) is an intramural program that provides training opportunities for students from under-represented groups who are interested in the scientific basis of drug abuse. In this program, students gain basic science and/or clinical laboratory experience, attend student seminars and participate in a summer poster presentation. The goal of this program is to expose students to the realities of research, from experimental design to data analysis, interpretation and presentation. To request an application or to receive additional information, contact: Christie Brannock at cbrann@intra.nida.nih.gov.

NIDA's New and Competing Awards Since January 2000

Abrams, David B. --- Miriam Hospital
Nicotine Dependence: Risk & Recovery Over Generations

Adler, Martin W. --- Temple University School of Medicine
College on Problems of Drug Dependence Annual Meeting

Balster, Robert --- Virginia Commonwealth University
The Behavioral Pharmacology of Phencyclidine

Bardo, Michael T. --- University of Kentucky
Novelty, Dopamine and Response to Amphetamine

Bickel, Warren K. --- University of Vermont
Improving Combined Buprenorphine- Behavioral Treatment

Booth, Robert E. --- University of Colorado
Intervention to Reduce Injection Drug Use

Budney, Alan J. --- University of Vermont State Agricultural College
Clinical Significance of Marijuana Withdrawal

Butelman, Eduardo R. --- Rockefeller University
Effects of Systemically Administered Dynorphins

Butler, Stephen F. --- Innovative Training Systems
A Spanish Adaption of the ASI -- Multimedia Version

Caggiula, Anthony R. --- University of Pittsburgh
Effects of Self-Administered vs Noncontingent Nicotine

Caron, Marc G. --- Duke University Medical Center
Genetic Analysis of Dopaminergic Reward Mechanism

Caudle, Robert M. --- University of Florida
Nociception and NMDA Receptor Phosphorylation

Chen, Hao --- Oceanix Biosciences Corporation
Profiling Data Base for Cocaine Medication

Corrigall, William A. --- ARF Division
Cholinergic and Opiate Mechanisms in Drug Reinforcement

Coscia, Carmine J. --- St Louis University School of Medicine
Opioid Modulation of Astrocyte Proliferation

Coussons-Read, Mary E. --- University Of Colorado
Effects of Morphine on Pulmonary Influenza Infection

Crowley, Thomas J. --- University of Colorado Health Science Center
Substance-Use and Conduct Disorder: Motility, Neuropsychology

Cunningham, Susanna L. --- University of Washington
Addiction: Hijacking the Brain

Dansereau, Donald F. --- Texas Christian University
Cognitive Enhancements for Treatment of Probationers

Deadwyler, Samuel A. --- Wake Forest University School Of Medicine
Long-Term Brain-Behavior Effects of Delta-9-THC

Deren, Sherry --- National Development and Research Institute
Drug Users in New York and Puerto Rico: HIV Risk Behavior

Devi, Lakshmi A. --- New York University School of Medicine
Post-Translational Regulation of Opioid Receptors

Donovan, Stephen J. --- Research Foundation of Mental/Hygiene Inc.
Temper, Mood Swings and Marijuana-A Treatable Syndrome

Drucker, Ernest --- Montefiore Medical Center
Office-Based Methadone Prescribing II

Dubner, Ronald --- University of Maryland, Baltimore
CNS Modulation of Persistent Pain and Spinal Plasticity

Edlin, Brian R. --- University of California, San Francisco
Syringe Exchange Peer Mobilization Intervention

Edlin, Brian R. --- University of California -Department of Family-Community Medicine
Hepatitis C Virus Transmission in Crack Cocaine Smokers

Evans, Suzette M. --- Research Foundation for Mental Hygiene
Vulnerability to Anxiolytic Abuse in Women

Fendrich, Michael --- University of Illinois, Chicago
Feasibility of Biological Measurement in Drug Surveys

Galizio, J. Mark --- University of North Carolina Wilmington
Drugs of Abuse and Complex Behavior

Garvey, Arthur J. --- Harvard School of Dental Medicine
Individualizing Treatment for Addicted Smokers

Gold, Michael S. --- University of Maryland at Baltimore
Inflammation-Induced Plasticity Trigeminal Sensory Neurons

Gudelsky, Gary A. --- University Of Cincinnati
Determinants and Consequences of MDMA Neurotoxicity

Guo, Jie --- University of Washington
Developmental Relations of Substance Use and Risky Sex

Harlan, Richard E. --- Tulane School of Medical
Thalamo-Striatal Mechanisms of Morphine Action

Houghten, Richard A. --- Torrey Pines Institute for Molecular Studies
Identification of Receptor Specific Opioid Ligands

Howell, Leonard L. --- Emory University
Cocaine Use and Monoamine Function in Nonhuman Primates

Johannes, Catherine B. --- New England Research Institute, Inc.
Pharmacology for Chronic Pain: An Interactive CD Rom

Kalivas, Peter W. --- Medical University of South Carolina
Glutamate and Craving for Cocaine

Kandel, Denise B. --- Columbia University
Nicotine Dependence Among U.S. Youths

Kosten, Thomas R. --- Yale University
Comorbidity in Cocaine and Opioid Pharmacotherapy

Kramer, Hal K. --- New York University Medical Center
Mechanisms Involved in Opioid Receptor Down-Regulation

Leonard, Sherry S. --- University of Colorado Health Science Center
Human Brain Nicotinic Receptors and Nicotine Addiction

Liu-Chen, Lee-Yuan --- Temple University School of Medicine
Molecular Characterization of Opioid Receptors

Loeber, Rolf --- Western Psychological Institute/Clinic UPMC
Development of Substance Use in Girls

Lysle, Donald T. --- University of North Carolina at Chapel Hill
Determinants of Opioid/Immune Interactions

Macdonald, J. Christie --- University of Sydney
Opioid Withdrawal Mechanisms in Midbrain Neurons

Magura, Stephen --- National Development and Research Institute Inc.
Service Outreach to Homeless Drug Users

Marcus, Marsha D. --- Western Psychology Institute and Clinic
Bupropion and Weight Control for Smoking Cessation

Mayes, Linda C. --- Yale University School Of Medicine
Arousal **Regulatory Functions in Cocaine-Exposed Children**

McLellan, A. Thomas --- University Of Pennsylvania
Drug Abuse Treatment Evaluation Center

Metherate, Raju S. --- University of California Irvine
Functions of Nicotine Receptors in Sensory Neocortex

Miller, Maureen --- National Development & Research
Networks, Resources and Risk Among Women Drug Users

Miller, Richard J. --- University of Chicago
Chemokine Receptor Function in the Nervous System

Moeller, Frederick G. --- University of Texas at Houston
Serotonin, Impulsivity and Cocaine Dependence Treatment

Morrissey, Joseph P. --- University of North Carolina at Chapel Hill
Impacts of Managed Care on Substance Abuse Service Linkages

Nader, Michael A. --- Wake Forest University School of Medicine
Social Stress: Vulnerability to Cocaine Abuse

Pacula, Rosalie L. --- Rand
Are There Economic Costs of Marijuana Use?

Pasternak, Gavril W. --- Sloan-Kettering Institute/Cancer Research
Pharmacology of Opioid Receptor Subtypes

Pentel, Paul R. --- Hennepin County Medical Center
Immunization to Block the Effects of Nicotine

Pentz, Mary A. --- University of Southern California
The Multi-State Prevention Teleconference Trial

Peoples, Laura L. --- University Of Pennsylvania
Cue-Controlled Drug Taking: Accumbal Neurophysiology

Perkins, Kenneth A. --- Western Psychology Institute and Clinic
Individual Variation in Nicotine Sensitivity in Humans

Pope, Harrison G, Jr. --- McLean Hospital
Cognitive Consequences of Long-Term Marijuana Use

Porco, Travis C. --- San Francisco Department/Public Health
Forecasting HIV Evolution in IDUs and Other Populations

Richter, Kimber --- University of Kansas Medical Center
Addressing Nicotine Addiction in Drug Abuse Patients

Roberts, Laura W. --- University New Mexico, Health Science Center
Stigma and Rurality: Drug Abuse, HIV/STD and Mental Illness

Roerig, Sandra C. --- LSU Medical Center
Spinal Nitric Oxide in Chronic Inflammatory Pain

Rotrosen, John P. --- NYU/NY VA Medical Center
NIDA Clinical Trials Network - NYR East Side Node

Sanders-Bush, Elaine --- Vanderbilt University Medical Center
Hallucinogens and Serotonin Signal Transduction

Schottenfeld, Richard S. --- Connecticut Mental Health Center
Improving Efficacy of Drug Abuse Treatment

Schottenfeld, Richard S. --- Connecticut Mental Health Center
Disulfiram for Cocaine Abuse in Buprenorphine Treatment

Sherman, Steven J. --- Indiana University
The Social Psychology of Group Perception and Smoking

Shi, Wei-Xing --- Yale University
DA-NE Interaction in Drug Abuse

Simone, Donald A. --- University of Minnesota
Cannabinoid Modulation of Hyperalgesia

Smith, James E. --- Wake Forest University School of Medicine
Neurobiology of Speedball Self-Administration

Smith, Sheryl S. --- Research Foundation of SUNY
Steroids and GABA: Physiology of Receptor Subunit Changes

Sopori, Mohan L. --- Lovelace Biomedical and Environmental Research Institute
Mechanism of Cigarette Smoke-Induced Immunosuppression

Stark, Michael J. --- Oregon Health Division
Reducing HIV and Domestic Violence Risk in Women Offenders

Stein, Elliot A. --- Medical College of Wisconsin
Functional MFRI of Human Drug Abuse

Stitzer, Maxine L. --- Society for Research on Nicotine
Society for Research on Nicotine and Tobacco Annual Meeting

Strauss, Shiela M. --- National Development and Research Institute Inc.
Drug Users' Self-Reported HIV Status: Validity/Methods

Tarter, Ralph E. --- Western Psychological Institute and Clinic
Drug Abuse Vulnerability: Mechanisms and Manifestations

Tietz, Elizabeth I. --- Medical College of Ohio
Hippocampal Benzodiazepine Tolerance

Tiffany, Stephen T. --- Purdue University
Laboratory Investigations of Craving for Cigarettes

Trzcinska, Monika M. --- Zebra Pharmaceuticals, Inc.
Behavioral Evaluation of Novel DAT Antagonist

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

Vanyukov, Michael M. --- Western Psychological Institute and Clinic
Substance Abuse and the Dopamine System Genes

Vathy, Ilona --- Albert Einstein College of Medicine
Opiates and CNS Development

Vlahov, David --- New York Academy of Medicine
Hepatitis C in New IDUs: Implications for HIV Prevention

Vogel, Zvi --- Weizmann Institute of Science
Mechanism of Adenylyl Cyclase Superactivation by Opiates

Vorhees, Charles V. --- Children's Hospital Research Foundation
Developmental Effects of Methlenedioxymethamphetamine

Walker, J. Michael --- Brown University
Pain Modulation by Endogenous Cannabinoids

Weinstein, Harel --- Mount Sinai School of Medicine
Hallucinogens and 5-Ht2a Receptors: Mechanisms and Effects

White, Francis J. --- FUHS/Chicago Medical School
Cocaine Addiction and Neuronal Excitability

Wilens, Timothy E. --- Massachusetts General Hospital
Substance Abuse in Juvenile Bipolar Disorder

Wines, James D. Jr. --- Alcohol and Drug Abuse Research Center
Drug-Related Suicidal and/or Homicidal Behavior

Winsauer, Peter J. --- LSU Medical Center
Cocaine Self-Adminstration: Effects on Learning

Winters, Ken C. --- University of Minnesota
Youth Drug Abuse, ADHD, and Related Disruptive Behaviors

Wolf, Marina E. --- FUHS/Chicago Medical School
Glutamate and Psychostimulant-Induced Neuroadaptations

Woods, James H. --- University of Michigan
Narcotic Drug and Opioid Peptide Basic Research Project

Woolverton, William L. --- University of Mississippi Medical Center
Determinants of Drug Choice in Monkeys

Worley, Paul F. --- Johns Hopkins University School of Medicine
Analysis of a Novel Cocaine-Induced IEG

Zacny, James P. --- University of Chicago
Characterizing Psychoactive Effects of Inhalants

Zemlan, Frank P. --- Mind Probes Inc.
Neurotoxin Discovery Platform - Drugs of Abuse

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

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

National Institute on Drug Abuse

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

May, 2000

Extramural Policy and Review Activities

Review Meetings

Chartered committee reviews of grant applications were completed for NIDA-E (Treatment Review Committee), NIDA-F (Health Services Review Committee), NIDA-L (Medications Development Committee), and NIDA-K (Training Committee). Two Special Emphasis Panels (SEPS) were held for conflicts in NIDA-E and NIDA-K, and several other SEPS were established for mechanism-based reviews such as those for centers, program projects, B-Start, and conference grants.

Contract reviews have been completed for the "Analytical Techniques Program," and for "Drug Supply Services Support" activities of the Division of Neurobiology and Basic Research. Contracts reviewed for the Division of Treatment Research and Development include "Medication Discovery Using Rat Models of Relapse to Cocaine Self-administration" and "Screening for Cocaine Pharmacotherapies Using the Rat Self-Administration Test." An SBIR review on prevention research dissemination was also held, and several concept reviews were completed. NIDA's Contracts Review Branch is collaborating with OSPC to complete the solicitations for SBIR concepts.

Extramural Staff Development

Dr. Mark Swieter, Scientific Review Administrator for the Basic Sciences Review Branch, OEA, has provided training on extramural issues to the NIDA Intramural Research Program in order to assist fellows there who will move to an extramural environment. In February 2000, he and Dr. Cindy Miner, OSPC, presented on opportunities for funding under K mechanisms. He presented "Review Issues in Grant Writing" on March 30, 2000.

As NIDA's representative to CSR's Workgroup on SRA Handbook Revisions, Dr. Susan Coyle took a lead role in updating and expanding Chapter 7, "Scientific Peer Review Group (SRG) Meeting Reports." The CSR Workgroup hopes to publish the revised Handbook in the summer of 2000.

The Office of Extramural Affairs Symposium Series continues to provide a forum for staff interchanges on topics related to extramural administration. Dr. Leshner engaged the NIDA staff in a lively question and answer session in January 2000. In February, Dr. Rita Liu, NIDA's Receipt and Referral Officer, and Dr. Teri Levitin, Director, OEA, presented information on NIDA's centers program and procedures for internal processing of applications. In March, Dr. Larry Seitz, a program official from the Division of Epidemiology, Services, and Prevention Research, led a discussion of the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) program. The April meeting used case studies to address complex decisions in extramural administration. The OEA Symposium Series is managed by Dr. William C. Grace, Deputy Director, OEA.

Extramural Outreach

Dr. Khursheed Asghar, Chief, Basic Sciences Review Branch, OEA, presented in April 2000 at the second annual Lonnie Mitchell National Historically Black Colleges and Universities Substance Abuse Conference in Baltimore. His

topic was "The Grants Review Process".

Dr. Teri Levitin, Director, OEA, and Dr. William Grace, Deputy Director, OEA, presented "Research Grants and the Peer Review Process" at the April 14-16, 2000 Conference on Human Development in Memphis, TN. They presented an overview of NIDA's resources and procedures for funding, the policy on inclusion of children in research, information on modular grants, and an introduction to becoming a peer reviewer.

Dr. Mark Swieter, Scientific Review Administrator for the Basic Sciences Review Branch, OEA, presented an overview of review at a grant writing workshop at the Society for Research on Nicotine and Tobacco meeting in Arlington, VA in February 2000; this workshop was organized by Drs. John Hughes, Jay Turkkan, Cathy Backinger, Scott Leischow, Maxine Stitzer, and Janine Pillitteri.

Dr. Swieter presented "Introduction to Research Grants" to the NIDA INVEST and Humphrey fellows meeting organized in February 2000 by Dr. Pat Needle.

At the March 2000 meeting of the Society for Research on Adolescents, Dr. Levitin presented on recent changes in the application, referral, and peer review process for social and behavioral research applications. She also chaired a small group discussion period, "Social and Behavioral Research on Adolescence at NIH: Funding Opportunities".

On May 1, 2000 Dr. William Grace presented an overview of NIDA's extramural program and NIH funding processes to a group of psychology students and staff at Walter Reed Army Medical Center.

Dr. Marina Volkov, Scientific Review Administrator for the Clinical, Epidemiological, and Applied Sciences Review Branch, OEA, presented information regarding extramural review policies and the grant review process at the annual meeting of the Cognitive Neuroscience Society in April 2000.

Publications

Dr. Marina Volkov authored an overview of peer review at NIH for the Early Career Prevention Network newsletter.

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

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

National Institute on Drug Abuse

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

May, 2000

Congressional Affairs

(Prepared April 4, 2000)

Appropriations - FY 2001

February 15, 2000 - NIH Overview Appropriations Hearing before the House

Dr. Ruth Kirschstein, Acting Director, NIH, accompanied by the Institute and Center Directors, appeared before the House Appropriations Subcommittee on Labor, Health and Human Services, and Education to discuss the FY 2001 budget request of $18.8 billion for NIH (a $1 billion or 5.6 percent increase over the FY 2000 level). In her opening remarks, Dr. Kirschstein reminded the Subcommittee of various medical breakthroughs that have arisen from collaborative efforts of the scientific community, detailed important scientific advances supported by NIH and then described principles that NIH uses to establish priorities for spending.

In general, the Subcommittee expressed support for the NIH and its activities. The following are some of the key topics of interest expressed by Members.

- "Buying Good Science" Several members expressed concerns about whether NIH is funding better proposals or dipping down to lower-rated applications. Others questioned whether NIH provided adequate supervision and stewardship.
- Funding Increases/Budget Justifications There were a number of questions concerning how NIH would spend additional increases. Among them was a request to provide the "incremental consequences" of a $500 million, $1 billion, and $1.5 billion funding increase for NIH for FY 2001; and the amounts that NIH spent last year on funding per death on diabetes, cancer, heart disease, HIV/AIDS, and stroke.
- Health Disparities and Funding to Minority-Serving Institutions Rep. Jackson asked Dr. Kirschstein several questions about health disparities. He said that the Office of Research on Minority Health (ORMH) should be a freestanding center and discussed his bill, H.R. 2391, to accomplish this. He asked Dr. Kirschstein how NIH is addressing the components of the bill, which includes a strategic plan for the elimination of health disparities, a "seat at the (IC) table" for the center head, grant making authority for the center, and infrastructure improvements at minority institutions.
- Among other topics of interest to the subcommittee were delayed obligations; under-represented states; and whether the Executive Branch was putting the NIH budget through a "political filter."

February 17, 2000 - NIDA Appropriations Hearing

The FY 2001 non-AIDS budget request for NIDA is $496.3 million, an increase of $27.1 million over the FY 2000 appropriation. Including the estimated allocation for AIDS, total support requested for NIDA is $725.5 million, an increase of $38.1 million over the FY 2000 appropriation. Funds for the NIDA efforts in AIDS research are included within the Office of AIDS Research budget request.

In his opening remarks, NIDA Director, Dr. Alan I. Leshner highlighted several of NIDA's ongoing activities and recent research accomplishments and reported that, as promised last year, the National Drug Abuse Treatment Clinical Trials Network is up and running, with 6 nodes already established and 5 more on the way. Moreover, 35 treatment centers have been established, and more are scheduled to open. The network will help eliminate health disparities because minority populations are disproportionately affected by drug abuse, and the network will help us understand better how to treat these populations. Dr. Leshner also discussed NIDA's "Genetics of Drug Addiction Vulnerability" initiative that is to examine the role of genetics in nicotine, cocaine, and heroin addiction. In addition, Dr. Leshner informed the Subcommittee of NIDA's extremely successful information dissemination efforts, including www.clubdrugs.gov and the publications "Preventing Drug Use Among Children and Adolescents: A Research-Based Guide" and "Principles of Drug Addiction Treatment: A Research-Based Guide."

After his remarks, Dr. Leshner fielded questions from the Subcommittee. In response to Mr. Porter, Dr. Leshner explained current drug use trends, including data suggesting a possible downturn in use. Mr. Hoyer asked about treatment for heroin addiction and alternatives to methadone treatment. Dr. Leshner described how new medications (buprenorphine and buprenorphine/naloxone), soon to be approved by the FDA, are likely to be the first such medications to actually be delivered in physicians' offices.

Ms. Pelosi noted that after prevention, substance abuse treatment is the most effective use of funds and asked what the future holds for substance abuse treatment technology. She also inquired as to the percentage of overall drug use for various abused substances. Dr. Leshner responded that drug abuse treatment would benefit from advances in neuroimaging, molecular genetics, information technology, and new understandings in behavioral research. He also noted that in the U.S. there are some 810,000 heroin users and 3 million cocaine addicts, and that in some areas, the use of methamphetamines exceeds cocaine use.

Mr. Jackson expressed concerns about NIDA's funding for health disparities and said that the U.S. prison population is overrun with addicts, a big percentage of whom are minorities. He said there is no treatment in prisons, leading to a "revolving door" effect increasing recidivism. He also noted that ORMH must have shared that information with NIDA and asked Dr. Leshner's opinion as to what percentage of the budget increase should be used on this problem. Dr. Leshner explained that NIDA was the source of the information on drug abuse treatment in the criminal justice system and, in fact, had provided it to ORMH. He explained that of NIDA's total budget, $101 million is for health disparities. He noted that drug use rates for young people are lower in African-American and Hispanic populations than for whites, but that in their twenties, that changes. He also noted that there is a disproportionate impact of consequences of drug use among different populations. Dr. Leshner emphasized that the relationship between NIDA and ORMH is very strong because the issue of health disparities is not at all new for NIDA, and that NIDA is spending more than other Institutes in this area.

March 30, 2000 - NIH Overview Appropriations Hearing before the Senate

Dr. Kirschstein delivered the opening statement for NIH's fiscal year 2001 budget before the Senate Appropriations Subcommittees on Labor, Health and Human Services, and Education. Mr. Millstein, Deputy Director, NIDA, who was among those who accompanied Dr. Kirschstein, was asked by Senator Harkin to tell him what progress has been made in research on methamphtetmine abuse and possible treatment options. In response, Mr. Millstein provided a brief update on the NIDA methamphetamine initiative. He explained that the Community Epidemiology Work Group (CEWG) has shown increases in use of methamphetamine in rural areas. He told the Senator that NIDA has already found out more about methamphetamine and violence, heart disease, and brain damage; and NIDA currently is conducting clinical trials in five different potential medications for treatment of methamphetamine abuse. NIDA is hopeful that we will soon be able to apply the growing body of knowledge to treatment populations as well as in prevention.

House Government Reform Subcommittee Hearing

March 14, 2000 - *Hearing before the House Government Reform Committee, Subcommittee on Criminal Justice, Drug Policy, and Human Resources, "HHS Drug Treatment Support: Is the Substance Abuse and Mental Health Services Administration (SAMHSA) Optimizing Resources?"*

Dr. Leshner was invited to testify at a hearing that was one in a series focusing on SAMHSA's use of resources for drug abuse treatment. Dr. Leshner discussed areas of research and recent accomplishments for NIDA during his testimony. In particular he stressed the potential for practical applications of scientific findings. He also described how NIDA is taking enormous steps to improve the quality of drug addiction treatment in this country by establishing the National Drug Abuse Treatment Clinical Trials Network. Rep. Mica asked both Dr. Leshner and Dr. Chavez, Administrator, SAMHSA, whether SAMHSA's Knowledge Development and Application (KDA) program overlaps with

NIDA's research mission and whether this function should be transferred to NIDA. Both replied that the agencies' programs involve minimal overlap. Rep. Mica remained interested in the possibility of moving the KDA program to NIDA and promised future hearings about the use of resources at SAMHSA.

International Drug Summit

February 8, 2000 - At the invitation of Rep. John Mica (R-FL), Chairman, House Government Reform Subcommittee on Criminal Justice, Drug Policy, and Human Resources, NIDA Director Dr. Alan Leshner participated in a Demand Reduction Panel of the International Drug Control Summit 2000. The event was conducted in conjunction with the UN International Drug Control Program. The U.S. Congress hosted the annual meeting of the international parliamentarians on February 8 and 9, 2000. The goal was to provide participants from the European Community, Japan, Canada, and the U.S. an opportunity to engage in strategic dialogue on the growing global drug crisis.

Dr. Leshner's statement focused on the role that science can play in confronting the global drug crisis. He shared with the participants some recent science discoveries and described how science has revolutionized our fundamental understanding of drug abuse and addiction. He illustrated his talk by showing a poster graphically illustrating very dramatic, persistent brain changes that last as long as three years after the addict stops taking drugs. He explained that the fact that long-term drug use has changed their brains is in large part why addicted people cannot stop using drugs and is precisely why they need treatment. He also emphasized that drug abuse treatment is as successful as treatment of other chronic, relapsing diseases, such as diabetes, hypertension and asthma. He described how NIDA will improve treatment throughout our country through a variety of activities, but the most dramatic means that will have the greatest impact is the National Drug Abuse Treatment Clinical Trials Network. This network is a vehicle through which we test new treatments in real-life settings with diverse types of patients and through which we can get new science-based treatments into actual use in practice.

Meetings/Briefings

January 5, 2000 - Dr. Elizabeth Robertson, Prevention Research Branch Chief, DESPR, accompanied Dr. Timothy P. Condon, Associate Director, NIDA to brief Ali Dekorsky, and several other members from the staff of Sen. Arlen Spector (R-PA), and staffers from the Senate Judicial Committee. The focus of the discussion was on successful Federal drug prevention programs. Other federal agencies participating in the meeting were SAMHSA, ONDCP, and the Department of Education.

March 2, 2000 - Dr. Frank Vocci, Director, Division of Treatment Research and Development, NIDA, briefed Rep. Kay Granger, R-TX, at her request. Rep. Granger was interested in scientific and medical information relating to detoxification of adolescents from various drugs of abuse and the effects of drugs on the adolescent brain and body, treatment effectiveness, and cost issues. Mary Mayhew, OSPC, accompanied Dr. Vocci.

March 23, 2000 - Dr. Joseph Frascella, Chief Neurobiology Branch, Division of Treatment Research and Development, participated in a briefing by ONDCP for staff to Sen. Bob Graham (D-FL), concerning Ecstasy. Dr. Frascella provided scientific information about the drug's toxicity, effects, and treatment and prevention approaches. He was accompanied by Keith Van Wagner, OSPC.

April 4, 2000 - Dr. Lula Beatty, Chief, Office of Special Populations, NIDA, briefed Earl Smith, staff to Congressman Charles Rangel (D-NY). Mr. Smith requested information about African American adolescents and young adults concerning trends in drug use, medical and other health consequences of drug abuse, and treatment and prevention approaches. Dr. Cindy Miner, Deputy Chief, Science Policy Branch, and Mary Mayhew, OSPC, also participated.

Bills of Interest

H.R. 2130 - Date Rape Prevention Act - On February 8, 2000, President Bill Clinton signed the Hillory J. Farias and Samantha Reid Date-Rape Drug Prohibition Act into law. Sponsored by Fred Upton (R-MI) this bipartisan bill aimed at curbing the abuse of three sedatives that have emerged as so-called "date rape" drugs, was approved August 5, 1999 by the House Commerce Committee. The measure would add GHB (gamma hydroxybutyric acid, also known as Liquid Ecstasy) and GBL (gamma butyrolactone) to Schedule I, and ketamine to Schedule III of the Controlled Substances Act (CSA). The legislation also would require the Justice Department to assist with the development of forensic tests to detect the ingestion of GHB or related substances; direct the HHS Secretary to submit annual reports to Congress estimating the number of sexual assault cases involving date-rape drugs; and require the HHS Secretary to develop a national awareness campaign to educate people about the dangers of date-

rape drugs and the strong CSA criminal penalties that could be imposed on those who abuse them. The bill was passed by the House on October 12, and was amended and passed by the Senate on November 19, 1999.

H.R. 2260 - Pain Reduction Relief Promotion Act of 1999 - Passed in the House on October 27, 1999 by a vote of 271-156. The bill was then sent to the Senate where it was placed before the Judiciary Committee on November 19, 1999. The bill was introduced on June 17, 1999 by Rep. Henry Hyde (R-IL) and is designed to amend the Controlled substances Act to promote pain management and palliative care without permitting assisted suicide and euthanasia.

H.R. 2391- National Center for Research on Domestic Health Disparities Act - This bill, originally introduced by Rep. Jesse Jackson, Jr. (D-IL) on June 30, 1999, has 15 new co-sponsors. Eighty-five Congressmen now endorse H.R. 2391, including nine Republicans, and one Independent. The bill would create at NIH a National Center for Research on Domestic Health Disparities, responsible for coordinating its activities with the national research institutes; developing a comprehensive plan for minority health research at NIH; and ensuring the inclusion of members of minority groups in clinical research. H.R. 2391 also would provide an advisory committee for the Center and authorize $100 million for FY 2000 and such sums as may be necessary for the four succeeding years, in addition to other authorizations of appropriations for the other agencies of the NIH. In addition, the bill would authorize the Center Director to carry out a program to facilitate minority health research by providing for research endowments at centers of excellence. H.R. 2391 was referred to the House Committee on Commerce.

H.R. 2987 - Methamphetamine Anti-Proliferation Act of 1999 - On September 30, 1999, Rep. Chris Cannon (R-UT) introduced this bill to provide for the punishment of methamphetamine laboratory operators, provide additional resources to combat methamphetamine production, trafficking, and abuse in the United States, waive certain requirements for practitioners who dispense schedule IV and V narcotic drugs for maintenance treatment or detoxification treatment, and for other purposes. H.R. 2987 was referred to the House Commerce Health and Environment Subcommittee on October 20, 1999. Further action is still pending.

S. 486 - Methamphetamine Anti-Proliferation Act of 1999 - On August 5, 1999, S. 486 was reported to the Senate with an amendment in the nature of a substitute and without a written report by the Senate Committee on the Judiciary. The bill has been placed on the Senate Legislative Calendar. S. 486 was introduced on February 25, 1999, by Sen. John Ashcroft (R-MO) and, as reported, includes several provisions of interest to NIH. S. 486 would require the head of each department, agency, and establishment of the Federal Government to place anti-drug messages on appropriate Internet websites; require the Secretary, HHS, to submit annually to Congress a report on the problems caused by methamphetamine consumption, and the incidence of and treatment available for methamphetamine abuse; authorize the Center for Substance Abuse Prevention to carry out school-based programs regarding the dangers of abuse and addiction; authorize the Director, NIDA, to expand current and on-going interdisciplinary research and clinical trials with treatment centers of the National Drug Abuse Treatment Clinical Trials Network relating to methamphetamine abuse and addiction; require the Secretary, HHS, in consultation with the Institute of Medicine, to conduct a study on the development of medications for the treatment of addiction to methamphetamine; and waive the requirement for practitioners, who dispense narcotic drugs to individuals for maintenance or detoxification treatment, to annually obtain a separate registration for that purpose. The language of S. 324, The Drug Addiction Treatment Act, was swept into S. 486 during markup. On November 19, 1999, S. 486 passed the Senate and was then referred to the House. On February 4, 2000 the bill was referred to the House Commerce Health & Environment Subcommittee.

S. 976 - The Youth Drug and Mental Health Services Act - On May 6, 1999, Sen. William Frist (R-TN) introduced The Youth Drug and Mental Health Services Act, which authorizes SAMHSA and introduces some new youth-related programs. On July 28, 1999 the bill was ordered reported by the full Senate Health, Education, Labor & Pensions Committee with an amendment in the nature of a substitute. Under the bill SAMHSA would end the practice of requiring states to expend a certain portion of federal funds on specified programs, but states would be required to file more comprehensive progress reports. The bill also would set up grant programs under SAMHSA to support: youth and adolescent substance abuse prevention and treatment initiatives; mental health initiatives designed to combat teen violence; mental health and substance abuse programs for the homeless; emergency funds for mental health and substance abuse needs; and treatment services for juvenile delinquents. The bill did not include a provision that would have permitted blending of substance abuse and mental health block grant funds without accountability for the purpose of servicing individuals diagnosed with co-occurring substance abuse and mental health disorders. Instead the bill restated current law. The Committee amended the bill by adopting a charitable choice provision that permits religious organizations to receive federal funds to provide alcohol and drug treatment and prevention services. On November 3, 1999 the bill was passed by the Senate with Unanimous Consent. S. 976 was then sent to the House and referred to the House Commerce Subcommittee on Health and Environment on November 12.

S. 1507 - Native American Alcohol and Substance Abuse Program Consolidation Act of 1999 - On August 5, 1999, Sen. Ben Nighthorse Campbell (R-CO) introduced S. 1507, the Native American Alcohol and Substance Abuse Program Consolidation Act of 1999. This bill would require the Secretary of the Interior, in cooperation with specified Federal agencies (including NIH), to authorize an Indian tribe to coordinate and consolidate Federally funded alcohol and substance abuse programs. According to Sen. Campbell's introductory remarks, funds available through NIH and NIAAA include several different grant programs for minorities and the prevention of alcohol abuse that could be integrated with other programs into a single program. S. 1507 was referred to the Senate Committee on Indian Affairs and hearings were held on the bill. On March 29, 2000 the Committee on Indian Affairs ordered S. 1507 to be reported with an amendment in the nature of a substitute favorably.

S. 1561 - Date Rape Control Act of 1999 - On August 5, 1999, Sen. Spencer Abraham (R-MI) introduced S. 1561, the Date Rape Control Act of 1999, which would amend the Controlled Substances Act to require the Attorney General to add gamma hydroxybutyric acid to Schedule I and ketamine to Schedule III. It also would require the Secretary of HHS to submit to Congress reports on the number of incidents of the abuse of date-rape drugs that occurred in the most recent one year period, and to develop a plan, in consultation with the Attorney General, for carrying out a national campaign to educate the public on the dangers of date-rape drugs. Finally, the Secretary of HHS would be required to establish an advisory committee to make recommendations to the Secretary on issues related to date rape. After being referred to the Senate Committee on the Judiciary, S. 1561 was incorporated as an amendment into H.R. 2130, a bill that eventually was passed by both the House and Senate.

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

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

National Institute on Drug Abuse

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

May, 2000

International Activities

NIDA and the Hungarian Ministry of Youth and Sports co-sponsored the **U.S./East Europe Regional Meeting on Methamphetamine and Ecstasy Abuse Research,** March 31-April 2, 2000, in Visegrád, Hungary. Drug abuse researchers from nine Eastern European nations, UNDCP, and the United States discussed scientific data about these drugs, sharing knowledge about how they act on the brain, how they produce their behavioral effects, and strategies for prevention and treatment. Speakers at the opening general session included Mr. Ákos Topolánszky, Deputy State Secretary, Hungarian Ministry of Youth and Sport; Dr. Gyula Telegdy, President, Hungarian Academy of Sciences Medical Section; and NIDA Director, Dr. Alan I. Leshner. The meeting was planned by an international organizing committee co-chaired by Dr. Anna Borsodi, Hungarian Academy of Sciences, Szeged; Dr. Tibor Wenger, Semmelweis University, Budapest; and Dr. M. Patricia Needle, NIDA International Program. In addition to Drs. Leshner and Needle, the U.S. delegation included five NIDA grantees: Dr. Marianna K. Baum, University of Miami; Dr. Patricia Case, Harvard University; Dr. Richard Rawson, University of California, Los Angeles; Dr. George A. Ricaurte, The Johns Hopkins University; and Dr. Claire Sterk, Emory University.

NIDA will shortly announce a new program to foster international collaborative research on drug abuse and drug-related consequences. **The Distinguished International Scientist Collaboration Program** supports 1- to 3-month professional visits to the United States by experienced drug abuse researchers from any other country to stimulate development of innovative collaborative research. The Program will support research exchange visits by researchers who meet the following standards: (1) a minimum of 7 years of experience beyond the postdoctoral level in drug abuse research, (2) a scientific record that includes peer-reviewed publications, (3) letters of concurrence from the home and host institutions, and (4) two letters of support.

Dr. Piotr Popik, Poland, and Dr. Kültegin Ögel, Turkey, have been selected as the **2000 WHO/NIDA/CPDD International Traveling Fellows.** The awards will support the researchers' collaborative visits with U.S. scientists and participation in two June 2000 scientific meetings, the NIDA-sponsored *Building International Research on Drug Abuse: Drug Abuse Treatment in the New Millennium,* and the College on Problems of Drug Dependence (CPDD) Annual Scientific Meeting. The competitive International Traveling Fellowships are supported by NIDA, the World Health Organization, and CPDD. Dr. Popik will visit the laboratory of Dr. Herbert H. Kleber, Columbia University College of Physicians and Surgeons, New York. Dr. Ögel will meet with researchers at the University of Michigan who conduct the NIDA-supported Monitoring the Future studies of drug abuse trends among American high school and college students, and will work with NIDA staff to begin planning a joint U.S.-Turkey workshop on drug abuse research that is scheduled for 2001.

The **1999-2000 INVEST Research Fellows visited NIDA in February** to learn how the Institute administers its research programs and meet with Institute staff. On February 24, 2000, Dr. Vaughan Rees, Australia; Dr. Abdel Assi, Egypt; and Dr. Elisa Mengual, Spain, met with scientists at the Intramural Research Program (IRP), including Dr. Barry J. Hoffer, IRP Scientific Director; Drs. Tsung-Ping Su, Mark Walter, and Ronald Herning, Cellular Neurobiology Branch, Molecular Neuropsychiatry Section; Dr. David Gorelick, Clinical Pharmacology and Therapeutics Branch, Clinical Pharmacology Section; and Dr. Jeffrey Witkin, Behavioral Neuroscience Branch. The following day, they met with program officers at NIDA headquarters, including Dr. Rebekka Rasooly, DNBR; Ms. Carol Cowell, DESPR, and Dr. David Thomas, DNBR. They also attended a seminar on the NIH grant application process presented by the following

NIDA staff members: NIDA Associate Director, Dr. Timothy P. Condon; Dr. M. Patricia Needle, International Program; Dr. Mark Swieter, OEA; Dr. David Thomas, DNBR; Dr. Jacques Normand, DESPR; and Dr. Lynda Erinoff, DESPR. The 1999-2000 Hubert H. Humphrey Drug Abuse Research Fellows also participated in the half-day seminar.

Three researchers have been awarded NIDA Hubert H. Humphrey Drug Abuse Research Fellowships for 2000-2001: Dr. Olga Vassioutina, Russia; Dr. Leonid Godlevsky, Ukraine; and Dr. Elvia Amesty de Torres, Venezuela. The three were selected by a review panel that included Dr. Dorynne Czechowicz, DTR&D; Dr. Lynda Erinoff, DESPR; and NIDA grantee Dr. David Metzger, University of Pennsylvania. The competitive, 10-month Fellowships are sponsored by NIDA in cooperation with the U.S. Department of State, the Institute of International Education, and The Johns Hopkins University. Through a combination of academic courses and professional experience, Fellows learn about NIDA-supported drug abuse research and the application of research to the development of prevention programs, treatment protocols, and government policy.

Dr. M. Patricia Needle, International Program, was in Mexico City April 4-7, 2000 to participate in the meeting of the U.S.-Mexico Binational Health Commission working group. Participants from both countries reviewed the joint activities of the two nations in the six Core Group areas: Substance Abuse, Women's Health, Migrant Health, Tobacco Use Prevention, Immunizations, and Aging, to prepare for the May annual meeting of the Binational Commission in Washington, D.C. In addition, Dr. Needle worked with CONADIC (Mexican Council Against Addictions) and the Mexican Institute of Psychiatry staff members HaydŽe Rosovsky and Maria-Elena Medina Mora, respectively, to plan the one-day research symposium that will precede the annual U.S.-Mexico Binational Conference on Demand Reduction, to be held in Phoenix, May 30-June 2, 2000.

On April 18-19, 2000, NIDA's Center on AIDS and other Medical Consequences of Drug Abuse (CAMCODA) hosted the Global Research Network (GRN) on HIV Prevention in Drug-Using Populations Planning Committee Meeting. This working meeting was attended by representatives of ten national and international co-sponsoring organizations to finalize the agenda and activities associated with the third annual meeting of the GRN that will precede the 13th International AIDS Conference in Durban, South Africa, on July 5-7, 2000.

Dr. Peter Delany and Dr. Kathy Etz, DESPR, and Dr. Patricia Needle, Director, International Program, OSPC, presented an overview of NIDA's prevention and services research to a group of 12 Russian drug abuse researchers and service providers on March 27, 2000 during the group's visit to NIDA.

Mr. Nicholas J. Kozel and Dr. Richard Needle, DESPR, participated in a meeting sponsored by the United Nations International Drug Control Programme and hosted by the European Monitoring Centre on Drugs and Drug Addiction in Lisbon, Portugal on January 20-21, 2000 entitled: **Consensus Seeking & Partnership Building to Produce More Comparable and Higher Quality Information on Illicit Drug Consumption Patterns**. The purpose of the meeting was to provide a forum for those involved in drug information gathering networks to discuss ways to (1) coordinate activities more effectively, (2) produce more comparable information, and (3) develop and support networking activities at a regional and global level. The need to discuss these issues, according to UNDCP, was based on the growth in epidemiologic activities around the world and the recognition of the importance of improving information on the nature of drug consumption patterns to inform policy formulation.

Mr. Nicholas J. Kozel, DESPR, participated in the biannual meetings of the **South African Community Epidemiology Network on Drug Use (SACENDU)** held in Cape Town, Port Elizabeth, Pretoria and Durban on March 14-22, 2000. Alcohol continues as the dominant substance of abuse throughout the country, while cannabis and Mandrax (methaqualone) used alone or in combination (white pipe) are the major illicit drugs of abuse, although Mandrax indicators are level or declining. In contrast, cocaine indicators of both availability and abuse are increasing. Heroin and club drugs, such as Ecstasy and LSD also are becoming more prominent. In addition, abuse of over-the-counter and prescription drugs, including Rohypnol, continues to be an issue across sites.

Ms. Moira O'Brien and Dr. Elizabeth Robertson, DESPR, Dr. Dorynne Czechowicz, DTR&D, and Dr. Patricia Needle, International Program, met with Dr. Juan Yaria, Head of the Buenos Aires, Argentina, Provincial Drug Secretariat, on March 10, 2000, at NIDA headquarters to discuss issues of epidemiology, prevention and treatment of drug abuse.

Dr. Barbara H. Herman, DTR&D, was invited to give a presentation and attend the **First Conference on the Neuroscience of Drug Addiction** held by the Istituto Superiore di Sanitˆ, Rome, Italy on Feb 11, 2000. The title of Dr. Herman's presentation was: "A Clinical Focus on Medications Development for Cocaine, Methamphetamine, and Opiate Addiction." Clinical research on selegiline, and dopamine agonists and antagonists for treating cocaine addiction was presented. The importance of developing medications for relapse for all these addictive disorders was emphasized, including the possibility that interoceptive or exteroceptive cues contribute to relapse.

Dr. Herman was also invited to meet with clinicians and investigators in Parma, Italy to discuss glutamatergic antagonists as new medication treatments for addiction disorders, at the invitation of Gilberto Gerra, M.D. at the

Servizio Tossicodipendenze, Az. USL, Distretto "Parma Citta" in Parma, Italy on February 14, 2000. Dr. Herman presented two consecutive one hour presentations on glutamatergic antagonists and addiction disorders, and medications development for cocaine and methamphetamine. These presentations highlighted the research of many NIDA grantees and others who have demonstrated a role for glutamate in the actions of both cocaine and methamphetamine related to addictive processes in animals.

Mr. Nicholas J. Kozel, DESPR, participated in a meeting sponsored by the United Nations International Drug Control Programme and hosted by the European Monitoring Centre on Drugs and Drug Addiction in Lisbon, Portugal on January 20-21, 2000 entitled: **Consensus Seeking & Partnership Building to Produce More Comparable and Higher Quality Information on Illicit Drug Consumption Patterns**. The purpose of the meeting was to provide a forum for those involved in drug information gathering networks to discuss ways to (1) coordinate activities more effectively, (2) produce more comparable information, and (3) develop and support networking activities at a regional and global level. The need to discuss these issues, according to UNDCP, was based on the growth in epidemiologic activities around the world and the recognition of the importance of improving information on the nature of drug consumption patterns to inform policy formulation.

Dr. Monique Ernst presented "Potential Relationship to Pain Syndromes in Lesch Nyhan Disease" at the **Pain Syndromes and Associated Disorders Meeting** Paris, France, February 3-4, 2000.

An AIDS supplement was awarded in the fall of 1999 to Don Des Jarlais, Ph.D. (NIDA Grant #R01 DA03574-16; "Risk Factors for AIDS among Intravenous Drug Users") for a unique and important research study on cross-border HIV prevention for injecting drug users and their sexual partners between Yunnan Province, China and Lao Cai, Vietnam. The Swedish International Development Agency (SIDA) and the Ford Foundation are also contributing financial support to the project. NIDA is supporting the design of the HIV prevention intervention and its evaluation in the project's first (current) year. Work will include site visits to candidate intervention villages and finalization of the intervention and evaluation designs in collaboration with the in-country partners in China and Vietnam. Dr. Des Jarlais will document the process of developing and implementing cross-border and multinational HIV prevention projects and strategies for assisting those seeking to develop cross-border collaborative projects. He and colleagues plan to build on their findings and expand their collaborative research efforts on HIV prevention among drug users. The study represents a new opportunity for research on coordinated programs that might reduce the spread of HIV across national borders in areas of the world in which the HIV epidemic is rapidly increasing among drug injectors.

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

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

National Institute on Drug Abuse

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

May, 2000

Meetings/Conferences

NIDA co-hosted with the Society for Women's Health Research a seminar entitled **Gender Differences in Addiction and Recovery** at the Smithsonian Institution, Washington, DC, on January 29, 2000. NIDA Director, Dr. Alan I. Leshner and experts in the field of addiction research, prevention, and treatment discussed the latest findings about such issues as use of multiple substances, family problems, violence, victimization, HIV/AIDS, and treatment programs. The event drew over 150 individuals from throughout the Washington metropolitan area, representing treatment professionals, women's groups, and members of the general public.

The **Fourth Annual PRISM Awards** were held on March 21, 2000, at the Beverly Hills Hotel in Beverly Hills, CA. NIDA co-sponsored the event with the Entertainment Industries Council and the Robert Wood Johnson Foundation. Other participants included the Centers for Disease Control and Prevention's Office of Smoking and Health. These awards are bestowed yearly to members of the entertainment community who have accurately depicted drug, alcohol and tobacco abuse, and addiction in their productions.

On April 14, 2000 NIDA sponsored **Steroids, Science, and Youth: A Research Roundtable on Anabolic Steroids** to mark the launch of a comprehensive public information initiative by NIDA in response to the increased use of steroids reported by young people throughout the United States. The meeting and a press conference were held in the National Press Club in Washington, DC.

On March 27, 2000, NIDA conducted a workshop entitled **Effects of *in Utero* Exposure to Methamphetamines**. Researchers and clinicians discussed what is known and what research is needed regarding the effects of methamphetamine and closely-related analogs (e.g., MDMA, or "ecstacy") on the developing fetus and child. The meeting was sponsored by the NIDA Child and Adolescent Workgroup, and was chaired by Dr. Jerry Frankenheim. A summary of the meeting will be available on the NIDA website in the very near future, and a report on the meeting is expected in *JAMA.*

NIDA, the Trans-NIH Non-Mammalian Models Committee, and the National Human Genome Research Institute co-sponsored a Genome Focus Group for NIH extramural scientists entitled **DNA Microarray Technology,** held on April 3, 2000 in the Lister Hill Auditorium on the NIH campus. The program focused on the basics of array experiments, with an emphasis on practical issues related to the review and funding of DNA microarray research. Dr. Rebekah S. Rasooly co-chaired the event.

Drs. Minda Lynch, Susan Volman, DNBR, and Joseph Frascella , DTR&D organized a workshop at the Society for Biological Psychiatry at the annual convention in May, 2000. The workshop, entitled **Frontal Cortical Function and Drug Abuse,** featured preclinical and clinical investigators who study frontal cortical functions in motivation, using lesion, neuroimaging, electrophysiological and neuropsychological techniques. A specific role was addressed for frontal cortical circuits, including complex neurotransmitter interactions, in both primary drug reward and incentive motivational processes. Modulatory functions of this prefrontal region in higher order cognition were considered.

A workshop co-sponsored by NIDA and co-chaired by Dr. Rebekah S. Rasooly, entitled **Molecular Genetics of Substance Abuse: Analyzing Complex Traits,** was held at the annual meeting of the Society for Biological Psychiatry in Chicago on May 12, 2000. The purpose of the workshop was to provide insight on how researchers in

human genetics are studying multi-gene traits such as alcohol abuse, drug abuse, and smoking, and traits, such as deafness, that are caused by defects in any one of many different genes.

The Intersection of Stress, Drug Abuse and Development, co-chaired by Drs. Nancy Pilotte and Pushpa Thadani, was held on January 19-20, 2000 at the Neuroscience Center. Proceedings will be published in Psychopharmacology.

A two-day **CTN Steering Committee Meeting** was held December 8-9, 1999, at the Gaithersburg Hilton Hotel. This was the first two- day meeting of the newly formed Steering Committee for the Clinical Trials Network. This meeting focused on procedures for submitting concepts to initiate research activities, development of time lines for clinical trials, and setting up subcommittees to address issues for data management, training, regulatory affairs, quality assurance, publications, and protocol development.

A conference was co-sponsored by the Treatment Workgroup and the CTN entitled **Bridging the Span - Research to Treatment** on January 6, 2000. Dr. Nancy Petry (University of Connecticut Health Center) and Dr. Chris Farentinos (Change Point, Portland, Oregon community treatment provider) shared their experiences from opposing viewpoints on how to bridge the gap from research to treatment.

A **CTN National Steering Committee Meeting** was held on January 18-19, 2000, in Los Angeles, California. Each of the five nodes proposed two protocol concepts for consideration by the entire CTN. The concepts were reviewed, voted upon, and prioritized by numerical score. Three concepts were selected for the first trials within the Network. Lead Investigators were selected to form across-node teams to draft and implement the new protocols.

On January 27, 2000, the first meeting of the **NIDA CTN Oversight Ad Hoc Group** met and was chaired by NIDA Director, Dr. Alan Leshner. The Group reviewed the first three clinical trial concepts selected at the January 18-19, 2000 Steering Committee Meeting in LA. The Oversight Ad Hoc Group unanimously approved the first three concepts: (1) Buprenorphine/NX as a Detoxification Medication for the Treatment of Opiate Abuse and Dependence, (2) Motivational Incentives for Improved Treatment Outcomes, and (3) Motivational Enhancement Treatment to Improve Engagement and Outcome.

A **CTN National Steering Committee Meetin**g was held on March 14-15, 2000, in Baltimore, Maryland. The two-day meeting focused on development of the three approved protocols, common assessment battery, AIDS trial opportunities, third party payers issues, and mission and responsibility for each of the subcommittees. Dr. Alan Leshner gave a Director's Report and updated the CTN members on the proposed future expansion of the Network. Members from the recently awarded New York Node were introduced and assigned committee responsibilities.

On March 16, 2000, the CTN co-sponsored a seminar with NIDA's Treatment Workgroup and Women and Gender Research Group. The meeting was entitled, **Relationship Psychology: A Schema of Women's Addiction**. The speaker was Dr. Nancy Waite-O'Brien, Director of Psychological Services at the Betty Ford Center, Palm Springs, California. The Betty Ford Center is one of the Community Treatment Providers in the Pacific Region Node of the Clinical Trials Network.

A day-long NIDA sponsored Symposium entitled **Treating the Multiple Drug Abuser: Science-Based Approaches** was held on Saturday April 15, 2000 at the American Society of Addiction Medicine Medical-Scientific Conference in Chicago, Illinois. The purpose of this meeting was to provide scientific information on behavioral and pharmacological treatment approaches for the multiple drug abuser. Dr. Frank Vocci, Director, Division of Treatment Research and Development, chaired the NIDA Symposium. Dorynne Czechowicz, M.D., Jack Blaine, M.D., and Betty Tai, Ph.D. organized this meeting.

A NIDA sponsored Workshop entitled **Office-Based Treatment with Buprenorphine** was held on Tuesday April 11, 2000 at the American Methadone Treatment Association Conference in San Francisco. Participants included: Dr. Frank Vocci, Director of DTR&D, NIDA; Robert Walsh, DTR&D, NIDA; Dr. Walter Ling, UCLA; Dr. Paul Casadonte, NYU Medical Center; and Dr. Donald Wesson, Friends Research, CA. The workshop reviewed the pharmacology of buprenorphine; the experience of the NIDA-supported office-based buprenorphine trials, and provided science-based clinical information that physicians will need to know to use buprenorphine effectively. Dr. Dorynne Czechowicz represented NIDA on the AMTA planning Committee and also organized the NIDA buprenorphine workshop.

NIDA co-sponsored a National Conference on **Drug Abuse Treatment in the Correctional System** with the National Development & Research Institute, Inc. (NDRI) in Bethesda, MD on March 15-17, 2000. Mr. Richard Millstein, Deputy Director, NIDA, and Dr. Fred Streit, NDRI welcomed the 140 participants and NIDA Director, Dr. Alan Leshner provided the keynote address. Drs. Peter Delany, DESPR, Cora Lee Wetherington, DNBR, Henry L. Francis, CAMCODA, and Bennett Fletcher, DESPR, and Drs. John Baumann, Harry Wexler, and Stan Sacks from NDRI acted as facilitators on the 7 panels with 42 speakers from the fields of corrections and treatment. Dr. Peter Delany,

DESPR, and Dr. John Baumann, NDRI, organized and co-chaired the meeting.

Dr. Kesinee Nimit, Scientific Review Administrator for the Clinical, Epidemilogical, and Applied Sciences Review Branch, OEA, organized a seminar in conjunction with the NIDA Treatment Research Subcommittee ("NIDA-E") in Washington, DC on February 29, 2000. Marilyn Huestis, Ph.D., Acting Chief of Chemistry and Drug Metabolism Section, Clinical Pharmacology and Therapeutics Research Branch, Intramural Research Program, NIDA, spoke on "Analysis of Drugs in Alternative Matrices; New Drug Monitoring Techniques." Lisa Onken, Ph.D., Associate Director for Behavioral Treatment Research, and Chief, Behavioral Treatment Development Branch, Division of Treatment Research and Development, NIDA, addressed "NIDA Behavioral Therapy Development Program." The seminar was well attended by the Treatment Research Subcommittee members and NIDA staff.

Dr. Steven Grant, DTR&D, organized and chaired a symposium entitled **Cognitive Neuroscience & Drug Addiction: Primed for Interaction?** at the annual meeting of the Cognitive Neuroscience Society in San Francisco, California, April 8-12, 2000. The participants were: Trevor W. Robbins from the University of Cambridge, who spoke on "From Experimental Animals to Human Drug Abusers in the Neuropsychopharmacology of Addiction"; Hans Breiter, MGH-NRM Center Harvard Medical School, "Using fMRI to Dissect Human Reward Function into Its Cognitive Subprocesses"; Jonathan D. Cohen, Princeton University, "The Role of Prefrontal Cortex, Anterior Cingulate and Locus Coeruleus in Cognitive Control and the Regulation of Behavior"; and Janet A. Metcalfe, Columbia University, "Hot/Cool Framework of Cognition and Emotion: Application to Drug Addiction."

Dr. Joseph Frascella co-organized a workshop with Dr. Linda Porrino on **Imaging in the New Millennium** at the Spring Brain Conference in Sedona, Arizona, March 10, 2000.

Dr. Kathy Etz, PRB, DESPR, planned and facilitated a meeting on **"Drug Abuse Prevention Research in the Native American Context"** co-sponsored by NIDA and the IHS held on April 6-7, 2000 in Washington, D.C. NIDA Deputy Director, Richard A. Millstein presented opening remarks and Dr. Elizabeth Robertson, PRB, DESPR, presented on prevention research at NIDA. Rick Harrison, OEA, also participated in the meeting.

The Community Research Branch, DESPR, sponsored a talk by William Vega, Ph.D., Professor, Department of Psychiatry, Robert Wood Johnson Medical School. Dr. Vega's talk entitled **A Profile of Crime, Violence, and Drug Use Among Mexican Immigrants** was held at the Neuroscience Center on March 15, 2000. Mr. Richard A. Millstein, NIDA Deputy Director and Acting Director, Division of Epidemiology, Services and Prevention Research presented opening remarks.

On March 15, 2000, NIDA's Prevention Research Branch, DESPR, sponsored a presentation by Dr. Kris Bosworth, University if Arizona, on the topic of Protective Schools.

Mr. Richard A. Millstein, Deputy Director, NIDA, testified before the Labor, Health and Human Services, Education and Related Agencies Subcommittee of the Senate Appropriations Committee on the President's Budget Request for NIDA, FY 2001, Washington, D.C., March 30, 2000.

Mr. Richard A. Millstein was a panelist at the Town Meeting of the Lonnie Mitchell HBCU Conference on Substance Abuse, Baltimore, Maryland, April 6, 2000.

Mr. Richard A. Millstein hosted ONDCP Director General Barry R. McCaffrey at a presentation of recent research findings by the NIDA Intramural Research Program and NIDA-funded scientists at the Johns Hopkins University Bayview Medical Center, Baltimore, Maryland, April 7, 2000.

Mr. Richard A. Millstein presented an overview of NIDA research programs and priorities to the Okura Mental Health Leadership Fellows, Rockville, Maryland, April 17, 2000.

Mr. Richard A. Millstein presented opening remarks at the Second Annual Meeting of NIDA-Funded Communications Researchers, Rockville, Maryland, April 24, 2000.

Mr. Richard A. Millstein presented opening remarks at the Second Annual Meeting of the NIDA Communications Researchers, ONDCP Anti-Drug Media Campaign staff, and Campaign Evaluators, Rockville, Maryland, April 25, 2000.

Mr. Richard A. Millstein presented on next steps and new directions to the DATOS researchers, Ft. Worth, Texas, May 8-9, 2000.

Dr. Timothy P. Condon, Associate Director, NIDA, provided an overview of brain research as it applies to recovery and implications for clinical practices leading to recovery at "An Open Forum on Behavioral Health Care in the Year 2000 and Beyond, Innovative Clinical Practices Leading to Recovery: A Summary of Research from the Decade of the Brain with Implications for Improved Treatment" on February 10, 2000. Dr. Condon's presentation, "Understanding Drug

Abuse and Addiction: Implications for Treatment and Prevention", to the L2000+ Leadership Development Academy for Emerging Leaders in Mental Health and Addiction Services Agencies at the John Glenn Institute for Public Service and Public Policy in Columbus, Ohio was followed by a discussion of the role of future behavior health care leadership in light of information on the brain and recovery.

Dr. Timothy P. Condon made a keynote presentation, "Focus on Methamphetamine", and participated as a panelist at a conference in Springfield, Missouri entitled "On Thin Ice: Confronting Methamphetamine in the Ozarks" on April 13, 2000.

Dr. Timothy P. Condon made a presentation entitled "Club Drugs in the LGBT Community" on April 29, 2000 at the "The March for Equality - Making Strides in LGBT Health and Policy" at George Washington University in Washington, DC.

On May 11, 2000, Dr. Timothy P. Condon gave a keynote presentation, "Addiction as a Brain Disease: Implications for Research and Practice", at a symposium entitled "The Many Masks of Depression" in Providence, Rhode Island sponsored by Harbor Healthcare Management and Blue Cross & Blue Shield of Rhode Island.

On February 4, 2000, Dr. Timothy P. Condon, Associate Director, NIDA and Dr. Jack B. Stein, Deputy Director, OSPC, conducted a NIDA Briefing for International Students in Action in Atlanta, GA on "Understanding Drug Abuse and Addiction: What the Research Reveals". Sessions hosted by Drs. Condon and Stein included: "Drugs and the Brain; Principles of Drug Abuse Prevention and Drug Addiction Treatment"; "Risks, Raves, and Research: Update on Club Drugs"; and "Putting the Research to Use: Overview of NIDA Resources and How to Access Them".

Dr. Timothy P. Condon, Associate Director, NIDA and Dr. Jack B. Stein, Deputy Director, OSPC conducted two repeated workshops on April 6 and 7, 2000 titled, "Raves, Risks, and Research: Update on Club Drugs" at the Parents Resource Institute for Drug Education (PRIDE) Youth Programs annual conference in Louisville, Kentucky, April 5-8, 2000.

Dr. Jack Stein, Deputy Director, OSPC, presented a workshop on "Understanding Drug Addiction" at the Commonwealth Prevention Alliance 2000 conference in State College, Pennsylvania on April 13, 2000.

Dr. Cindy Miner, Deputy Chief, Science Policy Branch, OSPC, attended the American Academy of Child and Adolescent Psychiatry's Annual K12 Retreat from March 2 - 5, 2000 to view the progress of the Academy's research training program and discuss NIDA's research training program.

Dr. Cindy Miner, OSPC, attended the Association of Neuroscience Departments and Programs annual meeting held on May 8, 2000 at Georgetown University, Washington, D.C. to discuss research training initiatives at NIDA.

Dr. Cindy Miner, OSPC, attended the American Psychiatric Association Committee on Research Training's fifth annual "Research Colloquium for Junior Investigators", May 14, 2000 at the University of Illinois in Chicago. The colloquium was designed to connect young investigators with their peers and with senior investigators to discuss research opportunities.

Dr. Cindy Miner, OSPC, was invited to represent NIDA at "NIAAA/NIDA/NIMH Grants and Career Development" at the 2000 American Psychiatric Association Annual Meeting held in Chicago, May 17, 2000. Dr. Miner discussed NIDA's research training program and funding opportunities in drug abuse and addiction research.

In recognition of Brain Awareness week, Dr. Cathrine Sasek, Dr. Cindy Miner, and Monica Jones, OSPC, participated in a two day event for 5-8th graders at the National Museum of Health and Medicine, held April 15-16, 2000. The students rotated through several stations in the museum where they had the opportunity to participate in activities and ask questions about a variety of brain related research areas. NIDA's station focused on how drugs act in the brain. In addition, Dr. Sasek conducted a plenary session entitled "Your Brain and Drugs."

On January 13, 2000, Dr. Lula Beatty, Chief, Special Populations Office, presented a session on opportunities in drug abuse research to participants in NIH's Extramural Associates program in Bethesda, Maryland.

On February 3, 2000, Dr. Lula Beatty presented grants development sessions for faculty from the Atlanta University center schools at Spelman College in Atlanta, GA.

On March 1-2, 2000, Dr. Lula Beatty was a representative of NIDA at the HHS Diversity Council conference in Washington, DC.

On March 9, 2000, Dr. Lula Beatty attended the advisory committee meeting of the Recruited Scientist Program at North Carolina Central University, one of the HBCUs in the HBCU cooperative agreement program jointly supported

by NIDA and ORMH.

On March 23-26, 2000, Dr. Lula Beatty attended the governance committee meetings of the American Psychological Association in Chantilly, VA. She participated in the Committee on Women in Psychology, a committee of the Public Interest Directorate.

On March 28, 2000, Dr. Lula Beatty participated in a CSAT sponsored meeting in Bethesda, Maryland to discuss their efforts to examine the long-term effects of treatment with adolescents.

On April 6-7, 2000 Dr. Lula Beatty attended the Lonnie E. Mitchell National Historically Black Colleges and Universities Substance Abuse Conference in Baltimore, MD. She moderated a session on epidemiological factors in drug abuse. The meeting was co-sponsored by NIDA.

Dr. Peter Hartsock, CAMCODA, organized and chaired a special conference at the Cosmos Club, Washington, D.C. on January 14, 2000 dealing with cutting edge assessment of the public health impact and cost effectiveness of AIDS intervention measures. Presenters consisted of scientists from Yale, Stanford, and UCSF who are working under a consortium headed by the Societal Institute of Mathematical Sciences (SIMS) and which is funded by NIDA. The object of the SIMS project has been to develop instruments for assessing the impact of AIDS intervention measures--from behavioral interventions through vaccines.

Dr. Peter Hartsock, CAMCODA, represented the Department at the annual Seniors Meeting of the Federal Interagency Arctic Research Policy Committee (IARPC), March 13, 2000, Washington, D.C. The meeting was convened by National Science Foundation Director and IARPC Chairperson, Dr. Rita R. Colwell, to approve the Federal Arctic Research Plan for submission to the White House and to plan new Arctic research initiatives. Dr. Hartsock's recommendation for a circumpolar emerging and re-emerging infectious diseases (EREIDs) monitoring system was adopted for further development. The groundwork for such a network has already been started by collaborative U.S.-Russian EREIDs research and monitoring initiated by Dr. Hartsock, colleagues at NIAID, and Russian colleagues, and taps into the already existing "anti-plague monitoring station system" which spans the former Soviet Union.

Dr. Frank Vocci, Director, DTR&D, presented at the 32nd. Annual Meeting of the Society for Adolescent Medicine, March 22-26, 2000. Dr. Vocci's address summarized recent findings on the neurobiology of addiction, new treatment efforts, and findings regarding adolescents and vulnerability to drug abuse.

On April 13, 2000, Dr. Frank Vocci, Director, DTR&D attended the Annual Meeting of the Society for Addiction Medicine in Chicago, Illinois. Dr. Vocci presented recent findings from NIDA sponsored research on "The Neurobiology of Addiction: Implications for Treatment" at the opening plenary session of the meeting.

On April 28, 2000 Dr. Frank Vocci, Director, DTR&D participated in a meeting at Elan-DSI to discuss the topic of naltrexone.

Dr. Elizabeth Rahdert and Dr. Dorynne Czechowicz, Behavioral Treatment Development Branch, DTR&D, participated in the NIDA Educational Display that was held at the Society of Adolescent Medicine Conference on March 24, 2000 at the Marriott Crystal Gateway Hotel, Arlington, VA.

On February 29, 2000, Dr. Lisa Onken, DTR&D, gave a presentation to the NIDA-E Treatment Research Subcommittee on NIDA's behavioral treatment research program.

Dr. Steven Grant, DTR&D, gave a seminar entitled "Imaging the Somatic-Marker Hypothesis in Addiction" at the Department of Neurology, University of Iowa, Iowa City, on March 10, 2000.

Dr. Steven Grant, DTR&D, gave an invited lecture on "Introduction to Brain Imaging" to first year medical students in a medical neuroscience course at the Finch Medical College of Chicago, North Chicago, Illinois, on March 22, 2000.

Dr. Steven Grant, DTR&D, gave a research seminar entitled "Cognitive Approaches to Addiction" at the Department of Neuroscience, Finch Medical College of Chicago, North Chicago, Illinois, on March 23, 2000. Drs. Joseph Frascella and Steven Grant, both of DTR&D, represented NIDA at the 8th Annual Meeting of the International Society for Magnetic Resonance in Medicine in Denver, Colorado, April 2-7, 2000. Also at this meeting, Dr. Frascella co-organized (along with Drs. Linda Chang and David Place) and participated in a workshop entitled "Strategies for Successful Clinical Research: FDA Approval, Grantsmanship, Funding Opportunities, and the Grants Process".

Drs. Steven Grant, DTR&D, Tony Simon, CAMCODA, David Shurtleff, DNBR, and Marina Volkov, OEA, represented NIDA at the annual meeting of the Cognitive Neuroscience Society in San Francisco, California, April 8-12, 2000. NIDA remains the only NIH institute to have an exhibitor's booth at this meeting.

Drs. Steven Grant, DTR&D, and Marina Volkov, OEA, conducted a NIDA-sponsored Grant-Writing Workshop at the annual meeting of the Cognitive Neuroscience Society in San Francisco, California, April 8-12, 2000. This was the first grant-writing workshop ever held at this meeting.

Dr. Steven Grant, DTR&D, represented NIDA at the inaugural meeting of the Motivational Network at Seabrook, South Carolina on April 15-17, 2000.

Dr. Joseph Frascella was invited to deliver a colloquium address entitled "Anatomy of Grant Writing: Dissecting the Process" at the Department of Psychology, Brown University, Providence, Rhode Island, February 16, 2000.

Dr. Joseph Frascella gave a presentation sponsored by the Western North Carolina Society for Neuroscience entitled "On Obtaining NIH Funding: Dissecting the Process," at the Wake Forest University School of Medicine on April 11, 2000.

Dr. Joseph Frascella gave an invited address at Marist College in Poughkeepsie, New York on strategies for obtaining NIH funding at a small liberal arts college, April 28, 2000.

Dr. Joseph Frascella was a science judge in the Seventh Annual Undergraduate and Graduate Science Research Symposium hosted by Morgan State University, MBRS RISE Program and The School of Computer, Mathematical and Natural Sciences, Baltimore, Maryland on April 20, 2000.

Dr. Elizabeth Robertson, DESPR, was appointed the NIDA representative to the National Prevention Coalition. The Coalition met on February 7, 2000 at the headquarters of the National Mental Health Association in Alexandria, VA.

Dr. Elizabeth Robertson, DESPR, participated in the Executive Seminar of the Aspen Institute held at the Federal Executive Institute in Charlottesville, VA from February 28 to March 3, 2000.

On April 10, 2000, Dr. Elizabeth Robertson, DESPR, presented at the Carolina Consortium on Human Development, the University of North Carolina at Chapel Hill on Developing a National Research Agenda: The Role of the NIH.

Dr. Kathy Etz, PRB, DESPR, represented NIDA at tribal research meetings at the Mille Lacs and Bois Forte bands of Ojibwe in Northern Minnesota on March 7 and 8, 2000.

Dr. Kathy Etz, PRB, DESPR, participated in a session on new program developments at NIH at the Society for Research on Adolescence, Chicago, IL, March 31, 2000.

Dr. Kathy Etz, PRB, DESPR, presented a paper on recommendations for Drug Abuse Prevention Research at the Indian Health Service Research Conference in Albuquerque, New Mexico on April 25, 2000.

Dr. James Colliver, DESPR, gave a presentation on the Patterns and Extent of Abuse of Smokable Substances at the American Chemical Society forum on Chemistry, Pharmacology, and Toxicology of Tobacco, Marijuana, and Related Substances: Pyrolysis Products, cosponsored by NIDA.

Dr. Leslie Cooper represented NIDA at the 2000 National Conference on African -Americans and AIDS on February 24 -25, 2000 in Washington, DC.

Dr. Leslie Cooper participated in the Department of Health and Human Services Diversity Conference in Washington, DC on March 1-2, 2000.

Ms. Susan David, DESPR, participated in a Symposium at Claremont Graduate University on February 26, 2000 entitled "Mass Media and Drug Prevention: Classic and Contemporary Theories and Research," which featured five NIDA prevention and communications research grantees, and will result in a book published by Erlbaum next year.

Beverly Jackson, OSPC, Dr. William Bukoski, DESPR, and, Dr. Elizabeth Robertson, DESPR, served as NIDA's representatives at a recent progress review meeting of the DHHS Secretary's Initiative on Youth Substance Abuse Prevention (YSAPI). The meeting was held with the Deputy Secretary, DHHS on February 10, 2000, in the Hubert Humphrey Building. The progress review included an update of NIDA's drug abuse prevention research initiatives and discussion of NIDA's media outreach program to the entertainment industry to include the PRISM awards.

Dr. William Bukoski, DESPR, serves as NIDA's representative to the Interagency Committee on School Health. The most recent meeting of the committee was held on February 15, 2000, at the Hubert Humphrey Building, Washington, D.C. The co-chairs of the committee are David Satcher, M.D., Ph.D., Surgeon General of the United States; Shirley Watkins, M.S., Under Secretary, Food, Nutrition and Consumer Services, U.S. Department of Agriculture; and Lloyd Kolbe, Ph.D., Director, Division of Adolescent and School Health, CDCP. Lead agencies of the Interagency Committee on School Health include the U.S. Department of Education, the U.S. Department of Health

and Human Services, and the U.S. Department of Agriculture in their collective efforts to increase the effectiveness of Federal efforts to improve the education and health of school-aged children, pre-kindergarten through the 12th grade.

On February 7, 2000, Dr. William Bukoski, DESPR, represented NIDA at a meeting of "The Exchange," a public-private sector group that discusses topics related to substance abuse prevention and treatment. The Exchange is affiliated with Join Together, a project funded by the Robert Wood Johnson Foundation, and the Center for Substance Abuse Prevention, SAMHSA.

Dr. William J. Bukoski, DESPR, represented NIDA at the January 20, 2000, meeting of the Evaluation Guidance Committee for CSAP's National Cross-site Evaluation of the State Incentive Grant Program (SIG). The purpose of the meeting was to provide an update of the SIG program and to discuss the status of the planning process for the cross-site evaluation of this national program.

On March 29, 2000, Dr. William Bukoski, DESPR, served as a review judge to assess school applications competing for the Washington Regional Alcohol Program's (WRAP) year 2000 GEICO Student Organization Awards for excellence in promoting zero tolerance and alcohol and drug-free lifestyles.

Drs. Peter Delany and Jerry Flanzer, SRB, DESPR, participated in a technical assistance workshop on January 28, 2000, on grantmanship for doctoral students and new faculty. This day-long workshop provided new investigators with information on the fundamentals of grant writing and review. This is the 3rd workshop for new investigators that has been held under the leadership of NIDA and the Institute for Advancement in Social Work Research.

Drs. Peter Delany and Jerry Flanzer, SRB, DESPR, presented on funding opportunities and the new Social Work Research Development Program to 85 symposium participants at the Society for Social Work Research on January 29, 2000 in Charleston, SC.

Drs. Peter Delany and Jerry Flanzer, SRB, DESPR, presented on funding opportunities and the new Social Work Research Development Program to 40 workshop participants at the Council on Social Work Education on February 28, 2000 in New York, NY.

Dr. Bennett Fletcher, SRB, DESPR, presented on the DATOS study at the annual meeting of State Needs Assessment Planners, sponsored by SAMHSA/CSAT.

Dr. Bennett Fletcher, SRB, DESPR, presented on NIDA's health services research program at a meeting on Practitioner Research Networks, sponsored by SAMHSA/CSAT.

On April 7, 2000, Dr. Tsung-Ping Su of the IRP, NIDA, was invited to present as the plenary speaker in an International Symposium at Denver, Colorado. The symposium was entitled: "Behavioral Effects of Selective Sigma-1 Receptor Ligands: New Therapeutic Opportunities" and was sponsored by the International Behavioral Neuroscience Society, the French INSERM, Parke/Davis of US, and Taisho Pharmaceuticals of Japan. Dr. Su presented a talk entitled "Calcium Signaling Via Sigma-1 Receptors: New Mechanism for Cognitive Enhancement". The symposium included scientists from the U.S., Japan, France, and Canada.

Dr. Jean Lud Cadet presented "Methamphetamine-induced Apoptosis: Cellular and Molecular Mechanisms" at the Brookhaven National Laboratory in New York, February 2000.

Dr. Jean Lud Cadet presented "Dose-dependent Cognitive Effects of Cocaine" at Xavier College in New Orleans, LA, February 2000.

Dr. Jean Lud Cadet presented "Critical Substance Abuse Research Issues for the New Millennium" at Howard University, March 28, 2000.

Dr. Roy Wise, NIDA, IRP, presented a paper, "Dopamine and Reward: Simple as That?" at an invitational workshop on The Neural Mechanisms of Addiction organized by the Juan March Foundation in Madrid on December 13-15, 1999. Dr. Wise was invited to write the meeting summary to appear in the April issue of Neuron.

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

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

See our **Contact Information**. .

National Institute on Drug Abuse

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

May, 2000

Media and Education Activities

Awards

NIDA's web site received the **Web Feet Seal of Approval** and will appear in *Web Feet: The Internet Traveler's Desk Reference.* Web Feet is the premier subject guide to the best web sites for students, researchers, and the general public and is the first comprehensive web guide that is interactive and updated monthly.

Press Releases

December 29, 1999 - **NIDA Announces Second-Round Competition for National Drug Abuse Treatment Clinical Trials Network.** NIDA announced the release of the second request for grant applications for participation in the National Drug Abuse Clinical Trials Network. Launched in January 1999, the Clinical Trials Network provides a critically needed research infrastructure that will test and disseminate science-based addiction treatments in real-life settings throughout the country.

January 7, 2000 - **Addiction and the Feminine Mystique: National Institute on Drug Abuse Hosts Seminar about Gender Differences in Addiction and Recovery.** This Save-the-Date provided information about a January 29, 2000, seminar at the Smithsonian Institution, Washington, DC, co-sponsored with the Society for Women's Health Research, where experts in the field of addiction research, prevention, and treatment discussed the latest findings and provided insight into related issues such as abuse of multiple substances, family problems, violence, victimization, and HIV/AIDS. The event drew over 150 individuals from throughout the Washington metropolitan area, representing treatment professionals, women's groups, and members of the general public. As a result of this event, coverage appeared in *AMA News.*

February 20, 2000 - **Nicotine Craving and Heavy Smoking May Contribute to Increased Use of Cocaine and Heroin.** Researchers supported by NIDA found that craving for nicotine appears to be linked to increased craving for illicit drugs among drug abusers who also smoke tobacco. In addition, scientists said, patients in drug treatment programs may be less likely to successfully stay off drugs if they are cigarette smokers. These were the findings from two studies published in the February issue of *Experimental and Clinical Psychopharmacology.* As a result of this news release, articles appeared in *Reuters Health, M2 Presswire,* and *Join Together Online,* as well as on *ABC News.*

March 1, 2000 - **NIDA Survey Finds Practitioners Would Treat Addicted Patients with Office Based Methadone.** A NIDA-supported survey of primary care physicians, physician assistants, and nurse practitioners working in New York City found that two-thirds of the clinicians are willing to provide methadone maintenance treatment in their offices to opiate addicted patients. Seventy-one clinicians at 11 sites in Manhattan and the Bronx took part in the survey, which was conducted by researchers at the Albert Einstein College of Medicine and Montefiore Medical Center in Bronx, NY. The full report appeared in the *Journal of Urban Health: Bulletin of the New York Academy of Medicine.* As a result of this news release, articles appeared in *M2 Presswire* and *Join Together Online,* as well as on *Fox News.*

March 7, 2000 - **New Study Underscores Effectiveness of Methadone Maintenance as Treatment for Heroin**

Addiction. New research clearly showed that longer-term methadone maintenance therapy combined with some psychosocial counseling is a far more effective treatment for heroin addiction than is simply the temporary use of methadone to detoxify patients and reduce drug craving, even when the detoxification is coupled with much more intensive psychosocial therapy. The study was published in the *Journal of the American Medical Association* by a research team from the University of California, San Francisco, and the San Francisco Veteran Affairs Medical Center. NIDA provided funding for the research. As a result of this news release, articles appeared in *salon.com, Associated Press & Local Wire, Join Together Online, Reuters Health, PSLGroup.com, Agence France Presse, M2 Presswire, USA Today Health T,* as well as on *Fox News.*

March 10, 2000 - **Students Learn What's Really on Their Minds: Brain Awareness Week Activities to be Held March 15-16.** Some local students were offered the chance to touch and feel and learn all about the human brain during a special program co-sponsored by the National Institutes of Health and the Dana Alliance for Brain Initiatives. The program took place at the National Museum of Health and Medicine, Walter Reed Army Medical Center, Washington, DC.

March 21, 2000 - **Oscar Nominee, "The Insider," Receives Top Honors at PRISM AwardsTM 2000.** The National Institute on Drug Abuse, in partnership with The Entertainment Industries Council, Inc. (EIC), and The Robert Wood Johnson Foundation, awarded the PRISM Awards 2000 for accurate depiction of drug, alcohol, and tobacco use and addiction in television, feature film, and comic book entertainment, as well as community service efforts and individual volunteerism. Coverage of the awards appeared in *USA Today, Daily Variety, The Hollywood Reporter, The Los Angeles Times, USA Today online, US magazine,* and local LA network affiliates.

March 27, 2000 - **Methamphetamine Abuse Linked to Long-Term Damage to Brain Cells.** New research shows that those who use methamphetamine risk long-term damage to their brain cells similar to that caused by strokes or Alzheimer's disease. In an article published in the March 28 issue of *Neurology,* scientists at the Harbor-UCLA Medical Center in Torrance, CA, used magnetic resonance spectroscopy to take measurements of three parts of the brains of 26 participants who had used methamphetamine and then compared them with measurements of the same regions in the brains of 24 people who had no history of drug abuse. As a result of this news release, articles have appeared in *Reuters Health, Eurekalert!, Press Association Newsfile,* as well as on *ABC News* and *Fox News.*

Opinion Pieces/Letters

December 22/29, 2000, *The Journal of the American Medical Association* - Commentary by Alan I. Leshner - "2020 Vision: NIH Heads Foresee the Future (National Institute on Drug Abuse)."

Articles of Interest

December 6, 1999, *US News & World Report* - Interview of Frank Vocci - "For Heroin Addicts, a Bizarre Remedy."

December 1999, *Men's Health* - Interview of Alan I. Leshner - "The Good Times' Toll: How to Undo the Damage of Your Reckless Youth."

December 30, 1999, *Associated Press* - Interview of Alan I. Leshner - "Drugs in Research Lightly Monitored" (this article appeared in *The Philadelphia Inquirer, The Washington Post, Lexis-Nexis Universe, The New York Times, The USA Today, Yahoo! News* and on *ABC News, Fox News,* and *MSNBC*).

January 12, 2000, *The Washington Post (Horizon Section)* - Interview of Alan I. Leshner - "The Dope on Drugs: How the Most Popular Substances Affect Your Brain, Body and Behavior" (this article was reprinted in *The Connecticut Post*).

January 26, 2000, *Fox News* - Interview of Alan I. Leshner - "Nicotine Vaccine Could Mean the End of Addiction."

February 1, 2000, *Physician's Weekly* - Interview of Alan I. Leshner - "Club Drugs: A Strange New Brew Has ED Doctors Frustrated, Feds Concerned."

February 7, 2000, *The Washington Post* - Interview of Alan I. Leshner and Frank Vocci - "Can an Antibody Gobble Up Cocaine Cravings?" (a shorter version of this article was reprinted in *The Amarillo Daily News*).

February 15, 2000, *Family Circle* - Interview of Alan I. Leshner - "What Every Parent Needs to Know, Special Survey Report: Teens and Drugs."

February 22, 2000, *Mobile (Alabama) Register* - Interview of Edward Cone - "Hair Testing Raises Doubts."

February 23, 2000, *Reuters Health* - Interview of Stephen Heishman - "Cigarette Craving Can Trigger Addicts' Drug Urge."

February 24, 2000, *USA Today* - Interview of Alan I. Leshner - "Experts: Cocaine Addicts Often Relapse."

February 25, 2000, *The Associated Press State & Local Wire* - Interview of Steven Gust - "Ole Miss Research Yields Suppository and Plant Fingerprinting."

March 6, 2000, *AMA News* - Interview of Alan I. Leshner - "New Study Highlights Gender's Impact on Addiction."

March 14, 2000, *APB News* - Interview of Frank Vocci - "Vaccine May Block the Cocaine High."

April 2, 2000, *Sun-Sentinel (Fort Lauderdale, FL)* - Interview of Timothy P. Condon - "Teens Find ÔClub Drugs' Anywhere; Accessibility Makes Them a Chief Threat."

NIDA Director, Dr. Alan I. Leshner was featured as the key panelist on a special satellite broadcast by Community Anti-Drug Coalitions of America (CADCA) titled, "Emerging Drug Epidemics: Club Drugs" on April 25, 2000 in St. Petersburg, Florida.

Other Activities

On February 2, Dr. Frank Vocci, Director, DTR&D gave the first of a series of presentations on Medicine for the Layman to NIDA-wide staff. Dr. Vocci spoke on the subject of drug craving.

A directory of Clinical Trial Network (CTN) participants was compiled and distributed at the March 14-15, 2000 Steering Committee Meeting of the CTN in Baltimore.

NIDA Exhibits Program

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

January 29, 2000	Smithsonian Institution: Gender Differences in Addiction and Recovery
February 18 - 20, 2000	Society for Research on Nicotine and Tobacco
February 23 - 25, 2000	Centers for Substance Abuse Prevention
March 3 - 6, 2000	The National Conference on Education
March 16 - 19, 2000	American Medical Student Association
March 24, 2000	32nd Annual Meeting of the Society of Adolescent Medicine
March 30 - April 2, 2000	Society for Research on Adolescence
April 1-7, 2000	International Society of Magnetic Resonance Medicine
April 5-8, 2000	Parent Resource Institute for Drug Education
April 5-8, 2000	The Lonnie E. Mitchell National HBCU Substance Abuse Conference
April 9-11, 2000	Cognitive Neuroscience Society
April 9-12, 2000	National Methadone Conference

April 12-16, 2000	American Society of Addiction Medicine
April 26-29, 2000	National Coalition of Hispanic Health and Human Services Organizations
April 29, 2000	Maryland National Capital Park and Planning Commission Sports & Learning Complex Grand Opening
May 7-9, 2000	HIV, AIDS, and Hepatitis Conference
May 13-17, 2000	Summit 2000-An Annual International Media Literacy Campaign
May 13-18, 2000	American Psychiatric Association

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

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

National Institute on Drug Abuse

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

May, 2000

Planned Meetings

A conference, **Assessing the Impact of Childhood Interventions on Subsequent Drug Abuse** (Dr. Meyer Glantz, OD, DESPR, chair), will be held in Washington, D.C., at the Hotel Washington on May 23-24, 2000. NIDA and NIMH are co-sponsoring this meeting to assess the impact of mental health treatments for childhood psychopathologies on subsequent risk for drug abuse to assist drug and mental health investigators develop this important research area. More details are available at http://www.nida.nih.gov/Meetings/AICISDA/AICISDA.html.

A symposium, **Drug Addiction Treatment for Women: Does Gender Matter?**, co-chaired by Drs. Cora Lee Wetherington, NIDA's Women's Health Coordinator, and Betty Tai, Director of NIDA's Clinical Trials Network, will occur at the June, 2000 meeting of the College on Problems of Drug Dependence in San Juan, Puerto Rico. Speakers will be Drs. Cora Lee Wetherington, Kenneth Perkins (University of Pittsburgh), Karla Moras (University of Pennsylvania), Kathleen Brady (Medical University of South Carolina), and Rolley Johnson (Johns Hopkins University). The symposium is co-sponsored by NIDA's Women and Gender Research Group and the Treatment Workgroup. In order to foster the conduct of research on women and gender differences by junior investigators, NIDA (via the Women and Gender Research Group) will award a Women and Gender Travel Award to 20 junior investigators who will present a paper or poster on this topic at the 2000 meeting of the College on Problems of Drug Dependence in San Juan, Puerto Rico. Nearly 60 junior investigators applied for this award.

Drs. Timothy Condon, Cindy Miner, and Mark Swieter are organizing a grant writing workshop to be held at the annual College on Problems of Drug Dependence meeting, June 17- 22, 2000 in San Juan, Puerto Rico.

NIDA's Behavioral Science Working Group is planning two events at the American Psychological Association convention in Washington D.C. this August in collaboration with the Science Directorate of the APA. A pre-convention workshop will be held on Thursday, August 3, 2000 which will focus on early career behavioral scientists who are interested in, or who may already be conducting research in drug abuse and addictions (including nicotine). The workshop begins with introductory remarks by Dr. Alan I. Leshner, NIDA Director. Breakout sessions for graduate students and postdocs will focus on a) drug addiction research topics, led by invited NIDA-supported researchers; and, b) more advanced investigators who would like help with grant writing. Participants will be given a notebook to guide them through the grants maze at NIH, and will hear from both program and review staff at NIDA. In addition, eight invited lectures throughout the Focus on Science program at APA (August 4-6, 2000) are planned along the theme of "Faces of Vulnerability to Drug Abuse". These lectures will be co-hosted by seven APA Divisions and NIDA and include: Kathleen Merikangas, The Search for Genes for Drug Abuse: Promises and Pitfalls; Nick Goeders, The Role of Stress in the Motivation for Drug Abuse -- Preclinical Models; Ralph Tartar, Etiology of Substance Abuse: From Individual Differences to Different Individuals; John Falk, Environmental Sources of Vulnerability to Drug Abuse; Jose Szapocznik, An Ecological Developmental Approach to Vulnerability; Alan Leshner, Vulnerability to Drug Abuse and Addiction: A Quintessential Biobehavioral Issue; Marilyn Carroll, Vulnerability to Drug Abuse: How it Can be Avoided or Accelerated?; and Howard Moss, Behavioral Undercontrol and Family Liability for Substance Abuse.

In collaboration with the NIH Office of Dietary Supplements, ODS, National Center on Complementary and Alternative Medicine, NCCAM, Dr. Jag Khalsa of the Center on AIDS and Other Medical and Health Consequences of Drug Abuse, CAMCODA, will conduct a workshop this Summer 2000 on **Intervention Modalities (chemo-& alternative) in Drug Abuse and HIV/AIDS.** The workshop participants will identify the gaps in knowledge in such major areas as

incidence and prevalence of metabolic and endocrine disorders in drug abusers with HIV/AIDS and various intervention modalities such as chemointervention, alternative and complementary therapies for the prevention/treatment of these clinical complications. It is anticipated that the speakers will provide NIDA, ODS, NCCAM and other attending researchers directions for future research on the subject. The abstracts and recommendations for future research will be placed on the NIDA website. In addition, an executive summary of the proceedings will be published in a professional biomedical journal.

National CTN Steering Committee Meetings are planned for the follow dates and locations: May 23-24, 2000, in Hartford, CT; July 19-20, 2000, in Portland, OR; September 19-20, 2000, in Philadelphia, PA; and November 1-2, 2000, in Bethesda, Maryland.

A second **CTN Kick-Off Meeting** is planned for October 31, 2000, Bethesda, MD, for the second round of awards for the CTN RFA.

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

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

National Institute on Drug Abuse

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

May, 2000

Publications

Research Report Series: Anabolic Steroids Abuse (Revision)
NIH Pub. No. 00-3721
PHD561
The Research Report Series provides an authoritative and unbiased overview of particular topics and brings together the more recent and pertinent scientific information in an individual issue, along with a reference list. The revisions to this publication reflect the most recent findings from research on anabolic steroid use and surveys on youth drug use.

Community Drug Alert Bulletin-Anabolic Steroid Abuse
NIH Pub. No. 00-4771
This publication alerts communities that steroid abuse is a growing problem among adolescents and elaborates on the dangers of steroid abuse. There is increasing concern about the use of steroids, and NIDA is in a prime position to provide research-based information. NIDA wishes to inform the public about attempts being made to control steroid abuse and to make the public aware that the Institute is a resource for information about the problem.

Community Drug Alert Bulletin-Hepatitis C
NIH Pub. No. 00-4663
There currently exists a substantial need to alert health care workers, the prevention community, and the general public about the health risks posed by hepatitis C infection and its association with injection drug use. The purpose of this Bulletin is to provide information about the link between injection drug use and hepatitis C infection. The Bulletin contains information as follows: scientific information on hepatitis C infection and disease; the effects of hepatitis C virus infection on the body; the adverse consequences on the disease process of ongoing substance abuse; current treatment options; the risk for infection posed by injection drug use; screening recommendations for testing for the virus; and prevention efforts. In addition, the Bulletin lists other information sources.

Epidemiologic Trends in Drug Abuse: Community Epidemiology Work Group
Volume I, December 1999
NIH Pub. No. 00-4739
This publication provides more detailed descriptions than the Advanced Report of drug abuse patterns, trends, and consequences. The report provides an ongoing assessment of the epidemiology of drug abuse in major metropolitan areas of the United States with the purpose of keeping both public and private sector policy makers and researchers informed with current and accurate data.

Epidemiologic Trends in Drug Abuse: Community Epidemiology Work Group
Volume II, December 1999
NIH Pub. No. 00-4740
The International Epidemiology Work Group (IEWG) is a network of drug abuse researchers from various countries, regions, and international organizations. The IEWG is an outgrowth of efforts to establish a global drug abuse surveillance network. The IEWG is based on recognition of the essential need to coordinate and share the most timely and accurate information about the changing dynamics of drug abuse worldwide.

National Survey Results on Drug Use from the Monitoring the Future Study,

1975-1999, Overview of Key Findings
NIH Pub. No. 00-4690
The Monitoring the Future Study is a large-scale epidemiological survey of drug use attitudes and behavior among the nation's youth. The survey is based on a national probability sample of approximately 16,000 public and private high school seniors in the contiguous United States. The Advance Report provides systematically recurring annual estimates of drug use among students. The trends are useful for understanding the changing drug abuse problems and for formulating the appropriate interventions (both prevention and treatment) and policies.

The Problems of Drug Dependence, 1999: Proceedings of the 61st Annual Scientific Meeting of the College on Problems of Drug Dependence
NIH Pub. No. 00-4737
This publication is more than just a "proceedings" from a meeting-it is valued as one of the only research tools and references for scientists and other professionals in the drug abuse field. The publication is the most comprehensive gathering of scientific information on all aspects of substance abuse and is invaluable to researchers and other scientists.

NIDA NOTES

NIDA NOTES Vol. 14, Issue 5
NIH Pub. No. 00-3478
NN0040

Drug addiction treatment research is highlighted in this issue beginning with the lead story, which announces NIDA's new Principles of Drug Addiction Treatment guide, and continuing in the Director's Column, which links Principles to the Institute's 25 years of treatment research. This issue's Tearoff sums up the 13 principles of effective drug addiction treatment from the guide. Other treatment articles discuss methadone dosage, the additive effects of additional counseling and 12-step programs in treatment, and the benefits of combining drug-counseling methods to treat cocaine addiction. Research on the use of peers to provide drug abusers with AIDS prevention information is featured, and an article on NIDA's science education program highlights efforts to introduce young women in rural Appalachia to hands-on science.

NIDA NOTES Vol. 14, Issue 6
NIH Pub. No. 00-3478
NN0041

NIDA's broad-based initiative to combat an alarming rise in the use of club drugs is highlighted in the lead article. An accompanying list describes common club drugs, how they are used, and the consequences of their use. The Director's Column warns of the dangers of this trend, especially for youngsters who may be uninformed or misinformed about the hazards of club drug use. The first six sites for NIDA's landmark Clinical Trials Network are announced in this issue, and highlights of a symposium celebrating NIDA's 25th anniversary are covered as well. Another article looks at how research is translated into practice as programs developed by NIDA-funded prevention research are instituted in communities.

NIDA NOTES Vol. 15, Issue 1
NIH Pub. No. 00-3478
NN0042

The lead story announces NIDA's partnership with the National Cancer Institute and the Robert Wood Johnson Foundation in launching seven tobacco research centers across the nation. In the Director's Column, Dr. Leshner describes how research seeks ways to address the medical consequences of drug abuse. The Tearoff presents facts about drug abuse and hepatitis C. Other articles examine promising findings for cocaine abuse treatment and report new information on marijuana and its abuse. In addition, results of the annual Monitoring the Future study on teen drug use are announced.

Other Publications

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

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

See our **Contact Information**. .

National Institute on Drug Abuse

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

May, 2000

Staff Highlights

Honors and Awards

NIDA's Buprenorphine Development Team received the DHHS Secretary's Award for Distinguished Service at the 2000 HHS Honor Awards Ceremony held on May 9, 2000. Team members include: Nora Chiang, Lee Cummings, Joel Egertson, Liza Gorgon, Richard Hawks, Sue Herbert, Deborah Leiderman, Moo Park, James Terrill, Robert Walsh, Peter Bridge, Betty Tai, Frank Vocci and the late James Hill.

Ana Anders, Senior Advisor on Special Populations, was elected by the NIH Hispanic Employee Organization as President-Elect to serve for the year 2001.

Dr. Peter Hartsock, CAMCODA, received a commendation from National Science Foundation Director, and Chairperson for the Federal Interagency Arctic Research Policy Committee (IARPC), Dr. Rita R. Colwell, for his exemplary service as the Departmental Co-Representative on the IARPC.

A patent was recently awarded entitled "Radiolabeled pyridyl-7-azabicyclo [2.2.1]heptanes." This invention involved the use of radiolabeled epibatidine analogues to image and quantify nicotinic acetylcholine receptors (nAChRs) in the brain. Selective nicotinic radiotracers can be used to study the underlying mechanisms of tobacco dependence and will be useful in the development and testing of therapies for tobacco dependence. Further benefits may be realized in elucidating the role of nAChRs in neurodegenerative disease states, specifically Alzheimer's disease, Parkinson's disease, and Tourette's syndrome, which are characterized, in part, by abnormalities in nicotinic receptors or neurotransmitter release modulated by nicotinic receptors. (London, E.D., Kimes, A.S., Horti, A.G., Dannals, R.F. and Kassiou, M., patent #5,969,144).

Staff Changes

Angela Benjamin joined the staff of the Office of Extramural Affairs as Grants Technical Assistant at the end of January 2000. Ms. Benjamin comes to NIDA from the Center for Scientific Review, NIH.

Loretta Beuchert joined the staff of the Office of Extramural Affairs as Program Assistant on February 28, 2000. Ms. Beuchert comes to NIDA from the National Institute of Neurological Disorders and Stroke.

Jahnavi Kharidia, Ph.D. joined NIDA's Division of Treatment Research and Development as a Pharmacokineticist in January 2000. Prior to joining NIDA, Dr. Kharidia was a reviewer at FDA for 3 years. Dr. Kharidia received her Ph.D. in Pharmacokinetics from University of Maryland in 1996.

LCDR Angela M. Martinelli, DNSc, RN joined the Science Policy Branch, OSPC in February 2000. Prior to coming to NIDA, Dr. Martinelli was a Nurse Consultant in the Division of Nursing, Health Resources and Services Administration. Dr. Martinelli has held faculty positions at Boston College and the Catholic University of America. She received her Doctor of Science in Nursing from The Catholic University of America and was a Postdoctoral Research Fellow in Health Promotion and Risk Reduction at the University of Michigan, Ann Arbor. Her research area of interest is

tobacco and nicotine prevention and health promotion.

Eve E. Reider, Ph.D. recently joined the Prevention Research Branch in the Division of Epidemiology, Services and Prevention Research as a Health Scientist Administrator. Prior to joining NIDA, Dr. Reider worked as a psychologist and Director of Clinical Training in Psychology in the Department of Psychiatry at Kennedy Krieger Institute. She was also an Instructor in the Department of Psychiatry at Johns Hopkins University School of Medicine. Dr. Reider received her Ph.D. in Psychology at Michigan State University.

Ming Shih, Ph.D., joined NIDA's CTN Office/DTR&D on January 31, 2000. Previously, Dr. Shih headed a research chemistry laboratory and directed a medical products development program for multi-center clinical trials with the U.S. Army, Department of Defense. In 1997, she did a tour of duty at NIH for extramural grant management. She has practiced as a clinical pharmacist in hospitals and community pharmacies. Dr. Shih received her Ph.D. in Physical Pharmacy and Pharmacokinetics from the University of Pittsburgh.

Edwina Smith, M.S. joined the Clinical/Medical Branch of the Division of Treatment Research and Development in April 2000 as a clinical trials monitor. Ms. Smith is an RN, certified by the American Nurse Association Credentialing Center (ANCC) in Psychiatric and Mental Health Nursing and is a Commander in the USPHS Commissioned Officers Corps. She holds a Master of Science Degree in Health Services Administration, and has 28 years experience as a registered nurse. She has held positions as staff nurse, nurse team leader, case manager, and supervisory psychiatric nurse. She has been employed at the Neuropsychiatric Research Hospital on the St. Elizabeth's Hospital Campus, at Greater Southeast Community Hospital, and most recently the Clinical Center at NIH as Nurse Case Manager of the Attention Deficit Hyperactivity Disorder (ADHD) Day Program. She is a member of many professional organizations, has received several awards and was recently approved for a Commendation Medal from the U.S. Public Health Service.

Nathalie Thiriet, Ph.D. has joined the Molecular Neuropsychiatry Section of NIDA's Intramural Research Program as a Visiting Foreign Fellow. Dr. Thiriet graduated in 1999 from the UniversitŽ Louis Pasteur, located in Strasbourg, France.

Dr. Ro Nemeth-Coslett of NIDA's Prevention Research Branch, Division of Epidemiology, Services, and Prevention Research recently assumed a detail in the Clinical Neurobiology Branch, Division of Treatment Research and Development.

Dr. Andrea Baruchin left NIDA at the end of April 2000 after serving as the Chief, Science Policy Branch, OSPC for almost three years. Dr. Baruchin will be going to Vanderbilt University in Nashville, Tennessee to become the Associate Director of the newly established Vanderbilt Brain Institute - a research infrastructure that will encompass all the brain research that is ongoing at the University.

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

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

National Institute on Drug Abuse

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

May, 2000

Grantee Honors

Dr. Timothy B. Baker, Professor of Psychology, University of Wisconsin and Associate Director of the University's Center for Tobacco Research and Intervention, was named Editor, Journal of Abnormal Psychology.

Dr. Lloyd D. Johnston and **Dr. Jerald G. Bachman** received The University of Michigan's Distinguished Research Scientist Award. This award modifies their titles to Distinguished Senior Research Scientist.

Dr. Lloyd D. Johnston received The Regents' Award for Distinguished Public Service, The University of Michigan.

Dr. Edward Kaplan, Yale University School of Organization and Management, has been awarded an endowed chair, the "Beach Professor of Management Sciences." Dr. Kaplan, who is also a professor of public health at the Yale School of Medicine, has been a leader in developing cutting edge methods of quantitatively evaluating HIV intervention programs. In this respect, he was the first federally (NIDA) funded researcher to evaluate the impact of needle exchange programs in preventing the spread of HIV/AIDS among injecting drug users. His needle exchange research has been the subject of special reviews by and accolades from the U.S. Congressional General Accounting Office, the National Academy of Sciences, and the Centers for Disease Control and Prevention.

Project STAR, a NIDA supported intervention created by **Mary Ann Pentz, Ph.D.,** University of Southern California, was selected by the Center for Substance Abuse Prevention as a model program. Dr. Pentz was recognized for her achievements at the 1999 Exemplary Substance Abuse Prevention Awards ceremony on May 16, 2000. The award is jointly sponsored by CSAP, the National Association of State Alcohol and Drug Abuse Directors, the National Prevention Network, and the Community Anti-Drug Coalitions of America.

Dr. Phillip Portoghese, Professor of Medicinal Chemistry at the College of Pharmacy of the University of Minnesota, and editor of the Journal of Medicinal Chemistry, received the Alfred Burger Award from the American Chemical Society for his career work on the structure and activity relationships of opioid compounds.

[Office of the Director][Report Index]

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