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

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Research Findings

Basic Research

Role for GDNF in Biochemical and Behavioral Adaptations to Drugs of Abuse

Drs. David Russell and Eric Nestler and their research team at the Yale University examined a role for Glial-Derived Neurotrophic Factor (GDNF) in adaptations to drugs of abuse. Infusion of GDNF into the ventral tegmental area (VTA), a dopaminergic brain region important for addiction, blocks certain biochemical adaptations to chronic cocaine or morphine as well as the rewarding effects of cocaine. Conversely, responses to cocaine are enhanced in rats by intra-VTA infusion of an anti-GDNF antibody and in mice heterozygous for a null mutation in the GDNF gene. Chronic morphine or cocaine exposure decreases levels of phosphoRet, the protein kinase that mediates GDNF signaling in the VTA. Together, these results suggest a feedback loop, whereby drugs of abuse decrease signaling through endogenous GDNF pathways in the VTA, which then increases the behavioral sensitivity to subsequent drug exposure. Messer, C.J., Eisch, A.J., Carlezon, W.A. Jr., Whisler, K., Shen, L., Wold, D.H., Westphal, H., Collins, F., Russell, D.S., and Nestler, E.J. Role for GDNF in Biochemical and Behavioral Adaptations to Drugs of Abuse. Neuron, 26(1), pp. 247-257, 2000.

Mechanisms Responsible for Methamphetamine-Induced Rapid Decrease in Dopamine Transporter Function

Single and multiple high-dose administrations of methamphetamine (METH) decrease dopamine (DA) transporter function, as assessed in striatal synaptosomes (approximately 33% and 78% reductions, respectively). These effects occur within 60 minutes after in vivo treatment and persist even after METH is removed from the synaptosomal preparation. The large reduction in DAT function after multiple METH injections appears to have two separate components with distinct underlying mechanisms. Phase I occurs after either a single or multiple METH administrations and is not dependent on drug-induced changes in dopaminergic function or hyperthermia. It is hypothesized that phase I is due to a METH-induced internalization of DAT causing a temporary loss of transporter function. Phase II only occurs after multiple METH administrations and is dependent on activation of DA receptors, hyperthermia and free radical formation. Even though there is no loss of DAT protein, it is possible this phase II response of DAT to METH is somehow related to the neurotoxic potential of this drug, as similar factors are necessary for this drug to induce long-term deficits in monoamine systems after multiple METH treatments. The precise nature of these two phases of METH-induced reduction in DAT activity requires further study and may be important for understanding both the short- and long-term consequences of abusing this drug. Metzger, R.R., Haughey, H.M., Wilkins, D.G., Gibb, J.W., Hanson, G.R., and Fleckenstein, A.E. Methamphetamine-Induced Rapid Decrease in Dopamine Transporter Function: Role of Dopamine and Hyperthermia. J. Pharmacol. Exp. Ther., 295(3), pp. 1077-1085, 2000.

Pigment Measurement is Important for Hair Testing for Several Drugs of Abuse

In rats with pigmented hair, cocaine, ecogonine methyl ester (EME) and norcocaine (NCOC) were detected in dose-related concentrations whereas in rats with non-pigmented hair none of these were detected. In rats with pigmented hair, cocaine was twice as likely as its metabolite benzoylecgonine (BE) to be detected. Melanin binds to basic drugs with a net positive charge. Cocaine concentrations in pigmented hair peaked after cocaine disappears from the blood. In rats with pigmented hair, maximal hair concentrations of cocaine were found three days after serum

concentrations became undetectable. In rats with non-pigmented hair, concentrations of cocaine were undetectable for two days. In rats, while amphetamine binds preferentially to pigmented hair, its non-basic analog, N-acetylamphetamine, is taken up equally in both pigmented and non-pigmented hair. In mice, while the cation 45CA2 associated with melanocytes and melanosomes of forming pigmented hair within 5 minutes of dosing, the anion 38Cl- did not associate in the hair of either pigmented or non-pigmented hair. Hubbard, D.L., Wilkins, D.G., and Rollins, D.E. The Incorporation of Cocaine and Metabolites into Hair: Effects of Dose and Hair Pigmentation. Drug Metab. Dispos., 28, pp. 1464-1469, 2000.

Heroin Modulation of Immune Status

Heroin use is associated with an increased incidence of several types of infections, including HIV, yet few studies have assessed whether heroin produces pharmacological alterations of immune status that might contribute to the increased rate of infections among heroin users. Two recent studies by Dr. Donald Lysle and his colleagues have evaluated the immunomodulatory effects of a single heroin injection in the rat. The first study investigated whether a single heroin administration produces dose-dependent alterations in immune status. The results show that heroin produces a dose-dependent, naltrexone-reversible suppression in stimulated proliferation of T-cells, B-cells, production of interferon-g, and cytotoxicity of natural killer (NK) cells in the spleen. Thus, heroin affects both functional and phenotypic measures of immune status. Fecho, K., Nelson, C.J., and Lysle, D.T. Phenotypic and Functional Assessments of Immune Status in the Rat Spleen Following Acute Heroin Treatment. Immunopharmacology, 46, pp. 193-207, 2000.

A second study examined the rate of splenocyte death by necrosis or apoptosis. The results showed that a single injection of heroin decreased the total number of leukocytes in the spleen in a dose-dependent, naltrexone-reversible manner. Moreover, the heroin-induced decrease in splenic leukocytes was not associated with an increase in circulating leukocytes. Fecho, K., and Lysle, D.T. Heroin-Induced Alterations in Leukocyte Numbers and Apoptosis in the Rat Spleen. Cellular Immunology, 202, pp. 113-123, 2000.

Endomorphin-1, Antinociception and Immune Modulation

Central opioid receptors have been known for some time to be involved in immunomodulation. However, only recently has an endogenous agonist possessing high selectivity and affinity for the mu opioid receptor, endomorphin-1, been identified. Little is known about the immunomodulatory and antinociceptive effects of endomorphin-1. Dr. Donald Lysle and his colleagues found in rats that endomorphin-1 produced naltrexone-reversible antinociception in both the hotplate assay and in the warm water tail withdrawal assay. However, there were no immunomodulatory effects up to 120 minutes after injection. These observations suggest that it may be possible to develop therapeutic strategies for separating antinociception and immunomodulatory properties through the m-opioid receptor. Carrigan, K.A., Nelson, C.J. and Lysle, D.T. Endomorphin-1 Induces Antinociception without Immunomodulatory Effects in the Rat. Psychopharmacology, 151, pp. 299-305, 2000.

Methamphetamine Neurotoxicity Has Behavioral Consequences in Rats

Dr. John F. Marshall's group has been studying the degeneration of neurons in the somatosensory cortex after repeated methamphetamine. Given the general lack of studies of cognitive functioning after neurotoxic regimens of methamphetamine, they studied a spatial (hippocampus-dependent) and a cued (caudate nucleus-dependent) water maze task one week after a neurotoxic regimen of methamphetamine. Rats treated with methamphetamine had impaired acquisition of the cued, but not the spatial, task. By contrast, the methamphetamine group had impaired retention (tested 24 hr after acquisition) of the spatial task. The swimming speed was not affected in any tests, indicating that these effects were not due to impaired motor function. Autoradiography demonstrated that dopamine transporter was markedly reduced in the striatum, and serotonin transporter was reduced in the hippocampus. Thus, methamphetamine neurotoxicity has different consequences on hippocampus- and caudate-dependent memory tasks in rats. Schršder, N., and Marshall, J. Differential Effects of Methamphetamine-Induced Neurotoxicity on Hippocampus-Dependent and Caudate Nucleus-Dependent Memory Processes. Society for Neuroscience Abstracts, 26, Abstract 484.14, p. 1311, 2000.

More Evidence for Glutamate's Role in Addiction

Sensitization in rodents, defined as an enhanced response to a drug due to previous exposure to that drug, appears to model the enhanced drug-seeking behavior over time of human drug addicts. For example, the locomotor activation produced by amphetamine in rats increases with repeated daily injections, and the locomotor response to amphetamine remains sensitized indefinitely, despite stopping the daily injections. Dr. Paul Vezina's group is investigating the roles of the neurotransmitters glutamate and dopamine in sensitization. They found that

microinjection of a compound that blocks glutamate reuptake into the nucleus accumbens enables enhanced locomotor responding to co-injection of a dopamine D1 receptor agonist (but not to a D2 agonist) in rats previously exposed to amphetamine. (Amphetamine releases dopamine, and thereby may lead to the activation of both D1 and D2 dopamine receptors.) This indicates that, in the n. accumbens, increased glutamate neurotransmission and activation of D1 dopamine receptors, neither of which is by itself sufficient, together contribute to the expression of locomotor sensitization by amphetamine. These new findings provide further evidence of the importance of the role of glutamate in the "switching" mechanism in the process of addiction. Kim, J-H., and Vezina, P. Rats Pre-Exposed to Amphetamine Show Enhanced Locomotion to a D1 Dopamine Receptor Agonist in the Nucleus Accumbens When Glutamate Reuptake is Inhibited. Society for Neuroscience Abstracts, 25, p. 2211, 1999.

Mechanism of Action of Bupropion

Since its approval in 1998 as a prescription drug in sustained-release oral form as a smoking cessation agent, mechanisms of the function of bupropion have been under investigation. Pharmacologically, the compound is an antidepressant structurally related to the phenethylamines, and is capable of causing an increase in extracellular dopamine in the nucleus accumbens, along with inhibiting the firing of noradrenergic neurons in the locus coerulus. It lacks binding affinity for the serotonin, dopamine, adrenergic, and muscarinic receptors. In a recent study by Dr. Billy Martin and his colleagues bupropion's action on nicotinic acetylcholine receptors was examined in-vitro (rat brain membrane binding and recombinant receptor subtypes in oocyte cells) and in-vivo (antinociception and behavioral testing). Electrophysiological cellular currents, induced by acetylcholine administration, were blocked at the alpha4beta2, alpha7, and alpha3beta2 receptor subtypes by various micromolar concentrations of bupropion, in a concentration dependent, reversible, noncompetitive, and voltage-independent manner. The relative order of receptor functional blocking observed was alpha3beta2>alpha4beta2>alpha7. The "alpha3"-containing subtypes have been shown from other work to be more resistant to functional inactivation by chronic nicotine exposure than alpha4beta2 or alpha7. Bupropion alone did not induce currents when acutely administered. In rat brain membranes, where the alpha4beta2 subtype is a predominant subtype, bupropion did not displace bound tritiated nicotine.

In behavioral tests of antinociception (hot plate and tail flick tests), motor effects, and convulsive seizures in mice, subcutaneous or intravenous injections of bupropion, prior to nicotine injections, antagonized at least some of the effects of injected nicotine, most notably its antinociceptive effects. The block of antinociception lasted approximately thirty to sixty minutes at a five mg/kg dose. This latter dose is similar to that previously used to show antidepressant behavioral effects in animals, and is higher than that required to produce dopamine reuptake blocking in animals. Future studies may address the question of the relative importance of nicotinic acetylcholine receptor blocking as compared to bupropion's effect on the dopamine and noradrenergic systems. Slemmer, J.E., Martin, B.L, and Damaj, M.I. The Journal of Pharmacology and Experimental Therapeutics, 295, pp. 321-327, 2000.

Opiate Receptors and Vascular Endothelial Cells

Studies have shown that in human and rat vascular endothelial cells, the mu opiate receptor is coupled to nitric oxide (NO) release and that these tissues exhibit stereo specific, saturable and naloxone-sensitive opiate binding sites. In a recent paper, Dr. George Stefano and his colleagues provide molecular evidence that mu-type opiate receptors are expressed in human vascular endothelia and that their expression can be regulated by pro-inflammatory cytokines. They observed that exposure of human endothelia to pro-inflammatory cytokines IL-1 led to a significant increase in the expression of mu transcript as well as in morphine-stimulated NO release measured ampherometrically. These findings advance our understanding of the physiological role of NO in the vascular and cardiac cellular function. Cadet, P., Bilfinger, T.V., Fimiani, C., Peter, D., and Stefano, G.B. Endothelium-New York, 7(3), pp. 185-191, 2000.

Opiates and Immune System

A recent study published by Dr. George Stefano and his associates demonstrates that in rat, after a latent period, brain morphinergic processes respond to peripheral immune challenges such as lipo-polysaccharide (LPS) injection or food deprivation stress. LPS, a bacterial product known to stimulate pro-inflammatory immune cascades, produced an increase in morphine levels in the rat brain in a time dependent manner with a peak reached at 36 hours. Increases in brain morphine levels were also observed in animals following 96 hours of food deprivation. This suggests that the latent period preceeding the increase in brain morphine levels is physiologically relevant as it probably allows the critical immune and neural excitatory processes to emerge and protect the organism from an overactive immune response. Goumon, Y., Bouret, S., Casares, F., Zhu, W., Beauvillain, J. and Stefano, G.B. Neuroscience Letters, 293, pp. 135-138, 2000.

Players in the Signal Transduction Pathways Induced by Cocaine and Morphine

G proteins are heterotrimeric proteins, made up of alpha, beta and gamma subunits. G proteins link receptors on the cell surface to intracellular signaling pathways. There are many genes encoding each G protein subunit, and so there are many versions of each subunit. The most unusual G alpha subunit is G_{zalpha}; it has the least similarity to others. When NIDA grantee Dr. Blendy and his co-workers made mice lacking this subunit, the animals showed several defects, including impaired platelet aggregation and altered responses to psychoactive drugs. The mutant mice exhibited a greatly exaggerated response to cocaine, a lowered response to the analgesic effects of morphine, and no response at all to the antidepressants desipramine and reboxetine. The authors concluded that G_z mediates the effects of specific receptors, defining a unique role for G_{zalpha} in platelets and the in the central nervous system. The importance of this work is that it shows that receptors interact selectively with G proteins, and that G protein subunits are not interchangeable. The importance of this work for drug abuse research is that it implicates the G_{zalpha} protein in the signaling pathways induced by cocaine and morphine, opening the way for further research on this part of the signal transduction cascade. Yang, J., et al. Loss of Signaling Through the G Protein, G_z, Results in Abnormal Platelet Activation and Altered Responses to Psychoactive Drugs. Proc. Natl. Acad. Sci. USA, 97, pp. 9984-9989, 2000.

Vesicle Transporters Regulate Neurotransmitter Release by Two Mechanisms

The vesicle monoamine transporter (VMAT2) is responsible for the uptake of monoamine neurotransmitters (such as dopamine) into synaptic vesicles. Amphetamines act by reversing the action of VMAT2. NIDA grantees Drs. Sulzer and Edwards and their co-workers found that overexpression of VMAT2 in small synaptic vesicles in cultured neurons led to an increase in the number of vesicles released per event (quantal size) and in the frequency of release. This is an unexpected result because transporters were not thought to be rate-limiting in vesicle accumulation. In light of these findings, it is clear that the regulation of vesicle transporter activity leads to rapid and profound changes in transmitter release. The result is a profound increase of released neurotransmitter to multiple post-synaptic sites and a resultant synaptic strengthening. The importance of this paper is that it points out an important regulatory role for VMAT2, a protein that is a target for amphetamine. Pothos, E.N., et al. Synaptic Vesicle Transporter Expression Regulates Vesicle Phenotype and Quantal Size. J. Neurosci., 20, pp. 7297-7306, 2000.

Modulation of Morphine-Induced Antinociception by Glucose

The analgesic potency of opioid drugs varies as a function of gender, and can be modified by the intake of palatable sweet-tasting solutions. Male and female Long-Evans rats were fed laboratory chow and water alone, or chow, water and either a 32% sucrose solution or a 0.15% saccharin solution. Following the administration of cumulative doses of morphine sulfate, the rats were tested in two analgesic paradigms, the tail-flick test and the hot-plate test. On the tail-flick test, morphine produced dose-related increases in antinociceptive responses. Chronic sucrose intake significantly augmented morphine's antinociceptive properties. On the hot-plate test, when the plate was heated to 51¼ C, morphine led to significant dose-related increases in antinociceptive responses, irrespective of sucrose intake. However, when the temperature of the hot plate was increased to 53¼ C, there was a trend for animals given sucrose to display greater antinociceptive responses. No differences in baseline pain sensitivity or morphine-induced analgesia were observed as a function of gender. Kanarek, R.B., Homoleski, B. Modulation of Morphine-Induced Antinociception by Palatable Solutions in Male and Female Rats. Pharmacology Biochemistry and Behavior, 66, pp. 653-659, 2000.

Heterodimerization of Mu and Delta Opioid Receptors: A Role in Opiate Synergy

Opiate analgesics are widely used in the treatment of severe pain. Three opioid-receptor types, delta, kappa and mu, have been identified. Pharmacological studies have suggested that mu and delta receptors interact and influence each other's properties. While most opiates exert their analgesic effects primarily via mu opioid receptors, delta receptor selective drugs have been shown to enhance their potency. The molecular basis for these findings has not been previously elucidated. NIDA grantees Lakshmi Devi and her coworkers have recently found that co-expression of mu and delta receptors in heterologous cells followed by selective immunoprecipitation results in the isolation of mu-delta heterodimers. Treatment of these cells with extremely low doses of certain delta selective ligands results in a significant increase in the binding of a mu receptor agonist. Similarly, treatment with mu selective ligands results in a significant increase in the binding of a delta receptor agonist. This robust increase is also seen in SK-N-SH cells that endogenously express both mu and delta receptors. Furthermore, we find that a delta receptor antagonist enhances both the potency and efficacy of the mu receptor signaling; likewise a mu antagonist enhances the potency and efficacy of the delta receptor signaling. A combination of agonists (mu and delta receptor selective) also synergistically binds and potentiates signaling by activating the mu-delta heterodimer. Taken together, these studies show that heterodimers exhibit distinct ligand binding and signaling characteristics. These findings have important clinical ramifications and may provide new foundations for more effective therapies. Gomes, I., Jordan, B.A., Gupta, A., Trapaidze, N., Nagy, V., and Devi, L.A. Heterodimerization of Mu and Delta Opioid Receptors: A Role in Opiate

Synergy. J. Neuroscience, 20, RC110: 1-5, 2000.

Morphine Induces Gene Expression in Human Lymphocytes

Opiate users constitute a large portion of the patient population contracting AIDS. The feasibility and success of human studies have always been hampered by the complexity of an individual's history of i.v. drug use. Thus, rhesus monkeys treated with opioids and infected with simian immunodeficiency virus (SIV) provide an excellent animal model for studying drug abuse and AIDS in a controlled manner. All HIV-1 strains studied to date use CCR5, CXCR4, or both receptors to enter cells. Research on several genetically divergent SIV isolates has revealed that SIV uses CCR5, and not CXCR4, for entry. CEM x174, a human lymphoid cell line, has been routinely used to cultivate and maintain various SIV strains. However, questions have arisen about how CEM x174, which reportedly was unable to express detectable amounts of CCR5 transcripts, efficiently supports the growth of SIV. Using a sensitive, competitive RT-PCR procedure, Dr. Ronald Y. Chuang and his colleagues at the University of California, Davis attempted to detect as well as quantify the amount of CCR5 expression. Their findings indicate that: (1) CEM x174 expresses CCR5; and (2) the amount of CCR5 is increased in cells pre-treated with morphine. These results correlate well with their previous observations that morphine treatment causes CEM x174 cells to be more susceptible to SIV-infection. Similar morphine effects were not observed on CEM x174 cells infected with SRV (simian retroviruses) that do not depend on CCR5 for entry. These findings suggest a plausible mechanism whereby opiate drug users render themselves more susceptible to HIV infection. These data contributing substantially to explaining the vast prevalence of HIV infection among endemic drug use populations. Miyagi, T., Chuang, L.F., Doi, R.H., Carlos, M.P., Torres, J.V. and Chuang, R.Y. Morphine Induces Gene Expression of CCR5 in Human CEMx174 Lymphocytes. J. Biol. Chem., 275, pp. 31305-31310, 2000.

Phosphorylation and Sequestration of Serotonin Transporters Differentially Modulated by Psychostimulants

Many psychotropic drugs interfere with the re-uptake of dopamine, norepinephrine and serotonin. The actions of serotonin are terminated by active transport. Whereas serotonin actions are mediated by more than 15 different types of receptors, a single serotonin transporter is responsible for extracellular serotonin clearance. NIDA grantee Randy D. Blakely and his coworkers at the Vanderbilt University School of Medicine have recently investigated whether the regulation of serotonin transporters was influenced by transport per se and whether serotonin transporter ligands differentially influenced serotonin transporter regulation. Transport capacity is regulated by kinase-linked pathways, particularly involving protein kinase C, leading to transporter phosphorylation and sequestration. Phosphorylation and sequestration of the serotonin transporter were significantly impacted by ligand occupancy. Ligands that can permeate the transporter, such as serotonin or the amphetamines, prevented protein kinase C-dependent serotonin transporter phosphorylation. Non-transported serotonin transporter antagonists such as cocaine and antidepressants were permissive for serotonin transporter phosphorylation. Protein kinase C-dependent serotonin transporter sequestration was also blocked by serotonin. These findings reveal activity-dependent modulation of neurotransmitter reuptake and identify novel consequences of amphetamine and cocaine action. Ramamoorthy, S. and Blakely, R.D. Phosphorylation and Sequestration of Serotonin Transporters Differentially Modulated by Psychostimulants. Science, 285(5428), pp. 763-766, 1999.

Characterization and Analysis of Biphalin - An Opioid Peptide with a Palindromic Sequence

In this study Dr. Hettiarachchi and his colleagues characterized and analyzed a structurally modified opioid peptide, biphalin, when standard techniques for peptide analysis were inadequate. Biphalin, an octapeptide consisting of two monomers of a modified enkephalin, attached via a hydrazine bridge, and with the amino acids assembled in a palindromic sequence, needed strict quality control because of certain drawbacks associated with its synthesis. Many techniques were used for its analysis including elemental analysis, amino acid analysis, amino acid sequence analysis (AASA), mass spectrometry (MS), 1H-NMR, 1H-correlated spectroscopy (COSY)-NMR, high performance liquid chromatography (HPLC), and capillary electrophoresis (CE). Electrospray ionization (ESI) mass spectrometry that included both ESI MS and ESI MS/MS, was performed to confirm the full sequence since AASA results alone could verify only the monomer sequence and not the full sequence. Although the 1H-NMR results led to a preliminary assignment of many protons, the 1H COSY-NMR results allowed for an unequivocal assignment of almost all protons. The peptide purity was determined by reversed phase HPLC and CE. Hettiarachchi, K., Ridge, S., Thomas, D.W., Olson, L., Obi, C.R., and Singh, D. Characterization and Analysis of Biphalin - An Opioid Peptide With A Palindromic Sequence, J. Peptide Research, 57, 1-12 (2001), 2000.

Dopamine and cAMP-Regulated Phosphorylation

Dr. Paul Greengard, one of the winners of the 2000 Nobel Prize in Medicine and Physiology, has been characterizing

the actions of dopamine and cAMP-regulated phosphoprotein of M(r) 32,000 (DARPP-32). DARPP-32 is a central player in mediating the actions of dopamine by regulating the amount of phosphorylation of proteins in spiny neurons of the striatum where dopamine receptors are localized. When DARPP-32 is phosphorylated it inhibits protein-phosphatase, an enzyme that decreases the amount of phosphorylation and, at the same time, augments the action of neurotransmitters that increase phosphorylation. Mice lacking the DARPP-32 gene show a reduced behavioral response to drugs of abuse such as cocaine and D-amphetamine.

In a recent paper, Dr. Greengard's group shows that mice lacking DARPP32 do not display long-term potentiation or long-term depression in synapses connecting the striatum to the cortex. These results are similar to those produced by blocking the dopamine D1 receptor. However, they report that distinct biochemical pathways seem to play a significant role in mediating the two forms of synaptic plasticity. Blockade of protein kinase A blocks the induction of long-term potentiation but not long-term depression while blockade of protein kinase G pathway blocks long-term depression and not long-term depression at corticostriatal synapses. These forms of plasticity may play an important role in addiction in term of habit formation and impulse control. Through understanding the biochemical pathways that control these forms of plasticity, researchers hope to develop new and more effective treatment interventions. Calabresi, P., Gubellini, P., Centonze, D., Picconi, B., Bernardi, G., Chergui, K., Svenningsson, P., Fienberg, A.A., and Greengard, P. Dopamine and cAMP-Regulated Phosphoprotein 32 kDa Controls Both Striatal Long-Term Depression and Long-Term Potentiation, Opposing Forms of Synaptic Plasticity. J. Neurosci.20(22), pp. 8443-8451, 2000.

Agmatine and Pain Control in Mammals

Dr. Carolyn Fairbanks and Dr. George Wilcox of the University of Minnesota examined the analgesic properties of agmatine. Agmatine, an amine known to exist in bacteria, plants, and invertebrates, has recently been found in the central nervous system (CNS) of mammals. Agmatine appears to function as a neurotransmitter/ neuromodulator within the CNS, where its activity includes the antagonism of NMDA receptors and the inhibition of nitric oxide synthase (NOS). The activation of both NMDA receptors and of the NOS have been implicated in plastic changes of the CNS responsible for chronic pain. Drs. Fairbanks and Wilcox have found that intrathecal administration of agmatine in rodents decreased chronic pain associated with inflammation and nerve injury, but did not alter normal acute pain perception. These analgesic actions were not associated with motor impairment, a common side effect of NMDA antagonists. This research suggests that agmatine may be an effective alternative to opioids in the treatment of chronic pain Fairbanks et al., Agmatine Reverses Pain Induced by Inflammation, Neuropathy, and Spinal Cord Injury. Proc. Natl. Acad. Sci., 97(19), pp. 10584-10589, 2000.

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

Behavioral Research

Economic Trade-Offs for Cigarette Puffs versus Nicotine Gum

Researchers from the University of Vermont compared smokers' preferences for cigarette puffs and nicotine gum at varying "prices" for these commodities. As expected, the researchers found that when only cigarette puffs were available, participants decreased smoking as the price per puff increased. In a second phase of the experiment, when participants were offered a choice between chewing nicotine gum at a low price, or purchasing cigarette puffs at different prices, they continued to purchase the same number of cigarette puffs at each price as in the previous experiment (i.e., when gum was previously unavailable). At higher prices for cigarette puffs however, nicotine gum chewing increased modestly. These data suggest that nicotine gum is a weak substitute for cigarettes in smokers unprepared to quit. Given that the gum was selected when the price of puffs was very high, and no puffs were purchased under these experimental conditions, the data suggest that under some economic situations nicotine gum is a weak substitute for cigarettes. Future experiments using this methodology may lead to the development and testing of pharmacotherapies that may better compete and substitute for cigarettes. Shahan, T.A. et al., Nicotine Gum as a Substitute for Cigarettes: A Behavioral Economic Analysis. Behavioural Pharmacology, 11, pp.71-79, 2000.

Postpartum Separation from Offspring Produces Long-Lasting Effects in Mother Rats

Prior research has shown that neonatal rat pups exposed to periodic separation from their mothers show an elevated stress-reactivity in adulthood that is manifest on both behavioral and physiologic indices. Researchers at the Emory University School of Medicine now show that this separation also produces long-lasting changes in the dams. Dams separated from their neonatal pups for 3 hours daily on postpartum days 2-14 and tested four to six weeks post-weaning, exhibited anxiety-like behaviors measured via (a) both entries and time spent in the open arms of an elevated plus-maze, (b) time spent in the center of a novel locomotor arena, and (c) ultrasonic vocalizations. The separation also resulted in reduced sensitivity to morphine as measured by tail-flick and hot-plate tests of analgesia. Kalinichev, M., Easterling, K.W., and Holtzman, S.G. Periodic Postpartum Separation from the Offspring Results in Long-Lasting Changes in Anxiety-Related Behaviors and Sensitivity to Morphine in Long-Evans Mother Rats. Pharmacology, 152, pp. 431-439, 2000.

Sex Differences, Estrus Cycle, and Regulation of Self-Administered Cocaine in Rats

Drs. Wendy Lynch and Marilyn Carroll of the University of Minnesota previously demonstrated that female rats acquire cocaine self-administration faster than male rats and that a larger percentage of female than male rats acquire cocaine self-administration. Using a choice procedure, these researchers now find that the mean infusion dose is lowest during metestrus/diestrus and highest during estrus and proestrus. The regulation of cocaine intake was measured by the correlation between the mean interdose interval and the preceding dose. Self-administration regulation was significantly more precise in males and in metestrus/diestrus females as compared to estrus and in proestrus females. Furthermore, there was no difference in regulation between males and metestrus/diestrus females. Lynch, W.J., Arizzi, M.N., and Carroll, M.E. Effects of Sex and the Estrous Cycle on Regulation of Intravenously Self-Administered Cocaine in Rats. Psychopharmacology, 152, pp. 132-139, 2000.

Sex Differences in Nicotine Self-Administration in Rats

Evidence has accumulated that there are sex differences in nicotine use and dependency in humans. However, until now there has been no corroborating evidence in animals. Drs. Eric Donny and Anthony Caggiula at the University of Pittsburgh found that at the lowest dose female rats acquired nicotine self-administration faster than males. Female rats reached higher break points on a progressive ratio schedule of self-administration, and therefore took more nicotine infusions. Female rats displayed a shorter latency before self-administering the first nicotine infusion in a session. No reasons for these differences were found. Self-administration in female rats did not vary with the estrus cycle. Nor were there sex differences in either up-regulation of nicotinic receptor binding sites or in brain or plasma nicotine levels. Donny, E.C., Caggiula, A.R., Rowell, P.P., Gharib, M.A., Maldovan, V., Booth, S., Mielke, M.M., Hoffman, A., McCallum, S. Nicotine Self-Administration in Rats: Estrous Cycle Effects, Sex Differences and Nicotine Receptor Binding. Psychopharmacology, 151, pp. 392-405, 2000.

Opiate Pharmacology and Gender Difference

Dr. Theodore Cicero and his associates demonstrated that morphine served as a positive reinforcer in a place-conditioning paradigm in both male and female rats. However, the dose response curves displayed marked differences by sex. In male rats, morphine at doses above 10 mg/kg ceased to act as a positive reinforcer. Since no gender differences were observed in the blood and brain levels of morphine during the conditioning phase, the investigators suggest that these results may demonstrate intrinsic sex-linked differences in the sensitivity of the CNS to morphine's reinforcing properties. Cicero, T.J., Ennis, T., Ogden, J., and Meyer, E.R. Pharmacology Biochemistry and Behavior, 65, pp. 91-96, 2000.

The Effects of Pain on Morphine Tolerance, Withdrawal and Reward

Although opiates are used primarily for analgesia in the clinical setting, most prior preclinical research on the tolerance, withdrawal and reinforcing effects of these drugs has been conducted in pain-free animals. Recently, Dr. Shepard Siegel and his colleagues from McMaster University in Hamilton, Ontario used a standardized pain-induction procedure in rats. To compare the effect of pain on tolerance, withdrawal and the reinforcing effects of drugs. Tolerance to morphine developed only when it was administered in the absence of pain. After a three-week wash-out period, the rats were again given three days of morphine treatment, with or without pain present, and then challenged with a narcotic antagonist to test for precipitated withdrawal. The rats administered morphine in the presence of pain showed an attenuated withdrawal response. When morphine was paired with a distinct set of environmental cues in the conditioned place preference procedure, both drug groups showed an increase in time spent on the drug-paired side of the chamber in comparison to controls, but this preference was greater for rats administered morphine in the presence of pain. Thus, Dr. Siegel and his colleagues found that pain reduced tolerance to, and withdrawal from, morphine. However, pain enhanced reinforcement as measured by conditioned place preference. While conditioned place preference is not a direct measure of opiate reward, the present observation suggests that pain may enhance the reinforcing effects of morphine. However, the consequences for continued drug-seeking and drug-taking behavior (i.e., abuse liability) remain to be determined. Bardin, L., Kim, J.A. and Siegel, S. The Role of Formalin-Induced Pain in Morphine Tolerance, Withdrawal, and Reward. Experimental and Clinical Psychopharmacology, 8, pp. 61-67, 2000.

Exaggerated Corticosterone Response in Animals More Reactive to Morphine-Conditioned Taste Aversions

Dr. Felipe Gomez and colleagues at Penn State College of Medicine examined parallels between self-administration of reinforcing drugs and the ability of these drugs to condition a taste aversion when paired with distinctive gustatory cues (a "conditioned taste aversion", CTA). Senior author Dr. Patricia Sue Grigson has previously argued that these parallels, among other sources of evidence, suggest that the CTA phenomenon may be attributed to anticipatory contrast (thus reflecting the drug's rewarding properties) rather than to drug aversion. For example, activation of the hypothalamic-pituitary axis (HPA) enhances both self-administration and the development of a CTA. In a recent study these investigators took plasma corticosterone (CORT) samples from rats prior to CTA conditioning with morphine. They found that while some animals more readily acquired a CTA to a saccharin Ôcue' paired with morphine, basal CORT was no different between this group and those acquiring a weaker CTA. However, when rats developing a strong CTA were compared with those who showed a weaker CTA, (i.e., less aversion for morphine, as evidence for more acceptability of the paired gustatory cue), the large suppressers had significantly higher plasma CORT levels following the last morphine-saccharin pairing. This observation is interesting in that basal CORT was not an indicator for which rats would be more likely to develop this classically conditioned association, but those who did acquire a strong CTA also appear to have a stronger conditioned activation of the HPA axis. These results provide further support for a role of endogenous stress systems in reinforcing the effects of this opiate. Gomez, F., Leo, N.A. and Grigson, P.S. Morphine-Induced Suppression of Saccharin Intake is Correlated with Elevated Corticosterone Levels.

Brain Research, 863, pp. 52-58, 2000.

Caffeine May Not Contribute to the Flavor of Caffeinated Soft Drinks

Dr. Roland Griffiths at the Johns Hopkins University School of Medicine in Baltimore, Maryland is studying the stimulant, caffeine, as a potential model of drug reinforcement and dependence. He recently examined the concentration of caffeine in cola soft drinks using a sensitive flavor detection procedure, with 25 adult volunteers who were frequent cola drinkers. Commercially available cola drinks were adulterated with additional caffeine in order to test caffeine concentrations from 0.05 to 1.6 mg/mL. The procedure was essentially a forced-choice test with trial-by-trial feedback to compare all of the concentrations versus a caffeine-free cola. The investigators found that at the concentration typically found in commercial colas, 0.1 mg/mL, only 2 of the 25 subjects (8%) could detect a flavor difference. Overall, percent mean trials correct in detecting a flavor difference was at chance (53%) for the 25 subjects. However, at 0.4 mg/mL, subjects correctly detected a difference on 96% of the trials conducted, most often reporting the caffeine-adulterated choice to be extremely unpleasant. Based on observations from these 25 volunteers, the authors suggest that the concentration of caffeine typically found in commercial colas may contribute little to the taste of the beverage and that regular cola consumption in adults may be driven in part by pharmacological properties of the drug caffeine. Griffiths, R.R. and Vernotica, E.M. Is Caffeine a Flavoring Agent in Cola Soft Drinks? Archives of Family Medicine, 9, pp. 727-734, 2000.

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

Research Findings

Treatment Research and Development

Task Persistence Predicts Success at Smoking Cessation

Dr. Thomas Brandon and colleagues at the University of South Florida conducted a study to determine if persistence on frustrating tasks predicts success at quitting smoking among patients in a standard smoking cessation program. Task persistence was assessed in 144 smokers by measuring mean time spent solving difficult anagrams and time spent tracing geometric figures viewed through a mirror. Following smoking cessation treatment, subjects were followed for 12 months. Results indicated that the anagram and mirror tracing measures of persistence were negatively correlated with nicotine dependence. Further, persistence on the mirror-tracing task predicted successful treatment outcome. Individuals who exhibited greater task persistence were more successful at maintaining abstinence. Nath, V., Juliano, L.M., Lazev, A.B., Irvin, J.E., Stavros, R.A., Herzog, T.A. and Brandon, T.H. Paper presented at Association for the Advancement of Behavior Therapy, New Orleans, November 2000.

Tobacco Withdrawal in Women and Menstrual Cycle Phase

This study examined tobacco withdrawal, mood measures, and menstrual discomfort in 78 premenopausal women who quit smoking during either the follicular (days 1-14 postmenstrual onset) or luteal (day 15+ postmenstrual onset) phase of the menstrual cycle. Women quitting during the luteal phase reported significantly greater increases in tobacco withdrawal and self-reported depressive symptoms than women quitting during the follicular phase. Results indicate that in order to attenuate withdrawal and negative affect in female smokers, they should consider selecting a quit-smoking day early in the follicular phase. Perkins, K.A., Levine, M.D., Marcus, M.D., Shiffman, S., D'Amico, D., Miller, A., Keins, A., Ashwom, J., and Broge, M. Journal of Consulting and Clinical Psychology, 68, pp. 176-180, 2000.

Toward a Developmental Family Therapy: The Clinical Utility of Research on Adolescence

Dr. Howard Liddle and colleagues at the University of Miami focus on selected determinants of adolescent growth and development and discuss how this knowledge can have a direct and clinically useful impact on the design of treatment. The authors describe how an understanding of normative processes and developmental psychopathology in adolescent-parent relationships (e.g., attachment; conflict), biological maturation (e.g., puberty; sexuality) and cognitive development (concrete versus abstract thinking) informed the development of multidimensional family therapy for drug abusing youth. Liddle, H. A., Rowe, C., Diamond, G., Sessa, F.M., Schmidt, S. and Ettinger, D. Journal of Marital and Family Therapy, 26 (4), pp. 485-500, 2000.

A Multivariate Process Model of Adolescent 12-Step Attendance and Substance Use Outcome Following Inpatient Treatment

Dr. Mark Myers and colleagues at the University of California, San Diego, examined (1) the relationship between attendance at community-based 12-step meetings and substance use outcome after discharge from an inpatient drug treatment program and (2) a process model of how 12-step attendance affects motivation, coping and self-efficacy which, in turn, affects substance use outcome. Adolescents (N=99; 14-18 years; 60% female) were assessed at 3 and 6 months post-treatment. Results indicate modest beneficial effects of 12-step attendance that were mediated by

motivation-for-abstinence but not by abstinence-focused coping or by feelings of self-efficacy. Although average attendance dropped considerably during the second 3-month period, abstainers attended approximately twice as many 12-step meetings during the first 3 months as did adolescents who relapsed. Myers, M.G., Brown, S.A. and Kelly, J.F. Psychology of Additive Behaviors, 14(4), pp. 376-389, 2000.

Comparing LAAM, Buprenorphine and Methadone

A 17-week randomized study of 220 patients compared three times a week levomethadyl acetate (LAAM, 75 to 115 mg) and buprenorphine (16 to 32 mg), and daily high-dose (60 to 100 mg) and low-dose (20 mg) methadone as treatments for opioid dependence. 51 percent of subjects completed the trial. LAAM, buprenorphine, and high-dose methadone substantially reduced the use of illicit opioids compared with low-dose methadone. 12 or more consecutive opioid-negative urine specimens occurred in 36% of the LAAM group, 26% of the buprenorphine group, 28% of the high-dose methadone group, and 8% of the low-dose methadone group (P=0.005). The mean (SE) number of days that a patient remained in the study was significantly higher for those receiving LAAM (896), buprenorphine (964), and high-dose methadone (1054) than for those receiving low-dose methadone (704, P<0.001). Continued participation in the study was also significantly more frequent among patients receiving high-dose methadone than among those receiving LAAM (P=0.02). Johnson R.E., Chutuape, M.A. Strain, E.C., Walsh, S.L., Stitzer, M.L. and Bigelow, G.E. A Comparison of Levomethadyl Acetate, Buprenorphine, and Methadone for Opioid Dependence. N Engl J Med, 343(18), pp 1290-1297, 2000.

Elevated Liver Enzymes with Buprenorphine and a History of Hepatitis

Liver enzyme levels were evaluated among 120 individuals before treatment and following a minimum of 40 days of buprenorphine treatment (2, 4, or 8 mg/70 kg/day). Among patients with a history of hepatitis, AST and ALT levels significantly increased ($p < .05$). The odds of observing an increase in AST were dependent upon buprenorphine dose ($p < .05$; odds ratio = 1.23 per 1 mg increase in dose). These results suggest that liver enzyme levels should be monitored carefully when patients with hepatitis are treated with buprenorphine. Petry, N.M., Bickel, W.K., Piasecki, D., Marsch, L.A. and Badger, G.J. Elevated Liver Enzyme Levels in Opioid-Dependent Patients with Hepatitis Treated with Buprenorphine. Am J Addict, 9(3), pp. 265-269, 2000.

Thrice Weekly Versus Daily Buprenorphine Maintenance

Retention was 71% in the daily and 77% in the 3x/week conditions. The proportion of opioid-positive urine tests decreased significantly from baseline in both groups and averaged 57% (daily) and 58% in 3x/week. There were no significant differences between groups in self-reported number of bags of heroin used for any day of the week, or in medication compliance (92%, 91%) and counseling attendance (82%, 82%). At an equivalent weekly dose of 112 mg/70 kg, thrice-weekly and daily sublingual buprenorphine appear comparable in efficacy with regard to retention and reductions in illicit opioid and other drug use. Schottenfeld, R.S., Pakes, J., O'Connor, P., Chawarski, M., Oliveto, A., and Kosten, T.R. Biol Psychiatry, 47(12), pp 1072-1079, 2000.

Disulfiram Treatment for Cocaine Dependence

Preliminary results in 15 completers showed that the total number of weeks abstinent from cocaine was significantly greater on disulfiram than on placebo (mean +/- SD: 7.8 +/- 2.6 vs. 3.3 +/- 0.5, $p < .05$) and the number of days to achieving 3 weeks of continuous cocaine abstinence was significantly lower with disulfiram than with placebo (24.6 +/- 15.1 vs. 57.8 +/- 7.7, $p < .01$). The number of cocaine-negative urine tests during the trial were also higher on disulfiram (14.7) than on placebo (8.6); furthermore, subjects in the disulfiram group achieved consistently higher rates of cocaine-negative urine tests in each 3-week interval and the increase over time was faster in the disulfiram group. George, T.P., Chawarski, M.C., Pakes, J., Carroll, K.M., Kosten, T.R. and Schottenfeld, R.S. Disulfiram vs Placebo for Cocaine Dependence in Buprenorphine-Maintained Subjects: A Preliminary Trial. Biol Psychiatry, 47(12), pp 1080-1086, 2000.

Initiating Cocaine Abstinence with $100

On Monday of the test week, 72 cocaine-abusing methadone patients were offered a $100 voucher if urine samples collected on Wednesday indicated that they had abstained from cocaine across that 2-day period. Overall, 79% of study patients showed urinalysis evidence of abstention from cocaine between Monday and Wednesday of the test week. In a sub-sample with complete data (n = 50), almost all patients (94%) decreased their benzoylecgonine concentration from Monday to Wednesday of the test week, a significantly greater percent than decreased the week before (56%) or after (48%) the test week. Furthermore, significantly more patients abstained from cocaine from Monday to Wednesday of the test week (84%) than the week before (36%) or after (32%). This highly efficacious

procedure may have clinical application where reliable abstinence initiation is desired, either on a temporary basis (e.g. sobriety sampling) or at the start of longer-term interventions. It may also be possible to use the brief abstinence test as an experimental model to assess the effects of other therapeutic interventions on abstinence initiation in treatment settings. Robles, E., Silverman, K., Preston, K.L., Cone, E.J., Katz, E., Bigelow, G.E., and Stitzer, M.L. The Brief Abstinence Test: Voucher-Based Reinforcement of Cocaine Abstinence. Drug Alcohol Depend, 58(1-2), pp. 205-12, 2000.

Quitting Spit Tobacco with Transdermal Nicotine

In withdrawal from spit tobacco, nicotine patch was effective in increasing short-term abstinence compared to placebo patch, and in reducing craving and withdrawal signs and symptoms. Mint snuff reduced craving and withdrawal symptoms, but was not effective in enhancing treatment outcome. Hatsukami, D.K., Grillo, M., Boyle, R., Allen, S., Jensen, J., Bliss, R., and Brown, S. Treatment of Spit Tobacco Users with Transdermal Nicotine System and Mint Snuff. J Consult Clin Psychol, 68(2), pp. 241-249, 2000.

Minors Purchase Snuff at Corporate- and Independently-Owned Convenience Stores

Two underage males attempted to purchase moist snuff at each of 90 convenience stores. Two corporate owned chains with the largest number of convenience stores were selected (n = 45), along with a random sample of 45 independently owned convenience stores that held current tobacco licenses. Overall, underage buyers were sold snuff on one out of four purchase attempts. Sales occurred significantly more often in independent stores (35.6%) than in corporate stores (13.3%). An important variable associated with sales was whether the store clerk requested identification. Hanson, K., Hatsukami, D., Boyle, R. and Brown, S. Addict Behav, 25(2), pp. 289-293, 2000.

fMRI Study of Cocaine Craving

Dr. H. Garavan and colleagues at the Medical College of Wisconsin presented cocaine abusers and healthy comparison subjects with videotapes showing cocaine use, heterosexual activity, or nature scenes during BOLD fMRI scans. Cocaine users exhibited activations in the frontal cortex, parietal cortex, insula, anterior cingulated and posterior cingulated. Similar regional activations were seen during presentation of the sexual tape in both cocaine abusers and comparison subjects. In the cocaine users only 3 regions (anterior cingulate, insula, and parietal cortex) showed larger activations to the cocaine video compared to the sexual video. Cocaine users exhibited less activation to the sexual tape compared to the control subjects. Results suggest that cocaine craving is not associated with a unique neuroanatomical circuit, but that drug cues are more evocative than sexual stimuli for cocaine abusers. Garavan, H. et al., American Journal of. Psychiatry, 157, pp. 1789-1798, 2000.

Stress Imagery and Drug-Cue Imagery both Induce Similar Psychological and Physiological Reactivity

Dr. Sinha and colleagues report that personalized imagery of a stressful situation and of a drug cue situation that had been followed by taking cocaine both induce increased cocaine craving, subjective anxiety, heart rate and cortisol levels compared a neutral image. In addition increases in negative emotions (e.g., sadness, anger, fear) and decreases in positive emotions (e.g., joy) were also reported by the subjects. These results support the hypothesis that psychological stress-induced and drug cue-induced craving produce similar patterns of psychobiological activation. One implication for treatment would be that the craving state would be a reasonable target for intervention. Sinha, R., Fuse, T., Aubin, L.-R. and O'Malley, S.S. Psychopharmacology, 152, pp. 140-148, 2000.

Brain, Blood and Hair GHB Concentrations Following Fatal Ingestion

Dr. Stephen J. Kish and colleagues reported post mortem results of brain, blood and hair levels of the club drug, gamma-hydroxybutyrate (GHB), in a 22-year old woman, who died following a single GHB exposure. This case report confirmed the drug exposure through analysis of her blood and brain, and analysis of her hair indicated an absence of GHB or any other drugs of abuse in the hair segments, suggesting that the subject was not a chronic user of GHB or other drugs. GHB is a CNS depressant that has been used to induce anesthesia, treatment of narcolepsy, and for opiate and alcohol withdrawal. It has been used as a food supplement and by bodybuilders for its supposed enhancement of growth hormone release. GHB recently has been used as a sexual assault drug, as at specific doses it causes amnesia. This drug is becoming more and more widely used as a drug of abuse. Importantly, this report reinforces the finding, which is generally not widely appreciated, that GHB alone can result in overdose death, and it clearly points to the dangers of this drug.

Effect of Cocaine Administration on MRS in Basal Ganglia

Dr. Christensen and colleagues at McLean Hospital used proton MRS to assay the effect of intravenous cocaine administration on water and metabolite concentrations in the basal ganglia in cocaine abusers. Cocaine, but not placebo, produced dose-dependent increases in choline-containing compounds and N-acetylaspartate (a neuronal marker). Christensen, J.D. et al., Biological Psychiatry, 48, pp. 685-692, 2000.

Buprenorphine Changes in mu-Opioid Receptor Availability in Heroin Addicts

Using (11-C) carfentanil as a radiotracer in a PET study to assay mu opioid receptors Dr. Zubieta and colleagues at Wayne State Univ, studied male heroin-dependent subjects undergoing treatment with buprenorphine. Heroin users had greater opioid receptor binding availability in the orbitofrontal cortex and anterior cingulate compared to healthy comparison subjects during placebo studies. Buprenorphine produced dose-dependent reductions in opioid receptor availability. Zubieta, J. et al., Neuropsychopharmacology, 23, pp. 326-334, 2000.

MDMA Abuse and High-Risk Sexual Behaviors in Gay Men

Dr. R. Klitzman and colleagues of Columbia University had gay and bisexual men in 3 New York City dance clubs complete an anonymous questionnaire. About 33% reported using MDMA at least monthly. MDMA use was strongly correlated with a history of unprotected sexual activity, even after controlling for age, ethnicity, and other forms of drug abuse (including alcohol). Klitzman, R. et al., American Journal of Psychiatry, 157, pp. 1162-1164, 2000.

Cocaine Plus/Minus Alcohol on Neurocognitive Performance

Dose-related effects of cocaine on the CNS, with or without chronic alcohol use, were measured by performance on a battery of neurobehavioral tests. Fifty-six chronic cocaine users were evaluated following 1-3 days of enforced abstinence and again after 4 wks of abstinence. In addition to using cocaine, approximately half of the volunteers reported consuming more than 10 alcohol-containing drinks per week. After controlling for the effects of age, sex, and intelligence on performance, dose-related associations between neurobehavioral performance and cocaine dose and alcohol dose were found. When the influences of cocaine and alcohol on neurobehavioral performance were taken separately, cocaine and alcohol each selectively affected performance on different neurobehavioral tests after 1-3 days of abstinence, with these effects persisting after 4 wks of abstinence. Bolla, K.I., Funderburk, F.R., and Cadet, J.L. Differential Effects of Cocaine and Cocaine + Alcohol on Neurocognitive Performance. Neurology, 54(12), pp. 2285-2292, 2000.

Review of Clinical Studies of MDMA on Serotonin-Induced Neurotoxicity

(+)3,4-methylenedioxymethamphetamine (MDMA, 'Ecstasy') is a brain serotonergic neurotoxin in experimental animals, including nonhuman primates. It is also an increasingly popular recreational drug of abuse, and doses of MDMA that are used recreationally overlap with those that produce serotonin [5-hydroxytryptamine (5-HT)] neurotoxicity in animals. This article reviews findings from clinical studies of MDMA-induced serotonin neuro-toxicity. Studies in human MDMA users probing for evidence of brain serotonergic neurotoxicity show that some MDMA users may incur MDMA-related 5-HT neural injury and, possibly, functional sequelae. MDMA users have selective decrements in cerebrospinal fluid 5-hydroxyindoleacetic acid and brain 5-HT transporters, similar to nonhuman primates with documented MDMA-induced neurotoxicity. Functional abnormalities seen in MDMA users that may be related to 5-HT injury include cognitive deficits, altered sleep architecture, altered neuroendocrine function, altered behavioral responses to 5-HT selective drugs, and increased impulsivity. McCann, U.D., Eligulashvili, V., and Ricaurte, G.A (+)3,4-Methylenedioxymethamphetamine ('Ecstasy')-induced Serotonin Neurotoxicity: Clinical Studies. Neuropsychobiology, 42(1), pp. 11-16, 2000.

Review of Animal Studies of MDMA on Serotonin-Induced Neurotoxicity

The popular recreational drug, (+)3,4-methylenedioxymethamphetamine (MDMA; 'Ecstasy') is a potent and selective brain serotonin [5-hydroxytryptamine (5-HT)] neurotoxin in animals. MDMA-induced 5-HT neurotoxicity can be demonstrated using a variety of neurochemical, neuroanatomical and, more recently, functional measures of 5-HT neurons. Although the neurotoxic effects of MDMA in animals are widely accepted, the relevance of the animal data to human MDMA users has been questioned, largely because dosages of drugs used in animals are perceived as being much higher than those used by humans. In the present paper, the authors review the extensive body of data showing that MDMA produced toxic effects on brain 5-HT neurons in animals and present new data indicating that levels of the type 2 vesicular monoamine transporter are reduced in MDMA-treated animals, providing further indication of MDMA's 5-HT neurotoxic potential. Further, the authors show, using principles of interspecies scaling, that dosages of MDMA known to be neurotoxic in animals fall squarely in the range of dosages used typically by

recreational MDMA users. Ricaurte, G.A., Yuan, J., and McCann, U.D. (+)3,4-Methylenedioxymethamphetamine ('Ecstasy')-induced Serotonin Neurotoxicity: Studies in Animals. Neuropsychobiology, 42(1), pp. 5-10, 2000.

Improvement in Gambling Behavior was Seen Following a Randomized, Double-Blind, Crossover Study Using the Selective Serotonin Reuptake Inhibitor (SSRI), Fluvoxamine

Dr. Hollander and associates at Mt. Sinai School of Medicine entered advertisement-recruited and referral subjects into a 16-week double-blind study using measures of gambling urge and gambling behavior as outcome variables to determine the effect of the SSRI, fluvoxamine. Co-morbid disorders (including drug abuse) were excluded; the subjects did not undergo concomitant psychosocial or supportive therapies. Subjects taking either the placebo or SSRI during the first 8 weeks improved but those taking placebo during the second 8 weeks (having switched from SSRI) got worse while the SSRI subjects continued to improve. These data suggest that this SSRI can be effective in treating pathological gambling - a form of addiction. While the study, was limited in sample size and the elimination of common comorbid disorders (e.g., drug abuse), it is a first step in discovering the underlying mechanisms involved in addictive disorders. Hollander, E., DeCaria, C.M., Finkell, J.N., Begaz, T., Wong, C.M. and Cartwright, C. Biological Psychiatry, 47, pp. 813-817, 2000.

Two Approaches Using Reusable Gel Pad Microarray were Developed to Search for Expression of Single Nucleotide Polymorphisms (SNPs)

Dr. Mary Jeanne Kreek and her colleagues at Rockefeller University collaborated with Dr. Mirzabekov of Argonne National Laboratory to develop an assay that uses a gel-pad microarray to determine the genotype of the mu opioid receptor gene in human DNA samples. They tested the genotype of the coding region, looking for the presence of two naturally occurring single nucleotide polymorphisms (SNPs). Gel-pad microarray technology is unique because the arrays are reusable. This study is significant because methods of genotyping using arrays are still being developed and are generally prohibitively expensive. The use of reusable arrays might reduce the cost significantly, making genotyping assays rapid and routine. LaForge, K.S., Shick, V., Spangler, R., Proudnikov, D., Yuferov, V., Lysov, Y., Mirzabekov, A., and Kreek, M.J. Amer. J. Med. Genet., 96, pp. 604-615, 2000.

Sequence Variants of the Opioid Preceptor Gene OPRM1 were Associated with Substance Dependence

In a study carried out, in part by Dr. Berrettini and colleagues, all known functionally relevant regions of the OPRM1 gene were analyzed by multiplex sequence comparison in 250 cases and controls. Forty-three variants were identified and 52 different haplotypes predicted in a subgroup of African-Americans. By clustering techniques, the haplotypes were classified by similarity into two groups, one of which was significantly more frequent in substance-dependent individuals. The following were characteristic variants among these individuals: -1793T→A, -1699Tins, -1320A-G, -111C-T, +17C-T(A6V). This study is important because it provides a successful example of associating gene pattern variants with a substance abusing phenotype. Hoehe, M.R., Kopke, K., Wendel, B., Rohde, K., Flachmeier, C., Kidd, K.K., Berrettini, W.H., and Church, G.M. Hum Mol Genet, 9(19), pp. 2895-2908, 2000.

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

Research Findings

Research on AIDS and Other Medical Consequences of Drug Abuse

Sharing of Drug Preparation Equipment is a Potential Route of Hepatitis C

Transmission Investigators examined the risk of hepatitis C (HCV) transmission in relation to the sharing of cookers used to melt the drug into injectable liquid, of cotton used to filter out particles as the drug is drawn into the syringe, and of water used to rinse the syringe. Injection with a syringe previously used by another injector, and use of a syringe to divide drug doses between users (backloading) were also evaluated. HCV seroconversion was measured in a cohort of IDUs who tested negative for HCV antibody at the time of recruitment to the study. During the recruitment period, 2879 IDUs were enrolled in the overall cohort study, and only 507 (17.6%) tested 8negative for HCV. Follow-up was completed on 317 (62.5%) of the initially HCV-negative IDUs. Fifty-three of the IDUs seroconverted to HCV during the follow-up period, for a cumulative HCV incidence of 16.7%. Among those who did not share syringes, HCV seroconversion was associated with sharing drug cookers and filtration cotton (adjusted risk ratio=5.9; 95% CI=1.1, 31.7); 54% of HCV infections in IDUs who did not share syringes were attributable to cooker/cotton sharing. These findings indicate that, among IDUs who do not share syringes, an important proportion of HCV infections may be attributable to cooker/cotton sharing. Hagan ,H., Thiede, H., Weiss, N., Hopkins, S., Duchin, J. et al. Sharing of Drug Preparation Equipment as a Risk Factor for Hepatitis C. Am J Public Health, 91, pp. 42-46, 2001.

A Comparison of HIV Risk Behaviors Among New and Long-Term Injection Drug Users

The purpose of this study was to characterize the injection and sexual risk behaviors of a cohort of active drug injectors who have initiated injection within the past 4 years and to compare their behaviors with the risk behaviors of long-term injectors who have been injecting drugs since 1984. A stratified, network-based sample was used to recruit injection drug users from the streets in Miami-Dade, Florida. After screening for eligibility, which included a urine test to confirm drug use, participants were administered a structured questionnaire that included basic demographic information, drug use history, and HIV risk behavior practices. Both injector groups displayed a high level of HIV injection risk behavior. Although new initiates into injection demonstrated lower risk behavior than long-term injectors at the first injection episode, the current risk behavior between new and long-term injectors is similar. Other findings of interest include: new heroin injectors are distributed across ethnic and gender sub-populations; are initiating injection at a much later age (on average in their late 20s) than did long-term injectors who on average initiated injection in their late teens. They represent a new cohort of injectors at risk for HIV exposure and transmission. New injectors were more likely than long-term injectors to have sniffed heroin before they initiated heroin injection. Heroin sniffers are at high risk for progression to injection and are a prime target population for prevention efforts. New injectors were less likely than long-term injectors to have used speedball (heroin and cocaine in combination) and less likely to have used Dilaudid. During their first injection episode new injectors were less likely than long-term injectors to have shared syringes and other related equipment such as cookers, cottons and rinse water. Current risk behaviors, however, were quite similar for both injector groups. Chitwood, D.D., Comerford, M., Kitner, K.R., Palacios, W., and Sanchez, J. Substance Use and Misuse, 36(1), pp. 1-21, 2001.

Quality of Life Measures in the Miami HIV-1 Infected Drug Abusers (MIDAS) Cohort: Relationship to Gender and Disease Status

Shor-Posner and colleagues at the University of Miami report that HIV-infected drug abusers, particularly women, have less social support than men. The investigators assessed activity, daily living, health, support and outlook by using the Physician-administered Spitzer Index in 75 HIV-infected drug abusers (51 men; 24 women) enrolled in the Miami HIV Infected Drug Abusers Study (MIDAS). Total composite scores were significantly lower in HIV-infected women than men ($p=0.03$). Most women (45%) were homeless or marginally housed as compared to 11% of the men. Women with low activity scores had less social support than women with high activity scores. Cocaine use was significantly related to reports of normal activity, and varied across genders; more men used cocaine than women ($p=0.03$). Compared to non-AIDS participants, AIDS patients were more likely to have lower scores in health ($p=0.009$) and poor outlook ($p=0.03$). These findings reveal specific deficits in areas of psychosocial capacity, particularly in HIV-1 infected women who abuse drugs, that may need to be strengthened in order to enhance function and adherence to treatment, as well as well-being. Shor-Posner, G., Lecusay, R., Miguez-Burbano, M.J., Quesada, J., Rodriguez, A., Ruiz, P., O'Mellan, S., Campa, A., Rincon, H., Wilkie, F., Page, B., and Baum, M. Quality of Life Measures in the Miami HIV-1 Infected Drug Abusers (MIDAS) Cohort: Relationship to Gender and Disease Status. Journal of Substance Abuse, 12, pp. 1-10, 2000.

Gonadal Hormone Levels in Injection Drug Users

Dobs group at Johns Hopkins reports preliminary findings showing that HIV-infected IVDUs have low levels of serum testosterone (<410 ng/dl) and may be at risk of hypogonadism. The subjects, 40 African-Americans (20 men, 20 women, mean age of 41.5±5.6 years) were a part of a cohort from an ongoing NIDA-funded ALIVE study (AIDS Linked to Intravenous Drug Experiences). Eight (20%) of these 40 subjects had low levels of testosterone. A larger, more diverse patient population that includes non-injection drug users as controls is underway to determine the relationship between drug use, HIV status and hormones Wahlstrom, J.T., Tang, A., Cofrancesco, J., Shah, N..Jr., Dobs, A. Drug and Alcohol Dependence. 60, pp. 311-313, 2000.

Cocaine, HIV, and Their Cardiovascular Effects: Is there a Role for ACE-inhibitor Therapy?

Margolin and his group at Yale University School of Medicine tested if fosinopril could be used in the treatment of HIV and cocaine-associated cardiovascular complications. Fosinopril is an angiotensin converting enzyme (ACE) inhibitor used in the treatment of hypertension. It also modulates dopamine and corticotropin releasing factor in the brain. The investigators conducted echocardiographic and platelet activation studies in 16 HIV-infected cocaine abusing patients, as well as tolerability and efficacy studies of fosinopril for the treatment of cocaine abuse in both HIV+ (n=6) and HIV- (n=5) methadone-maintained cocaine abusers. Results showed that HIV+ cocaine abusing patients possessed abnormalities of diastolic heart function and platelet activation that are potentially reversible with fosinopril therapy. Findings also suggested that fosinopril was well tolerated regardless of HIV status, does not appear to cause hypotension, and may possess effectiveness for reducing cocaine use. The authors concluded that ACE-inhibitor therapy may offer a new pharmacologic approach to the treatment of cocaine abuse and its complications, and that controlled research of this class of agents may be promising. Margolin, A., Avants, S.K., Setaro, J.F., Rinder, H.M., Grupp, L. Drug and Alcohol Dependence. 61, pp. 35-45, 2000.

Human T-Lymphotropic Virus Type II RFLP Subtypes a0 and b4/b5 are Associated with Different Demographic and Geographic Characteristics in the United States

Murphy's group (Liu et al. 2000) has found that the human T-lymphotropic virus type II (HTLV-II), the prevalence of which is the highest among injection drug users and their sexual partners when compared to general US population and Native American Indians, exists in RFLP (restriction fragment length polymorphism) subtypes a0, a3, a5, a6, a7, b4 and b5 and in different populations. The investigators obtained blood specimens from 493 blood donors from five cities (Baltimore/Washington area, Detroit, Oklahoma, Los Angeles, San Francisco) and obtained the HTLV-II subtypes. HTLV-II subtype a0 was associated with age over 30 and with Black race/ethnicity, while subtype b4 and b5 were more common among Native Americans. The authors state that there may have been at least two transmission foci of HTLV-II in the US: a modest subtype a0 epidemic of unknown source in the 1960s and 1970s spread predominantly among Black persons in several geographic areas and a smaller focus of HTLV-II subtypes b4/b5 among non-Black individuals in Oklahoma and perhaps in other areas (not examined in this study). Liu, H., Leung, P., Glynn, S., and Murphy, E.L. Virology, 279, pp. 90-96, 2001.

HIV Risk Behaviors Differ Among IDUs, Crack Smokers, and IDUs Who Smoke Crack

A study was conducted to assess differences in sex-related risk behaviors between IDUs who did not smoke crack cocaine, crack smokers who did not inject drugs, and drug users who both injected drugs and smoked crack. Current drug users from 22 cities were recruited and assessed. The sample of 26,892 included 28% IDUs only, 42% crack smokers only, and 30% who injected drugs and smoked crack. Results showed that active drug users were at risk of

HIV through sexual transmission: in the 30 days prior to the interview, 28% reported sex with two or more individuals, 23% had an IDU sex partner, and 24% exchanged sex for drugs or money. In addition, more than 80% did not use a condom during sex. Crack smokers only, and crack smokers who also injected were more likely than IDUs only to report multiple sex partners and exchanging sex. Because of these high risk behaviors, condom use was of particular importance. The number of days of alcohol use and having an IDU sex partner were independently associated with not using a condom. Crack smoking injectors reported the highest average number of days of alcohol consumption and were the most likely to have had an IDU sex partner. Booth, R.E., Kwiatkowski, C.F., and Chitwood, D.D. Sex-Related HIV Risk Behaviors: Differential Risks Among Injection Drug Users, Crack Smokers, and Injection Drug Users Who Smoke Crack. Drug and Alcohol Dependence, 58, pp. 219-226, 2000.

Relapse to Unsafe Sex Explained by Cognitive Escape Model

A qualitative study was conducted to explore why men who have reduced their sexual behaviors to prevent HIV periodically engage in risky sex, even though they know their lapses put them at risk for acquiring HIV. Men (N=41) who have sex with men participated in semi-structured interviews during the course of the study. Findings indicate that MSM recognize strong normative expectations for using condoms during sex, and usually comply with these expectations. Constant awareness of HIV and the AIDS epidemic and the need to comply with safer sex practices were identified as sources of stress. The men noted that the intoxicating effects from use of illicit drugs and alcohol facilitated cognitive disengagement (a "time out") from the norms of safer sex. A cognitive escape model appears to explain the lapses of MSM who report periodic unprotected sex. Williams, M.L., Elwood, W.N., and Bowen, A.B. Escape from Risk: A Qualitative Exploration of Relapse to Unprotected Anal Sex Among Men Who Have Sex With Men. *J Psych Human Sexual.,* 11(4), pp. 25-49, 2000.

Network Saturation May Explain Continuing Stable HIV Prevalence in IDUs in New York

A study was conducted to consider how HIV incidence could remain moderate at seroprevalence levels that would give maximum incidence. Previous explanations include behavioral risk reduction and network saturation within high-risk groups. Among 767 IDUs studied during a period of stable high seroprevalence in New York City (i.e., from 1991-1993), risk behaviors were common and networks were far from saturated. This study explored a different network-based mechanism: in stable high-prevalence situations, the relatively small sizes of sub-networks of linked seronegatives -- within larger networks of both infected and uninfected persons-- may limit infectious outbreaks. Any primary infection outbreak would probably be limited to members of connected subcomponents of seronegatives, and the largest such subcomponent in the study included only 18 members (of 415 seronegatives). Research and mathematical modeling could explore conditions that may affect the size and stability of subcomponents of seronegatives. Finally, if the existence of small, connected components of seronegatives prevents secondary outbreaks, this protection may weaken, and vulnerability to new outbreaks increase, if HIV seroprevalence falls. Thus, in situations of declining prevalence, prevention programs should be maintained or strengthened. Friedman, S.R., Kottirl, B.J., Neaigus, A., Curtis, R., Vermund, S.H., and Des Jarlais, D. Network-Related Mechanisms May Help Explain Long-Term HIV Seroprevalence Levels That Remain High but Do Not Approach Population Group Saturation. Am J Epidemiol. 152(10), pp. 913-22, 2000.

Study Compares Computer-Administered and Face-to-Face Interviews

Researchers assessed the reliability of responses to HIV risk behavior questions obtained using a voice-enhanced, computer-administered self-interview (audio-CASI) system with touch-screen response compared with those obtained via face-to-face interviews administered by trained and experienced interviewers. Bias that may be attributable to an audio-CASI data collection format was also assessed. A 4-group crossover design was used, with random assignment to one of four study conditions: audio-CASI interview at both intake and retest; face-to-face interview at both intake and retest; audio-CASI interview at intake and face-to-face interview at retest; and face-to-face interview at intake and audio-CASI interview at retest. The study was conducted with a sample of drug users at risk for HIV infection interviewed in nonclinical settings. Data were collected at intake and 48 hours after intake. Analyses show that data obtained using voice-enhanced computer interviewing with touch screen response are reliable and are comparable to data obtained using interviewer administered face-to-face interviews. However, bias was associated with data collection format and may be partially attributable to the complexity of the questionnaire. Williams, M.L., Freeman, R.C., Bowen, A.M., Zhao, Z., Elwood, W.N., et al. A Comparison of the Reliability of Self-Reported Drug Use and Sexual Behaviors Using Computer-Assisted vs. Face-to-Face Interviewing. AIDS Education and Prevention, 12(3), pp. 199-213, 2000.

Syringe Acquisition and Use of SEPs Differ in Puerto Rican IDUs in P.R. and N.Y.

Alternative sources of syringes, including syringe exchange programs (SEPs) were compared for 165 Puerto Rican

IDUs in East Harlem, NY and 115 in Baymon, PR. IDUs in PR obtained, on average, 45% of their syringes from "syringe sellers," 18% from pharmacies, and 17.6% from a SEP. By contrast, IDUs in NY obtained 55% of their syringes from SEPs and 23% from "syringe sellers." Compared to their island counterparts, IDUs in NY received significantly more syringes from SEPs (NY, 104.5 vs PR, 9.2) in the prior 30 days, and were more likely to be referred by SEPs to drug treatment and HIV/TB-testing services. The restrictive syringe exchange policies in PR reduce access to new, sterile syringes and enhance HIV risks, indicating that PR should examine and eliminate its restrictive policies, reform drug paraphernalia laws to protect SEP clients, and address police harassment related to carrying syringes. Finlinson, A., Oliver-Velez, D., Colon, H., Deren, S., Robles, R., et al. Syringe Acquisition and Use of SEPs by Puerto Rican IDUs in New York and Puerto Rico: Comparisons Based on Quantitative and Qualitative Methods. AIDS and Behavior, 4(4), pp. 341-351, 2000.

Trends in Crime and the Introduction of a Needle Exchange Program

In this study, researchers determined whether the introduction of a needle exchange program (NEP) was associated with increased crime rates. Trends in arrests were compared in program and nonprogram areas before and after introduction of a NEP in Baltimore. Trends were modeled and compared by way of Poisson regression. No significant differences in arrest trends emerged. Over the study period, increases in category-specific arrests in program and nonprogram areas, respectively, were drug possession, 17.7% and 13.4%; economically motivated offenses, 0.0% and 20.7%; resistance to police authority, 0.0% and 5.3%; and violent offenses, 7.2% and 8.0%. the lack of association of overall and type-specific arrest data with program implementation argues against the role of NEP in increasing crime rates. Marx, M., Crape, B., Brookmeyer, R., Junge, B., Latkin, C. et al. Trends in Crime and the Introduction of a Needle Exchange Program. Am J Public Health, 90, pp. 1933-1936, 2000.

Comparison of Participants and Non-Participants Using Geographic Information System

Comparability of study participants with non-participants is customarily assessed in research studies by contrasting the distributions of sociodemographic characteristics. Such comparisons do not necessarily provide insight into whether or not participants of a given subgroup are similar to non-participants of the same subgroup. A geographical information system (GIS) may provide such insight by visually displaying the spatial distributions of participants and non-participants. In earlier research on heterosexuals at elevated risk for human immunodeficiency virus (HIV), traditional methods suggested distributional differences in the demographic characteristics of participants and non-participants. In this study, researchers used residential address coordinates for each subgroup member and the subgroup's centroid as the origin. They constructed a 360¡ series of overlapping box plots of the distance of subgroups members to the origin, thereby producing closed polygons for each of the box plot demarcators. The rotational box plots revealed similar geographical distributions for most participant and non-participant subgroups, with the exception of African-American men and women. The researchers conclude that observed differences resulted in part from the study design and provide some insight into sampling problems encountered in social network studies. Based on Tobler's supposition that Ônearby things tend to be alike', the rotational box plot represents a useful additional tool for investigating sample bias. Muth, S., Potterat, J. and Rothenberg, R. Birds of a Feather: Using a Rotational Box Plot to Assess Ascertainment Bias, Intl J Epidemiol, 5, pp. 899-904, 2000.

Accuracy of Drug Users' Recall Assessed for Use in Predicting Spread of HIV

To evaluate the accuracy of self-reports on sexual and drug use behaviors, data from a network study of HIV transmission among a sample of drug users and nonusers were used to compare reports of sexual and drug use behaviors by partners who engaged in those behaviors. Partner concordance (self-report agreement between two people) was used as an estimate of validity. Results showed that persons are able to recall and report about 85% of their recent partners (15%-20% less for recent drug use partners). For relationships that were reported by both partners, a high degree of concordance existed about recent behaviors (83%-96%) and variable agreement about frequency (0.48 Naltrexone Administration Attenuates Surgery-induced Immune Alterations in Rats

Surgery is a commonly performed procedure which produces substantial alterations in immune function in both humans and animals. To better understand the mechanism of surgery-induced immunomodulation, the present study investigated the effect of the opioid antagonist naltrexone on surgery-induced immune alterations in rats. Based on previous investigations in our laboratory, rats underwent a 6-cm laparotomy with no internal manipulation and immunological assessments were completed 24 hours following the surgical procedure. Naltrexone was administered at the time of surgery and every 4 hours thereafter until immune assessment. Results showed that naltrexone attenuated the surgery-induced decrease in natural killer cell cyto toxicity, B cell proliferation, T-cell proliferation, and production of the cytokine IFN-gamma. These results are among the first to show that pharmacological antagonism of opioid receptors can prevent deleterious immune changes in the postoperative state, suggesting a detrimental role of the endogenous opioids in surgical procedures. Nelson, C.J., Carrigan, K.A. and Lysle, D.T. Journal of Surgical

Research, 94, pp. 172-177, 2000.

Study Examines Stage of Change for Condom Use Among Women Crack Users

Attitudes-norms research (the theories of planned behavior and reasoned action) has been successful in accounting for many types of behavior change. One of the strengths of this approach has been to combine individual beliefs and normative influences in the explanation of behavior change. However, the conceptualization of normative influence in these theories makes very strong assumptions about self-awareness in the selection of normative referents. These assumptions are particularly problematic when applied to female cocaine smokers, who report frequent sex while under duress or while cognitively impaired. In this study the original conceptualization of normative influence and two alternatives (assuming emotion-based and interaction-based selection of normative referents) are operationalized to evaluate stage of change for condom use among women who are heavy crack cocaine users with multiple sex partners. Results show that stage of change for use of condoms with nonmain partners is best accounted for by interaction-based selection of normative referents. Richard, A.J., Bell, D.C., Montoya, I.D. Normative Influence on Condom Use in the Personal Networks of Female Cocaine Smokers. AIDS Educ Prev, 12(4), pp. 357-374, 2000.

Natural History of Hepatitis C Infection: Host, Viral and Environmental Factors

Hepatitis C virus (HCV) infection may resolve through viral clearance, persist with no complications, or progress to end stage liver disease (ESLD). A study to determine the incidence and determinants of viral clearance and ESLD was performed in a cohort of 1667 HCV antibody positive IDUs with median follow-up of 8.8 years. Of 919 patients assessed, persistent viremia was observed in 722 (78.6%), viral clearance in 90 (9.8%), and in 107 (11.6%), viremia was not resolved. Viral clearance occurred more frequently in non-African Americans (OR 5.15), and in those without HIV infection (OR 2.19). Forty cases of ESLD were observed during follow-up, for an incidence rate of 3.1/1000 person years. The risk of ESLD was higher for persons >= 38 years of age (adjusted relative incidence 3.67) and among those who ingested >260 g of alcohol per week (adjusted relative incidence 3.60). Only 1/1667 HCV antibody positive IDUs in this cohort had received treatment for HCV. Further research is important to understand the less frequent clearance of HCV infection among African Americans and to enhance HCV treatment utilization among eligible HCV-infected IDUs. Thomas, D.L., Astemborski, J., Rai, R.M., Anania, F.A., Schaeffer, M., Galai, N., Nolt, K., Nelson, K.E., Strathdee, S., Johnson, L., Laeyendecker, O., Boitnott, J., Wilson, L.E. and Vlahov, D. Journal of American Medical Association, 284, pp. 450-456, 2000.

Childhood Trauma as a Correlate of Lifetime Opiate Use in Psychiatric Patients

Tardiff's group (Heffernan et al. 2000) at Cornell University Medical Center found that the opiate abusers were 2.7 times more likely to have a history of childhood sexual and/or physical abuse than non-opiate users. The investigators examined the relationship between childhood abuse and opiate abuse in particular among 763 men and women consecutively admitted for psychiatric hospitalization between 1991 and 1992. Patients (age 18-59) were interviewed about demographic information, alcohol and drug use, and history of interpersonal violence. About 18% of the patients reported heavy opiate use. Childhood abuse was reported by 41.6% of the sample (17.2% physical abuse only, 9.3% sexual abuse only, and 14.8% both). Opiate use was higher among those reporting physical abuse alone (24%) or both physical and sexual abuse (27%) than among those reporting sexual abuse alone (8.8%) indicating that impact of physical abuse may create greater risk for opiate use. Heffernan, K., Coitre, M., Tardiff, K., Marzuk, P.M., Portera, L. and Leon, A.C. Addictive Behaviors, 25(5), pp. 797-803, 2000.

Prostitution and the Sex Discrepancy in Reported Number of Sexual Partners

Brewer and colleagues report that prostitute women are underrepresented in national household sexual surveys. In their examination of sampling bias to explain previous survey findings that men report more sex partners than women do, the investigators note that the proportion of heterosexual men and women in the United States is roughly balanced and that in the aggregate, men and women in a closed population have relatively the same number of sex partners. The investigators find that prostitutes have been under-represented primarily because their residences or lodgings place them outside sampling frames for household surveys and that when this undersampling is taken into consideration, the discrepancy in sexual behavior survey findings disappears. After adjusting for prostitution-related factors, such as estimated prevalence of prostitutes and their high number of sex partners (Potterat et al., Sexual, drug-using and social networks of persons presumed to be at high risk for HIV infection), the investigators conclude that essentially all the discrepancy is accounted for by undersampling of prostitutes rather than by sex-linked reporting bias such as men's reluctance to report that their partners include prostitutes. Brewer, D.B., Potterat, J.J., Garrett, S.B., Muth, S.Q., Roberts, J.M., Kasprzyk, D., Montano, D.E., and Darrow, W.W. The Proceedings of the National Academy of Sciences, 97(22), pp. 12385-12388, 2000.

Personality, Stress, and Social Support in HIV Risk Prediction

One-hundred and forty-one male veterans in treatment for alcohol and other drugs, were evaluated in terms of whether baseline levels of avoidant, antisocial, and dependent personality features and perceived stress and social support, predict 12-month follow-up levels of unprotected sex. These patients received substance abuse treatment that included an HIV transmission risk reduction component. Pretreatment levels of unprotected sex and dependent personality significantly predicted unprotected sex during follow-up. Avoidant personality was associated with reduced risk linked with lower levels of sexual involvement. Perceived stress and social support did not significantly predict level of unprotected sex during follow-up. Implications for developing personality sensitive HIV prevention interventions are discussed. McMahon, R.C., Malow, R.M., Jennings, T.E. AIDS and Behavior, 4, pp. 399-410, 2000.

Verbal Working Memory in HIV-Seropositive Drug Users

The performance of 30 HIV-seropositive male drug users (mean age 39.4 yrs) and 30 risk-matched seronegative controls (mean age 41.65 yrs) on 2 measures of verbal working memory, the Listening Span and the verbal Self-Ordered Pointing Task, was performed. The results show that impaired working memory performance was significantly more common among HIV-seropositive persons compared to controls, with the highest incidence of deficit among symptomatic participants. These findings indicate that working memory deficits in persons with HIV are not domain-specific and can be demonstrated reliably in drug users. Farinpour, R., Martin, E.M., Seidenberg, M., Pitrak, D.L., Pursell, K.J., Mullane, K.M., Novak, R.M., Harrow, M. Verbal Working Memory in HIV-seropositive Drug Users. Journal of the International Neuropsychological Society, 6(5), pp. 548-555, 2000.

Drug Use, Partner Violence, and HIV Risk

This study analyzed in-depth interviews with women in methadone maintenance treatment programs (MMTPs) who reported having experienced physical or sexual violence by an intimate partner during the past year. 87% of the women reported experiencing a minor physical assault from an intimate partner within the past year, 58% reported experiencing a severe assault, 64.5% reported experiencing minor sexual coercion, and 12.9% reported severe sexual coercion. 40% of the women indicated that both she and her partner were involved in drug-related activities during the most recent occurrence of partner abuse, 35% reported that only the partner was drug-involved, and only 6.4% of the women indicated that they alone were drug-involved. 20% reported using drugs immediately after the violent event because they were upset or in pain. Crack/cocaine was the drug most frequently mentioned by women reporting drug use before, during, or after the most recent violent event. For male partners, alcohol and crack/cocaine use were the most prevalent substances reported in conjunction with the most recent violent event. In terms of HIV risk behavior, 20% of the women reported having unwanted sex after the most recent incident. Few women reported using condoms with their main partners; yet, two-thirds reported that they had outside relationships or suspected their partners of having outside relationships. 20% reported having exchanged sex for money/drugs within the past 90 days. 20% reported injection drug use within the past year. The multiple ways in which drugs of abuse are related to partner violence and HIV risk behaviors suggest the need for specific interventions for preventing drug relapse, and HIV and HCV infection among abused women in MMTPs. Gilbert, L.,El-Bassel, N., Rajah, V. Foleno, A., Fontdevila, J., Frye, V., and Richman, B.L. The Converging Epidemics of Mood-Altering-Drug Use, HIV, HCV, and Partner Violence: A Conundrum for Methadone Maintenance Treatment. Mt. Sinai J. Med., 67(5-6), pp. 452-464, 2000.

HIV Risk Behavior Among Bisexual and Heterosexual Drug Users

This study examined the sexual and drug use behaviors for bisexual and heterosexual drug users (n=11,435 males and n=5,636 females) who participated in the NIDA AIDS Cooperative Agreement study. Results of the study suggest that, for males, bisexuality was highly associated with being homeless, having ever been paid for sex, having five or more sex partners in the month preceding the interview, having an IV drug-using sexual partner in the month preceding the interview, using crack, and sharing injection equipment in the month preceding the interview. For females, bisexuality was associated with ever having been arrested, past substance abuse treatment, ever having been paid for sex, ever having paid for sex, having five or more sexual partners in the month preceding the interview, ever using cocaine, and sharing injection equipment in the month preceding the interview. Overall, results from this study indicate that both male and female bisexuals, when compared to heterosexuals, were at higher risk for HIV and were more likely to be HIV positive. One implication of these results is that a universal prevention message may not be as effective as targeting prevention messages specifically for bisexual males and females. Logan, T. K., Leukefeld, C. J Psychoactive Drugs, 32, pp. 239-48, 2000.

Delivery of HIV Risk-Reduction Services in Drug Treatment Programs

Receipt of services targeted at HIV risk reduction was examined using data from 4,412 participants in the national Drug Abuse Treatment Outcome Study (DATOS). A higher percentage of individuals in long-term residential programs received HIV-related services, compared with clients in short-term inpatient, methadone maintenance, and outpatient drug-free programs. More men than women received HIV services. Although individuals who engaged in sex work had a higher likelihood than others of receiving HIV-related services, individuals with high-risk or multiple sexual partners were no more likely than others to receive HIV services. More comprehensive service delivery is needed in order to reduce the risk for HIV among clients in drug treatment. Grella, C.E., Etheridge, R.M., Joshi, V., and Anglin, M.D. Journal of Substance Abuse Treatment, 19(3), pp. 229-237, 2000.

Antidepressant Treatment and Health Services Utilization Among HIV-Infected Medicaid Patients Diagnosed With Depression

This study identified the prevalence and predictors of diagnosed depression among persons with HIV on Medicaid, determined who among those diagnosed received antidepressant treatment, and compared utilization and costs between depressed HIV-infected individuals treated with and without antidepressant medications. Merged Medicaid and surveillance data were used to compare health services utilized by depressed individuals who were or were not treated with antidepressant medications, controlling for other characteristics. The study population comprised Medicaid recipients in New Jersey who were diagnosed with HIV or AIDS by March 1996 and received Medicaid services between 1991 and 1996. Results indicate that women were more likely and African Americans were less likely to be diagnosed with depression. Women and drug users in treatment were more likely to receive antidepressant treatment. Depressed patients treated with antidepressants were more likely to receive antiretroviral treatment than those not treated with antidepressants. Monthly total expenditures were significantly lower for individuals diagnosed with depression and receiving antidepressant therapy than for those not treated with antidepressants. After controlling for socioeconomic and clinical characteristics, treatment with antidepressant medications was associated with a 24% reduction in monthly total health care costs. The results suggest that depressed HIV-infected patients treated with antidepressants were more likely than untreated subjects to receive appropriate care for their HIV disease. Antidepressant therapy for treatment of depression is associated with a significantly lower monthly cost of medical care services. Sambamoorthi, U., Walkup, J., Olfson, M., Crystal, S. J Gen Intern Med, 15(5), pp. 311-320, 2000.

Burnout in Substance Abuse Counselors - Impact of Environment, Attitudes, and Clients With HIV

Many substance abuse treatment counselors have clients with HIV or AIDS. The contribution of various hypothesized predictors of burnout was studied in 134 substance abuse counselors working with clients with HIV/AIDS. The three burnout dimensions were emotional exhaustion, depersonalization, and personal accomplishment. Emotional exhaustion was significantly predicted by less support, less efficacy, and working in a methadone clinic. Depersonalization was predicted by less efficacy, less support, and working in a methadone clinic. Personal accomplishment was predicted by having a lower percentage of clients with HIV/AIDS, and more efficacy; support, and education. Suggestions for interventions to prevent or limit burnout are presented. Shoptaw, S., Stein, J.A., Rawson, R.A. Journal of Substance Abuse Treatment, 19(2), pp. 117-126, 2000.

Delays in Seeking HIV Care Due To Competing Caregiver Responsibilities

This study described characteristics of HIV-infected persons who delay medical care for themselves because they are caring for others. HIV-infected adults (N = 2864) enrolled in the HIV Cost and Services Utilization Study (1996-1997) were interviewed. Results indicate that the odds were 1.6 times greater for women than for men to put off care. Persons without insurance and with CD4 cell counts above 500 were also significantly more likely to put off care. Those with a child in the household were 1.8 times more likely to put off care. Women or those with a child in the household should be offered services to allow them to avoid delays in seeking their own medical care. Stein, M.D., Crystal, S., Cunningham, W.E., Ananthanarayanan, A., Andersen, R.M., Turner, B.J., Zierler, S., Morton, S., Katz, M.H., Bozzette, S.A., Shapiro, M.F. and Schuster, M.A. Am J Public Health, 90(7), pp. 1138-1140, 2000.

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February, 2001

Research Findings

Epidemiology, Etiology and Prevention Research

Monitoring the Future (MTF) Study

Results from the MTF study were released on December 14, 2000. The major findings are summarized below. For more information, go to http://www.nida.nih.gov and to http://monitoringthefuture.org, the MTF website at the University of Michigan.

Results from the 2000 Monitoring the Future (MTF) study indicate that use of marijuana and most other illicit drugs by 8th, 10th, and 12th grade students remained stable from 1999 to 2000, continuing their recent moderating trend. However, MDMA (ecstasy) use increased among students in each grade, and steroid use increased among 10th graders; this is the second year of increases for these drugs. Past year heroin use by seniors increased to its highest level since the survey began, based largely on an increase in noninjection use of the drug. On the positive side, hallucinogen use decreased among 10th and 12th graders, and cocaine use declined among 12th graders. Notably, use of cigarettes decreased in each grade. Alcohol use remained mostly unchanged. Attitudes toward substance use, which are often seen as harbingers of changes in use, showed little systematic change from 1999 to 2000. Exceptions to that included increases in disapproval of trying marijuana among 8th and 12th graders, declines in perceived risk of cocaine use among 10th graders, increases in perceived risk of cigarette use among 8th and 10th graders, and a decrease in perceived risk of steroid use among 12th graders. Unless otherwise noted, the changes discussed are statistically significant.

Illicit Drug Use

- For the second year in a row, lifetime, past year, past month, and daily use of **marijuana/hashish** *remained unchanged* from 1999 to 2000. The same held true for the **any illicit drug use** measure. Seniors' rate of lifetime **marijuana** use is at the lowest point since 1997.

- Use of **MDMA (ecstasy)** in the lifetime and past year *increased* among 8th and 12th graders, and current use of the drug increased among 8th and 10th graders. This continues a trend seen last year for the older students and extends it to the younger students in the study.

- Lifetime and past year **steroid** use by 10th graders *increased,* continuing an increase begun last year; steroid use among 8th and 12th graders remained stable.

- Among seniors, past year use of **cocaine in any form** *decreased* from 1999 to 2000. Lifetime use of **crack** and current use of **other cocaine** also *declined* for seniors.

- **Hallucinogen** use in general and use of **LSD** in particular *declined* among 10th and 12th graders, with current use down for both grades and past year use down among 12th graders.

- **Heroin** use showed *mixed* trends, with an *increase* in past year overall heroin use and use **without a needle** among 12th graders and a *decline* in past year use overall use and use **with a needle** in the lifetime and past

year among 8th graders.

- Ever use of **inhalants** by 8th graders *decreased* in 1999 to its lowest level since 1993.
- Use of **marijuana, PCP, narcotics other than heroin, methamphetamine, crystal methamphetamine ("ice"), barbiturates, tranquilizers, and Rohypnol** remained stable for all three grades and for lifetime, past year, past month, and daily (where applicable) use.

Perceived Harmfulness, Disapproval, and Perceived Availability of Illicit Drugs

- Disapproval of trying **marijuana** once or twice *increased* among 8th and 12th graders.
- Perceived harmfulness of taking **crack** occasionally or taking **cocaine powder** once or twice or occasionally *decreased* among 10th graders.
- Perceived harm from **steroid** use *decreased* among seniors, the only class for whom measured.
- Disapproval of regular **LSD** use *decreased* among 8th graders.
- Perceived availability of **MDMA** and of **hallucinogens other than LSD** *increased* among seniors.
- Perceived availability of **crack** and **cocaine powder** *decreased* among 10th graders.

Alcohol Use

- Most measures of **alcohol** use *remained unchanged* from 1999 to 2000. The sole exception was a *decrease* in **daily alcohol use** among 8th graders.
- Perceived harm from trying one or two drinks of an **alcoholic** beverage decreased among 12th graders, and perceived availability of alcohol declined among 8th graders.

Use of Cigarettes and Smokeless Tobacco

- Use of **cigarettes** *decreased* notably in several categories from 1999 to 2000. Lifetime cigarette use declined among 8th and 10th graders; past month use decreased for 8th and 12th graders; and daily use in the past month and use of _ pack or more per day decreased among 10th and 12th graders.
- Perceived harm from **cigarette** use *increased* among 8th and 10th graders, and perceived availability of cigarettes declined among 8th and 10th graders (availability is not measured for seniors). Perceived harm from regular use of smokeless tobacco increased among 10th graders.

Community Epidemiology Work Group The 49th biannual meeting of the Community Epidemiology Work Group (CEWG) chaired by Mr. Nicholas J. Kozel, DESPR, was held in San Francisco, California, on December 12-15, 2000. 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 abuse, and negative health and social consequences. Reports are based on a variety of 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 findings from focus groups and qualitative research studies.

The following are highlights from the meetings:

Cocaine/Crack - Indicators continue to decline, a trend reported in 18 of the 21 CEWG areas. The downward trend is especially striking in areas where abuse of these drugs has been highly concentrated in the past, such as the Northeast, mid-Atlantic, and northern Midwest region of the Nation. There appears to be an aging factor among crack abusers. Nevertheless, cocaine/crack indicators remain elevated in most CEWG areas, and cocaine ranked first in DAWN ME drug-related deaths in nine CEWG sites. Indicator data show that cocaine is frequently used concurrently or sequentially with other substances.

Heroin - Indicators are trending upward in 15 CEWG sites located across the Nation. Heroin/morphine ranked first in DAWN ME drug-related mentions in eight CEWG areas. As in the past, CEWG members continued to report increases in heroin indicators among young populations. Data also show that heroin is often used in combination with cocaine (either concurrently or sequentially).

Marijuana - Indicators were mixed across CEWG areas, but there were signs that abuse of the drug is stabilizing in some areas after the dramatic upsurge from 1990-1998. While decreases or stabilization were characteristic of such indicators as ED mentions, almost all CEWG members reported increases in primary marijuana treatment admissions. Recent indicator data also show that marijuana is more likely than other illicit drugs to be used in combination with different substances, including hydrocodone and MDMA (methylenedioxymethamphetamine or ecstasy).

Methamphetamine - Indicators, which appeared to be trending downward from 1997 through the first half of 1999, showed signs of increasing again during the last half of 1999. Reports from 11 CEWG areas indicate that methamphetamine is being used along with other drugs at dance venues such as raves. There are signs also that methamphetamine is increasing in areas where it has not been a major problem in the past. A serious and sometimes fatal practice of using Viagra in combination with methamphetamine and other drugs is being reported by ethnographers.

MDMA (ecstasy) - is being closely monitored in CEWG areas. CEWG members from 17 areas report that ecstasy abuse has become more widespread recently. Members also report that ecstasy is now being used in a variety of settings, including raves, house parties and singles bars and age groups appear to be getting younger. DAWN ED mentions show that MDMA use in combination with marijuana/hashish increased from 8 in 1990 to 796 in 1999.

Emerging Drugs - Among emerging drugs of abuse are several licit substances: clonazepam (a benzodiazepine) and hydrocodone, hydromorphone, and oxycodone (controlled substances). Hydrocodone, e.g., Lorect, Lortab, appears to be the most widely abused. From 1993 to 1999, DAWN ED hydrocodone mentions increased 139 percent (from 6,115 to 14,639).

Links Between School Misbehavior, Academic Achievement, and Cigarette Use

The directionality of the association between substance abuse behaviors and negative school behaviors is unclear. In a study using the Monitoring the Future follow-up panel data, investigators at the University of Michigan examined relations among academic achievement, school bonding, school misbehavior, and cigarette use from 8th to 12th grade in two national panel samples of youth (n=3056). A series of competing conceptual models developed a priori was tested using structural equation modeling (SEM). The findings suggest that during middle adolescence the predominant direction of influence is from school experiences to cigarette use. School misbehavior and low academic achievement contribute to increased cigarette use over time both directly and indirectly. Two-group SEM analyses involving two cohorts -- gender and ethnicity -- showed robust findings. In addition, comparisons between high school dropouts and non-dropouts and between 8th grade cigarette use initiators and nonusers revealed few differences in direction or magnitude of effects. Results suggest that prevention programs that attempt to reduce school misbehavior and academic failure, as well as to help students who misbehave and have difficulty in school constructively avoid negative school- and health-related outcomes, are likely to be effective in reducing adolescent cigarette use. Bryant, A.L., Schulenberg, J., Bachman, J.G., O'Malley, P.M., and Johnston, L.D. Understanding the Links Among School Misbehavior, Academic Achievement, and Cigarette Use: A National Panel Study of Adolescents. Prevention Science, 1(2), pp 71-87, 2000.

Executive Cognitive Functioning Mediates the Relation Between Language Competence and Antisocial Behavior in Conduct-Disordered Adolescent Females

Researchers affiliated with the Center for Education and Drug Abuse Research (CEDAR) at the University of Pittsburgh conducted a study to determine (1) whether adolescent females with a conduct disorder (CD) demonstrate inferior language skills and lower executive cognitive functioning (ECF) compared with controls and (2) whether the relations between language abilities and different forms of antisocial behavior (ASB) are mediated by ECF. Language skills were measured using the Test of Language Competence-Expanded, ECF was measured using multiple neuropsychological tests, and ASB was assessed using various self-report and psychiatric interview indices reflecting

mild delinquency to severe violence. Subjects were 223 adolescent females with a CD and 97 normal controls ranging between 14 and 18 years of age (N = 320). The CD group demonstrated significantly poorer language skills and lower ECF compared with the controls. Moreover, even when controlling for chronological age and socioeconomic status, ECF still fully mediated the relations between language competence and each measure of ASB. The results are discussed in relation to a neurobehavioral model of ASB. Giancola, P.R. and Mezzich, A.C. Executive Cognitive Functioning Mediates The Relation Between Language Competence and Antisocial Behavior in Conduct- Disordered Adolescent Females. Aggressive Behavior, 26(5), pp. 359-375, 2000.

Learning Disorders in Boys with Parental History of Substance Use Disorders

In an analysis based on the CEDAR sample, investigators examined whether learning disorders (LDs) among 10- to 12-year-old boys are related to a parental history of alcohol and other substance use disorders (SUDs). Subjects were boys with (SA+; n = 179) and without (SA-; n = 203) a parental history of SUDs. LD diagnoses were made according to DSM-IV criteria using several standardized intelligence tests, and mother and teacher reports of academic and cognitive difficulties. The results indicated a higher rate of DSM-IV LDs in SA+ compared to SA- boys. This association remained significant after accounting for the effects of socioeconomic status and ethnicity. SA+ boys with a lower socioeconomic status had particularly high rates of LDs (15.3%). The results suggest that LDs are associated with a parental history of SUDs. SA+ children with lower SES may be at particularly high risk for cognitive and academic difficulties. Martin, C.S., Romig, C.J., and Kirisci, L. DSM-IV Learning Disorders in 10- to 12-Year-Old Boys With and Without a Parental History of Substance Use Disorders. Prevention Science, 1(2), pp. 107-113, 2000.

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

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

Inhalant Use Among High School Students in Illinois

Researchers at the University of Illinois at Chicago analyzed data from two years (1993 and 1995) of a statewide survey of high school students on drug use. Changes in the rates of inhalant use, and associations between inhalant use and sociodemographic variables, were examined across the two survey years. Measures of inhalant use included lifetime use, past year use, and past month use. Analyses showed no significant difference in the rates of inhalant use across years. Associations with sex, ethnicity, and age were partly consistent with previous research findings. Both lifetime and recent inhalant use were more prevalent among males than females. Blacks were less likely to use inhalants (lifetime and recent) than other racial/ethnic groups in both survey years. Native Americans showed elevated rates of recent inhalant use in 1993 but not in 1995. While patterns in age-specific rates in the 1993 survey were consistent with expectations, those in the 1995 survey were not: recent inhalant use was constant across age groups in the 1995 sample. Also contrary to expectations, inhalant use was not more prevalent in low-income or high- poverty areas. The associations of inhalant use with family intactness and academic performance varied by race/ethnicity. Family intactness was a significant protective factor only for whites and Hispanics. Poor grades were not a significant predictor of lifetime inhalant use for blacks, and the protective effect of high grades was found only for whites. Poor grades were highly predictive of lifetime inhalant use for Asians. Mackesy-Amiti, M.E. and Fendrich, M. Trends in Inhalant Use Among High School Students in Illinois: 1993-1995. American Journal of Drug and Alcohol Abuse, 26(4), pp. 569-590, 2000.

Gender Differences in Validity of Drug Use Reporting by Juvenile Arrestees

In an exploratory study, investigators at the University of Illinois at Chicago looked at the validity of drug use reporting among arrestees. Past studies on this topic have not included enough females to study gender differences. This study examined gender differences in the validity of drug use reporting among juvenile arrestees, using a gender-matched sample (n = 6,377) drawn from the Drug Use Forecasting Program for 1992-1996. Self-reported marijuana and crack and/or cocaine use was compared to urinalysis results to test gender differences in the accuracy of disclosure. Among urine positives, girls were more willing than boys to disclose past month and lifetime marijuana use. Gender was not a significant main effect for cocaine use reporting but interacted with race/ethnicity and family structure in predicting valid disclosure. Hispanic girls were significantly more likely than Hispanic boys to under report recent cocaine use. Among arrestees from homes with one or no parents, girls were significantly more likely than boys to disclose recent cocaine use. Kim, J.Y., Fendrich, M., and Wislar, J.S. The Validity of Juvenile Arrestees' Drug Use Reporting: A Gender Comparison. Journal of Research in Crime and Delinquency, 37(4), pp. 419-432, 2000.

Decreased Drug Reporting in a Cross-Sectional Student Drug Use Survey

Longitudinal cohort studies have suggested that reinterviews about drug use often lead to decreased reports of lifetime substance use (recanting). Respondents may edit their answers on reinterview because of perceptions regarding question threat. Since reinterviews usually occur after long periods of time, the influence of inadequate recall (memory), cannot be ruled out. In order to evaluate the relative importance of editing and memory on recanting, researchers examined a cross-sectional survey administered in 1993 to a probability sample of Illinois students who were in the 7th through 12th grade. Two sets of self-administered survey questions assessed drug use in this survey: the I-SAY drug-use questionnaire, and a supplemental questionnaire asked at the end of the survey. Rates of "new use " (i.e., cases where use of a drug was not reported in the I-SAY questionnaire but was reported on the supplement) with rates of recanting (use for a drug reported on the I-SAY but no use for the drug reported on the supplement). Findings indicate that recanting was generally more pronounced than was new use, especially for cocaine, heroin, marijuana, and inhalants. Those classified as light or inconsistent users on the I-SAY were significantly more likely to recant their drug use reports. Fendrich, M. and Mackesy-Amiti, M.E. Decreased Drug Reporting in a Cross-sectional Student Drug Use Survey. Journal of Substance Abuse, 11(2), pp. 161-172, 2000.

Adolescents' Reactions to Rock Stars in Anti-Drug-Abuse Commercials

Two studies by Michael Newcomb and his affiliates examined adolescents' perceptions and effectiveness of rock stars in antidrug-abuse public-service announcements (PSAs). In the pilot study (N = 24 teenagers), adolescents expected rock musicians, and in particular heavy metal musicians, to be drug users. In this experimental study (N = 78 high school students aged I5 to 16 years), one group was shown 4 PSAs produced by Rock Against Drugs®, using rock stars Jon Don Jovi, Aimee Mann, Gene Simmons, and Belinda Carlysle as spokespersons. The comparison group was shown 4 equivalent PSAs that were created using unknown actors selected for their similarity to the rock stars in terms of age, ethnicity, and gender, but without any reference to rock music. PSA ratings were taken on 4 scales: attractiveness, expertness, trustworthiness, and overall PSA rating. Pretest and posttest measures of drug attitudes supported the hypotheses that countermessages from rock stars denormalize the connection between rock music and drugs, and that adolescents respond more positively to PSAs with rock stars than to PSAs without rock stars. Newcomb, M.D., Mercurio, C.S., and Wollard, C.A. Rock Stars in Anti-drug-abuse Commercials: An Experimental Study of Adolescents' Reactions. Journal of Applied Social Psychology, 30(6), pp. 1160-1185, 2000.

Implicit Cognition, Polydrug Use, and HIV Risk Behavior

Implicit cognition theory differs from most other approaches to health behavior in that it emphasizes neurobiologically plausible and experimentally documented memory association processes rather than rational decisions, considerations of pros and cons, or beliefs. In a study of adults from a community population, investigators examined the predictive effects of implicit cognition, as well as behavioral and personality variables (sensation seeking, hostility, conscientiousness, and polydrug use), on risky sexual behaviors (lack of condom use, sex after drug use, and multiple sexual partners). In addition, the study investigated the predictors in both a high-risk and a low-risk sample. Results showed that polydrug use was the strongest and most consistent predictor of the sexual behaviors. The implicit cognition indicator was a significant, independent predictor of lack of condom use in the high-risk sample. Sensation seeking also had an important predictive effect. The results encourage more research on implicit cognition in health behavior and further document links among drug use, personality, and HIV risk behavior. Stacy, A.W., Newcomb, M.D., and Ames, S.L. Implicit Cognition and HIV Risk Behavior. Journal of Behavioral Medicine, 23(5), pp. 475-499, 2000.

Predictors of Early High School Dropout

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

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

Dr. Michael Newcomb collaborated with investigators from the University of Minnesota in developing a structural equation model looking at substance abuse problem severity, psychosocial risk and protection, and treatment variables as factors in adolescent drug abuse treatment outcome pathways across 6- and 12-month follow-up points. Findings on resiliency factors and an empirical method adapted from previous research were used to select and assign 10 psychosocial factors to either a multiple protective factor index or a risk factor index. Gender, substance abuse problem severity, treatment modality, treatment length, and aftercare participation were also examined as outcome predictors. The findings suggest that treatment intensity decisions may be better informed by pretreatment psychosocial risk level rather than by substance abuse problem severity. The present study also suggests that drug-abusing adolescents who receive sufficiently long treatment, participate in aftercare, and possess at least 1 individual or interpersonal protective factor during their recovery process have the best chance to maintain gains made during treatment. Latimer, W.W., Newcomb, M., Winters, K.C., and Stinchfield, R.D. Adolescent Substance Abuse Treatment Outcome: the Role of Substance Abuse Problem Severity, Psychosocial, and Treatment Factors. Journal of Consulting and Clinical Psychology, 68(4), pp. 684-696, 2000.

Risk and Protective Factors Influencing Adolescent Problem Behavior

Investigators at Oregon Research Institute examined the dynamic relations between adolescent- problem behaviors (alcohol, marijuana, deviance, academic failure) over time and predictors of these behaviors using data from the National Youth Survey, which included 1,044 adolescents (53.5% male; mean age at year 1 = 13.20). Dependent measures were adolescent alcohol use, marijuana use, deviance, and academic failure; assessments were conducted annually over 4 years. Independent measures included age, gender; marital status, income, family time, family support, time with friends, friend deviance, knowledge of friends, activities, and neighborhood problems. An associative latent growth modeling (LGM) analysis showed significant increases and relations between the four behaviors in both initial status and development. Second-order multivariate LGM analyses indicated that the four behaviors could be modeled by a higher-order problem behavior construct. Significant effects on the common problem behavior intercept or slope included time with friends, deviant friends, age, marital status, family time, and support. Additional effects were found to be specific to the initial status and slopes of individual problem behaviors. Overall, results indicate the importance of assessing the relations between adolescent problem behaviors as they change over time and identifying risk and protective factors that have both common and individual influences on these behaviors. Duncan, S.C., Duncan, T.E., and Strycker, L.A. Risk and Protective Factors Influencing Adolescent Problem Behavior: A Multivariate Latent Growth Curve analysis. Annals of Behavioral Medicine, 22(2), pp. 103-109, 2000.

School Dropout and Injecting Drug Use in a National Sample of White Non-Hispanic American Adults

Researchers at Johns Hopkins conducted a study to extend their previous finding of an association between school dropout and injecting drug use (IDU) among African Americans by testing the association in a sample of White non-Hispanic Americans. A nationally representative sample of White non-Hispanic Americans age eighteen years and older was drawn from public use data files of the 1995-1996 National Household Surveys on Drug Abuse (NHSDA). Adults with a self-report history of IDU were identified, and were matched to non-IDU adults in the same neighborhoods of residence. Conditional logistic regression was used to estimate the association between dropping out of high school and the occurrence of IDU. White non-Hispanic American high school dropouts were more likely than high school graduates to have injected a drug at least once. The findings of this research on non-Hispanic Whites are generally consistent with earlier evidence on the association between educational status and a history of

IDU among African-American adults. School dropout prevention programs may merit attention in an overall strategy of preventing injecting drug use and HIV/AIDS. Obot, I.S. and Anthony, J.C. School Dropout and Injecting Drug Use in a National Sample of White Non-Hispanic American Adults. Journal of Drug Education, 30(2), pp. 145-155, 2000.

Clusters of Drug Involvement in Panama

Researchers at Johns Hopkins University reported on the first epidemiological investigation of clustering of tobacco, alcohol, inhalant, and other drug involvement within individual schools using data from Panama's 1996 National Youth Survey on Alcohol and Drug Use. Clustering was estimated with the Alternating Logistic Regression method. Adjusted estimates of pair-wise cross-product ratios (PWCPR), a measure of clustering, show modest clustering (i.e. PWCPR > 1.0) at the school level for tobacco smoking (PWCPR = 1.41; 95% confidence interval, CI = 1.22-1.64), alcohol consumption (PWCPR = 1.33; 95% CI = 1.22-1.45), use of inhalants, (PWCPR = 1.35; 95%CI = 1.07-1.69), and other drug use (PWCPR = 1.38; 95%CI = 1.14-1.68). These findings provide preliminary evidence that the odds of drug use among youth who attend school increase when other youth in the same school use drugs. This suggests the need for new research on within-school diffusion, which should include the identification of school-level factors that contribute to student drug use. Delva, J., Bobashev, G., Gonzalez, G., Cedeno, M., and Anthony, J.C. Clusters of Drug Involvement in Panama: Results from Panama's 1996 National Youth Survey. Drug and Alcohol Dependence, 60(3), pp. 251-257, 2000.

Implications of Genetic Epidemiology for the Prevention of Substance Use Disorders

Despite advances in characterizing human genotypes, the complex process through which genes exert their influence limits the application of molecular genetics to human diseases. Substance use disorders are necessarily complicated by gene-environment interaction because exposure to an exogenous substance is required for their development. The methods of genetic epidemiology are specifically designed to identify sources of complexity that impede etiologic findings and prevention efforts. Researchers at Yale report a study illustrating the application of family study methods to identify risk factors for substance abuse and their implications for prevention. The Yale Family Study is a controlled family study of the comorbidity of substance and psychiatric disorders. The sample consists of 223 probands with substance use and/or an anxiety disorders and community controls, 1218 adult first degree relatives and spouses, and 203 offspring (ages 7-17) followed for 8 years. Results indicated familial aggregation of substance disorders in adults and children, independence of familial aggregation of alcoholism and drug dependence, and specificity of familial clustering of some drugs of abuse. Familial factors are more strongly associated with substance dependence than abuse, with an attributable risk of 55%. Premorbid psychiatric disorders -social phobia and bipolar affective disorder in adults, and depression, anxiety, conduct, and oppositional defiant disorders in children - were strongly associated with the subsequent development of substance dependence (attributable risks ranging from 44 to 86%). A family history of substance abuse and premorbid psychopathology are strongly associated with the development of substance use disorders. As specific genetic vulnerability markers for substance use disorders become identified, application of the tools of genetic epidemiology may be employed to identify specific environmental risk factors that may serve as targets for prevention. Merikangas, K.R. and Avenevoli, S. Implications of Genetic Epidemiology for the Prevention of Substance Use Disorders. Addictive Behaviors, 25(6), pp. 807-820, 2000.

Methamphetamine Use by High School Students

Researchers at the Tri-ethnic Center for Prevention Research at Colorado State University analyzed data on 9th through 12th graders' methamphetamine use reported in the American Drug and Alcohol Survey (n=629,722). From 1989 through 1992, methamphetamine use rates remained relatively stable. Since then, rates have increased, almost doubling, especially in Western states. There were no significant differences in methamphetamine use across year in school, but males were more likely to use than females though use among females has also increased. American Indians and Hispanics were more likely to use methamphetamine, followed (in order) by Asian Americans, White non-Hispanics, and African Americans. Compared to other heavily drug involved youth, methamphetamine users were more likely to use other drugs. The most commonly reported other drugs used by students who used methamphetamine were alcohol, marijuana, hallucinogens, uppers, and cocaine. Methamphetamine users were also more likely than other drug users to suffer drug use consequences such as traffic tickets, car accidents, being arrested, trouble at school, fighting, and other adverse consequences. Oetting, E.R., Deffenbacher, J.L., Taylor, M.J., Luther, N., Beauvais, F., and Edwards, R.W. Methamphetamine Use by High Schools Students: Recent Trends, Gender and Ethnicity Differences, and Use of Other Drugs. Journal of Child and Adolescent Substance Abuse, 10(1), pp. 33-50, 2000.

Childhood Sexual Abuse Predicts Adult Psychiatric and Substance Use Disorders in Women

Dr. Kenneth Kendler and colleagues at the Medical College of Virginia used a genetically-informed design and

population-based sample of 1411 female adult twins to explore the association between childhood sexual abuse and adult psychiatric disorders, including alcohol and substance abuse, assessed retrospectively. They found that women who reported childhood sexual abuse are at substantially increased risk to develop a range of psychopathologic outcomes, particularly alcohol and substance use disorders, primarily due to more severe sexual abuse. Of note, this relationship held when parental psychopathology was controlled in the analyses, suggesting that the relationship between childhood sexual abuse and adult outcomes is indeed causal. Although the association between sexual abuse and psychopathology has been reported previously, this study is remarkable for applying methodology that can help distinguish between association and causation by including family factors and using a co-twin report method in a population-based sample. Kendler, K.S., Bulik, C.M., Silberg, J., Hettema, J.M., Myers, J., and Prescott, C.A. Childhood Sexual Abuse And Adult Psychiatric And Substance Use Disorders In Women: An Epidemiological And Cotwin Control Analysis. Archives of General Psychiatry, 57, pp. 953-959, 2000.

Nicotine Dependence Rates Vary by Gender, Ethnicity, and Age

This study used data from the National Household Survey on Drug Abuse to look at the relationship between numbers of cigarettes used and symptoms of nicotine dependence, for various groups. The authors found that rates of nicotine dependence were highest among females, whites, and adolescents and younger adults (below age 50); each of these groups experienced more dependence symptoms while using the same or fewer number of cigarettes. Dependence rates increase sharply up to half a pack of cigarettes smoked per day. This study is unusual in using epidemiologic data from a large study to begin examining population prevalence and differential rates of nicotine dependence symptoms. It suggests that different thresholds of quantity and duration of smoking should be used in assessing different groups for risk for nicotine dependence, and that the risk for developing dependence increases sharply at lower levels of smoking (up to half a pack per day). Of particular note is the finding that adolescents, women, and whites were particularly vulnerable to the development of dependence symptoms at lower levels of consumption than their counterparts. Kandel, D.B. and Chen, K. Extent of Smoking and Nicotine Dependence in the United States: 1991-1993. Nicotine and Tobacco Research, 2, pp. 263-274, 2000.

Heritability of Tobacco Consumption Varies by Gender and Time Cohort

This article reports the largest and most comprehensive analysis to date of twin data yielding heritability estimates for tobacco use. The probands were obtained from a Swedish registry of twins born since 1886. By comparing monozygotic (MZ) and dizygotic (DZ) twin pairs, heritabilities for males was 56% with considerably lower contributions to the variance for use of tobacco; 24% and 20% for familial-environment and individual-specific environment risk factors, respectively. The pattern for females was not the same and subsequent analyses were needed to understand the differences. What seemed to matter for females was the era of their birth: those born in the first and second third of the cohort had much less heritability than those born in the last third (since 1940). In fact, those females born most recently had essentially the same heritability as males. The authors' conclude that "a reduction in the social restrictions on smoking in women in Sweden as the twentieth century progressed permitted genetic factors influencing the risk for regular tobacco use to increasingly express themselves."

A second result from this study is noteworthy. Twin correlations for amount of tobacco consumed were significant in MZ twins but not DZ twins, supporting the hypothesis that substance use is a two stage process: initiation and continued use (or misuse). Finally, the large number of twins studied allowed comparison of both MZ and DZ twin pairs who were either reared together or reared apart. This is important to address what is known as the "equal environment assumption" that assumes MZ and DZ twins are correlated in their exposure to their environment. In analyses addressing this issue, it was found that that the equal environment assumption was sufficiently valid so as not to introduce particular environmental biases due to zygosity. Kendler, K.S., Thornton, L.M., and Pedersen, N.L. Tobacco Consumption in Swedish Twins Reared Apart and Reared Together. Archives of General Psychiatry, 57, pp. 886-892, 2000.

Ethnicity and Gender in Polydrug Use

The purpose of this study was to determine if ethnic and gender differences in polydrug use exist among a cohort of inner-city adolescents during the three-year middle school period. Students in 22 urban schools completed self-report questionnaires with measures of drug use (smoking, drinking, and marijuana use) at three annual assessments. For participating students, (N=2354), analyses of variance were conducted to test for ethnic group (Asian, Black, Hispanic, and White) and gender differences in polydrug use. Ethnic differences were found for polydrug use measures at each assessment point. Asian and Black adolescents generally reported less polydrug use than White and Hispanic youth. When gender differences were evident, boys engaged in more use than girls. The relatively high rates of polydrug use indicate that prevention intervention programs that target multiple substances may be more efficient in reducing overall risk than prevention programs that focus on a single substance (e.g., smoking prevention

only). Epstein, J.A., Botvin, G.J., Griffin, K.W., and Diaz, T. Role of Ethnicity and Gender in Polydrug Use Among a Longitudinal Sample of Inner-City Adolescents. Journal of Alcohol and Drug Education, 45, pp. 1- 12, Fall 2000.

Risk Factors for Early Tobacco Experimentation

This prospective study examines the relations between the mother's prenatal and current smoking and the offspring's smoking experimentation. A low SES birth cohort of 589 10-year-olds, who have been followed since their gestation, completed a self-report questionnaire about their substance use. Half were female, and 52% were African-American. Detailed data on exposure to tobacco and other substances in the prenatal and postnatal periods were collected from the mothers. During pregnancy, 52.6% of the mothers were smokers; 59.7% were smokers when their children were 10. Six per cent of the children (37/589) reported ever-smoking cigarettes, 3% had had one full alcoholic drink, and none had started to use other drugs. Maternal smoking during pregnancy was significantly associated with an increased risk of the child's tobacco experimentation. Offspring exposed to more than _ pack per day during gestation had a 5.5-fold increased risk for early experimentation. Structural equation modeling showed that prenatal tobacco exposure had a direct and significant effect on the child's smoking and that maternal current smoking was not significant. Prenatal tobacco exposure also predicted child anxiety/depression and externalizing behaviors, and these outcomes affected child smoking through the mediating effect of peer tobacco use. Cornelius, M.D., Leech, S.L., Goldschmidt, L., and Day, N.L., Prenatal Tobacco Exposure: Is It A Risk Factor For Early Tobacco Experimentation? Nicotine & Tobacco Research, 2, 45-52, 2000.

Monthly Bursts in Adolescent Drug Use

The goal of this study was to determine the extent to which monthly bursts in substance use (i.e., tobacco, marijuana, alcohol) were related to family and peer relations. Using a structured protocol, monthly interviews were conducted with 181 young adolescents, ages 11-14 yrs old, and their parents. Scores derived from monthly telephone reports described variation in parent involvement, exposure to deviant peers, peer conflicts, and level of family stress. Consistent with an ecological framework of development, environmental factors varied by gender and family membership. Across gender in both 1- and 2-parent families, exposure to peer problem behavior co-varied with increased substance use in the same month. Other monthly predictors varied by gender. Findings suggest that intervention programs for high-risk youth targeting adolescent problem behavior need to focus on managing the peer environment. Dishion, T.J. and Medici Skaggs, N. An Ecological Analysis of Monthly "Bursts" in Early Adolescent Substance Use. Applied Developmental Science, 4(2), pp. 89-97, 2000.

Youth Violence

This study replicates earlier research findings on developmental risk factors for youth violence and explores the effects of violent behavior on factors shown to increase risk for other problem behaviors. Risk factors from the individual, family, school, peer, and community domains are examined. Prospective longitudinal data on 808 young people participating in the Seattle Social Development Project were used. Potential risk factors for violence at age 18 measured at ages 10, 14, and 16 years. Results show that at each age examined, risk factors strongly related to later violence were distributed among the 5 domains. Ten of 15 risk factors measured at age 10 were significantly predictive of violence at age 18. Twenty of 25 constructs measured at age 14 and 19 of 21 constructs measured at age 16 were significantly predictive of later violence. The hyperactivity, low academic performance, peer delinquency, and availability of drugs, were measured at all 4 ages and all 4 predicted later violence. Subjects exposed to multiple risks were more likely than others to engage in later violence. The overall accuracy in predicting those who 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.

Aggression and Drug Use Related in Inner-City Youth

In a study of 517 inner-city eighth graders, investigators found that self-reported aggressive and unsafe behaviors were associated with initiation of drug use (use of tobacco, alcohol, and marijuana). Sex differences were found for aggressive behavior, victimization, and unsafe behavior. Epstein, J.A., Botvin, G.J., Diaz, T., Williams, C., and Griffin, K. Aggression, Victimization and Problem Behavior Among Inner-City Minority Adolescents. J. of Child and Adolescent Substance Abuse, 9(3), pp. 51-66, 2000.

Reducing Adolescent Aggressive Behavior

Data from a randomized trial including 22 public schools assigned either to the Iowa Strengthening Families Program or a control condition were examined for long-term effects of this seven-session intervention for parents and their

sixth-grade children on aggressive and hostile behaviors of adolescents. Analyses supported sample representativeness of this general population study and failed to show differential attrition effects 4 years after baseline. The multi-informant, multi-method measures included independent observer ratings of adolescent aggressive and hostile behaviors in adolescent-parent interactions, family-member report of aggressive and hostile behaviors in those interactions, and adolescent self-report of aggressive and destructive conduct across settings. Data were collected during the 6th (pre- and post-intervention), 7th, 8th, and 10th grades. All measures showed a generally positive trend in intervention compared to the control group over time. During 10th grade, significant intervention-control differences were found for adolescent self-report of aggressive and destructive conduct with relative reduction rates ranging from 31.7% to 77.0%. Significant differences were shown for observer-rated aggressive and hostile behaviors in adolescent-parent interactions; differences in family member reports of those behaviors were not significant. Supplemental analyses interaction behavior measures, specific to parent gender, indicated significant experimental group differences in interactions with mothers for both measures, but not with fathers. Spoth, R.L., Redmond, C., and Shin, C. Reducing Adolescents' Aggressive and Hostile Behaviors - Randomized Trial Effects of a Brief Family Intervention Four Years Past Baseline. Archives of Pediatrics and Adolescent Medicine, 154 (12), pp. 1248-1257, 2000.

Psychosocial and Behavioral Factors Predict Heavy Drinking

A longitudinal study found that heavy drinking in 12th grade was predicted by multiple factors measured in the 7th grade, including experimentation with alcohol or cigarettes, having had a majority of friends who drink and having had poor behavioral self-control. Several effects were limited to either boys or girls. For example, positive alcohol expectancies in 7th grade predicted greater heavy drinking later in boys, while friends' smoking predicted later heavy drinking in girls. Griffin, K.W., Botvin, G.J., Epstein, J.A., Doyle, M.M. and Diaz, T. Psychosocial and Behavioral Factors in Early Adolescence as Predictors of Heavy Drinking Among High School Seniors. J. of Studies on Alcohol 61(4), pp. 603-606, 2000.

Results Linking Parenting Practices and Problem Behavior Replicated With Urban Minority Youth

A study of 228 6th grade urban minority youth found that boys from single-parent families engaged in the highest rates of problem behavior. The relationship between parenting practices and outcomes was moderated by family structure and gender. More parental monitoring was associated with less delinquency overall, as well as less drinking in boys only. Eating family dinners together was associated with less aggression overall, as well as less delinquency in youth from single-parent families and in girls. Unsupervised time at home alone was associated with more smoking for girls only. Griffin, K.W., Botvin, G.J., Scheier, L.M., Diaz, T. and Miller, N.L. Parenting Practices as Predictors of Substance Use, Delinquency, and Aggression Among Urban Minority Youth: Moderating Effects of Family Structure and Gender. Psychology of Addictive Behaviors, 14(2), pp. 174-184, 2000.

Competence Skills Protect Inner-City Adolescents from Alcohol Use

In a three-wave longitudinal study of inner city students in middle or junior high school at baseline, investigators found that decision making and self-efficacy predicted higher refusal assertiveness relative to alcohol use. Refusal assertiveness in turn predicted less drinking at the 2-year follow-up. Earlier drinking also predicted 2-year follow-up drinking. Epstein, J.A., Griffin, K.W. and Botvin, G.J. Role of General and Specific Competence Skills in Protecting Inner-City Adolescents from Alcohol Use. J. of Studies on Alcohol, 61(3), pp. 379-386, 2000.

The Relation of Perceived Neighborhood Danger and Childhood Aggression

Data from a school-based sample of 732 inner city predominantly African American 5th graders were analyzed to determine whether two mediational mechanisms, parenting practices and children's beliefs about aggression, accounted for the relationship between perceived neighborhood danger and childhood aggression. Results suggested that perceived neighborhood danger was associated with strong positive beliefs about aggression, which in turn was associated with high levels of aggression. The hypothesized mediating role of parenting practices (restrictive discipline, parental monitoring, and parental involvement) on the relation between perceived neighborhood danger and child aggression was not supported. The current findings suggest that children's positive beliefs about aggression mediated the relationship between restrictive discipline and aggression. Colder, C.R., Mott, J., Levy, S., and Flay, B. The Relation of Perceived Neighborhood Danger to Childhood Aggression: A Test of Mediating Mechanisms. American Journal of Community Psychology, 28(1), pp. 83-103, 2000.

Children's Beliefs About Long-Term Health Effects of Alcohol and Cocaine Use

The objective of this study was to assess age differences in children's beliefs about the long-term health effects of alcohol and cocaine, to use such beliefs to predict attitudes toward and intentions to use these substances, and to establish whether accurate beliefs are more predictive of attitudes and intentions than inaccurate ones. Children ages 6 to 12 (N=217) responded to an open-ended question about the effects of long-term alcohol and cocaine use and to 12 structured questions about drug effects. Differentiation of alcohol, cocaine, and tobacco effects was limited but increased with age. Beliefs about health effects had no impact on alcohol attitudes and intentions, but intentions to drink were stronger among older and white children. Anti-cocaine attitudes and intentions were associated with being older and non-White and with having accurate knowledge of cocaine's true health effects-but also with believing falsely that cocaine has tobacco-like effects and that drugs in general have catastrophic effects. With age, children differentiated more sharply between substances. Sigelman, C., Leach, D., Mack, K., Bridges, L., Rinehart, C., Dwyer, K., Elizabeth, D. and Sorongon, A. Children's Beliefs About Long-Term Health Effects of Alcohol and Cocaine Use. Journal of Pediatric Psychology, 25(8), pp. 557-566, 2000.

Development of a Training Program for Workplace Substance Abuse Prevention

This research describes the empirical and theoretical development of a workplace training program to help reduce/prevent employee alcohol and drug abuse and enhance aspects of the work group environment that support ongoing prevention. The paper (1) examines the changing social context of the workplace (e.g., teamwork, privacy issues) as relevant for prevention, (2) reviews studies that assess risks and protective factors in employee substance abuse (work environment, group processes, and employee attitudes), (3) provides a conceptual model that focuses on work group processes (enabling, neutralization of deviance) as the locus of prevention efforts, (4) describes an enhanced team-oriented training that was derived from previous research and the conceptual model, and (5) describes potential applications of the program. It is suggested that the research and conceptual model may help prevention scientists to assess the organizational context of any workplace prevention strategy. The need for this team-oriented approach may be greater among employees who experience psychosocial risks such as workplace drinking climates, social alienation, and policies that emphasize deterrence (drug testing) over educative prevention. Limitations of the model are also discussed. Bennett, J.B., Lehman, W, and Reynolds, G.S. Team Awareness for Workplace Substance Abuse Prevention: The Empirical and Conceptual Development of a Training Program. Prevention Science, 1 (3), pp. 157-172, 2000.

Effects of the "Preparing for the Drug Free Years" Curriculum on Growth in Alcohol Use and Risk for Alcohol Use in Early Adolescence

Preparing for the Drug-Free Years (PDFY) is a curriculum designed to help parents learn skills to consistently communicate clear norms against adolescent substance use, effectively and proactively manage their families, reduce family conflict, and help their children learn skills to resist antisocial peer influences. This study examined the effects of PDFY on the trajectories of these factors, as well as on the trajectory of alcohol use from early to mid adolescence. The sample consisted of 424 rural families of sixth graders from schools randomly assigned to an intervention or a control condition. Data were collected from both parents and students at pretest, posttest, and 1, 2, and 3 1/2-year follow-ups. Latent growth models were used to examine the data. PDFY significantly reduced the growth of alcohol use and improved parent norms regarding adolescent alcohol use over time. Implications for prevention and evaluation are discussed. Park, J., Kosterman, R., Hawkins, D.J., Haggerty, K.P., Duncan, T.E., Duncan, S.C. and Spoth, R. Effects of the "Preparing for the Drug Free Years" Curriculum on Growth in Alcohol Use and Risk for Alcohol Use in Early Adolescence. Prevention Science, 1 (3), pp. 125-138, 2000.

Childhood Sexual Abuse Among Female Addicts and Subsequent Parenting

The relationship between childhood sexual abuse (CSA), family of origin and the status of 248 female narcotic addicts currently raising adolescent children was examined. Seventy-eight of these women reported a history of CSA. The CSA group and the non- CSA group were compared on variables related to parental substance abuse, parenting behavior, and other family dynamics (retrospectively for families of origin and contemporaneously for current families). Findings suggest that the abuse of alcohol by the mothers of some of the CSA subjects was a contributing factor in creating an environment or set of circumstances in which the abuse took place. The two groups also differed on variables such as involvement, attachment, responsibility, discipline, and punitive actions. CSA was also related to addiction careers, parental substance use, adult psychological symptoms, and home atmosphere. Blatchley, R.J., Hanlon, T.E., Nurco, D.N., and O'Grady, K. Childhood Sexual Abuse Among Female Addicts and Changes in Parenting Across Two Generations. Fishbein, D.H. (Ed), et al. The Science, Treatment and Prevention of Antisocial Behaviors: Application to the Criminal Justice System, Kingston, NJ, US: Civic Research Institute, pp. 27-25, 2000.

Group Self-Identification and Prediction of Drug Use and Violence in High-Risk Youth

This study provides a 1-year prospective analysis of group self-identification as a predictor of adolescent drug use and violence. In most comparisons, 1 year later, a high-risk group reported greater levels of drug use and violence-related exposure than other groups, and the statistical relation between group self-identification and drug use or violence remained after controlling for baseline assessment of the drug use or violence measure. This is the first study to demonstrate that group self-identification is a significant prospective predictor of drug use and other problem behaviors. Sussman, S., Dent, C.W., and McCullar, W.J. Group Self-Identification as a Prospective Predictor of Drug Use and Violence in High-Risk Youth. Psychology of Addictive Behaviors, 14(2), pp. 192-196, 2000.

Prediction of Drug Use from Stress-Related Variables

Six stress-related variables, gender, age, and ethnicity were investigated as concurrent and prospective predictors of three types of drug use (cigarettes, alcohol, and illicit drug use) among 875 "high risk" adolescents. The stress-related variables were socioeconomic status, "missing" one's parent(s), family conflict, victimization, perceived stress, and stress-drug beliefs. In general, findings indicated that those who were lower in socioeconomic status, held beliefs favorable toward drug use and who had been victimized in the last year were more likely to be cigarette, alcohol, or illicit drug users. Those who had used drugs at baseline and had been victimized in the last year were relatively more likely to use drugs the next year. Significant predictors in the multivariable models accounted for between 56 and 85% of those subjects who were above the median on later drug use. Victimization is a relatively important source of stress in the prediction of future drug use. Thus, drug-use interventions need to provide supportive services to those who have been victims of violent attacks on their person or property. Sussman S., and Dent C.W. One-Year Prospective Prediction of Drug Use from Stress-Related Variables. Substance Use & Misuse, 35(5), pp. 717-735, 2000.

Skill Training Appears to Reduce Recidivism in Juvenile Offenders

This study compared juvenile offenders' recidivism following nonrandom assignment to juvenile diversion, juvenile diversion plus skill training, or juvenile diversion plus mentoring. Juvenile diversion with skill training was shown to be most effective, with a re-arrest rate of 37% two or more years after intake compared to 51% in the mentoring program and 46% in the diversion only program. Skills training was also most cost-effective, achieving a 14% relative reduction in recidivism at a savings of $33,600. Blechman, E.A., Maurice, A., Buecker, B. and Helberg, C. Can Mentoring or Skill Training Reduce Recidivism? Observational Study with Propensity Analysis. Prevention Science 1(3), pp. 139-156, 2000.

Paper vs. Computer-assisted Self Interview for Alcohol, Tobacco, and Other Drug Surveys

School surveys of alcohol, tobacco, and other drug use (ATOD) play an important role in evaluating prevention programs and developing policy. Until recently, most surveys are conducted with paper and pencil (PAP) instruments, but computer-assisted self-interviews (CASI) methods are becoming more common. Evidence on CASI methods indicates that they elicit higher rates of positive responses to sensitive questions than traditional measures. This study examines whether ATOD school surveys using CASI are feasible and improve the quality of data. Seventh, ninth, and eleventh grade students in two California communities were randomly assigned to PAP or to CASI (n=2296). The findings indicate that while CASI did not increase reported rates of substance use over PAP it significantly improved the speed of data processing and decreased the incidence of missing data. CASI was well accepted by students and school staff despite problems such as lack of computer resources. Hallfors, D., Khatapoush, S., Kadushin, C., Watson, K., and Saxe, L. A Comparison of Paper vs. Computer-assisted Self Interview for School Alcohol, Tobacco, and Other Drug Surveys. Evaluation and Program Planning, 23, pp. 149-155, 2000.

Trauma, Drugs and Violence Among Juvenile Offenders

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

Differences in Young Adult Psychopathology Among Drug Abstainers, Experimenters, and

Frequent Users

Shedler and Block offered the provocative proposal that individuals who experiment with drugs are psychologically healthier than either those who abstain completely or those who are frequent users. Not all studies have come to such conclusions, however. In an effort to specify under what conditions Shedler and Block's conclusions might hold, the present study examined three groups of drug users (abstainers, experimenters, frequent users) classified according to three different criteria: (a) marijuana use at age 20; (b) alcohol use during 10th grade; and (c) alcohol use at age 20. The three groups were compared at age 20 in terms of personality, deviant behavior, and psychopathology. The results revealed that abstainers were never more psychologically impaired, and were occasionally healthier, than experimenters. Frequent users of marijuana were consistently more impaired than both the abstainers and experimenters, in terms of both internalizing and externalizing disorders. Classification according to marijuana use appeared to be more related to psychopathology than did classification according to alcohol use. Milich, R., Lynam, D., Zimmerman, R., Logan, T.K., Martin, C., Leukefeld, C., Portis, C., Miller, J. and Clayton, R. Differences in Young Adult Psychopathology among Drug Abstainers, Experimenters, and Frequent Users. J Subst Abuse, 11, pp. 69-88, 2000.

Cigarette Smoking and Anxiety Disorders

Cigarette smoking has been shown to be associated with some anxiety disorders, but the direction of the association between smoking and specific anxiety disorders has not been determined. This investigation assessed the longitudinal association between cigarette smoking and anxiety disorders among adolescents and young adults. A community-based sample of 688 youths (51% female) participating in this prospective longitudinal study were interviewed in the years 1985-1986, at a mean age of 16 years, and in the years 1991-1993, at a mean age of 22 years. Participant cigarette smoking and psychiatric disorders in adolescence and early adulthood were measured by age-appropriate versions of the Diagnostic Interview Schedule for Children. Results show that heavy cigarette smoking (>/=20 cigarettes/d) during adolescence was associated with higher risk of agoraphobia (10.3% vs. 1.8%; odds ratio [OR], 6.79; 95% confidence interval [CI], 1.53-30.17), generalized anxiety disorder (20.5% vs. 3.71%; OR, 5.53; 95% CI, 1.84-16.66), and panic disorder (7.7% vs. 0.6%; OR, 15.58; 95% CI, 2.31-105.14) during early adulthood after controlling for age, sex, difficult childhood temperament; alcohol and drug use, anxiety, and depressive disorders during adolescence; and parental smoking, educational level, and psychopathology. Anxiety disorders during adolescence were not significantly associated with chronic cigarette smoking during early adulthood. Fourteen percent and 15% of participants with and without anxiety during adolescence, respectively, smoked at least 20 cigarettes per day during early adulthood (OR, 0.88; 95% CI, 0.36-2.14). These results suggest that cigarette smoking may increase risk of certain anxiety disorders during late adolescence and early adulthood. Johnson, J.G., Cohen, P., Pine, D.S., Klein, D.F., Kasen, S. and Brook, J.S. Association between Cigarette Smoking and Anxiety Disorders during Adolescence and Early Adulthood. JAMA, 284(18), pp. 2348-2351, 2000.

Development of Marijuana Use From Childhood to Young Adulthood

The present study was designed to examine the relationship between unconventionality and marijuana use over time. The sample for this paper consisted of 532 male and female participants interviewed during early adolescence, late adolescence, their early twenties, and their late twenties. Latent growth modeling was used. The findings indicated that (1) the influence of initial unconventionality (T2) on initial marijuana use (T2) was stronger for males, (2) unconventionality at T2 was not significantly related to overall rate of growth in marijuana use, and (3) change in unconventionality was related to overall growth rate of marijuana use. The implications of the findings for prevention and treatment are discussed. Brook, J.S., Whiteman, M., Finch, S.J., Morojele, N.K. and Cohen, P. Individual Latent Growth Curves in the Development of Marijuana Use from Childhood to Young Adulthood. J Behav Med 23(5), pp. 451-464, 2000.

Consequences of Adolescent Drug Use on Psychiatric Disorders in Early Adulthood

This article summarizes the existing literature on the relationship between adolescent drug use and abuse and the development of psychiatric disorders in adulthood. In recent years, there has been increased awareness of the co-occurrence of drug abuse and psychiatric disorders in adolescence and young adulthood. Few longitudinal studies, however, have examined specifically the impact of earlier drug use and abuse on later psychiatric disorders. The literature suggests three possible models to explain the relation between drug use and abuse and psychiatric disorders. According to the first model, adolescent psychiatric disorders precede drug use and abuse. A second model postulates that psychiatric disorders and drug use are correlated because they share one or more common etiological factor(s). The third model posits that drug use and abuse predict or precede certain psychiatric disorders. We present data from a recent longitudinal study to support this latter model. As drug use and abuse have been shown to increase the likelihood of psychiatric disorders, it is clear that medical attention needs to be given to adolescents who

use drugs of abuse. It is expected that a decrease in adolescent drug abuse should lead to an accompanying reduction in later psychiatric disorders. Brook, J.S., Richter, L. and Rubenstone, E. Consequences of Adolescent Drug Use on Psychiatric Disorders in Early Adulthood. Ann Med., 32(6), pp. 401-407, 2000.

Associations Between Bipolar Disorder and Other Psychiatric Disorders

This study investigated cross-sectional and longitudinal associations between bipolar disorder and other psychiatric disorders during adolescence and early adulthood. Psychiatric interviews were administered to a representative community sample of 717 youths and their mothers in 1983 (mean age of youths=14 years) and again in 1985-1986, and 1991-1993. Findings show a wide range of psychiatric disorders co-occurred with bipolar disorder during adolescence and early adulthood. Adolescent anxiety disorders were uniquely associated with increased risk for early adulthood bipolar disorder after adolescent bipolar disorder was accounted for. Manic symptoms during adolescence were associated with increased risk for anxiety and depressive disorders during early adulthood after adolescent anxiety and depressive disorders were accounted for. Researchers concluded that adolescents with anxiety disorders might be at increased risk for bipolar disorder or clinically significant manic symptoms during early adulthood. Adolescents with manic symptoms may be at increased risk for anxiety and depressive disorders during early adulthood. Johnson, J.G., Cohen, P., and Brook, J.S. Associations between Bipolar Disorder and Other Psychiatric Disorders during Adolescence and Early Adulthood: A Community-Based Longitudinal Investigation. Am J Psychiatry 157(10), pp. 1679-1681, 2000.

Personality Disorders Associated With Violence and Criminal Behavior

This community-based, longitudinal prospective study investigated whether personality disorders during adolescence are associated with elevated risk for violent behavior during adolescence and early adulthood. A community-based sample of 717 youths from upstate New York and their mothers were interviewed in 1983, 1985-1986, and 1991-1993. Axis I and II disorders were assessed in 1983 and 1985-1986. Antisocial personality disorder was not assessed because most participants were less than 18 years of age in 1983 and 1985-1986. Violent behavior was assessed in 1985-1986 and 1991-1993. Results show that adolescents with a greater number of DSM-IV cluster A or cluster B personality disorder symptoms were more likely than other adolescents in the community to commit violent acts during adolescence and early adulthood, including arson, assault, breaking and entering, initiating physical fights, robbery, and threats to injure others. These associations remained significant after controlling for the youths' age and sex, for parental psychopathology and socioeconomic status, and for co-occurring psychiatric disorders during adolescence. Paranoid, narcissistic, and passive-aggressive personality disorder symptoms during adolescence were independently associated with risk for violent acts and criminal behavior during adolescence and early adulthood after the covariates were controlled. Cluster A and cluster B personality disorders and paranoid, narcissistic, and passive-aggressive personality disorder symptoms during adolescence may increase risk for violent behavior that persists into early adulthood. Johnson, J.G., Cohen, P., Smailes, E., Kasen, S., Oldham, J.M., Skodol, A.E. and Brook, J.S. Adolescent Personality Disorders Associated with Violence and Criminal Behavior during Adolescence and Early Adulthood. Am J Psychiatry, 157(9), pp. 1406-1412, 2000.

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

Research Findings

Services Research

Comparison of Outcomes By Gender and for Fee-For-Service Versus Managed Care: A Study of Nine Community Programs

During-treatment services and 7-month post-treatment entry outcome of cocaine- or alcohol-dependent men (N = 145) and women (N = 149) Target City patients receiving either standard fee-for-services (N = 183) or managed care treatment funding (N = 111) in nine community outpatient programs were compared. No differences were found in treatment services received by the various subgroups. Regression analyses compared the four described subgroups (Gender x Type of Funding) on their seven Addiction Severity Index composite scores at 7 months post-admission controlling for the respective baseline composite score and several background variables on which the groups differed. Surprisingly few outcome differences were revealed between men and women patients and patients receiving the two forms of treatment funding. The only difference noted was that patients treated via managed care showed more improvement in the drug area. The need for further evaluation of the effects of managed care is emphasized. Alterman, A.I., Randall, M., McLellan, A.T. J Subst Abuse Treatment, 19(2), pp. 127-134, 2000.

Generalizability of the Clinical Dimensions of the Addiction Severity Index To Nonopioid-Dependent Patients

Clinical dimensions (CDs) for the Addiction Severity Index recently have been established for application among opioid-dependent patients in methadone treatment. The generalizability of CDs to other substance-dependent patients was examined in a sample of 2,027 adult nonopioid-dependent patients, comprised of 581 primarily cocaine-dependent, 544 primarily alcohol-dependent, 803 polydrug-dependent patients, and 99 patients dependent on other varied drugs. Generality of dimensions was assessed through confirmatory components analysis, structural congruence, internal consistency, and variance partitioning in higher order factoring. The CDs were found generalizable overall and to specific nonopioid-dependent subgroups, and across patient gender and age, and to African American and White patients. Preliminary concurrent and predictive validity data supported the CD structure. Alterman, A.I., McDermott, P.A., Cook, T.G., Cacciola, J.S., McKay, J.R., McLellan, A.T., Rutherford, M.J. Psychology of Addictive Behaviors, 14(3), pp. 287-294, 2000.

History of the Methamphetamine Problem

Methamphetamine (MA), called meth, crystal, or speed, is a central nervous system stimulant that can be injected, smoked, snorted, or ingested orally. Until the late 1980s, illicit use and manufacture of MA was endemic to California, but the MA user population has recently broadened in nature and in regional distribution, with increased use occurring in Midwestern states. An estimated 4.7 million Americans (2.1% of the U.S. population) have tried MA at some time in their lives. Short-and long-term health effects of MA use include stroke, cardiac arrhythmia, stomach cramps, shaking, anxiety, insomnia, paranoia, hallucinations, and structural changes to the brain. Prolonged use at high levels results in dependence. Children of MA abusers are at risk of neglect and abuse, and the use of MA by pregnant women can cause growth retardation, premature birth, and developmental disorders in neonates and enduring cognitive deficits in children. MA-related deaths and admissions to hospital emergency rooms are increasing. Although inpatient hospitalization may be indicated to treat severe cases of long-term MA dependence, optimum treatment for MA abusers appears to be an intensive outpatient setting with three to five visits per week of

comprehensive counseling for at least the first three months. Anglin, M.D., Burke, C., Perrochet, B., Stamper, E., Dawud-Noursi, S. J Psychoactive Drugs, 32(2), pp. 137-141, 2000.

Risk and Prevalence of Treatable Sexually Transmitted Diseases at a Birmingham Substance Abuse Treatment Facility

The prevalence of sexually transmitted disease (STD) was evaluated in patients entering residential drug treatment. Of 311 patients, crack cocaine use was reported by 67% and multi-substance use was reported by 71%. STD risk behaviors were common. The prevalence of infection was as follows: Chlamydia trachomatis, 2.3%; Neisseria gonorrhoeae, 1.6%; trichomoniasis, 43%; and syphilis, 6%. STD counseling and screening may be a useful adjunct to inpatient drug treatment. Bachmann, L.H., Lewis, I., Allen, R., Schwebke, J.R., Leviton, L.C., Siegal, H.A., Hook, E.W. Am J Public Health Oct; 90(10), pp. 1615-1618, 2000.

Resistance To Drug Abuse Treatment: A Comparison of Drug Users Who Accept Or Decline Treatment Referral Assessment

For largely unknown reasons, many drug abusers do not seek formal treatment. Treatment referral assessment was offered to a sample of 283 drug users. Only 58 subjects (20.5%) accepted this offer. Differences were examined between those who accepted the treatment referral assessment and those who declined. Predictors of acceptance included higher levels of severity in drug use and higher scores on a motivation and readiness scale. Among those who declined the assessment, 43.1% denied drug use, 37.3% thought their drug use was not a problem, and 16.4% expressed no interest in treatment. Further analysis showed that scores on motivation and readiness were positively related to a higher level of severity in employment problems, family problems, drug use, and to having a history of prior treatment. Boyle, K., Polinsky, M.L., Hser, Y.I. Journal of Drug Issues, 30(3), pp. 555-574, 2000.

Program Variation in Treatment Outcomes Among Women in Residential Drug Treatment

Multilevel modeling was used to assess the program characteristics associated with treatment retention among 637 women in 16 residential drug treatment programs in the Drug Abuse Treatment Outcome Study. Women who were pregnant or had dependent children had higher rates of retention in programs in which there were higher percentages of other such women. Programs with higher proportions of pregnant and parenting women provided more services related to women's needs. Longer retention was associated with higher rates of post-treatment abstinence. The findings support provision of specialized services and programs for pregnant and parenting women. Grella, C.E., Joshi, V., Hser, Y.I. Eval Review, 24(4), pp. 364-383, 2000.

A Search for Strategies To Engage Women in Substance Abuse Treatment

In order to remain in treatment, patients must initially engage in the treatment process, and clinicians seek motivational strategies to draw each patient into the treatment process. This study found that outpatient clients who received engagement services during the intake period showed increased use of these services, relative to a comparison group, throughout the treatment process. Tangible engagement services provided to women during the intake period for outpatient substance abuse treatment had no significant effect on the rates of admission, discharge, and service utilization. Comfort, M., Loverro, J., Kaltenbach, K. Social Work in Health Care, 31(4), pp. 59-70, 2000.

Access to Substance Abuse Treatment Services Under the Oregon Health Plan

The 1995 implementation of a capitated substance abuse benefit within the Oregon Health Plan, a Medicaid managed care plan, provided an opportunity to study the impact of funding mechanisms on access to publicly funded substance abuse treatment. Statewide treatment data for all Medicaid-eligible persons aged 12 to 64 years enrolled in the Oregon Health Plan before (1994) and after (1997) implementation of the capitated benefit were analyzed. An increase was found in access to substance abuse treatment for Medicaid-eligible persons in Oregon after a shift to managed care. Results show that the percentage of Medicaid-eligible persons admitted to substance abuse treatment programs during a calendar year increased from 5.5% of the average number of enrolled members per month in 1994 to 7.7% in 1997, following managed care. After case mix adjustment, access rates varied considerably among the 7 largest prepaid health plans. Operating characteristics of these health plans, such as the method of reimbursing treatment providers, were significant predictors of access. Deck, D.D., McFarland, B.H., Titus, J.M., et al. J Am Med Assoc, 284(16), pp. 2093-2099, 2000.

Modified Therapeutic Community for Homeless Mentally Ill Chemical Abusers: Treatment Outcomes

Two modified therapeutic community programs (TC1 and TC2) were compared with treatment as usual (TAU) for 342 homeless mentally ill chemical abusers (MICA). Follow-up interviews were obtained at 12 months post-baseline and at an average of about 2 years post-baseline. Outcome measures assessed drug use, crime, HIV risk behavior, psychological symptoms, and employment. Individuals in both modified TC groups showed significantly greater behavioral improvement than TAU at both follow-up time intervals. TC2, with lower demands and more staff guidance, was superior to TC1. Completers of modified TC programs showed significantly greater improvement than either TC dropouts or a subgroup of TAU clients with high exposure (i.e., more than 8 months) to other treatment protocols. The findings support the effectiveness and longer-term stability of effects of modified TC programs for treating homeless MICA clients. De Leon, G., Sacks, S., Staines, G., McKendrick, K. American J Drug Alcohol Abuse, 26(3), pp. 461-480, 2000.

To Thine Own Self Be True: Self-Concept and Motivation for Abstinence Among Substance Abusers

Individuals on a wait-list to enter public-sector addiction treatment were interviewed regarding their reasons for attempting abstinence. Follow-up interviews were completed 3 to 6 months after participants' removal from county-controlled treatment wait-lists. Rates of continuous self-reported abstinence for 90 days preceding follow-up were positively associated with motivation linked to discrepancies between substance use and self-standards. Characteristics associated with high identity-linked motivation were cocaine preference, a history of reducing self-dissatisfaction through substance use, low rewards and high costs associated with using, and low support for the user identity among significant others. The perception of discrepancies between substance use and self-standards was an effective motivator of abstinence even among those who reported previous use of substances to dampen self-dissatisfaction. Downey, L., Rosengren, D.B., Donovan, D.M. Addictive Behaviors, 25(5), pp. 743-757, 2000.

Benefit-Cost Analysis of Residential and Outpatient Addiction Treatment in the State of Washington

A benefit-cost analysis of full continuum (FC) residential and partial continuum (PC) outpatient care was conducted on a sample of substance abusers from the State of Washington. Economic benefits were derived from client self-reported information at treatment entry and at 9 months postadmission using an augmented version of the Addiction Severity Index. Results strongly indicate that both treatment options generate positive and significant net benefits to society. Average per client economic benefits of treatment from baseline to follow-up were statistically significant for both FC and PC for most variables and in the aggregate. The overall difference in average economic benefit between FC and PC was positive ($8,053) and statistically significant, favoring FC over PC. The average cost of treatment amounted to $2,530 for FC and $1,138 for PC. Average net benefits were estimated to be $17,833 for FC and $11,173 for PC, a statistically significant difference. French, M.T., Salome, H.J., Krupski, A., McKay, J.R., Donovan, D.M., McLellan, A.T., Durell, J. Evaluation Review, 24(6), pp. 609-634, 2000.

Measuring Client Clinical Progress in Therapeutic Community Treatment: The Therapeutic Community Client Assessment Inventory, Client Assessment Summary, and Staff Assessment Summary

Measuring changes in the individual during treatment is a first step in the effort to understand the change process and what can be done to improve treatment effectiveness. The development of the therapeutic community (TC) Client Assessment Inventory (CAI), Client Assessment Summary (CAS), and Staff Assessment Summary (SAS) is described. These instruments, derived from a comprehensive theory of TC treatment and recovery, measure client self-report and staff evaluation of client progress along 14 domains of behavior, attitude, and cognitive change. Analyses of scale properties indicate that both client and staff instruments reliably differentiate clinical changes during treatment. Client self-ratings are initially consistently higher than staff ratings. Kressel, D., De Leon, G., Palij, M., Rubin, G. J Substance Abuse Treatment, 19(3), pp. 267-272, 2000.

Support, Mutual Aid and Recovery from Dual Diagnosis

In recovery from substance abuse and mental health disorders (dual-diagnosis), social support can have a buffering role in stressful situations. The associations among social support (including dual-recovery mutual aid), recovery status, and personal well-being were investigated in dually-diagnosed individuals (N = 310) using cross-sectional self-report data. Persons with higher levels of support and greater participation in dual-recovery mutual aid reported less substance use and mental health distress and higher levels of well-being. Participation in mutual aid was indirectly associated with recovery through perceived levels of support. The association between mutual aid and recovery held for dual-recovery groups but not for traditional, single-focus self-help groups. Laudet, A.B., Magura, S.,

Vogel, H.S., Knight, E. Community Mental Health Journal, 36(5), pp. 457-476, 2000.

Correlates of Outpatient Drug Treatment Drop-Out Among Methamphetamine Users

California Alcohol and Drug Data System (CADDS) data were used to provide information on retention and drop-out for 2,337 methamphetamine users entering public outpatient treatment programs in California from 1994 - 1997. Overall, 23.3% of methamphetamine users completed 180 or more days of treatment, a rate similar to that for users of other drugs throughout California. Methamphetamine users who were older (40 years or over), had less severe drug use patterns (used less than daily or did not inject), or who were under coerced treatment were significantly more likely to complete treatment that other methamphetamine users. Men were significantly more likely to drop out of treatment before 180 days. Maglione, M., Chao, B., Anglin, M.D. J Psychoactive Drugs, 32(2), pp. 221-228, 2000.

Detoxification Centers: Who's in the Revolving Door?

Data from 443,812 admissions to publicly funded detoxification centers in Massachusetts from 1984 to 1996 were analyzed to assess changes in the population served. Substantial increases in admissions of women, African Americans, and Hispanics were apparent. Mean age at admission declined and unemployment increased. A 25% decline in admissions reporting alcohol use was coupled with a twofold increase in reported cocaine use and a fourfold increase in heroin use. Detoxification services have evolved. The older, white, male alcoholic is no longer the primary consumer. Policy initiatives (e.g., increased services for women) and the changing epidemiology of drugs abuse (e.g., increased access to heroin) contributed to the changing population served in detoxification centers. McCarty, D., Caspi, Y., Panas, L., Krakow, M., Mulligan, D.H. J Behav Health Serv Res, 27(3), pp. 245-256, 2000.

Predictors of Substance Abuse Treatment Retention Among Women and Men in an HMO

Although research has examined treatment retention in public drug treatment programs, little is known about factors that influence treatment retention in an insured outpatient population. All eligible intakes to a health maintenance organization's outpatient alcohol and drug treatment programs (abstinence based day hospital and traditional outpatient modalities) were recruited during a 2-year period, for a sample of 317 women and 599 men. One general pattern of predictors of increased retention was shared by women and men -- fewer and less severe drug problems. Most other predictors were gender-specific. Among women, higher retention was predicted by having higher incomes, belonging to ethnic categories other than African American, being unemployed, being married, and having lower levels of psychiatric severity. Among men, predictors of higher retention included being older, receiving employer suggestions to enter treatment, and having abstinence goals. These findings suggest treatment factors that may enhance retention among insured populations, including employer referrals, psychiatric services, and drug-related services. Mertens, J.R., Weisner, C.M. Alcohol Clin Exp Res, 24(10), pp. 1525-1533, 2000.

Managed Care Risk Contracts and Substance Abuse Treatment

This study estimates how one managed care arrangement, shifting risk to the organization managing care, affects substance abuse treatment. Full risk plans do not differ in access rates to any substance abuse treatments or inpatient treatment, but they significantly lower costs per user (by about $470, or 17%). Sturm, R. Inquiry - The Journal of Health Care Organization Provision and Financing, 37(2), pp. 219-225, 2000.

A Comparison of Substance Abuse Patients' and Counselors' Perceptions of Relapse Risk: Relationship To Actual Relapse

This study compared substance abuse patients' and their counselors' perceptions of relapse risk during treatment and evaluated whether these perceptions predict actual relapse 2 years later. Participants (N = 240) completed the Relapse Risk Index (RRI), which assesses confidence in abilities and need for services across four domains: coping skills, social support, resources, and leisure activities. Participants reported greater confidence and greater needs than counselors reported. Determinants of counselors' relapse risk perceptions included income, whereas participants' perceptions were related to polysubstance use. Counselors' ratings of coping skills predicted alcohol relapse; counselors' ratings did not predict drug relapse. Participants' ratings of coping skills and leisure activities predicted alcohol relapse; social support predicted drug relapse. When including background characteristics, counselors' ratings did not predict alcohol or drug relapse; participants' ratings predicted alcohol relapse but not drug relapse. Findings suggest the potential utility of considering patient perceptions to understand and possibly prevent relapse. Walton, M.A., Blow, F.C., Booth, B.M. J Substance Abuse Treatment, 19(2), pp. 161-169, 2000.

Addiction Severity Index Data from General Membership and Treatment Samples of HMO Members: One Case of Norming the ASI

The purpose of this study was to enhance the value of the Addiction Severity Index (ASI), a widely used drug abuse treatment planning and evaluation tool, by obtaining comparative data from nonclinical samples. The study included four ASI scales collected on samples of adult subscribers to a large health maintenance organization (HMO) in northern California, as well as an adult clinical sample from the same geographic region with the same HMO insurance. Interviews (N = 9,398) of non-alcohol-dependent or abuse adults from a random sample of members of a large HMO were analyzed. Complete ASI data were collected on the alcohol, drug, medical, and psychiatric composite scales and partial data on the employment scale. A sample of 327 adult members of the same HMO from one of the counties included in the survey, who were admitted to treatment for alcohol and/or drug addiction, was administered the same ASI items at treatment admission. Analyses compare problem severities in the two samples by age and gender. The general membership reported some problems in most of the ASI problem areas, although at levels of severity that were typically far below those seen in the clinical sample. General membership and clinical samples were somewhat similar in medical status and in employment. Alcohol, drug, and psychiatric status were much more severe in the clinical sample. The data from the HMO general membership sample provide one potential comparison group against which to judge the severity of problems presented by drug- and alcohol-dependent patients at treatment admission and at post-treatment follow-up. One implication of this study is that treatment-seeking substance dependent individuals may need a wider range of services than those focused simply on alcohol and drug use. Weisner, C., McLellan, A.T., Hunkeler, E.M. J Substance Abuse Treatment, 19(2), pp. 103-109, 2000.

The Outcome and Cost of Alcohol and Drug Treatment in an HMO: Day Hospital Versus Traditional Outpatient Regimens

Outcome and cost-effectiveness of two primary addiction treatment options, day hospitals (DH) and traditional outpatient programs (OP), were compared in a managed care organization. New admissions to a large HMO's chemical dependency program in California were interviewed between April 1994 and April 1996, with follow-up interviews eight months later. Admissions were randomly assigned to DH or OP; those who refused random assignment were also studied to determine the impact of self selection to treatment. Among randomized subjects, both treatment options showed significant improvement in all drug and alcohol measures. There were no differences overall in outcomes between DH and OP, but DH subjects with midlevel psychiatric severity had significantly better outcomes, particularly for alcohol abstinence (OR = 2.4; 95% CI = 1.2, 4.9). The average treatment costs were $1,640 and $895 for DH and OP programs, respectively. In the midlevel psychiatric severity group, the marginal cost of obtaining abstinence from alcohol in the DH cohort was approximately $5,464. Among the 405 self-selected subjects, DH was related to abstinence (OR = 2.1; 95% CI = 1.3, 3.5). Although significant benefits of the DH program were not found in the randomized study, DH treatment was associated with better outcomes in the self-selected group. For subjects with midlevel psychiatric severity in both the randomized and self-selected samples, the DH program produced higher rates of abstention and was more cost-effective. Understanding self-selection effects in studies that randomize patients to services requiring very different levels of commitment may be important in interpreting findings for clinical practice. Weisner, C., Mertens, J., Parthasarathy, S., Moore, C., Hunkeler, E.M., Hu, T., Selby, J.V. Health Service Research, 35(4), pp. 791-812, 2000.

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

Monitoring Opiate Use in Substance Abuse Treatment Patients by Sweat and Urine Testing

Although urine testing remains the standard for drug use monitoring, sweat testing for drugs of abuse is increasing. This study was designed to compare the efficacy of sweat testing versus urine testing for detecting drug use. Paired sweat patches applied and removed weekly were compared to consecutive urine specimens collected three times per week from patients in a methadone maintenance outpatient treatment program. Patches were analyzed by ELISA immunoassay for opiates and by GC/MS. Urine specimens were subjected to qualitative analysis by EMIT. Opiates were detected in 38.5% of the sweat patches with the ELISA screen. GC-MS analysis confirmed 83.4% of the screen-positive sweat patches for heroin, 6-acetylmorphine, morphine and/or codeine and 90.2% of the screen-negative patches. Heroin and/or 6-acetylmorphine were detected in 78.1% of the GC/MS positive sweat patches. Agreement in paired sweat patch test results was 90.6% by ELISA analysis. Analysis of sweat patches provides an alternate method for objectively monitoring drug use and provides an advantage over urine drug testing by extending drug detection times to one week or longer. In addition, identification of heroin and/or 6-acetylmorphine in sweat patches confirmed the use of heroin in 78.1% of the positive cases and differentiated illicit heroin use from possible ingestion of codeine or opiate-containing foods. However, the percentage of false negative results, at least in this treatment population, indicates that weekly sweat testing may be less sensitive than thrice weekly urine testing in detecting opiate use. Huestis M. A., Cone, E. J., Wong, C. J., Umbricht, A., and Preston, K. L. Journal of Analytical Toxicology, 24, pp. 509-521, 2000.

Cocaine and Metabolite Elimination Patterns in Chronic Cocaine Users During Cessation: Plasma and Saliva Analysis

It has been suggested that cocaine may accumulate in tissues following chronic administration and be detectable for an extended period of time compared to acute dosing. This study was designed to investigate the elimination patterns of cocaine and metabolites in the body fluids of chronic high-dose cocaine users. Male and female cocaine-using volunteers were housed on a closed research ward where blood and saliva specimens were collected periodically for up to 12 hours beginning immediately upon their entry to the ward. Specimens were analyzed by gas chromatography mass spectrometry for cocaine, benzoylecgonine, ecgonine methyl ester and other metabolites. On average, subjects had a history of cocaine use of approximately eight years and current cocaine use of approximately 10 days in the past 2 weeks. Time since last illicit reported use of cocaine prior to sample collection ranged from 2.5 to 63 hours. Plasma cocaine (COC) was detected in 16 subjects with an intake mean of 13.4 ± 37.0 ng/ml (highest 162.2). The mean and highest concentration of cocaine in saliva were 19.5 ± 41.4 ng/mL and 170.7 ng/mL, respectively. Where cocaine was detected in both plasma and saliva, the mean saliva-to-plasma (s/p) ratios was 5.2 ± 6.1 (range 0.7 to 16.1). These data suggest that low concentrations of unmetabolized cocaine and higher concentrations of metabolites can be detected in both plasma and saliva several hours after last use. While cocaine s/p ratios were comparable to those reported from studies of acute administration, these data suggest that EME accumulates as a result of chronic administration. Moolchan, E. T., Cone, E. J., Wtsadik, A., Huestis, M. A., and Preston, K. L. Journal of Analytical Toxicology, 24, pp. 458-466, 2000.

Sweat Testing for Cocaine, Codeine and Metabolites by Gas Chromatography Mass Spectrometry

Sweat testing for drugs of abuse provides a convenient and considerably less invasive method for monitoring drug exposure than blood or urine. Numerous devices have been developed. The most common device for collection of sweat specimens in current use is the PharmChek™ Sweat Patch which usually is worn by an individual for five to ten days. This device has been utilized in several field trials comparing sweat test results to conventional urinalysis with favorable results. Two new Fast Patch devices have been developed and tested that allow rapid collection of sweat specimens. The Hand-held Fast Patch was applied to the palm of the hand and the Torso Fast Patch was applied to the abdomen. Both patches employed heat-induced sweat stimulation and a larger cellulose pad for increased drug collection. Sweat specimens were collected for 30 min at various times following administration of cocaine or codeine in controlled dosing studies and analyzed by GC-MS simultaneously for cocaine, codeine and metabolites. Cocaine and codeine were the primary analytes detected in sweat. Peak cocaine and codeine concentrations ranged from 33-3579 ng/patch and 11-1123 ng/patch, respectively, across all doses for the Hand-held Patch compared to 22-1463 ng/patch and 12-360 ng/patch, respectively for the Torso Fast Patch. Peak concentrations generally occurred 4.5-24 h after dosing and were considerably higher than those reported for the PharmChek™ Sweat Patch. Multiple mechanisms appear to be operative in determining the amount of drug and metabolite secreted in sweat including passive diffusion from blood into sweat glands and outward transdermal migration of drug. Additional important factors are the physico-chemical properties of the drug analyte, specific characteristics of the sweat collection device, site of sweat collection, and in this study, the application of heat to increase the amount of drug secreted. Huestis, M. A., Oyler, J. M., Cone, E. J., Wtsadik, A. T., Schoendorfer, D., and Joseph, R. E. Journal of Chromatography B, 733, pp. 247-264, 1999.

Tolerance to Nicotine in Nonsmokers

When administered acutely to nonsmokers, nicotine's effects on performance are inconsistent, perhaps because of suboptimal dosing or initial dysphoria that could interfere with performance. The purpose of this study was to determine if a range of nicotine doses administered for 8 days to nonsmokers would enhance psychomotor and cognitive abilities and to document the development of nicotine tolerance or sensitization. Twelve male volunteers, who reported ever smoking 5 cigarettes or less, participated in 8 consecutive experimental days in which they were administered four doses of nicotine polacrilex gum each day in this order: 0, 2, 4, and 8 mg. Performance, subjective, and physiological measures were assessed before and after each dose. Plasma nicotine concentration ranged from 6.9 to 11.5 ng/ml following the 8 mg dose. Nicotine increased rate of responding and decreased response time on working memory (digit recall); however, accuracy was impaired. Nicotine also decreased accuracy on visual scanning and attention (two-letter search), and the 8 mg dose impaired gross motor coordination (circular lights). Tolerance did not develop to the performance impairing effects of nicotine. Nicotine produced dose-related increases in ratings of dysphoria and negative mood, including tension, anxiety, nervousness, turning of stomach, and sedation. Tolerance developed to some, but not all, of these aversive effects. Tolerance also was not observed to the increased cardiovascular measures. Although tolerance developed to some of the aversive effects of nicotine, performance enhancement was not observed. These data do not support the hypothesis that nicotine-induced performance enhancement contributes to the reinforcing effects of tobacco use during the early stages of dependence development. Heishman, S. J., and Henningfield, J. E. Psychopharmacology, 152, pp. 321-333, 2000.

Development and Plasticity Section, Cellular Neurobiology Research Branch

Neuropathology of Bipolar Disorder

The literature on the neuropathology of bipolar disorder (BD) is reviewed. Postmortem findings in the areas of pathomorphology, signal transduction, neuropeptides, neurotransmitters, cell adhesion molecules, and synaptic proteins are considered. Decreased glial numbers and density in both BD and major depressive disorder (MDD) have been reported, whereas cortical neuron counts were not different in BD (in Brodmann's areas [BAs] 9 and 24). In contrast, MDD patients showed reductions in neuronal size and density (BA 9, BA 47). There are a number of findings of alterations in neuropeptides and monoamines in BD brains. Norepinephrine turnover was increased in several cortical regions and thalamus, whereas the serotonin metabolite, 5-hydroxyindoleacetic acid, and the serotonin transporter were reduced in the cortex. Several reports further implicated both cyclic adenosine monophosphate and phosphatidylinositol (PI) cascade abnormalities. G protein concentrations and activity increases were found in the occipital, prefrontal, and temporal cortices in BD. In the PI signal cascade, alterations in PKC activity were found in the prefrontal cortex. In the occipital cortex, PI hydrolysis was decreased. Two isoforms of the neural cell adhesion molecules were increased in the hippocampus of BD, whereas the synaptic protein marker, synaptophysin, was not

changed. The findings of glial reduction, excess signal activity, neuropeptide abnormalities, and monoamine alterations suggest distinct imbalances in neurochemical regulation. Possible alterations in pathways involving ascending projections from the brain stem are considered. Larger numbers of BD brains are needed to further refine the conceptual models that have been proposed, and to develop coherent models of the pathophysiology of BD. Vawter, M.P., Freed, W.J., and Kleinman, J.E. Biological Psychiatry, 48, pp. 486-504, 2000.

Kinetics of Recovery at Mu Opioid Receptors

To investigate a previous observation that classical antagonists behave as agonists at mutant H297N and H297Q mu opioid receptors, we compared the kinetics of recovery from opioids at wild-type and mutant mu receptors expressed in voltage-clamped Xenopus oocytes. The cDNA for the potassium channel GIRK1 was coinjected into the oocytes with that of the mu receptors to transduce agonist binding into a coupled electrophysiological response. The kinetics of recovery were estimated by brief test pulses of the agonist normorphine given at a frequency of 0.67 or 1 per min. After treatment with a variety of agonists, the receptors recovered from desensitization at rates that depended on the agonist, but there was little difference between mutant and wild-type receptors. Antagonists, however, induced agonist-like currents and demonstrated faster recovery at the mutant receptors. These results suggest that His-297 may comprise part of an antagonist subsite. This conclusion, when coupled with the steric theory that intrinsic activity depends on independent binary equilibration of a drug between agonist and antagonist subsites, could unify the paired observations that antagonists become agonists and recover faster at the mutant than at the wild-type receptors. Spivak, C.E. and Beglan, C.L. Synapse, 38, pp. 254-260, 2000.

Dysregulation of the Neural Cell Adhesion Molecule and Neuropsychiatric Disorders

Cell adhesion molecule proteins play a diverse role in neural development, signal transduction, structural linkages to extracellular and intracellular proteins, synaptic stabilization, neurogenesis, and learning. Three basic mRNA isoforms and potent posttranslational modifications differentially regulate these neurobiological properties of the neural cell adhesion molecule (N-CAM). Abnormal concentrations of N-CAM 105-115 kDa (cN-CAM), N-CAM variable alternative spliced exon (VASE), and N-CAM secreted exon (SEC) are related to schizophrenia and bipolar neuropsychiatric disorders. These N-CAM isoforms provide potential mechanisms for expression of multiple neurobiological alterations between controls and individuals with schizophrenia or bipolar illness. Multiple processes can trigger the dysregulation of N-CAM isoforms. Differences in neuropil volume, neuronal diameter, gray matter thickness, and ventricular size can be related to N-CAM neurobiological properties in neuropsychiatric disorders. Potential test of the N-CAM dysregulation hypothesis of neuropsychiatric disorder is whether ongoing dysregulation of N-CAM would cause cognitive impairments, increased lateral ventricle volume, and decreased hippocampal volume observed in schizophrenia and to a lesser extent in bipolar disorder. An indirect test of this theory conducted in animal experiments lend support to this N-CAM hypothesis. N-CAM dysregulation is consistent with a synaptic abnormality that could underlie the disconnection between brain regions consistent with neuroimaging reports. Synapse stability and plasticity may be part of the molecular neuropathology of these disorders. Vawter, M.P. European Journal of Pharmacology 405, pp. 385-395, 2000.

Molecular Neuropsychiatry Section, Cellular Neurobiology Research Branch

Methamphetamine-induced Neurotoxicity is Attenuated in Transgenic Mice with a Null Mutation for Interleukin-6

Increasing evidence implicates apoptosis as a major mechanism of cell death in methamphetamine (METH) neurotoxicity. The involvement of a neuroimmune component in apoptotic cell death after injury or chemical damage suggests that cytokines may play a role in METH effects. In the present study, IRP investigators examined if the absence of IL-6 in knockout (IL-6-/-) mice could provide protection against METH-induced neurotoxicity. Administration of METH resulted in a significant reduction of [(125)I]RTI-121-labeled dopamine transporters in the caudate-putamen (CPu) and cortex as well as depletion of dopamine in the CPu and frontal cortex of wild-type mice. However, these METH-induced effects were significantly attenuated in IL-6-/- animals. METH also caused a decrease in serotonin levels in the CPu and hippocampus of wild-type mice, but no reduction was observed in IL-6-/- animals. Moreover, METH induced decreases in [(125)I]RTI-55-labeled serotonin transporters in the hippocampal CA3 region and in the substantia nigra-reticulata but increases in serotonin transporters in the CPu and cingulate cortex in wild-type animals, all of which were attenuated in IL-6-/- mice. Additionally, METH caused increased gliosis in the CPu and cortices of wild-type mice as measured by [(3)H]PK-11195 binding; this gliotic response was almost completely inhibited in IL-6-/- animals. There was also significant protection against METH-induced DNA fragmentation, measured by the number of terminal deoxynucleotidyl transferase-mediated dUTP nick-end-labeled (TUNEL) cells in the cortices. The protective effects against METH toxicity observed in the IL-6-/- mice were not caused by differences

in temperature elevation or in METH accumulation in wild-type and mutant animals. Therefore, these observations support the proposition that IL-6 may play an important role in the neurotoxicity of METH. Ladenheim, B., Krasnova, I. N., Deng, X., Oyler, J. M., Polettini, A., Moran, T. H., Huestis, M. A., and Cadet, J. L. Molecular Pharmacology, 58, pp. 1247-1256, 2000.

Methamphetamine-induced Apoptosis is Attenuated in the Striata of Copper-Zinc Superoxide Dismutase Transgenic Mice

Administration of methamphetamine caused significant increases in terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL)-positive cells, in poly (ADP-ribose) polymerase (PARP) cleavage, as well as in caspase-3 activity in the striata of C57BL/6J mice. In contrast, all these effects were markedly suppressed in the copper-zinc superoxide dismutase transgenic mice. These results indicate that superoxide radicals might be important factors in METH-induced cell death. Deng, X. and Cadet, J. L. Brain Research Molecular Brain Research, 83, pp. 121-124, 2000.

Preclinical Pharmacology Section, Behavioral Neuroscience Research Laboratory

Self-administration Behavior is Maintained by the Psychoactive Ingredient of Marijuana in Squirrel Monkeys

Most drugs abused by humans are intravenously self-administered by experimental animals. The lack of such evidence with marijuana (cannabis) or its psychoactive ingredient THC has led some to assume that marijuana is less addicting and dangerous than other "hard" drugs such as crack cocaine or heroin. We have now demonstrated that THC is actively and persistently self-administered by squirrel monkeys. The THC self-administration behavior was comparable in intensity to that maintained by cocaine in a control group of monkeys under identical conditions and was obtained using a range of doses in agreement with the single doses self-administered by humans smoking marijuana cigarettes. Also, treatment with a drug (SR141716A) that blocks the action of THC at cannabinoid receptors in the brain (CB 1 receptors), almost completely eliminated THC self-administration behavior but did not reduce cocaine self-administration behavior. The methodology provides an exciting opportunity for studying brain mechanisms involved in cannabinoid self-administration behavior. It also provides an exciting opportunity to study possible therapeutic strategies for treating marijuana abuse and to develop drugs possessing therapeutic efficacy similar to or better than marijuana or THC but lacking their potential for abuse. Tanda, G., Munzar, P., and Goldberg, S. R. Nature Neuroscience, 3, pp. 1073-1074, 2000.

Clinical Psychopharmacology Section, Medications Discovery Research Branch

Evidence for Possible Involvement of 5-HT2B Receptors in the Cardiac Valvulopathy Associated with Fenfluramine and other Serotonergic Medications

Serotonergic medications with various mechanisms of action are used to treat psychiatric disorders and are being investigated as treatments for drug dependence. The occurrence of fenfluramine-associated valvular heart disease (VHD) has raised concerns that other serotonergic medications might also increase the risk of developing VHD. We hypothesized that fenfluramine or its metabolite, norfenfluramine, and other medications known to produce VHD, have preferentially high affinities for a particular serotonin receptor subtype capable of stimulating cell growth on heart valves. Medications known or suspected to cause VHD (positive controls) and medications not associated with VHD (negative controls) were screened for activity at eleven cloned serotonin receptor subtypes using ligand binding methods and functional assays. The positive control drugs were (±)-fenfluramine, (+)-fenfluramine, (-)-fenfluramine, its metabolites (±)-norfenfluramine, (+)-norfenfluramine, (-)-norfenfluramine, ergotamine, methysergide and its metabolite, methylergonovine. The negative control drugs were phentermine, fluoxetine, its metabolite, norfluoxetine, trazodone and its active metabolite, m-chlorophenylpiperazine (mCPP). (±)-, (+)- and (-)-Norfenfluramine, ergotamine and methylergonovine all had preferentially high affinities for the cloned human serotonin 5-HT2B receptor and stimulated the 5-HT2B receptor. Our data imply that activation of 5-HT2B receptors is necessary to produce VHD and that serotonergic medications which do not activate 5-HT2B receptors are unlikely to produce VHD. We suggest that all clinically available medications with serotonergic activity as well as their active metabolites be screened for agonist activity at 5-HT2B receptors and that clinicians consider suspending their use of medications with significant activity at 5-HT2B receptors. Rothman, R.B., Baumann, M.H., Savage, J.E., Rauser, L., McBride, A., Hufisein, S., and Roth, B.L. Circulation, 102, pp. 2836-2841, 2000.

Amphetamine-type Central Nervous System Stimulants Release Norepinephrine More

Potently than they Release Dopamine and Serotonin

A large body of evidence supports the hypothesis that mesolimbic dopamine (DA) mediates, in animal models, the reinforcing effects of central nervous system stimulants such as cocaine and amphetamine. The role DA plays in mediating amphetamine-type subjective effects of stimulants in humans remains to be established. Both amphetamine and cocaine increase norepinephrine (NE) via stimulation of release and inhibition of reuptake, respectively. If increases in NE mediate amphetamine-type subjective effects of stimulants in humans, then one would predict that stimulant medications that produce amphetamine-type subjective effects in humans should share the ability to increase NE. To test this hypothesis, we determined, using in vitro methods, the neurochemical mechanism of action of amphetamine, 3,4-methylenedioxymethamphetamine (MDMA), (+)-methamphetamine, ephedrine, phentermine, and aminorex. As expected, their rank order of potency for DA release was similar to their rank order of potency in published self-administration studies. Interestingly, the results demonstrated that the most potent effect of these stimulants is to release NE. Importantly, the oral dose of these stimulants, which produce amphetamine-type subjective effects in humans, correlated with their potency in releasing NE, not DA, and did not decrease plasma prolactin, an effect mediated by DA release. These results suggest that NE may contribute to the amphetamine-type subjective effects of stimulants in humans. Rothman, R.B., Baumann, M.H., Dersch, C.M., Romero, D.V., Rice, K.C., Carroll, F.I. and Partilla, J.S. Synapse, 39, pp. 32-41, 2001.

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

Program Activities

New NIDA PAs and RFAs

On November 6, 2000, NIDA released a Program Announcement entitled **"Exploratory/ Developmental Grant Applications (R21)" (PA-01-012).** This is a re-issuance of PA-98-004 published in the NIH Guide for Contracts and Grants, on October 24, 1997, Volume 26, Number 36. The objective of the exploratory/developmental grant (R21) mechanism is to encourage applications from individuals who are interested in testing innovative or conceptually creative ideas that are scientifically sound and may advance our understanding of drug abuse and addiction. The exploratory/developmental mechanism of grant support is intended to enable an investigator to explore the feasibility of an innovative research question or approach.

On November 7, 2000, NIDA issued a Program Announcement entitled **"Economics of Drug Abuse Treatment and Prevention Services" (PA-01-013)**, replacing PA-096-075 in its entirety. This PA encourages research on the economics of drug abuse treatment and prevention services. The economic studies will be supported jointly by the Services Research Branch and the Prevention Research Branch of the Division of Epidemiology, Services and Prevention Research as part of NIDA's health services research program.

On November 8, 2000, NIDA published a Program Announcement entitled **"Behavioral Science Track Award for Rapid Transition" (PAR-01-014).** This PA replaces PAR-97-046 and is intended to facilitate the entry of beginning investigators into the field of behavioral science research. Through this PA, NIDA invites newly independent investigators to submit applications for small-scale, exploratory, or pilot research projects related to NIDA's behavioral science mission. Funding of B/START awards is relatively rapid; i.e., within approximately six months of the date of receipt of the application.

On November 30, 2000, NIDA issued a Program Announcement entitled **"Drug Abuse Aspects of HIV/AIDS and Other Infections" (PA-01-023)** which seeks to stimulate a range of investigator-initiated studies to advance the scientific knowledge base on drug abuse aspects of HIV/AIDS and other serious infections. Through this PA, researchers are invited to address diverse and cross-cutting issues in multiple disciplines, including virology, etiology, therapeutics and vaccines, ethnography and epidemiology, and the behavioral and social sciences.

On January 2, 2001, NIDA issued a Program Announcement entitled **"Collaborative Clinical Studies in Drug Abuse" (PAR-01-039).** Through this PA, NIDA seeks to increase the collaboration of investigators at different sites in order to address clinical issues in drug abuse research that require sample sizes greater than a single site can reasonably attain. The expectation for the collaborative effort is that there will be implementation of common protocols across different sites in order to study patient outcomes, patient factors, provider factors, setting characteristics, interactions of these, or other effects where pooled samples are appropriate and necessary for the hypotheses under consideration.

On September 6, 2000, NIDA issued an RFA entitled **"Services Research on the National Drug Abuse Treatment Clinical Trials Network" (DA-01-003)** to encourage research on changes in clinical management and organizational practices of community treatment providers participating in NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN); research to improve the ability of non-network providers to adopt new research-based treatments; and research on the cost-effectiveness of treatments tested in the CTN compared with typical treatment. Research on other health services issues related to the CTN and its overarching goal to improve drug abuse treatment nationwide is also encouraged. Letter of Intent Receipt Date for this RFA: November 20, 2000; Application

Receipt Date: December 19, 2000.

On November 21, 2000 NIDA issued an RFA entitled **"The Transition from Drug Use to Addiction: Unearthing the Switch" (DA-01-004).** The intent of this RFA is to stimulate research on the processes and mechanisms underlying the transition from drug use to drug addiction from a wide variety of academic disciplines and approaches. Research from epidemiologic, basic and clinical disciplines, including research on other transitional states with relevance to addiction, will be supported under this RFA. Letter of Intent Receipt Date: January 23, 2001; Application Receipt Date: February 23, 2001.

On January 15, 2001, NIDA issued an RFA entitled **"Health Disparities: Drug Use and Its Adverse Behavioral, Social, Medical, and Mental Health Consequences" (DA-01-008).** This RFA is part of the NIH-wide initiative to eliminate health disparities in racial and ethnic minority populations and builds on NIDA's efforts over the past several years to understand better and address drug abuse and addiction among and across racial and ethnic minority populations. It is designed to stimulate epidemiological, prevention, treatment, and services research that addresses issues relating to the differential drug use patterns and/or their associated behavioral, social, medical, and mental health consequences within and across racial and ethnic minority populations. Letter of Intent Receipt Date for this RFA: March 16, 2001; Application Receipt Date: April 16, 2001.

On January 15, 2001, NIDA issued an RFA entitled **"The Next Generation of Drug Abuse Prevention Research" (DA-01-009).** This RFA encourages a new generation of drug abuse prevention research. Applications are solicited to examine elements that may account for program effectiveness of drug abuse prevention interventions that have either been empirically validated or are currently undergoing rigorous efficacy/effectiveness trials. The purpose is to gain a better understanding of what accounts for program effectiveness through: empirical tests of theoretically derived processes; identification of patterns related to differential effectiveness; generating and testing alternate hypotheses accounting for effectiveness based on differential outcomes from current or previous research; and specification and testing of elements singularly and in combination that contribute to effectiveness. Letter of Intent Receipt Date: March 16, 2001; Application Receipt Date: April 16, 2001.

On January 25, 2001, NIDA issued an RFA entitled **"Health and Developmental Consequences of Prenatal Exposure to Methamphetamine" (DA-01-005).** The purpose of this RFA is to support research on the health and development of children exposed to methamphetamine in utero. In order to maximize the timeliness of the research, NIDA supports the establishment of collaborative Community Research Networks (CRNs) to meet this goal. The aim of the CRNs is to forge partnerships between Research Directors (RDs) and Community Research Partners (CRPs). The Research Directors will be researchers with capabilities to conduct longitudinal cohort studies on the effects of in utero exposure to illicit drugs. The CRPs will be clinicians and researchers from communities where methamphetamine use is prevalent. Letter of Intent Receipt Date: March 19, 2001; Application Receipt Date: April 19, 2001.

On January 25, 2001, NIDA issued an RFA entitled **"Responding to Club Drugs and Other Emerging and Current Drug Abuse Trends" (DA-01-010).** This RFA will support research to characterize the nature and extent of emerging/current drug abuse trends within local contexts and identify associated heath, social and behavioral consequences; to elucidate individual, social, cultural, and contextual factors influencing drug using behaviors; to enhance our ability to identify, monitor, and assess emerging drug abuse trends; to reveal processes and patterns of development and diffusion of new drug trends; and to identify community- or context-specific prevention and health services needs and interventions. Letter of Intent Receipt Date: March 16, 2001; Application Receipt Date: April 16, 2001.

On January 25, 2001 NIDA released an RFA entitled **"Research on GHB and Its Precursors" (DA-01-014).** This RFA is being issued in response to the recent emergence of GHB, GBL and 1,4-BD as public health concerns. NIDA intends to support a broad range of scientific research that is expected to lead to a reduction in the abuse of these sedative-hypnotic "club drugs", and to the development of treatments for GHB abuse. Letter of Intent Receipt Date: March 19, 2001; Application Receipt Date: April 17, 2001.

On January 25, 2001, NIDA in conjunction with numerous other NIH Institutes, issued RFAs entitled **"Tools for Insertional Mutagenesis in the Mouse" (DA-01-011)** and **"Tools for Insertional Mutagenesis in the Mouse: SBIR/STTR Initiative" (DA-01-012).** These RFAs solicit proposals for development of tools and techniques for the establishment of random and targeted sequence-tagged insertion libraries of embryonic stem (ES) cells that can be used to generate mutant mice in which the expression of the tagged gene could be controlled temporally and spatially. The development of such a resource for wide distribution to the scientific community would make it possible to scan the sequence database for any gene of interest and order the corresponding targeted ES cell line. Ideally, the insertional mutagenesis system developed would permit a wide range of genetic analyses and manipulations, including enhancer-trapping, conditional knockouts, conditional expression or overexpression, etc. It also would

permit the larger community of investigators to utilize genomic resources efficiently. Letter of Intent Receipt Date: March 11, 2001; Application Receipt Date: April 11, 2001

On January 29, 2001, NIDA issued a new RFA entitled **"International Studies on Drug Abuse and HIV/AIDS" (DA-01-006).** This RFA is intended to build on lessons learned in developed countries in response to the intertwined epidemics of drug abuse and the spread of HIV/AIDS and other infectious diseases. It seeks to foster cross-national and international research collaborations that, through both independent research and the recruitment, training and mentoring of new, multi-disciplinary researchers, lead to the development, adaptation, replication, and evaluation of effective interventions and approaches to slow or reverse the spread of HIV and other infections in vulnerable drug-using populations. Letter of Intent Receipt Date: February 28, 2001; Application Receipt Date: March 28, 2001.

On January 29, 2001, NIDA issued a new RFA entitled **"HIV/AIDS and Drug Use Among Adolescents" (DA-01-007).** The purpose of this RFA is to support drug use/abuse focused HIV/AIDS studies that address the particular challenges and needs of HIV-infected and at-risk adolescents. Specifically, research applications are sought on (a) prevention of HIV infection and related infectious diseases among adolescents; (b) transmission by HIV-positive youth; (c) accessibility, integration and management of adolescent-specific medical, mental health, and drug treatment services and interventions relative to HIV infection; (d) outreach strategies for high-risk adolescent sub-populations; and (e) analysis of infectious comorbidities and their influence on HIV progression. Letter of Intent Receipt Date: February 28, 2001; Application Receipt Date: March 28, 2001.

Other Program Activities

GHB Antidote Initiative

On October 19, 2000, NIDA's interdisciplinary team held a one-day meeting to consider the necessity of developing an antidote for gamma-hydroxy-butyrate (GHB) poisoning and a diagnostic tool for rapid testing of GHB in blood of victims. The participants were NIDA scientists and clinical experts who are national experts in dealing with cases of GHB poisoning and dependence.

Annual Review of DTRD P-50 Grants

On October 25, 2000, DTR&D held an annual meeting with investigators of current P-50 grants to review their progress in evaluating different medications for the treatment of stimulant and opiate dependence. Investigators from the following centers participated: University of Pennsylvania (Helen Pettinati, PI), New York State Psychiatric Institute (Herbert Kleber, PI); Research Foundation for Mental Hygiene & NY Psychiatric Institute (Marian Fischman, PI); Yale University (Tom Kosten, PI); Friends Research Foundation, Los Angeles (Walter Ling, PI); University of Texas (John Grabowski, PI); University of Minnesota (Dorothy Hatsukami, PI); John's Hopkins University (George Bigelow, PI). Highlights of the meeting included: the emergence of disulfiram as a potential medication for the treatment of cocaine dependence; imaging data that suggests that the brains of some chronic cocaine abusers may operate in a fundamentally different way with respect to release of dopamine; and a study that demonstrated that LAAM (75 to 115 mg), buprenorphine (16 to 32 mg) and high dose methadone (60 to 100 mg) have a comparable efficacy.

Clinical Trials Network (CTN) Update

Five additional awards were made in September, increasing the number of CTN nodes from six to eleven. These new nodes are located at the Medical University of South Carolina, the University of Miami, Wayne State University, the University of Cincinnati, and the University of Colorado Health Sciences Center. In January 2001, three additional awards were made to the University of Washington, New York Psychiatric Center and Duke University, bringing the total number of CTN nodes to fourteen.

The Methamphetamine Clinical Program

To implement the recommendations of the Methamphetamine Addiction Treatment Think Tank (MATTT) meeting, a process was started to establish a group of sites to conduct clinical trials in methamphetamine dependent patients. Five sites have been selected based in areas where the epidemic is currently concentrated: two are in the Midwest (Des Moines, Iowa, and Kansas City, Kansas), and the other three are in Los Angeles, San Diego, CA, and Honolulu, HI. The first medication study protocol was finalized (bupropion) and sent to local IRBs for review. Selegiline, the next medication to be studied, will be first evaluated in inpatient clinical pharmacology studies at UCLA and UCSF for

safety interactions with amphetamine. Following these studies and, if safety is not an issue, selegiline will be advanced to outpatient studies following completion of the bupropion study.

Clinical Research Efficacy Screening Trial (CREST-I) Study

On April 26, 2000, consultants reviewed the data from each NIDA/VA Medications Development Research Unit (MDRU) in their CREST studies (three medications each and an unmatched placebo). Out of the 15 medications reviewed, three medications were shown to reduce cocaine use in these screening pilot studies. Reserpine, the anti-hypertensive medication, gave the strongest signal while cabergoline (dopamine agonist) and Hydergine (brain metabolic and blood flow enhancer) gave weaker signals. The recommendations of the consultants were to follow up with larger phase II studies on these medications.

Clinical Research Efficacy Screening Trial (CREST-II) Study

Similar to CREST-I, the second phase of rapid drug screening started following the completion of CREST-I. This second round involves eight different medications. The data from these trials are scheduled to be analyzed and reviewed by consultants by February 2001.

Cocaine Clinical Trials Operations

A group of four academic clinical sites has been established to replace the former Department of Veterans Affairs MDRU sites to conduct clinical trials for the treatment of cocaine addiction. The sites are UCLA, the University of Cincinnati, the Medical University of South Carolina, and the University of Texas at San Antonio. Seven protocols have been submitted for the sites to study: three are phase I interaction studies (Modafnil, Metyrapone, Tolcapone, and Disulfiram); one is a phase IIa study (Ondansteron); and two are phase IIb studies (resperpine and cabergoline). These studies began in January 2001.

Methylphenidate In Cocaine Dependant Individuals With ADD

An open label feasibility study showed a 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. This study is approximately half completed.

Selegiline

The selegiline IR study has been completed and data are currently being analyzed. The VA Cooperative Studies Program review committee and its central IRB have approved the phase III 300 subject Selegiline Transdermal System study protocol. The protocol was sent out to local investigators for review by local IRBs and was also submitted to FDA by Somerset Pharmaceuticals, Inc. for review. A kick-off meeting for this study was held at the end of January 2001.

Lofexidine for Heroin Withdrawal Study

This phase III multi-site study protocol was recently approved by the VA CSP central IRB. A kick-off meeting of the three participating sites (Los Angeles, Philadelphia VA, and Columbia University) was held in Long Beach, CA in January 2001.

Evaluation of the National Youth Anti-Drug Media Campaign

In November 2000, NIDA and ONDCP released the first report of findings from the Evaluation of the National Youth Anti-Drug Media Campaign, conducted under contract by Westat, Inc., and the Annenberg School for Communications, University of Pennsylvania. This report, entitled Evaluation of the National Youth Anti-Drug Media Campaign: Campaign Exposure and Baseline Measurement of Correlates of Illicit Drug Use From November 1999 Through May 2000, reported on the attitudes, beliefs and behaviors of parents and youth during the first wave of the full-blown campaign.

Because these data will serve as baseline, no correlations were done to compare media exposure with specific attitudes and behaviors. The first report to produce such findings will be released in March 2001. Some of the findings

include:

- Using general exposure measures, and summing across all media,
  - 90 percent of parents and 93 percent of youth recalled exposure to one or more anti-drug ads each month. General exposure measures include both Campaign and other advertising.
  - Sixty-eight percent of parents and 70 percent of youth recalled exposure to one or more anti-drug ads each week.
  - The median general recall by parents was 10 ads per month (i.e., at least half of parents saw 10 or more per month and at least half saw 10 or fewer). The media recall by youth was around 11 ads per month.
- Using specific aided recall measures
  - The median recall of specific youth TV ads by youth was 4 exposures in recent months.
  - The median aided recall of specific parent TV ads by parents was 3 exposures in recent months.
- Parent-child reporting of past year marijuana use shows that, in general, parents have a pretty good idea of marijuana use among their children-e.g., 2.9% of parents report that their 12-13 year old child has used marijuana in the past year, and 3.3% of children this age report use; among 16-18 year olds, there is a greater gap in reporting with 19.5% of parents reporting marijuana use in the past year, and 29% youth reporting such use.
- Most youth report that they receive offers to use marijuana, but they claim they rarely accept. Almost 50% of youth (16-18) reported that they had received offers of marijuana in the past 30 days, but 13% reported having smoked marijuana in that time.

NIH Summer Internship Program (SIP) and the Minority Recruitment & Training Program (MRTP)

The NIH Summer Internship Program (SIP) and the Minority Recruitment & Training Program (MRTP) are now accepting applications for Summer 2001. Both programs provide training opportunities for students 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. For information and an application for the SIP, go to www.training.nih.gov or contact Dr. Stephen Heishman (sheish@intra.nida.nih.gov). For an application or to receive information about the MRTP, contact Christie Brannock (cbrann@intra.nida.nih.gov)

NIDA's New and Competing Grants Awarded Since September 2000

Adler, Martin W. -- Temple University
Center on Intersystem Regulation By Drugs of Abuse

Akbarian, Schahram -- Massachusetts General Hospital
Conditional Mutagenesis In Addiction Circuitry

Altice, Frederick L. -- Yale University
Directly Observed Anti-Retroviral Therapy Among Active Drug Users

Amara, Susan G. -- Oregon Health Sciences University
Expression Profilling of Psychostimulant-Regulated Genes

Bainton, Roland J. -- University of California, San Francisco
A Genetic Study of Drosophila Responses To Cocaine

Barnes, Grace M. -- Research Institute on Addiction
Sports, Gender and Adolescent Substance Use

Bartlett, John G. -- Johns Hopkins University School of Medicine
Johns Hopkins Center For AIDS Research

Becker, Jill B. -- University of Michigan, Ann Arbor
Gender Differences In Drug Abuse

Belenko, Steven R. -- CASA at Columbia University
Impact Evaluation of the DTAP Diversion Program

Bell, David C. -- Affiliated Systems Corporation
Community-Based Research on Drug Use Networks

Bell, Jeanne E. -- University of Edinburgh
Drug Related CNS Damage-Synergy With Effects of HIV

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

Bierut, Laura J. -- Washington University
Family Study of Cocaine Dependence

Bloom, Alan S. -- Medical College of Wisconsin
Effects of THC on Regional Brain Activity: A fMRI Study

Booth, Robert E. -- University of Colorado
Rocky Mountain Regional Clinical Trials Node

Botvin, Gilbert J. -- Cornell University Medical College
Drug Abuse and Violence Prevention with Minority Youth

Bowen, Gary L. -- Flying Bridge Technologies
SSP Drug Abuse Prevention Screening Tool: Development

Bowser, John J. -- Compact Membrane Systems, Inc
Concentration Method for Thermally Labile Pharmaceutical

Brady, Kathleen T. -- Medical University of South Carolina
Southeastern Node of the Clinical Trials Network

Brot, Michelle D. -- University of Washington
Drugs of Abuse In Dopamine-Deficient Mice

Brown, Emma J. -- University of Central Florida
An Ethnography: Drug Use Among African American Women

Brue, Vesta -- Lifetechniques, Inc.
Duration Adjustments In Scheduled Reduced Smoking

Butler, Stephen F. -- Innovative Training Systems
Computerized ASI Consultation For Addictions Counselors

Carlezon, William A. -- McLean Hospital
Role Of Nucleus Accumbens Ca2+ Flux In Cocaine Reward

Carroll, Kathleen M. -- Yale University
Psychotherapy of Substance Use Disorders

Chernen, Leslie -- Accurate Assessments
Enhancing the ASI with Gambling & ADHD Domains

Chiauzzi, Emil -- Innovative Training Systems
Multimedia Safe Driving Program For Adolescents

Cicchetti, Dante -- University of Rochester
Teen Drug Use/Abuse: Pathways From Child Maltreatment

Clark, DJ -- Videodiscovery, Inc
Computer Health Performance Assessment

Clentano, David -- Johns Hopkins University
HPTU - Thailand

Coatsworth, J. D. -- Pennsylvania State University
Clinical Processes In Drug Abuse Prevention

Colbern, Deborah L. --Beemnet, Inc.
National Kids Judge! Neuroscience Fairs Partnership

Collins, Linda M. -- Pennsylvania State University
Center For Prevention Methodology

Compton, Wilson M. -- Washington University
Psychiatric Comorbidity In Drug Abusers

Cook, Royer F. -- ISA Associates
A Workplace CD-Rom Drug Prevention Program for Parents

Cornish, James W. -- University of Pennsylvania
Naltrexone Treatment of Opioid Dependent Parolees

Cronin, Christopher J. -- Saint Leo College
Intervention For Marijuana Use Among College Students

Crowley, Thomas J. --University of Colorado Health Sciences Center
Genetics of Adolescent Antisocial Drug Dependence

Cubells, Joseph F. -- Yale University School of Medicine
Genetics of Cocaine Induced Psychosis

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

Dehovitz, Jack A. -- SUNY Health Sciences Center
SUNY AIDS International Training Program

Del Rio, Carlos -- Emory University School of Medicine
Persons Without HAART: Characteristics and Determinants

Delorey, Timothy M. -- Moltech Corporation
Design of New Benzodiazepine Ligands as Memory Enhancers

Des Jarlais, Don C. -- National Development & Research Institute, Inc.
HIV Risk Behaviors Among Urban Nomad Drug Injectors

Dewey, William L. -- Virginia Commonwealth University
Effects of Opiates on Cellular Mechanisms

Dingman, Sherry -- Marist College
Perfluoro Analogues for Imaging B: MRI/Behavioral Study

Dishion, Thomas J. -- University of Oregon
Enhancing Family-Based Prevention of Adolescent Drug Use

Donovan, Dennis M. -- University of Washington
Clinical Trials Network: Pacific Northwest Node

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

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

Dusenbury, Linda -- Tanglewood Research
Video-Based Teacher Training In Drug Prevention

Erb, Judith L. --IA, Inc.
Immunophore Test Strips for Screening Steroids of Abuse

Esposito, Noreen W. -- Columbia University
Women Drug Abusers and Post Sexual Assault Care

Farzadegan, Homayoon -- Johns Hopkins University
Epidemiology of Drug-Resistant HIV-1 In IDUs

Fattom, Ali -- NABI
Vaccination For Treatment of Nicotine Dependence

Ferris, Craig F. -- Insight Neuroimaging Systems
Noninvasive Device for FMRI Studies In Cocaine Abuse

Flanigan, Timothy P. -- Miriam Hospital
Directly Observed HAART For Active Substance Abusers

Frankel, Wayne, N. -- The Jackson Laboratory
Production & Screening of Mouse Neurological Mutations

Fraser, Mark W. -- University of North Carolina
Making Choices: A Social Development Program

French, Michael T. -- University of Miami School of Medicine
Chronic Drug Use, Depression, and Labor Supply

Friedmann, Peter D. -- Rhode Island Hospital
Linkage To Health Services In Drug Abuse Treatment

Garland, Marianne -- Columbia University
Glucuronyl-Transferase Activity In the Fetal Primate

Gastfriend, David R. -- Massachusetts General Hospital
Improving Drug Abuse Treatment Planning Criteria

Giles, Steven M. -- Tanglewood Research, Inc.
Modeling Drug Prevention Program Fidelity

Glang, Ann E. --Oregon Center for Applied Sciences, Inc.
Interactive Program For Effective Playground Supervision

Golder, Seana --University of Washington
Modeling Women's Involvement In High Risk Behavior

Goldowitz, Daniel -- University of Tennessee - Memphis
Targeted Mutagenesis of Mouse Genome & Neural Phenotype

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

Greenblatt, David J. -- Tufts University
Antiretroviral Therapies and Substance Abuse

Guay, Laura A. -- MU-JHU Research Collaboration
HPTU- JHU/MCAIDS Uganda

Haggerty, Kevin P. -- University of Washington
Examining The Efficacy of 'Parents Who Care'

Halkitis, Perry N. -- New Jersey City University
Club Drug Use and Men's Health: A Community Study

Haller, Deborah L. --Virginia Commonwealth University
Adherence Therapy for Opioid Abusing Pain Patients

Haney, Margaret -- New York State Psychiatric Institute
THC and Marijuana: Effects In Individuals With HIV/AIDS

Hansen, William B. -- Tanglewood Research, Inc.
All Stars, Jr.: Drug Prevention For Elementary Schools

Hauser, Kurt F. -- University of Kentucky
Opiates: Neuronal and Glial Vulnerability To HIV

Henderson, Leslie P. -- Dartmouth Medical School
GABA A Receptor Modulators In the Developing Rat Forebrain

Hershow, Ronald C. -- University of Illinois, Chicago
Early Natural History of HCV Infection Among IDUs

Hill, Karl G. -- University of Washington
Intergenerational Influence of Substance Use on Children

Hillhouse, Maureen P. -- University of California
Replicating the Addicted-Self Model of Recovery

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

Hops, Hyman -- Oregon Research Institute
Drug Use & HIV Risk:Treatment of Hispanic & Anglo Youth

Hser, Yih-Ing -- UCLA Drug Abuse Research Center
A 12-Year Follow-Up Of a Cocaine-Dependent Sample

Huang, Tien L. -- Xavier University of Louisiana
Novel Anti-PCP Agents With Neuroprotective Properties

Hubbard, Robert L. -- Duke University Medical Center
National Drug Abuse Treatment Clinical Trials Network

Hussong, Andrea M. -- University of North Carolina at Chapel Hill
Self Medication and Adolescent Substance Use

Jackson, J. B. -- Johns Hopkins University
HPTU- JHU/MCAIDS China

Jason, Leonard A. -- DePaul University
Abstinent Social Support In Oxford House

Johns, Josephine M. -- University of North Carolina at Chapel Hill
Cocaine and Maternal Neglect: Intergenerational Effects

Johnson, Bankole A. -- University of Texas Health Sciences Center, San Antonio
Medication Development for Methamphetamine Dependence

Johnson, Lawrence L. -- Trudeau Institute, Inc
Effect of Morphine on Immune Resistance to T Gondii

Jones, Hendree E. -- John Hopkins University
Treating the Partners of Drug Using Pregnant Women

Justice, Joseph B. -- Emory University
Ligand Binding Sites on the Dopamine Transporter

Kantak, Kathleen M. -- Boston University
New Method for Studying Drug Self-Administration In Mice

Kaplan, Andrew H. -- University of North Carolina
Adherence To HAART Among Incarcerated Substance Users

Karim, Salim S. -- Mailman School of Public Health
International Training Program In Epidemiology of AIDS

Karpatkin, Simon -- New York University School of Medicine
AIDS and Thrombocytopenia: Drug Abusers and Homosexuals

Khanna, Pyare L. -- Discoverx
Complementation Assay for G Protein Linked Receptors

Koob, George F. -- Scripps Research Institute
Dopamine Partial Agonists and Psychostimulant Dependence

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

Lahoste, Gerald J. -- University of New Orleans
Gap Junctions and Dopamine Plasticity

Lally, Michelle A. -- Miriam Hospital
HIV/Infectious Disease Test/Treatment In Substance Abuse

Laudet, Alexandre -- National Development & Research Institute, Inc.
Referral To Self-Help: Clinicians and Clients Views

Leukefeld, Carl G. -- University of Kentucky
HIV Risk Reduction Among Rural Drug Abusers

Lewis, Michael P. -- The Athena Group, Inc.
Lord Kelvin: A Computer-Based Science Learning System

Li, Ming D. -- University of Tennessee, Memphis
Gene Expression Profiling During Exposure To Nicotine

Liberty, Hilary J. -- Social Sciences Innovations
Detecting Crack and Other Cocaine Use With Fast Patches

Likness, Mark A. -- Plowshare Technologies, Inc.
A Portable Device For Measuring Smoking Topography

Lysle, Donald T. -- University of North Carolina at Chapel Hill
Behavioral Factors In Heroin's Effect On Nitric Oxide

Magura, Stephen -- National Development & Research Institute, Inc.
Innovative Job Placement Model For Methadone Patients

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

Makriyannis, Alexandros -- University of Connecticut
Studies On Cannabinoid Effects and Cannabimimetic Drugs

Malow, Robert M. -- University of Miami School of Medicine
Cognitive Behavioral Treatment of HIV + Drug Abusers

Margolin, Arthur -- Connecticut Mental Health Center
Acupuncture and Coping Skills Training For Cocaine Abuse

Martinez, Diana -- Columbia University
Imaging Mesolimbic DA Receptors In Cocaine Abuse

Martinez, Joe L. -- University of Texas, San Antonio
Enkephalins and Learning

Mazure, Carolyn M. -- Yale New Haven Hospital
Yale IWHR Scholar Program On Women and Drug Abuse

Mcchargue, Dennis E. -- University of Illinois, Chicago
Depression-Prone Smokers and Cigarette Craving

McNeese-Smith, Donna K. -- University of California, Los Angeles
Substance Abuse Treatment In Two Managed Care Structures

Meng, Fan -- University of Michigan
Novel Microarray for SNP and Methylation Detection

Miles, Michael F. -- Ernest Gallo Clinic & Research Center
Analyzing Gene Expression Profile Clusters By Comparison

Moncher, Michael S. -- Intersystems, Inc.
Drug Abuse Prevention Among Adolescent Women

Moore, Richard D. -- Johns Hopkins University
Mid Career Investigator Award

Neumeyer, John L. -- Brain Research Lab, Inc.
Dopamine Agonists For the Therapy of Cocaine Addiction

Nicholson, Katherine L. -- Virginia Commonwealth University
Effect Of NMDA Antagonists on Acute Opioid Dependence

Nickerson, Deborah -- University of Washington
Starnet: Research Experiences for Students and Teachers

Nunes, Edward V. -- New York State Psychiatric Institute
CU Partners: NY/Long Island Regional Node

Ortabasi, Llse M. -- Kinder Magic Software
Science Snoops-Life Science Investigations

Ouellet, Lawrence J. -- University of Illinois at Chicago
Noninjected Heroin Use, HIV & Transitions To Injection

Paul, Elizabeth H. -- National Health Promotion Associates, Inc.
Life Skills Training Through CD-ROM Technology

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

Pettegrew, Jay W. -- University of Pittsburgh
In Vivo 31p-1h MRSI and MRI Brain Studies of Nicotine

Pickens, Roy W. -- Virginia Commonwealth University
Building Research Careers In Women's Health

Podell, Michael -- Ohio State University
A Feline Model of NeuroAIDS and Drug Abuse

Potashkin, Judith -- Finch University of Health Sciences
Cocaine Regulation of FOSb Splicing

Rakela, Jorge L. -- Mayo Clinic Scottsdale
Hepatitis C Virus Coinfection In HIV-1 Infected Subjects

Ramsay, Douglas S. -- University of Washington
A Small-Animal Model of Inhalant Self-Administration

Rapoza, Darion -- Entertainment Science, Inc.
A Single-Player Drug Abuse Prevention Video Game

Ricaurte, George A. -- Johns Hopkins University
Gene Expression and Methamphetamine Neurotoxicity

Riggs, Paula D. -- University of Colorado Health Sciences Center
Substance Dependent Teens: Impact of Treating Depression

Robinson, Terry E. -- University of Michigan
Neuroplastic Adaptations Engendered By Drugs of Abuse

Robles-Sotelo, Elias -- University of Arkansas
Delay Discounting & Impulsiveness In Methadone Patients

Rocha, Beatriz D. -- University of Maryland Baltimore Professional School
Cocaine Self-Administration In The DAT Knockout Mice

Roffman, Roger A. -- University of Washington
Motivating Marijuana Cessation

Sanna, Pietro P. -- Scripps Research Institute
Gene Expression Bases of Cocaine Dependence and Relapse

Schmitz, Joy M. -- University of Texas Houston Health Science Center
Integrated Treatment for Cocaine and Mood Disorders

Schoenbaum, Ellie E. -- Montefiore Medical Center
Natural History of Menopause In HIV Infected Drug Users

Schottenfeld, Richard S. -- Yale University
Research Training Fellowship In Substance Abuse

Schuster, Charles R. -- Wayne State University School of Medicine
Great Lakes Clinical Trials Network Regional Node

Schwarz, Kathleen B. -- Johns Hopkins University
Viral Hepatitis In Children of Injection Drug Users

Self, David W. -- Yale University School of Medicine
Gene Expression and Cocaine In Prolonged Abstinence

Shelton, Keith L. -- Wake Forest University School of Medicine
Diazepam Discrimination In GABA Subunit Knockout Mice

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

Singer, Merrill -- Hispanic Health Council
Effects of Partner Violence Victimization In Drug Use

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

Smith, James E. -- Wake Forest University
Neurobiological Mechanisms of Drug Reinforcement

Somoza, Eugene C. -- University of Cincinnati
Clinical Trials Network, Ohio Valley Node

Spielberg, Freya -- Harborview Medical Center
Counseling Strategies To Reduce HIV Risk Among IDU

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

Stein, Lynda A. -- Brown University
Motivational Interviews for Incarcerated Teens

Stein, Michael D. -- Rhode Island Hospital
A Trial To Reduce Hepatitis C Among Infection Drug Users

Stiffman, Arlene R. -- Washington University
Adolescent American-Indian Multisector Help Inquiry

Stiffman, Arlene R. -- Washington University
GWB Social Work Center For Addictions Research

Stitzer, Maxine L. -- Johns Hopkins University
Novel Lapse-Responsive Approach To Smoking Cessation

Strombeck, Rita D. -- Healthcare Education Association
HIV/AIDS Prevention for Women In Drug Treatment

Suhadolik, Robert J. -- Temple University
Effect of Opiods on 2-50as/Pkr Pathway In HIV Infection

Sussman, Steven Y. --University of Southern California
Project Towards No Drug Abuse Components Analysis

Swaim, Randall C. -- Colorado State University
Using Media To Prevent Violence Among Rural Youth

Szapocznik, Jose -- University of Miami
Florida Node of the Drug Abuse Clinical Trials Network

Taffe, Michael -- Scripps Research Institutes
Neuropharmacology of Primate Cognition

Taha, Taha E. -- Johns Hopkins University
HIV Prevention Trials Unit - Malawi

Tank, A. W. -- University of Rochester
Nicotine Effects on the Adrenal Medulla and Brain

Tarter, Ralph E. -- University of Pittsburgh
Drug Abuse Vulnerability: Mechanisms and Manifestations

Thio, Chloe L. -- Johns Hopkins University School of Medicine
Hepatitis C Clearance and Host Genetic Factors

Thomas, David L. -- Johns Hopkins University
HIV-HCV Coinfection: Antiviral Therapy and Fibrosis

Tompkins, Christopher -- Brandeis University
Development of Case Rates For Substance Abusers

Trupin, Eric W. -- University of Washington
Developing Prime Time Project for Double Jeopardy Youth

Tsien, Joe -- Princeton University
Genetic Analysis of Temporal Phases of Memory Consolidation

Tully, Tim -- Cold Spring Harbor Laboratory
Genome Responses to Drosophila Addiction Using DNA Chips

Valentine, Fred T. -- New York University Medical Center
Center for AIDS Research

Vlahov, David -- New York Academy of Medicine
Evaluating Supervised HAART In Late Stage HIV In IDUs

Von Zastrow, Mark E. -- University of California, San Francisco
Proteins Regulating Endocytosis of Opioid Receptors

Vrana, Kent E. -- Wake Forest University School of Medicine
Functional Genomics of Cocaine Self-Administration

Wagner, Edward J. -- Oregon Health Sciences University
Cannabinoid-Induced Disruption of the Reproductive Axis

Walker, Bruce D. -- Massachusetts General Hospital Partners/Fenway/Shattuck
Center for AIDS Research

Walwyn, Wendy M. -- University of California, Los Angeles
Opioid Receptor Desensitization, Internalization & Tolerance

Wang, Hong -- Weill Medical College of Cornell University
Postnatal Targeting of Striatal Opioid & NMDA Receptors

Wawer, Maria J. -- Columbia University
HPTU- Rakai, Uganda

Wehner, Jeanne M. -- University of Colorado
Genetics of Alcohol and Substance Abuse

Wenzel, Suzanne L. -- Rand
Drug Abuse, Violence, and HIV/AIDS In Impoverished Women

Wesson, Donald R. -- Drugabuse Sciences, Inc.
SR Buprenorphine for Treatment of Opiate Dependence

Whitbeck, Leslie B. -- Institute for Social & Behavioral Research
Pathways to Substance Abuse Among Ojibwe Children

Williams, Robert W. -- University of Tennessee, Memphis
Informatics Center for Mouse Neurogenetics

Wilson, Emery A. -- University of Kentucky
Interdisciplinary Research Careers In Women's Health

Wong, Dean F. -- Johns Hopkins University School of Medicine
Human Imaging Research In Neuropsychiatry & Drug Abuse

Wright, Teresa L. -- Northern California Institute for Research & Education
HCV Variants and Immune Response In Injection Drug Users

Yu, Xiao-Fang -- Johns Hopkins University School of Public Health
Viral & Host Factors on HIV Transmission/Pathogenesis

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Extramural Policy and Review Activities

Review Meetings

During this Council cycle, the Office of Extramural Affairs (OEA) arranged and managed fifteen committee meetings for review grant applications and seven for review of contract proposals. In addition, 24 contract concepts were reviewed.

The reviews for NIDA's chartered committees were held, which include NIDA-E (Treatment Review Committee), NIDA-F (Health Services Review Committee), NIDA-L (Medications Development Committee), and NIDA-K (Training Committee). Five Special Emphasis panels were also held to review applications in conflict with the chartered committees. Four Special Emphasis Panels were constituted for reviews of specific mechanisms: program projects, centers, B/STARTs, and conference grants. Two meetings were held for RFA reviews, as follows:

DA-01-001	Cognitive Approaches to Addictive Processes
DA-01-002	Development of Behavioral Methods for Drug Abuse Studies in the Mouse

The Contracts Review Branch, OEA, managed the following reviews of proposals:

N01DA-0-1200	National Hispanic Science Network
N43DA-1-8812 (SBIR Topic 032)	Dosage Form Development
N01DA-1-1104	Technical and Logistical Support for OSPC
N43DA-1-5505 (SBIR Topic 035)	Instrument Development for Assessing Community Factors that Affect Drug Use Consequences
N43DA-1-5511 (SBIR Topic 033)	Develop Drug Abuse Screening/Assessment and Intervention for Youth for Primary Care/Managed Care Providers
N43DA-1-7721 (SBIR Topic 009)	Chemical Libraries for Drug Development
N43DA-1-7712 (SBIR Topic 037)	Novel Drug Delivery System for the Mouse

In addition, the Contracts Review Branch is currently planning and managing the reviews of an additional thirteen Small Business Innovation Research (SBIR) contract projects. These reviews are expected to be completed by March, 2001.

Staff Training and Policy Development

The OEA Symposium Series met monthly to provide a forum for staff exchange of ideas and training related to extramural administration. In September, Mr. Robert Walsh, Division of Treatment Research and Development, NIDA, presented "The Emerging Role of Data and Safety Monitoring Boards." October's session was devoted to topics raised by the participants, followed by a case study on conference grants. Ms. Michelle Muth, Office of Science Policy and Communications, NIDA, led a discussion in November of NIDA's efforts to disseminate the results of its research. The final session of the year was an update on policy and procedure changes at NIH. Dr. William C. Grace, Deputy Director, OEA, coordinates the symposium series.

OEA hosted a seminar, "The NIH Freedom of Information Office," in October. Ms. Susan Cornell, NIH Freedom of Information Officer, and Ms. Connie Caldwell, NIH Freedom of Information Act Specialist, discussed the Freedom of Information Act and recent revisions to Office of Management and Budget Circular A110.

OEA coordinated an internal working group that developed policies for distributing e-mail to large numbers of non-Federal recipients. This group will continue to work with staff to ensure coordination of large distributions.

A training session for consumer representatives serving as reviewers of NIDA grant applications was held on January 25, 2000. Dr. Mark Green, Chief, Clinical, Epidemiological, and Applied Sciences Review Branch, OEA, organized the training with assistance from Ms. Lana Le, Grants Technical Assistant, OEA.

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Congressional Affairs

Intramural Research

FY 2001 Appropriations

On December 21, 2000, following an unusually complex legislative process, President Clinton signed into law the omnibus spending package (HR4577), which includes the FY 2001 Labor-HHS-Education bill (HR5656). Among many provisions, the bill continues the congressional commitment to double funding for the NIH over a 5-year period by providing $20.313 billion, which is $1.5 billion over the President's budget request and $2.5 billion more than last year.

FY 2001 Appropriations Conference Bill and Report Language for H.R. 4577- H.Rept. 106-1033

NIH Funding:

FY 2001 President's Budget	$18.813 billion
FY 2001 House Bill	$20.513 billion
FY 2001 Senate Bill	$20.513 billion (+ 15%)*
FY 2001 Conference	$20.313 billion (+ 14%)
Transfer to the Secretary for newly formed	
Office for Human Research Protection	$5.8 million

NIDA Funding:

FY 2001 President's Budget	$725.467 million
FY 2001 House Bill	$788.201 million
FY 2001 Senate Bill	$790.038 million (+15%)
FY 2001 Conference	$781.327 million (+13.7%)

*(% increase over FY 2000)

Bill Language - H.R. 4577 --- NIH

- Provides a specific appropriation of $130.2 million for National Center on Minority Health and Health Disparities (NCMHD).

Maintains transfer authorities consistent with FY 2000 appropriation language.

- Provides $75 million for extramural facilities construction grants.
- Provides $500,000 for the NIH Foundation.
- Provides $48.271 million for the operations of the Office of AIDS Research.
- Provides $47.3 million within B&F (Buildings and Facilities) for the National Neuroscience Research Center.
- Prohibits NIH from using appropriated funds on a contract for the care of the 288 chimpanzees acquired by the NIH from the Coulston Foundation unless the contractor is accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care International or has a PHS assurance, and has not been charged with any violations of the Animal Welfare Act.
- Waives the matching requirement for facilities construction grants for nonhuman primate research facilities of special interest of NIH.
- Permits the NIH Director to enter into and administer a long-term lease for facilities for the purpose of providing laboratory, office and other space for biomedical and behavioral research at the Bayview Campus in Baltimore, Maryland.
- Requires NIH to transfer $5.8 million to the Office of the Secretary, General Departmental Management to support the newly established Office for Human Research Protection.
- Expands the intramural loan repayment program for clinical researchers from disadvantaged backgrounds to the extramural community.
- Clarifies that the Acting Director of NIH may continue to serve under this title rather than Principal Deputy Director until a new Director of NIH is confirmed by the Senate.
- Names the National Neuroscience Research Center for Representative John E. Porter.
- Raises the salary cap for extramural investigators to Executive Level I from Level II . The 2000 Executive Schedule annual rate is $157,000 for Level I and $141,300 for Level II.
- Increases the one percent evaluation tap by $76.404 million over FY 2000 to finance CDC and AHRQ.
- Extends the authority for the Physicians Comparability Allowance for five years.
- The Departments of Labor, HHS and Education are reduced by $25 million for an across-the-board administrative and related expenses cut.

Conference Report Language - H. Report 106-1033 --- NIH

Conferees indicate that in implementing the agreement, the Department and agencies should comply with the language and instructions set forth in House Report 106-645 and Senate Report 106-293. However, with respect to provisions in the House and Senate reports that specifically allocate funds, those that are jointly concurred in have been included in this joint statement. The conferees direct DHHS to submit to the Committees on Appropriations operating plans for discretionary appropriations within 30 days of enactment.

NCRR: Conferees earmark $100 million for the IDeA grants as proposed by the House instead of $60 million as proposed by the Senate and endorse the use of the funds as identified in the House report.

NIAMS: Conferees encourage NIAMS to support loan repayment for researchers working in the areas of childhood rheumatic diseases.

AIDS Funding: The report indicates that the conferees understand that NIH expects to provide $2,266,987,000 in AIDS research funding.

Study of NIH Structure: Conferees concur with language in the Senate report instructing NIH to fund the NAS study of the structure of NIH. The study is to determine if the current structure and organization is optimally configured for scientific needs. The Committees expect to receive a report with recommendations one year from the date of confirmation of the new NIH Director.

Return on NIH Investments: The conferees drop language added by Representative Bernard Sanders (I-VT) and Senator Ron Wyden (D-OR) relating to drug pricing and add language directing NIH to prepare by July 2001 a listing of therapeutic drugs which are FDA approved, have reached $500 million per year in U.S. sales and have received NIH funding.

Autism: Conferees strongly urge NIH to implement an intensified research effort regarding autism consistent with the Children's Health Act of 2000. The NIH Director should report to the House and Senate Committees on Appropriations by March 1, 2001, on a plan for establishing the Centers of Excellence on Autism program authorized in the Act.

Plaza Designation: Conferees urge the Director of NIH to designate the plaza in front of the James Shannon building on the NIH campus as the Paul G. Rogers Plaza and to commemorate it in his honor.

Fetal Tissue Practices - GAO Study: The Conferees drop the Senate language requesting a GAO study into Federal fetal tissue practices.

Other Bills of Interest

Children's Health Act

H.R. 4365, the Children's Health Act of 2000, was signed into law by President Clinton on October 17, 2000 (PL 106-310). The bill covers the entire range of child-health-related topics, expanding research, creating new programs, and developing new initiatives at NIH for, among other areas, autism, juvenile arthritis, diabetes, epilepsy, adoption awareness, oral health, and obesity. The Act also contains many provisions relating to substance abuse including reauthorization of the Substance Abuse and Mental Health Services Administration (SAMHSA).

Included in this comprehensive bill is the "Drug Addiction Treatment Act" (DATA) which allows qualified physicians to prescribe certain anti-addiction medications in an office setting. HR 4365 also includes the "Methamphetamine Anti-Proliferation Act of 2000," which amends Section 464N of the PHSA authorizing the Director of NIDA to "make grants or enter into cooperative agreements to expand the 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 and other biomedical, behavioral, and social issues related to methamphetamine abuse and addiction." An authorization of appropriations of "such sums as may be necessary" is included. One provision requires the Secretary of Health and Human Services, in consultation with the Institute of Medicine, to conduct a study on the development of medications for the treatment of addiction to amphetamine and methamphetamine and report results to the Committees on the Judiciary of the Senate and House. Another bill swept into HR4365 is the "Ecstasy Anti-Proliferation Act of 2000," which, in part, encourages adequate funding for NIDA to accomplish the following: identify those most vulnerable to using ecstasy and develop science-based prevention approaches; understand how ecstasy produces its toxic effects and how to reverse neurotoxic damage; develop treatments, including new medications and behavioral treatment approaches; better understand the effects that ecstasy has on developing children and adolescents; and translate research findings into useful tools and ensure their effective dissemination.

Health Improvement Act

On November 13, 2000, President Clinton signed into law H.R. 2498, the Health Improvement Act (PL 106-505). Sponsored by Rep. Cliff Stearns (R-FL), the bill initially only included language that was to provide Federal buildings with emergency equipment to treat heart attack victims. However, the measure, also known as the "Minibus bill" came to include provisions from 9 other, separate House and Senate health bills. Three of the bills - HR 762, the Lupus Research Act; S. 1243, the Prostate Cancer Research Act; H.R. 4015, the Alzheimer's Clinical Research and Training Awards Act of 2000 - expanded the resources for clinical research in disease specific areas. Two of the bills

rolled into H.R. 2498, S. 1813, the Clinical Research Enhancement Act; and S. 1268, the 21st Century Research Laboratories Act, increase broad support for clinical research efforts, particularly at NIH. H.R. 2498 also includes S. 2731, the Public Health Therapies Act, which will enhance the nation's capacity to address public health threats and emergencies, as well as S. 2625, the Organ Procurement Organization Certification Act. This section of H.R. 2498 will revise the performance standards and certification process for organ procurement organizations. In addition, the "Minibus" contains provisions on Sexually Transmitted Disease research and technical changes to the Children's Health Act of 2000.

Biomedical Imaging and Bioengineering Establishment Act

The Senate passed the National Institute of Biomedical Imaging and Bioengineering Establishment Act (HR1795) by unanimous consent on December 15, 2000 and cleared it for the President's signature. The bill had been passed in the House on September 27, 2000. The President signed the bill into law on December 29, 2000 (PL 106-580). The bill establishes a new institute at NIH to coordinate activities in this technology and provide funding equal to the amount obligated by NIH for biomedical imaging and bioengineering in FY 1999, adjusted for inflation. In establishing the Institute, the Director of NIH is authorized to transfer personnel, use appropriate facilities to house the new Institute, and obtain administrative support from other agencies of NIH. The Institute is expected to have a 12-member advisory council, and prepare a plan to address the consolidation and coordination of NIH biomedical imaging and engineering programs, as well as related activities of other federal agencies.

Senate Majority Leader Trent Lott, R-Miss., who sponsored similar legislation (S1110) said biomedical imaging and engineering allows breakthroughs at the molecular level and said the NIH has not invested enough in this area in recent years. The House Commerce Committee adopted an amendment to change the proposed name of the new institute, inserting "Bioengineering" in place of "Engineering". Earlier this year, NIH moved forward with plans to create an Office of Bioengineering, Bioimaging and Bioinformatics, OBBB, or OB3. However, this legislation will require a significant course change. The new office was established in April 2000 within the Office of the NIH Director, and rolled together the Bioengineering Consortium (BECON), which was established in 1997 to provide a focus for bioengineering activities and now includes bioimaging, and the Biomedical Science and Technology Initiative Consortium (BISTIC), created this Spring to further research in bioinformatics.

Small Business Reauthorization Act

On December 15, 2000, the House and Senate passed H.R. 5667, the Small Business Reauthorization Act of 2000. The legislation reauthorizes and makes improvements to virtually all of the Small Business Administration's (SBA) programs, including the Small Business Innovation Research (SBIR) program. H.R. 5667 passed the Congress as part of the FY 2001 Omnibus Appropriations Act which was signed by the President December 21, 2000.

Chimpanzee Health Improvement, Maintenance, Protection Act

On December 20, 2000, the President signed H.R. 3514, the Chimpanzee Health Improvement, Maintenance, and Protection Act, into law (P.L. 106-551), which requires NIH to enter into a contract with a nonprofit private entity for the purpose of operating a sanctuary system for the long-term care of chimpanzees.

Minority and Health Disparities Research and Education Act

Signed by the President on November 22, 2000, the legislation (P.L. 106-525) creates in statute a National Center on Minority Health and Health Disparities (NCMHD) at the NIH to coordinate health disparities research performed or supported by NIH; a grant program through the new NCMHD to further biomedical and behavioral research education and training; an endowment program to facilitate minority and other health disparities research at centers of excellence; and a loan repayment program to train members of minority or other health disparities populations as biomedical research professionals.

107th Congress

NIH authorizing and appropriations committees will see several changes in the 107th Congress. Representative John Edward Porter (R-IL), Chairman of the Subcommittee on Labor, Health and Human Services, and Education of the House Committee on Appropriations, retired at the end of the 106th Congress. Representative Ralph Regula (R-OH) has been named by the full Committee Chairman, C.W. (Bill) Young (R-FL), to serve as the new Chairman of the Subcommittee. Representative Thomas Bliley (R-VA), Chairman of the House Commerce Committee, retired at the end of the 106th Congress. The Committee has been renamed the House Energy and Commerce Committee, and the

new Chairman is Representative W.J. Tauzin (R-FL). Senator Arlen Spector (R-PA) will remain as Chairman of the Subcommittee on Labor, Health and Human Services, and Education of the Senate Appropriations Committee.

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NIDA and the World Health Organization Department of Child and Adolescent Health and Development assembled 37 representatives from 16 nations at **Street Children and Drug Abuse: Social and Health Consequences**, held September 17-19, 2000, in Marina Del Rey, California. The researchers and community-based organizers met to enhance networks for communication and cooperation, examine science-based interventions from around the world, and adopt action priorities for a collaborative, cross-national, multidisciplinary research agenda that will promote the health and well-being of young people. The organizing committee was co-chaired by Dr. M. Patricia Needle, International Program, and Dr. Andrew Ball, WHO Department of Child and Adolescent Health and Development, and included Dr. Mary Jane Rotheram-Borus, University of California, Los Angeles; Dr. John Howard, Macquarie University, Sydney, Australia; and Ms. Moira O'Brien, DESPR. Other participants included Ms. Sheryl Massaro, OSPC; Dr. Jacques Normand, DESPR; and NIDA grantees Dr. Philippe Bourgois, University of California at San Francisco, and Dr. Michael Clatts, National Development and Research Institutes, Inc., New York. The U.S. Department of State provided financial support for the meeting.

NIDA and the Thai Ministry of Public Health cosponsored the **Pacific Regional Research Conference on Methamphetamine and Other Amphetamine-Type Stimulants** in Bangkok, Thailand, November 14-17, 2000. Researchers and treatment professionals discussed the latest scientific findings on the epidemiology, ethnography, and neuropsychopharmacology of methamphetamine use, clinical and treatment research issues, the impact of methamphetamine abuse on HIV/AIDS, and an Asia Pacific research agenda. NIDA Director Dr. Alan I. Leshner addressed the opening plenary session; NIDA Associate Director Dr. Timothy P. Condon chaired the session on epidemiology and ethnography. The international organizing committee included Dr. M. Patricia Needle, NIDA International Program; Dr. Jirot Sindhvananda, Thai Ministry of Public Health; and NIDA grantee Dr. Walter L. Ling, University of California, Los Angeles. NIDA grantees who participated included Dr. Patricia Case, Harvard Medical School; Dr. Linda Chang, Brookhaven National Laboratory; Dr. Michael Clatts, National Development and Research Institutes, Inc., New York; Dr. Robert T. Malison, Yale University School of Medicine; and Dr. David Segal, University of California San Diego School of Medicine.

NIDA selected three senior researchers as recipients of the first **Distinguished International Scientist Collaboration Program Awards:** Dr. Tibor Wenger, Semmelweis University, Budapest, Hungary; Dr. Christian SchŸtz, Ludwig-Maximilians University, Munich, Germany; and Dr. Anton Bespalov, Pavlov Medical University, St. Petersburg, Russia. Designed to encourage international collaborative research on drug abuse, the awards support short-term visits to NIDA grantees by established researchers from other countries. Dr. Wenger will work with Dr. Billy Martin, Virginia Commonwealth University, using immunohistochemistry to determine the anatomical relationship between cannabinoid and dopamine systems. Dr. SchŸtz will collaborate with Dr. John Krystal, Yale School of Medicine, to prepare a research grant proposal for a pilot study of the effects of the opioid antagonist naloxone on a challenge with the NMDA antagonist memantine. Dr. Bespalov will collaborate with Dr. Athina Markou, The Scripps Research Institute, to expand her study of the intravenous self-administration of nicotine in nicotine-dependent mice.

NIDA welcomed the 2000-2001 **Hubert H. Humphrey Drug Abuse Research Fellows** with an orientation program December 1, 2000. Three Fellows are supported by NIDA: Dr. Olga Vassioutina, Russia; Dr. Vedran Marde_ic, Croatia; and Ms. Elvia Amesty de Torres, Venezuela.

The 2000-2001 **INVEST Research Fellows** have begun their postdoctoral research and training with NIDA grantees. A senior clinical consultant at Linkoping University Hospital, Sweden, Dr. Henrik Druid will work with Dr. Deborah C.

Mash, University of Miami School of Medicine. Dr. Druid will study the neurochemical mechanisms involved in the deaths of chronic cocaine abusers. A psychiatrist and postdoctoral fellow at the National Institute on Drug Dependence in Beijing, China, Dr. Chuang Liu will work with Dr. Elliot A. Stein, Medical College of Wisconsin, Milwaukee. He will study the underlying mechanisms contributing to craving by using functional magnetic resonance imaging to determine which neuroanatomical sites are activated during cue-induced nicotine craving.

On October 5, 2000, Dr. Elizabeth Robertson met with Sergio Haro Cordero and Jorge Alejandro Medellin, Mexican investigative news reporters interested in prevention programming and outcomes in the United States.

Ms. Susan David, DESPR, met with Mr. Timo S. Jetsu, Administrator, Secretariat General of the Drugs Coordination Unit, The European Commission, on September 21, 2000, to discuss new research in drug abuse prevention and how those findings can be applied to European drug problems.

Ms. Susan David and Dr. Kathy Etz, DESPR, met with Drs. Chung, Chung, and Lee from Korea on September 27, 2000, discussing prevention research in both the U.S. and Korea.

Dr. Kathy Etz met with Ms. Maria Paz from Chile on October 2, 2000, to discuss plans for broadly disseminating drug abuse prevention in Chile, exploring how U.S. based research can inform this effort.

Ms. Moira O'Brien, CRB, DESPR, participated in the **Inter-American System of Uniform Drug Use Data Expert Advisory Meeting**, sponsored by the Organization of American States Drug Abuse Control Commission (OAS/CICAD), held in Panama City, Panama, September 26-28, 2000.

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Meetings/Conferences

A meeting on **Cardiovascular Complications of HIV and Substance Abuse** (cocaine, alcohol) planned, organized and conducted by Lan-Hsiang Wang, Ph.D. of the NHLBI and Jag H. Khalsa, Ph.D., of CAMCODA, NIDA was held September 18-19, 2000. A group of nationally and internationally recognized clinicians and scientists (funded by NHLBI and NIDA-co-sponsored RFAs) presented and discussed current data on the etiology and underlying pathophysiology of cardiovascular complications of HIV/AIDS, and substance abuse (cocaine, alcohol) and HIV infection. They also made a number of recommendations for future research. A brief summary, agenda and the roster of participants appears on the NIDA website. An executive summary is in preparation for publication in a professional journal.

NIDA held its **Fifth Annual Research Training Grant Directors Meeting** on October 13, 2000 in Bethesda, Maryland. Dr. Timothy P. Condon, Associate Director, NIDA, updated the training directors on NIDA's research initiatives; Drs. Cindy Miner and Angela Martinelli, Science Policy Branch, OSPC, discussed current research training activities at NIDA; Dr. Mark Swieter, Office of Extramural Affairs, updated the directors on current extramural review policies; and Dr. Lula Beatty, Director of NIDA's Special Populations Office, presented NIDA's Health Disparities Plan.

NIDA, the University of California Los Angeles, MATRIX, the Los Angeles County Alcohol and Drug Program Administration, and the Robert Wood Johnson Foundation co-sponsored a conference, **"Blending Clinical Practice and Research to Enhance Drug Addiction Treatment,"** on November 1-2, 2000, in Los Angeles, CA, to disseminate research-based information on drug abuse and addiction. Researchers and practitioners examined ways to enhance ongoing efforts to ensure research is incorporated into practice settings.

A satellite meeting to the Society for Neuroscience Annual Meeting, sponsored by the NIDA Neuroscience Consortium, was held on November 4, 2000. The meeting, organized by Drs. Rita Liu, OEA, and Roger Brown, DNBR, was entitled **"NIDA Neuroscience: Current Status and Future Directions,"** and included presentations and panel discussions led by NIDA staff on NIDA activities and neuroscience-related research interests. NIDA participants included: Drs. Timothy Condon, Glen Hanson, David McCann, Dionne Jones, Peter Delany, Teri Levitin, Barry Hoffer, Rita Liu, Roger Brown, Joseph Frascella, David Shurtleff, Minda Lynch, Jane Acri, Cora Lee Wetherington and Pushpa Thadani.

NIDA sponsored a satellite symposium at the Annual Meeting of the Society for Neuroscience held in November 2000 in New Orleans, LA entitled **"Cellular and Molecular Mechanisms of Synaptic Vesicle Trafficking".** This symposium, organized by Drs. Jonathan Pollock and Rebekah Rasooly, both of DNBR, presented new results regarding key players mediating and regulating exocytosis and vesicle recycling.

Drs. Nancy Pilotte and Minda Lynch, DNBR, co-chaired a satellite symposium at the Society for Neuroscience meeting in November 2000, in New Orleans entitled **"Cross-Sensitization Between Drugs: A Behavioral and Neural Basis for "Gateway"?"** The purpose was to examine evidence that prior drug exposure modifies subsequent reactivity to a different drug of abuse, e.g., neurobiological substrate changes, behavioral data, human lab studies and anecdotal reports, and the relevance to vulnerability for addiction.

Dr. Pushpa Thadani, DNBR, chaired a NIDA-sponsored satellite forum **"Minority Scholars: Research and Funding Opportunities at the National Institute on Drug Abuse"** at the Annual Meeting of the Society for Neuroscience, in New Orleans, LA in November 2000. The event was co-hosted by Xavier University, an HBCU in New Orleans. The forum showcased various NIDA Minority training and research programs including MIDARP and Minority Supplement program designed to attract underrepresented minorities in Drug Abuse Biomedical Research. The forum also showcased students' research findings generated under the MIDARP (Xavier University and SUNY, Stonybrook NY)

and Minority Supplement programs. Over 70 people attended the forum and the attendees included undergraduate and graduate students, postdoctoral fellows, faculty, NIDA training directors and researchers as well as NIDA staff.

NIDA sponsored a panel on Hepatitis C at the American Public Health Association conference, moderated by David Anderson, MS, editor, NIDA NOTES, in Boston, MA, on November 11, 2000. The panel addressed **"Research Update on Hepatitis C among Drug Abusers: What are the Health Consequences and Implications for Treatment, Prevention, and the Community?"**

A NIDA sponsored scientific workshop titled: **"Bridging Neurobiological, Behavioral, and Prevention Sciences,"** co-chaired by Dr. Bill Bukoski, Associate Director for Prevention Research Coordination, DESPR and Dr. Minda Lynch, Acting Chief, Behavioral Sciences Research Branch, DNBR was held on November 15, 2000 at the Gaithersburg Hilton Hotel. The workshop convened senior and early career scientists from the disciplines of basic, behavioral, and prevention research to explore the relevance and possible future directions of "multidisciplinary" research and research training opportunities that could advance drug prevention theory and the development of innovative prevention interventions to better reach youth and young adults at high risk for drug abuse and addiction.

NIDA participated as a co-organizer in the trans-NIH conference: **"The Science of the Placebo: Toward an Interdisciplinary Research Agenda,"** held November 19-20, 2000 in Bethesda, MD. This conference brought together researchers from a wide range of disciplines to examine the biological, behavioral, social, cultural, and ethical aspects related to the placebo effect. Dr. Lisa Onken represented NIDA on the executive planning committee for this conference, and also served as a co-chair for a breakout session on the placebos in behavioral treatment research.

NIDA, the American Academy of Pediatrics, and the American Academy of Child and Adolescent Psychiatry were co-sponsors of the American Society of Addiction Medicine's Conference, entitled **"Adolescent Substance Abuse for the Practitioner"**, held on November 3-5, 2000 at the Omni Shoreham Hotel, in Washington, D.C. The conference presented science-based information on identification of and intervention with adolescents involved in (or at risk for) use of alcohol, tobacco, and other drugs. The conference workshops focused on translating clinical and behavioral research into approaches that can be used by practitioners in a number of settings, including primary care. NIDA Director, Dr. Alan Leshner, gave the keynote presentation on the Neurobiology of Addiction: Implications for Practice. Dorynne Czechowicz, M.D., DTR&D represented NIDA on the conference planning committee.

On November 30, 2000, the Special Populations Office, NIDA convened a special one-day **Meeting of NIDA's Four Racial/Ethnic Advisory Work Groups** including the African American Researchers and Scholars, National Hispanic Science Network, Native American/Alaskan Native and Asian American and Pacific Islander Work Groups in Bethesda, Maryland. The meeting was designed to focus on NIDA's Health Disparity Initiative and to allow individual work groups time to continue ongoing strategies in addressing drug abuse research efforts relevant to their communities.

On December 1, 2000, a **NIDA and Managed Behavioral Healthcare Summit Meeting** was held in Washington, D.C. Dr. Leshner chaired the meeting that focused on areas of common interest, simplified provider reporting, and roadblocks to supporting clinical trials.

Dr. Jacques Normand and Ms. Moira O'Brien, CRB, DESPR, organized and chaired a meeting, **Research on Emerging and Current Drug Abuse Trends: Agenda Setting**, in San Francisco, California, on December 11, 2000, held in conjunction with the biannual meeting of the NIDA CEWG. Mr. Nicholas Kozel, DESPR, also participated in the meeting. The meeting convened several NIDA-supported researchers and CEWG participants to discuss issues pertaining to the timely identification and monitoring of new drug abuse trends, and enhancing the linkages between drug abuse monitoring and problem-focused research.

On December 14, 2000, the Special Populations Office held a one-day **MIDARP Planning Meeting** to receive feedback from grantees and reviewers on the current structure of the program.

On January 11, 2001, NIDA sponsored a meeting, **"Turning Scientific Breakthroughs Into Science News,"** at the Natcher Conference Center at the National Institutes of Health, Bethesda, MD, for NIDA and grantee university public information staff. Special lectures addressed topics such as the dissemination of research results and the challenges of promoting research. In addition, a "Health Science and the Media" panel discussion included speakers from The Washington Post, CNN, WebMD, USA Today, and Science Magazine.

The **First Steering Committee Meeting of the National Hispanic Science Network on Drug Abuse**, which is being implemented through a contract with the University of Miami, took place on January 18 and 19, 2001. Ana Anders, Senior Advisor on Special Populations, serves as Project Officer on the contract.

Dr. Gordon Duval addressed the ethical issues in conducting randomized clinical trials with court diverted patients at

a seminar sponsored by the CTN and NIDA's Treatment Work Group held on January 26, 2001.

A **CTN National Steering Committee Meeting** was held August 21-22, 2000, in Washington, D.C. The members met to review and approve policies and procedures for the CTN; discuss plans for Year 2 of the Network; and to approve a reorganization of the CTN Steering Committee with the establishment of a new executive Operating Committee to focus on the everyday protocol implementation activities of the CTN.

NIDA sponsored a **Clinical Trials Network meeting** on September 18, 2000, at Yale University, which is the New England node of NIDA's National Drug Abuse Clinical Trials Network. At the meeting, NIDA launched the NIDA Clinical Toolbox: Science-Based Materials for Drug Abuse Counselors. The toolbox, packaged in a bright gray box with a large "Tx" on the front, was sent to nearly 12,000 drug treatment programs around the country.

The **NIDA CTN Ad Hoc Oversight Board**, chaired by Dr. Leshner, met on September 11, 2000, in Bethesda, MD. The Board reviewed and approved the next wave of five new concepts for development into CTN wide protocols.

A **CTN National Steering Committee Meeting** was held September 19-20, 2000, in Philadelphia, PA. The keynote speaker was Mark Bencivengo, Deputy Secretary of Health, City of Philadelphia. The members discussed the status of the ongoing protocols, plans for development of the approved concepts into protocols, and the expansion of the CTN from the current 6 nodes. The Steering Committee members signed a Declaration of Interdependence.

The **first meeting of the CTN Data and Safety Monitoring Board (DSMB)** was held September 27, 2000, in Rockville, MD. The members discussed the mission, vision of the Board, agreed to review the CTN DSMB policies and SOPs, current protocols, and made plans to meet on a regular basis.

Site Initiation visits were held at 7 Community Treatment Programs starting on October 4, 2000 and ending on October 27, 2000. The meetings were held to assess the readiness of the clinical sites before implementation of the buprenorphine/naloxone detoxification protocols (CTN 00001 and 00002).

A **CTN Protocol Kick Off Meeting** was held October 17-19, 2000, in New Haven, CT, for the Motivational Enhancement Therapy and Motivational Interviewing Therapy protocols (CTN 00004 and 00005). Participating members from all the CTN Community Treatment Programs attended the meeting.

A **New CTN Nodes PI Orientation Meeting** was held on October 23, 2000, in Bethesda, MD, to welcome the newly awarded grantees into the CTN. Dr. Leshner gave opening remarks and welcomed the new members to the CTN. Members were briefed on the CTN infrastructure, policies and procedures, current protocols, guidelines for publications, and other pertinent issues.

The **CTN National Steering Committee** met in Los Angeles on October 30, 2000, followed on October 31, 2000, by the CTN Kick Off Meeting. All eleven nodes participated in the meetings including attendees from other organizations interested in joining the CTN.

The **CTN Data and Safety Monitoring Board** met on December 8, 2000, in Bethesda, MD. The Board reviewed the initial CTN protocols.

A **CTN Steering Committee Meeting** was held January 8-10, 2001 in Tampa FL.

A **CTN Training Subcommittee Meeting** to welcome members from the new nodes was held January 29-30, 2001, in Bethesda, MD.

A **GRP (Good Research Practice) Train the Trainer Session** was held on January 31, 2001 in Bethesda, MD.

A two-day **CTN Quality Assurance Subcommittee Meeting** to welcome new node members was held February 1-2, 2001, in Rockville, MD.

At the Sixth Annual Latino Behavioral Health Institute Conference on September 22, 2000, in Los Angeles, CA, NIDA announced a Latino campaign in early 2001 to include radio Public Service Announcements (PSAs) and a brochure in Spanish to encourage parents to talk to their children about the consequences of drug abuse. The conference offered 50 workshops on Latino behavioral health, and attracted over 1,000 participants including family, consumers, and providers of behavioral health services to the Latino community.

At the Society for Advancement of Chicanos and Native Americans in Science (SACNAS) National Conference in Atlanta, GA, on October 12-15, 2000, NIDA released an intergenerational, year 2001 Indian Country Calendar for Native Americans, "Walking A Good Path." NIDA printed 100,000 calendars, and as of December 2000 has distributed 76,580. In addition, at the SACNAS conference, NIDA announced the availability of a variety of new and recently

translated NIDA research brochures.

Mr. Richard A. Millstein, NIDA Deputy Director, was keynote speaker at the Utah Fall Substance Abuse Conference, St. George, Utah, September 27, 2000.

Mr. Millstein participated as a panel member of the IMPAC Teen Illicit Drug Expert Panel of the Robert Wood Johnson Foundation-funded Andrews University Project, Arlington, VA, September 29, 2000.

Mr. Millstein was keynote speaker at the Friends Research Institute Awards Dinner, Baltimore, MD, October 5, 2000.

Mr. Millstein was a speaker at the conference "Drug Abuse and Addiction: Global Answers to a Problem without Frontiers", co-sponsored by the United Nations Drug Control Programme and the Rainbow Coalition of Therapeutic Communities, Rimini, Italy, October 27, 2000.

Mr. Millstein greeted attendees at the Association for Medical Education and Research in Substance Abuse (AMERSA), Alexandria, VA, November 2, 2000.

Mr. Millstein spoke on the science of addiction at the Tobacco Free Suffolk County Conference, Smithtown, NY, November 13, 2000.

Mr. Millstein welcomed participants to a NIDA Workshop, "Bridging Neurobiological, Behavioral, and Prevention Science", Gaithersburg, Maryland, November 15, 2000.

Mr. Millstein was guest lecturer on drug abuse epidemiology, and on drug abuse policy issues, Johns Hopkins University School of Public Health, Baltimore, MD, November 29, 2000.

Mr. Millstein presented opening remarks at the combined meeting of NIDA's four racial and ethnic minority researchers and scholars groups, Bethesda, MD, November 30, 2000.

Dr. Timothy P. Condon Associate Director, NIDA, served as an advisory board member at the Addiction Institute Workshop in Winston-Salem, NC on September 8, 2000.

Dr. Timothy P. Condon presented "Updates on Drug Abuse Research: Implication for Science-based Prevention and Treatment" at the Michigan Substance Abuse Conference: Working Together-Sharing Solutions, in Grand Rapids, MI on September 19, 2000.

Dr. Timothy P. Condon presented "NIDA Prevention Principles" at the Fifth Annual Statewide Prevention Providers Meeting: Strengthening the Voice of Prevention in Phoenix, AZ on September 22, 2000.

Dr. Timothy P. Condon presented "Raves, Risks, and Research: Update on Club Drugs" at the Thirteenth Cape Cod Symposium on Addictive Disorders: Addiction Across the Lifespan: Prevention, Identification and Healing in Hyannis, Cape Cod, MA on October 6, 2000.

Dr. Timothy P. Condon spoke at the 30th Anniversary Celebration of Operation PAR's program in Clearwater, FL on October 19, 2000.

Dr. Timothy P. Condon presented "Research Advances in Drug Abuse and Drug Addiction: Science Replacing Ideology" at the 24th Annual Training Conference for Alcohol, Tobacco, and Other Drugs, Treatment and Prevention Professionals in Atlantic City, NJ on October 24, 2000.

Dr. Timothy P. Condon presented "Identification, Assessment and Early Intervention in Children and Adolescents at High Risk for Development of Substance Use Disorders" at the 47th Annual Meeting of the American Academy of Child and Adolescent Psychiatry in New York, NY on October 25, 2000.

Dr. Timothy P. Condon presented "Using Science and Research to Discuss Substance Abuse as a Chronic Treatable Condition" at the Demand Treatment! San Jose Regional Meeting in San Jose, CA on October 26, 2000.

Dr. Timothy P. Condon presented "Neuroscience at the National Institute on Drug Abuse" at the 30th Annual Society for Neuroscience Conference in New Orleans, LA on November 4, 2000.

Dr. Timothy P. Condon presented "Minority Scholars: Research and Funding Opportunities at NIDA" at the 30th Annual Society for Neuroscience Conference in New Orleans, LA on November 6, 2000.

Dr. Timothy P. Condon presented "The Epidemiology/ Ethnography of Methamphetamine Use" at the Pacific Regional Research Conference on Methamphetamine and Other Amphetamine-Type Stimulants in Bangkok, Thailand on

November 14, 2000.

Dr. Timothy P. Condon presented "Neurobiology of Addiction" at the Hubert H. Humphrey Drug Abuse Research Fellows Orientation to NIDA in Bethesda, MD on December 1, 2000.

Dr. Timothy P. Condon presented "Addiction is a Brain Disease" at the Colorado State Assembly on Offenders with Drug/Alcohol and Mental Health Issues: Partnerships for Effective Policy in Denver, CO on December 4, 2000.

Dr. Timothy P. Condon officiated at the ribbon cutting ceremony for the expansion of the Brookhaven National Laboratory's Center for Imaging and Neurosciences in Upton, Long Island, NY on December 7, 2000.

Dr. Timothy P. Condon and Dr. Jack Stein, Deputy Director, OSPC, presented an "Update on NIDA's Research/Practice Blending Activities" at the CTN National Steering Committee Meeting in Tampa, FL on January 8, 2001.

Dr. Timothy P. Condon presented "Science Advances in the Emerging Drug Problem: What We Have Learned" at the American Society of Addiction Medicine/Florida Society of Addiction Medicine (ASAM/FSAM) Conference 2001 in Orlando, FL on February 10, 2001.

Dr. Jack Stein, Deputy Director, OSPC, presented "Research Advances in Drug Abuse" to the staff of the A&E Television Network in New York, NY on November 13, 2000.

Dr. Jack Stein presented "Principles of Drug Abuse Treatment" at Join Together's, Demand Treatment! Hunt Valley Regional Meeting in Baltimore, MD on November 9, 2000.

Dr. Cindy Miner, Chief, Science Policy Branch, OSPC, organized and participated in the "NIDA Grant Writing Workshop" at the annual meeting of the American Academy of Child and Adolescent Psychiatry, October 27, 2000 in New York.

Dr. Angela M. Martinelli, Science Policy Branch, OSPC, organized and participated in "NIH Funding and Training Opportunities" at the American Public Health Association Annual Meeting held in Boston, MA on November 5, 2000.

Dr. Khursheed Asghar, Chief, Basic Sciences Review Branch, OEA, made a presentation on the review process and conducted a mock SRG meeting at a November meeting of the Special Populations Research Development Seminar, "Grant Application Development and Proposal Review - Follow-up to the Summer Workshop.

Mr. Richard Harrison, Chief, Contracts Review Branch, OEA, attended the American Indian Science and Engineering Society conference in Portland, OR from November 9-12, 2000, where he participated in the NIDA exhibit booth and recruiting activities. Mr. Harrison also represented the NIH Office of Equal Opportunity at the annual meeting of the National Congress of American Indians in St. Paul, MN, November 13-18, 2000 and served as the NIH representative on the Inter-Agency Committee for American Indian-Alaskan Native Heritage Month for the Washington area ceremonies and activities.

Drs. Rita Liu, Mark Green, Mark Swieter, and Bill Grace, all of OEA, participated in a planning meeting addressing the NIDA Minority Institutions Drug Abuse Research Development Program on December 14, 2000. This meeting was organized by the NIDA Special Populations Office.

Dr. Teri Levitin, Director, OEA, served as an evaluator of projects for the INTEL High School Science Talent Search in December 2000.

On December 7, 2000, Dr. Marina Volkov, Clinical, Epidemiological, and Applied Sciences Review Branch, OEA, along with Dr. Kathy Etz, Division of Epidemiology, Services and Prevention Research, addressed the Maryland Peer Counselors Conference on Avoiding the Brain Change: The Biology and Prevention of Addiction.

Dr. Lula Beatty, Chief, Special Populations Office, participated in the meeting of the Committee on Women in Psychology of the American Psychological Association on September 23-24, 2000 in Washington, DC.

Dr. Lula Beatty gave a presentation entitled "Funding Mechanisms at NIH: What You Need to Know" at a technical assistance workshop on research on HIV/AIDS adherence and treatment for minority investigators sponsored by the NIH Office on AIDS on October 27, 2000 in Crystal City, VA.

Dr. Lula Beatty presented an address entitled "Women Abusing Drugs: Building the Knowledge Base for Effective Prevention and Treatment" at the annual meeting of the American Association of Behavioral Therapists, on November 19, 2000 in New Orleans, LA.

Dr. Lula Beatty participated in a meeting cosponsored by the Special Populations Office and the Women's Office of the

American Psychological Association to discuss developing leadership in translational research for women on December 15, 2000 in Washington, DC.

Ana Anders, Special Populations Office, participated in planning the Hispanic Heritage Month Observance at NIH held on October 4, 2000 at which Dr. Jose Szapocznik, NIDA grantee, made a presentation.

Ana Anders participated in planning the annual conference of the Latino Behavioral Health Institute held in Los Angeles, CA September 20-22, 2000. Four drug abuse research workshops were held, and Ms. Anders was the moderator for two.

Ana Anders is a member of the WHO/PAHO planning committee for the World Health Day celebration that will be held on April 6, 2001 in Washington, D.C.

On December 4, 2000 Ana Anders made a presentation to the Upcounty Latino Network Mental Health Committee on NIDA's mission, with particular emphasis on the Institute's Hispanic Initiative.

Flair Lindsey, Program Analyst, Special Populations Office, gave a presentation on the effects/consequences of drug abuse to 7th and 8th grade students at the Hip Hop to Health Conference held at Howard University on October 13, 2000 in Washington, DC.

Flair Lindsey gave a presentation on the effects of marijuana to pre-teens at the Teen Life Choices Center on October 23, 2000 in Washington, DC.

Dr. Frank Vocci, Director, DTR&D, presented on NIDA's Stimulant Medications Discovery Program at the Workshop on New Knowledge in Methamphetamine Medications Development at UCLA on September 28, 2000.

Dr. Frank Vocci presented at two workshops at the Blending Clinical Practice and Research: Forging Partnerships to Enhance Drug Addiction Treatment conference in Los Angeles on November 1, 2000. Drs. Mary Jeanne Kreek and Ron Jackson were his co-presenters.

Dr. Frank Vocci participated in the Center for Substance Abuse Treatment's Physicians Summit on Buprenorphine Education on November 30, 2000 in Bethesda, MD.

Dr. Frank Vocci presented on the Research Programs of the Division of Treatment Research and Development at the Hubert H. Humphrey Drug Abuse Research Fellows Orientation to the National Institute on Drug Abuse at the NSC on December 1, 2000.

Dr. Betty Tai, DTR&D, gave a presentation on the CTN at the CSAT/NIDA National Addiction Technology Transfer Centers Network Meeting on November 15-16, 2000, in Bethesda, MD. Several of NIDA's CTN staff also participated in the ATTC/CSAT meeting as moderators for workshops.

Dr. Joseph Frascella, DTR&D, participated as a faculty mentor in a Special Populations Research Development Seminar Series entitled "Grant Application Development and Proposal Review - Follow-up to the Summer Workshop" in Rockville, MD, November 27-28, 2000.

Dr. Joseph Frascella participated in the "Joint Meeting of NIDA Work Groups on the Topic of Health Disparities" in Bethesda, MD, November 30, 2000.

Dr. Steven Grant presented a talk entitled "Brain Activity Differentiates Drug Abusers and Controls During Gambling Task Performance" at the conference on Co-Morbidity of Pathological Gambling, Las Vegas, NV, December 3-5, 2000.

Dr. Steven Grant presented a talk entitled "Differential Brain Networks in Drug Abusers and Controls During Gambling Task Performance: A PET FDG-Study" in the symposium "Addiction as a Disease of the Orbitofrontal Cortex" at the annual meeting of the American College of Neuropsychopharmacology meeting in San Juan, Puerto Rico, December 10-14, 2000.

Dr. Ahmed Elkashef presented on NIDA's Methamphetamine Medications Portfolio and future plans at the Workshop on New Knowledge in Methamphetamine Medications Development at UCLA on September 28, 2000.

Dr. Ahmed Elkashef presented on NIDA's Medications Discovery Program at a continuing education training course at the Drug Abuse Counselors of Northern Virginia chapter meeting held, May 2000.

Dr. Cora Lee Wetherington, DNBR and NIDA's Women and Gender Research Coordinator, gave an invited talk, "Gender Matters in Drug Abuse" in the "Drug Addiction" panel at the Society for Women's Health Research Tenth Scientific Advisory Meeting, October 26, 2000, Washington, D.C. She was also the moderator for the panel in which

she spoke.

Dr. Cora Lee Wetherington gave an invited talk, "Does Gender Matter in Your Drug Abuse Research?," at the Behavioral Pharmacology Research Unit at Johns Hopkins University, December 7, 2000.

Dr. Minda Lynch, Behavioral Sciences Research Branch, DNBR, directed a break-out group on NIH Career Development Awards at the "Meeting on Training Opportunities" sponsored by NIH and NSF at the Society for Neuroscience annual convention held in New Orleans, LA in November 2000.

Dr. Nancy Pilotte participated in a White House Task Force on Sports and Drugs in Salt Lake City, November 6-7, 2000.

Dr. James Colliver, ERB, DESPR, represented NIDA at the annual meeting of the National Advisory Committee to Monitoring the Future (MTF) at the University of Michigan in October 2000 and presented an overview of environmental factors affecting MTF from the Federal perspective.

Dr. Leslie Cooper, ERB, DESPR, participated in a special session to formalize national efforts for the elimination of Health Disparities held at the American Public Health Association's Annual Meeting in Boston, MA, November 4, 2000.

Dr. Leslie Cooper, ERB, DESPR, participated in the National Stakeholder's Meeting October 16, 2000, to discuss the launching of National Minority Health Month, organized by the former Secretary of Health and Human Services, Dr. Louis Sullivan. The focus of the meeting was the elimination of Health Disparities among racial and ethnic minorities.

Dr. Leslie Cooper, ERB, DESPR, participated in an evaluation effort for the DC Developing Families Center, along with other DHHS agencies and the community held December 15, 2000. The purpose was to plan an evaluation effort that includes the identification of improved perinatal outcomes; methodological issues in designing community based studies; and the identification of historical interventions that have been successful with similar populations.

Dr. Leslie Cooper, ERB, DESPR, represented NIDA in the HHS Diversity Workshop December 12, 2000, entitled "All of Us...Beyond Race and Gender" which was follow-up to the HHS Conference on Diversity held March 1-2, 2000.

Dr. Coryl Jones, ERB, DESPR, and Bernie Auchter of the National Institute of Justice co-hosted a pre-conference Institute, Violence Against Women and Within the Family, October 1-3, 2000, at the National NIJ Research Conference on Violence Against Women. Research presented at the meeting and the researcher-practitioner conference was the result of 10 grants ($5.5M) supported by the NIH Consortium on Violence Against Women and Within the Family. Dr. Jones served as the program official for all grants funded by the NIH Consortium.

Dr. Coryl Jones, ERB, DESPR, was member of the steering committee and presenter at The Federal Child Neglect Research Consortium meeting held November 30 and December 1, 2000, held under the auspices of the NIH Consortium on Child Neglect. It was the first of five annual Technical Assistance Meetings for Grantees funded by the Consortium, which includes seven NIH institutes, the Administration on Children, Youth, and Families (Children's Bureau), the Office of Justice Programs (NIJ and OJJDP), and the Department of Education (Office of Special Education Programs). This meeting focused on instrumentation, data sharing, definitional, legal, and human subject issues, and establishing a cross-institute and cross-agency base of operations.

Dr. Yonette Thomas, ERB, DESPR, was an invited speaker for the National Academies' Ford Foundation Fellows Program and participated in a panel on career development and opportunities for research held at the Annual Conference of Ford Fellows at the Beckman Center in Irvine, CA, October 14, 2000.

Dr.Yonette Thomas, ERB, DESPR, also served as the NIDA representative to the National Institute of Justice's Third Annual International ADAM (Arrestee Drug Abuse Monitoring Program) Conference held September 21-23, 2000.

Dr. Yonette Thomas, ERB, DESPR, participated in the National Leadership Forum XI of the Community Anti-Drug Coalitions of America, December 6-8, 2000.

Dr. Elizabeth Robertson and Ms. Susan David, PRB, DESPR, participated in a planning conference with other Federal representatives of anti-drug programs, October 30-31, 2000. Dr. Robertson presented a paper on the future of NIDA prevention research. The meeting was convened by the Robert Wood Johnson Foundation to develop recommendations on future directions for substance abuse prevention research and services.

Ms. Susan David and Dr. Bill Bukoski, DESPR, participated in a Prevention Roundtable, November 16, 2000, sponsored by SAMHSA, which included representatives from DHHS programs targeted to youth who are at-risk for substance abuse problems. The purpose was to develop collaborative programming to expand the reach of Department prevention efforts.

Dr. Elizabeth Robertson and Ms. Susan David, DESPR, represented NIDA at a meeting held on December 1, 2000, sponsored by the Office of National Drug Control Policy, to identify sources of data on parent and mentoring programs to incorporate into their Program Measurement for Effectiveness System (PME). NIDA presented an overview of its research portfolio on family research and the Westat Campaign Evaluation which will produce information about the attitudes, beliefs, and behaviors of parents and their children.

Dr. Elizabeth Robertson and Ms. Susan David, DESPR, presented a paper and participated in planning work groups at the Worldwide Inaugural Conference, December 5-7, 2000, on "The Promotion of Mental Health and Prevention of Mental and Behavioral Disorders," at The Carter Center, Atlanta, GA. The purpose of the conference was to examine how to integrate mental health promotion with the prevention of mental and substance abuse disorders, and cross-cultural transfer of science-based prevention research into cultures around the world. The focus of the paper was to outline NIDA's goals for the next generation of prevention research and encourage new applications to address these goals.

Dr. Eve Reider, PRB, DESPR, gave a presentation on drug abuse prevention research on behalf of Dr. Elizabeth Robertson at The Fall Research Conference: Bridging the Gaps Between Research, Policy and Practice held by Washington State Department of Social & Health Services-Division of Alcohol and Substance Abuse and Northwest Frontier Addiction Technology Transfer Center. The conference was held at the Embassy Suites in Tukwila, WA on December 11 -12, 2000.

Dr. Kathy Etz, PRB, DESPR, served as a rapporteur for the meeting, Preventing Adolescent Problem Behaviors on November 20-21, 2000 in Washington DC.

Dr. Kathy Etz presented information on drug abuse prevention at the Maryland Peer Helpers Association meetings in Ocean City, Maryland on December 7, 2000.

Dr. Bill Bukoski, DESPR participated as an expert panelist in a CSAT-sponsored meeting held November 30-December 1, 2000 and titled: "Preadolescent Screening Instrument (PASI) --- Second Expert Panel Meeting." The purpose of the conference was to explore innovative multiple-gating assessment procedures that could be employed to identify and assist children at possible risk to subsequent onset of drug abuse and other psychological and educational behavioral disorders.

Dr. Lynda Erinoff, CRB, DESPR, represented NIDA at the Principal Investigators (PI) Meeting of the NIH Youth Violence Consortium December 12-13, 2000. The PIs all were recently funded under the RFA "Research on the Development of Interventions for Youth Violence" and exchanged information about human subjects issues, study design and measurement issues.

Dr. Jacques Normand and Ms. Moira O'Brien, CRB, DESPR, participated in the NIDA sponsored meeting, Street Children and Drug Abuse: Social and Health Consequences, held in Marina Del Rey, California, September 17-19, 2000.

Dr. Bennett Fletcher, Services Research Branch, DESPR, presented on NIDA's health services research goals at the Little Rock Conference on Substance Abuse Health Services Research: Research in Practice, November 1-3, 2000, Little Rock, Arkansas.

Dr. Bennett Fletcher participated in the planning meeting of the Veterans with HIV/AIDS Cohort Study (VACS), a study currently supported by the National Institute on Aging, the National Institute for Mental Health, and the Veterans Affairs Administration on October 26, 2000 in Pittsburgh, PA.

Dr. Jerry Flanzer, Services Research Branch, DESPR, led a workshop on the implications of recent NIDA neuroscience findings for social work practice. NASW National Conference, November 3-4, 2000, Baltimore, MD.

Dr. Jerry Flanzer led a panel on NIDA's efforts on Drug Court Research at the Annual Conference of the American Society on Criminology, November 15-16, 2000, San Francisco, CA.

Dr. Jerry Flanzer participated on a Steering Committee to review the latest Practice Research Network findings of the NASW. December 1-2, 2000 in Washington, DC.

Dr. Henry Francis, Director of NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA), made a presentation on "Hepatitis C" to health care service providers at the Year 2000 World Conference on Co-Existing Medical Conditions, San Francisco, CA, September 2, 2000.

Dr. Henry Francis made a presentation on "Infections in Injecting Drug Users" at a "Meet the Professor Session" of the 38th Annual Meeting of the Infectious Diseases Society of America, New Orleans, Louisiana, September 8, 2000.

Dr. Henry Francis presented on "Hepatitis C, the Silent Epidemic" to the founders of the Maryland State Hepatitis Coalition, Inc., Frederick, MD, November 17, 2000.

Dr. Henry Francis presented on "Substance Abuse Trends and Practices in the New Millennium: Implications for STD Prevention" at a Symposium on "Confronting Emerging Challenges for STD Prevention: New Paths, New Approaches" at the 2000 National STD Prevention Conference, Milwaukee, WI, December 5, 2000.

Drs. Henry Francis and Peter Hartsock participated in the Yale University AIDS in Africa Day and AIDS Research Day, where cutting edge NIDA-supported research findings were presented in New Haven, CT, September 21-22, 2000.

Helen Cesari, CAMCODA, presented an overview of the Global Research Network on HIV Prevention in Drug-Using Populations at the Fogarty International Center AITRP/TBITRP Network Meetings, Washington, DC, October 26, 2000.

Dr. Dionne Jones, CAMCODA, attended and participated in workshops at the American Public Health Association Annual Meeting, Boston, MA, November 13-16, 2000.

Helen Cesari, CAMCODA, attended and participated in workshops at the 2000 National STD Prevention Conference, Milwaukee, WI, December 4-7, 2000.

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Media and Education Activities

Awards

NIDA's 3-minute introduction for the addiction supplement to the NIH High School Curriculum won the Silver (second place) in the Mercury Awards; NIDA's PSA campaign, "Keep Your Brain Healthy. Don't Use Drugs," won Bronze (third place) in the Mercury Awards competition.

NIDA's *Treatment Solutions* video was a finalist in the behavioral diseases category of the 2000 FREDDIE Awards/International Health and Medical Media Awards, sponsored by Time Inc Health.

NIDA's Mind Over Matter was featured on HomeworkSpot.com, a new educational web site that simplifies the search for the best free online K-12 homework resources.

Press Releases

July 26, 2000 - **Medication Reduces Metabolism of Nicotine, Decreasing Urge to Smoke.** Researchers at the University of Toronto found that methoxsalen, a compound used to treat skin disorders, partially blocks the body's ability to break down nicotine and significantly improves the effectiveness of oral nicotine replacement in reducing a smoker's urge for nicotine. In addition, when smokers do light up, they take fewer and shorter puffs on each cigarette, the scientists say. Dr. Edward Sellers and colleagues at the University of Toronto describe the research in the July 2000 issue of *Clinical Pharmacology and Therapeutics.* Coverage of this publication appeared in *USA Today, USAToday.com, CNN.com, New Scientist, Join Together Online, Business Week,* and *Alcoholism & Drug Abuse Weekly.*

August 13, 2000 - **Study Finds Acupuncture Shows Promise for Treating Cocaine Addiction.** In the August 14/28 issue of the Archives of Internal Medicine, researchers reported that cocaine-addicted patients who received a course of auricular acupuncture (acupuncture needles inserted into four specific points in the outer ear) were more likely to be free of cocaine during treatment than those not receiving acupuncture. Coverage of this publication appeared in *The New York Times, Chicago Tribune, LA Times, The Washington Times, The Washington Post, USA Today, EurekAlert!, CNN.com, HealthSCOUT, MSNBC.com, ABCnews.com, Reuters Health,* and other media outlets.

September 11, 2000 - **New National Public Service Campaign Highlights How Drugs Damage the Brain. *"Keep Your Brain Healthy. Don't Use Drugs."*** That's the message of a new, nationwide public service campaign launched by NIDA. The campaign, which features radio and television public service announcements in English and Spanish, is designed to help America's youth understand the risks associated with drug use. NIDA's partners in this public service campaign include Dr. Drew Pinsky, co-host of Loveline and drDrew.com; Major General Arthur T. Dean (ret.), CEO of Community Anti-Drug Coalitions of America (CADCA), and Sue Rusche, Executive Director, National Families in Action. As a result of this launch, coverage appeared in *USA Today, Reuters Health, Alcoholism & Drug Abuse Weekly, The Eagle (American University Student Newspaper),* and *Newsday.com.*

September 14, 2000 - **Street Children and Drug Abuse: Social and Health Consequences.** This media advisory announced an international working meeting to discuss and define a research agenda for addressing the social and health consequences of drug abuse by the world's street children. NIDA, the World Health Organization, and the National Inhalant Prevention Coalition co-sponsored the meeting, which was held September 17-19, 2000, in Los Angeles, CA. At this meeting, NIDA launched an updated research report that discusses recent studies on the use of

inhalants among adolescents in the United States with the goal of alerting the public to the widespread use of inhalants and the dangers inherent in such use. As a result of this meeting, coverage appeared in *Reuters Health.*

September 15, 2000 - **NewsScan: NIDA Addiction Research News.** In this issue, research advances included the following: genes play increasing role in risk for tobacco use among women (Sept 2000 issue of Archives of *General Psychiatry*); new study highlights addictive potential of cocaine (September 5, 2000, issue of *The Journal of Neuroscience*); natural compound may offer new treatment for chronic pain (September 2000 issue of *Proceedings of the National Academy of Science*); and nicotine may negatively affect nonsmokers (*Psychopharmacology* 152/3).

September 18, 2000 - **NIDA Clinical Toolbox Provides the Latest Information about Drug Treatment Strategies: Comprehensive science-based materials to be distributed to all drug treatment programs nationwide.** Nearly 12,000 drug treatment programs around the country received *NIDA Clinical Toolbox: Science-Based Materials for Drug Abuse Counselors.* The toolbox, packaged in a bright gray box with a large "Tx" on the front, is large enough to store all current NIDA drug treatment publications; it also has room for material that will result from future NIDA-sponsored research. As a result of this launch, coverage appeared in *Alcoholism & Drug Abuse Weekly, Progress Notes, About.com, Yale Bulletin & Calendar,* and *Join Together Online.*

September 19, 2000 - **NIDA Launches Spanish PSAs at Latino Behavioral Health Institute Conference.** ***"Manten Tu Cerebro Saludable. No Uses Drogas." ("Keep Your Brain Healthy. Don't Use Drugs.")*** This media advisory announced the launch of NIDA's Spanish PSAs at the 6th Annual Latino Behavioral Health Institute Conference on September 22, 2000, in Los Angeles, CA. These PSAs are targeted to parents and adolescents, and feature cutting-edge brain scans showing the effects of drugs on the human brain.

September 25, 2000 - **Teens, Women, and Whites More Vulnerable Than Others to Becoming Nicotine-Dependent.** An analysis of the data from the National Household Survey on Drug Abuse interviews with 22,292 smokers showed that adolescents, women, and whites are particularly vulnerable to developing nicotine-dependence symptoms, according to researchers who published their findings in the September 2000 issue of *Nicotine and Tobacco Research.* Coverage of this publication appeared in *Reuters Health, Join Together Online, EurekAlert!,* and *news.excite.com.*

October 24, 2000 - **Access to Substance Abuse Treatment for Medicaid Clients Improves with Oregon Model for Financing Treatment under Managed Care.** Researchers at the Oregon Health Sciences University found that implementation of a capitated substance abuse benefit appeared to increase access to related services for state Medicaid clients in Oregon. The single benefit broadened the array of covered substance abuse treatment services formerly offered Medicaid patients, and improved integration of health care services among providers. The study appeared in the October 25 issue of *Journal of the American Medical Association.*

October 25, 2000 - **NIDA Researchers Find That Animals Exposed to Marijuana's Active Component Will Self-Administer the Drug.** Scientists at NIDA have demonstrated that laboratory animals will self-administer marijuana's psychoactive component, THC (delta-9-tetrahydrocannabinol), in doses equivalent to those used by humans who smoke the drug. Self-administration of drugs by animals, long considered a model of human drug-seeking behavior, is characteristic of virtually all addictive and abused drugs. Coverage of this publication appeared in *The New York Times, MSNBC, LA Times, Associated Press, Seattle Post-Intelligencer, CNN, The Columbus Dispatch, Philadelphia Daily News, ABC News, Join Together Online, The San Francisco Examiner,* and *salon.com* and in various news media outside the United States.

October 30, 2000 - **National Meeting in Los Angeles to Focus Attention on Drug Addiction and Treatment.** This media advisory announced two NIDA-sponsored meetings from October 30-November 2, 2000, in Los Angeles, CA. The larger meeting, "Blending Clinical Practice and Research: Forging Partnerships to Enhance Drug Treatment," focused on catalyzing partnerships to facilitate moving drug addiction research into clinical practice. Prior to this meeting, NIDA convened its National Drug Abuse Treatment Clinical Trials Network investigators to discuss research and treatment advances that have evolved out of this program. As a result of these meetings, coverage appeared in *Yahoo! Finance.*

October 31, 2000 - **National Drug Abuse Treatment Clinical Trials Network Expands: Network now includes 11 research centers and nearly 70 treatment programs.** The National Drug Abuse Treatment Clinical Trials Network launched by NIDA with grants to six research facilities has been expanded to include an additional five regional research centers and a total of almost 70 community based treatment programs. The five newly funded centers each will receive a total of $11 million over five years. The total funding for all 11 components of the Clinical Trials Network is $121 million over five years. As a result of this press release, coverage appeared in *Alcoholism & Drug Abuse Weekly and Join Together Online.*

November 1, 2000 - **High Success Rates for Variety of Heroin Addiction Treatment Medications.** A recent

study has shown that levomethadyl acetate (LAAM), buprenorphine, and high doses of methadone (60-100 mg) were much more effective in treating heroin addiction than low-dose methadone maintenance (20 mg). LAAM and methadone are available for clinicians to prescribe. Buprenorphine is currently under review by the Food and Drug Administration and is used only in research studies. This study appeared in the November 2 issue of *New England Journal of Medicine.* Coverage of this publication appeared in *CNN, MSNBC, LA Times, USA Today, Join Together Online,* and *Fox News.*

November 3, 2000 - **Neuroscience at NIDA-A Series of Satellite Symposia-Will Highlight Current Neuroscience Research and Issues during Annual Society for Neuroscience Meeting.** NIDA sponsored a series of satellite symposia at Society of Neuroscience 2000, held throughout the society's annual meeting in New Orleans on November 4-9, 2000. The symposia highlight the latest in NIDA neuroscience research, NIDA research directions, and opportunities for minority research scholars at the agency. As a result of this meeting, coverage appeared in *Yahoo! Finance.*

November 7, 2000 - **Researchers Link Adolescent Cigarette Smoking with Anxiety Disorders during Early Adulthood.** Scientists supported by the National Institute of Mental Health and NIDA have documented that chronic cigarette smoking during adolescence may increase the likelihood that these teens will develop a variety of anxiety disorders in early adulthood. These disorders include generalized anxiety disorder, panic disorder, and agoraphobia (the fear of open spaces). The research appeared in the November 8 issue of *Journal of the American Medical Association.* As a result of this press release, coverage appeared in *The New York Times, The Washington Times, The Washington Post,* and *Fox News.*

November 15, 2000 - *Walking A Good Path 2001 Calendar: American Indian Organizations and NIDA Produce Free, Science-based Calendar on Drug Abuse and Addiction.* In an effort to raise awareness about the health risks of drug abuse and addiction, as well as prevention and treatment, American Indian experts and organizations nationwide collaborated with NIDA to create an intergenerational year 2001 calendar, "Walking A Good Path." As a result coverage appeared in *Yahoo! Finance.*

December 2000 - **NewsScan: NIDA Addiction Research News.** In this issue, research advances included the following: gender differences may affect substance abuse treatment retention (October 2000 issue of *Alcoholism: Clinical and Experimental Research*); craving for cocaine involves same brain sites as other cravings (November 2000 issue of *American Journal of Psychiatry*); and NIDA funds innovative research facility to enhance social workers' involvement in substance abuse treatment research. Coverage of these publications appeared in *Join Together Online* and *Yahoo! Finance.*

December 14, 2000 - 2000 **Monitoring the Future Survey Released: Moderating Trend Among Teen Drug Use Continues.** Overall use of illicit drugs among teenagers remained unchanged from last year, according to the 26th annual Monitoring the Future Survey released by the Department of Health and Human Services. The 2000 Monitoring the Future Survey, conducted by the University of Michigan's Institute for Social Research and funded by NIDA, surveyed over 45,000 students in 435 schools across the nation about lifetime use, past year use, past month use, daily use of drugs, alcohol, and cigarettes and smokeless tobacco. As a result of the survey, coverage appeared in *The New York Times, The Washington Times, USA Today, The Washington Post, The Deseret News (Salt Lake City, UT), The Record (Bergen County, NJ), The Palm Beach Post,* and *Associated Press.*

Opinion Pieces

August 14, 2000, *New York Magazine*-Letter to the Editor by Alan I. Leshner, Ph.D.-"The X-Files" (Responding to the article, "E-commerce," which chronicles the widespread use of the drug ecstasy)

August 29, 2000, *Newark Star-Ledger*-Article by Alan I. Leshner, Ph.D.-"Ecstasy Can Lead to Agony for Drug's Users"

September 2000, *New York State Bar Association Journal*-Article by Alan I. Leshner, Ph.D.-"Treatment Option for Drug Offenders is Consistent with Research Findings"

November 21, 2000, *New York Resident*-Article by Alan I. Leshner, Ph.D.-"Ecstasy: The Complete Story"

Articles of Interest

July 31, 2000, *HealthSCOUT*-Interview of Steven Gust, Ph.D.-"Joints for Your Joints"

August 2, 2000, *The Orlando Sentinel*-Interview of Alan I. Leshner, Ph.D.-"Ecstasy is Hardly a Pleasure"

August 7, 2000, *ABC News.com*-Interview of Alan I. Leshner, Ph.D.-"A Shot in the Arm: A Tobacco Vaccine in Rats Lowers Blood Levels of Nicotine"

August 8, 2000, *Reuters Health*-Interview of Alan I. Leshner, Ph.D.-"Anti-smokers Gird in Chicago for New Products, Ads"

August 13, 2000, *Newsday (New York, NY)*-Interview of Stephen Heishman, Ph.D.-"Drug Problem: When Pain-Killers Kill More Than Pain"

August 21, 2000, *The Washington Post*-Interview of Frank Vocci, Ph.D.-"A Not-Quite-Legal Lifeline"

August 22, 2000, *Newsday (New York, NY)*-Interview of Wallace Pickworth, Ph.D.-"In the War on Smoking, It's Best to Use All the Ammo"

August 24, 2000, *HealthSCOUT*-Interview of Alan I. Leshner, Ph.D.-"Drug Use a Family Affair"

August 24, 2000, *USA Today*-Interview of Barry Hoffer, M.D., Ph.D.-"Mixed Signals on Stroke Therapy"

August 26, 2000, *The Washington Post*-Interview of Alan I. Leshner, Ph.D.-"Maryland Mobilizes Against Use of Ecstasy"

August 28, 2000, *The Christian Science Monitor*-Interview of Alan I. Leshner, Ph.D.-"When Parents Are a Part of the Drug Problem"

August 28, 2000, *The Detroit News*-Interview of Alan I. Leshner, Ph.D.-"Club Drug Becomes Suburban Sensation"

August 29, 2000, *The Tennessean*-Interview of Frank Vocci, Ph.D.-"Controversial Cure"

September 2000, *Matrix: The Magazine for Leaders*-Interview of Alan I. Leshner, Ph.D.-"Club Drugs Go to College"

September 2000, *Science & Vie*-Interview of Alan I. Leshner, Ph.D.-"ActivitŽ CŽrŽbrale AltŽrŽe"

September 2000, *Monitor on Psychology*-Interview of Meyer Glantz, Ph.D.-"Earning Certification in Substance Abuse"

September 1, 2000, *Salon.com*-Interview of Timothy P. Condon, Ph.D.-"Chemical Ravings"

September 19, 2000, *CNN.com*-Interview with Jacques Normand, Ph.D.-"Quitting Cigarettes for Two"

September 25, 2000, *Alcoholism & Drug Abuse Weekly*-Interview of Alan I. Leshner, Ph.D.-"SAMHSA Bill Plays Politics with 10 to 12 Million Lives"

October 2000, *The Economics of Neuroscience*-Interview of Alan I. Leshner, Ph.D.-"The TEN Interview"

October 10, 2000, *Salon.com*-Interview of Alan I. Leshner, Ph.D.-"The Drug War's Tweedledee"

October 20, 2000, *Join Together Online*-Interview of Frank Vocci, Ph.D.-"Buprenorphine Legislation Hailed as Treatment Breakthrough"

October 30, 2000, *HealthSCOUT*-Interview of Stephen Heishman, Ph.D.-"Pot Use Up Sharply at Colleges"

November 13, 2000, *Time (Asian Edition)*-Interview of Alan I. Leshner, Ph.D.-"The Lure of Ecstasy"

November 18, 2000, *Associated Press*-Interview of Steven Gust, Ph.D.-"Is Marijuana Really Medicine? At Last It's Being Put to the Test"

November 30, 2000, *CBS 48 Hours*-Interview of Alan I. Leshner, Ph.D.-Show about ecstasy aired on CBS and MTV; Dr. Leshner also participated in a website chat following the airing

November/December 2000, *The Journal of Addiction and Mental Health*-Interview of Timothy P. Condon, Ph.D. and Beverly Jackson-"The Addict as TV Entertainment: Hollywood Recognizes Substance Abuse as Storytelling Gold Mine"

December 11, 2000, *Time*-Interview of Alan I. Leshner, Ph.D.-"Downey's Downfall"

December 11, 2000, *Alcohol & Drug Abuse Weekly*-Interview of Jack Stein, Ph.D.-"Federal Approval of Buprenorphine Expected Next Month"

December 13, 2000, *Today Show*-Interview of Alan I. Leshner, Ph.D.-Story about Robert Downey; Dr. Leshner

addressed topics of addiction and treatment

January 11, 2001, *CBS Health Watch*-Interview of Jerry Frankenheim, Ph.D.-" ÔParty Drug' Has Deadly Effects Even Without Alcohol"

NIDA Exhibits Program

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

September 9-10, 2000	Black Family Reunion
September 15, 2000	Hispanic Heritage Month Celebration
September 18, 2000	Yale CTN Meeting
September 20-22, 2000	Latino Behavioral Health Institute
October 4, 2000	Hispanic Heritage Month Celebration
October 12-15, 2000	Society for Advancement of Chicanos and Native Americans
October 21, 2000	An Exposition of Health Resources from NIH To Its Neighbors
October 22-25, 2000	National TASC: 7th Conference on Drugs and Crime
October 24-28, 2000	American Academy of Child and Adolescent Psychiatry
November 1-2, 2000	Blending Clinical Practice and Research
November 1-4, 2000	National Association of Social Workers
November 4-7, 2000	14th Annual Conference on Hispanic Association of Colleges and Universities
November 4-9, 2000	Society for Neuroscience Annual Conference
November 9-11, 2000	American Indian Science & Engineering Society
December 6-9, 2000	Community Anti-Drug Coalitions of America
December 7-10, 2000	American Academy of Addiction Psychiatry
January 11-13, 2001	National Association of Drug Court Professionals

Training and Other Activities

A two-day CTN training session was held for Motivational Enhancement Therapy and Motivational Interviewing in Albuquerque, NM on August 17-18, 2000. Representatives from all of the nodes participating in these protocols attended the meetings.

There was a two-day CTN training session for the Buprenorphine/Naloxone protocols on September 7-8, 2000, in Los Angeles, CA. Members from all of the participating sites attended the meetings.

A two-day CTN training session was held October 10-11, 2000, on the Motivational Incentives protocols. The meeting was held in Baltimore, MD, and included members from all sites across the CTN participating in the two protocols.

Two training sessions were held on the ASI-Lite, a common assessment battery instrument to be used throughout the CTN. The first meeting was held in Philadelphia on December 7-8, 2000, and the second meeting was held in Portland, OR on December 14-15, 2000. Attendees from all of the nodes came to these training sessions.

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Planned Meetings

NIDA will be sponsoring a **national prevention research conference** on August 9-10, 2001, in Washington, D.C. Top drug abuse prevention scientists will share research findings from the past five years with community leaders, educators, and other practitioners. Family, school, media, and multi-context prevention projects will be presented. Determining effective practices and interventions for particular communities will be a major focus. Emerging trends in drug abuse prevention will be highlighted.

NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA) is planning to hold a working meeting on May 3-4, 2001 in Rockville, MD on **"The Network Paradigm in Research on Drug Abuse, HIV, and Other Blood-Borne and Sexually Transmitted Infections: New Perspectives, Approaches, and Applications."** The purpose of the meeting is to bring together social networks researchers and experts in STDs, HIV/AIDS, and drug abuse to provide scientific presentations, exchange data and information, identify research gaps, and discuss future directions in research on STDs and HIV/AIDS in drug-using networks.

The **Fifth Annual PRISM Awards** will be held on April 4-5, 2001, in Los Angeles, CA. NIDA will sponsor the event with the Entertainment Industries Council and the Robert Wood Johnson Foundation. These awards are bestowed yearly to members of the entertainment community who have accurately depicted drug, alcohol and tobacco abuse, and addiction in their productions.

A NIDA **conference on MDMA research** is planned for July 19-20, 2001, in the Natcher Auditorium on the NIH campus. The symposium will focus on the scientific research on methylenedioxymethamphetamine (MDMA), including MDMA neuropharmacology, addiction liability, neuropathology and its long-term behavioral consequences, ontogenetic effects, other toxicology, drug interactions, patterns of abuse, perceptions of risk, prevention research, and the toxicology of amphetamines sometimes replacing MDMA (such as PMA and PMMA).

National CTN Steering Committee Meetings are planned for the follow dates and locations: April 2-4, 2001, in Bethesda, MD; July 16-18, 2001, in Denver, CO; and October 22-24, 2001, in Bethesda, MD.

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Publications

Bringing the Power of Science to Bear on Drug Abuse and Addiction: Five Year Strategic Plan 2000
NIH Pub. No. 00-4774

NIDA's strategic plan serves as a framework for the Institute's scientific future. The overarching goal of NIDA's strategic plan is to significantly reduce the behavior, health and social consequences of drug abuse and addiction. It provides the reader with a three-pronged approach as to how NIDA will fulfill its goal over the next five years: to provide communities science based tools to prevent drug abuse and addiction; to use scientific activities to improve the quality of drug abuse treatment nationwide; and to disseminate research discoveries to educate the public about the true nature of drug abuse and addiction.

NIDA's Clinical Toolbox: Science-Based Materials for Drug Abuse Treatment Providers
NCADI CLNBOX

The toolbox is a collection of materials based on NIDA-supported research, including the first three in a series of drug treatment therapy manuals and NIDA's recent publication, *Principles of Drug Addiction Treatment: A Research-Based Guide.* It also includes several of NIDA's recent Research Reports and other information products.

Indian Country Calendar
NIH Pub. No. 00-4673

The National Institute on Drug Abuse has collaborated with Native experts and organizations across the country to create an inspirational and education calendar, "Walking a Good Path," on drug abuse and addiction. Every month features a powerful image, an insightful quote, and useful information to help American Indian and Alaska Native parents and elders speak to children about the dangers of drug use.

NIDA NOTES

NIDA NOTES, Volume 15, Issue 4
NIH Pub. No. 00-4378
NCADI 0045

The lead story in this issue reports on NIDA research that has found that, in mice, methamphetamine causes more extensive brain damage than previously thought. NIDA's research to reverse the damaging effects of methamphetamine on the brain is also featured. In the Director's Column, Dr. Leshner talks about how NIDA's research seeks to discover how different drugs damage the brain and what can be done to treat this damage. Other articles discuss the gender differences in drug abuse risk and treatment, prevalence of drug abuse, and opportunities to use drugs. Other topics discussed in this issue include a report on how doses of anabolic steroids can cause adverse psychiatric symptoms in men; a report of a conference on the linked issues of drug abuse, HIV/AIDS, and hepatitis C; and the release of clinical guidelines for treating nicotine addiction.

NIDA NOTES, Volume 15, Issue 5

NIH Pub. No. 00-4378
NCADI NN0046

The lead story reports on NIDA research on a vaccine that prevents nicotine from reaching the brains of rats and that may offer hope for smokers trying to break their addiction. In the Director's Column, Dr. Leshner talks about scientific approaches to combat nicotine addiction. Other articles discuss prenatal exposure to cigarette smoke, which appears to increase risk of drug abuse on conduct disorder; a genetic variation that makes some individuals less liable to become addicted to nicotine; findings that nicotine craving increases craving for other drugs among drug abusers; and a new approach that relieves chronic pain without adverse effects. Other topics include a national media campaign to impress young people that drugs can permanently damage health and highlights of recent gains by NIDA-funded researchers in knowledge about nicotine and tobacco.

NIDA NOTES, Volume 15, Issue 6
NIH Pub. No. 01-4378
NCADI NN0047

The lead story in this issue reports on the first seven treatment protocols approved and put into placed by NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN). In the Director's Column, Dr. Leshner discusses the importance of blending drug abuse research and clinical practice to improve treatment and cites the accomplishments of the CTN in its first year of operation. Another story lists the five new research sites added to the CTN and another describes the Clinical Toolbox, which was mailed to more than 12,000 practitioners across the country. Other stories discuss rat brain changes due to cue-induced craving for opiates; NIDA staff and grantee participation in the 11th World Conference on Tobacco OR Health; NIDA's involvement in two conferences in South Africa on HIV/AIDS and drug abuse; and how the research of this year's Nobel Prize winners in Medicine provided the foundation for understanding how drugs affect the brain. Other stories report on the appointment of Dr. Glen Hanson as the Director of the Division of Neuroscience and Behavioral Research; abuse of opioids by steroid users; acupuncture as a treatment for cocaine abuse; and the latest Research Report on inhalant abuse.

Other Publications

Oyler, J.M., Cone, E.J., Joseph, R.E. Jr., and Huestis, M.A. Identification of Hydrocodone in Human Urine Following Controlled Codeine Administration, Journal of Analytical Toxicology; 24, pp. 530-535, 2000.

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

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

Ladenheim, B., Krasnova, I.N., Deng, X., Oyler, J.M., Polettini, A., Moran, T.H., Huestis, M.A. and Cadet, J.L. Methamphetamine-Induced Neurotoxicity Is Attenuated in Transgenic Mice with a Null Mutation for Interleukin-6. Mol Pharmacol 58(6), pp. 1247-1256, 2000.

Deng, X. and Cadet, J.L. Methamphetamine-induced Apoptosis is Attenuated in the Striata of Copper-Zinc Superoxide Dismutase Transgenic Mice. Mol Brain Res 83(1-2), pp. 121-124, 2000.

Sharpe, L.G., Pilotte, N.S., Shippenberg, T.S., Goodman, C.B. and London, E.D. Autoradiographic Evidence that Prolonged Withdrawal from Intermittent Cocaine Reduces Mu-Opioid Receptor Expression in the Limbic Regions of the Rat Brain. Synapse, 37, pp. 292-297, 2000.

Tudge, J.R.H., Hogan, D.M., Snezhkova, I.A., Kulakova, N.N., and Etz, K.E. Parents' Child-Rearing Values and Beliefs in the United States and Russia: The Impact of Culture and Social Class. Infant and Child Development, 9, pp. 105-121, 2000.

Drs. David Shurtleff, Herb Weingartner, Susan Volman and Karen Skinner coordinated NIDA's written contribution and support of a supplement to Nature Neuroscience entitled "Computational Approaches to Brain Function," which was published in November 2000. The supplement publication was also sponsored by, NIMH, NINDS, and NIAAA. The issue covers the history and current state of computational neuroscience, and each of the supporting NIH institutes describes their interests in computational neuroscience with NIDA describing its emerging interests in this area. Approximately 5,000 copies of the supplement were distributed at the November 2000 Society for Neuroscience

meeting in New Orleans, and additional copies will be mailed to Nature Neuroscience subscribers. The entire text of the supplement is available on-line at: http://www.nature.com/neuro/journal/v3/n11s/full/nn1100_1160.html

Jag H. Khalsa, Sander Genser, and Henry Francis of CAMCODA and Bernadette Marriott of the Office of Dietary Supplements (ODS), NIH, co-authored/co-edited a major publication entitled: Metabolic, Endocrine, and Gastrointestinal (MEG) Disorders in Drug Abuse and HIV/AIDS that appeared in the Journal of Acquired Immune Deficiency Syndromes (JAIDS), 25: supplement 1, October, 2000. The supplement consists of an introduction (Khalsa et al.) and 12 chapters contributed by nationally and internationally recognized experts in the field of HIV/AIDS and drug abuse who participated in a NIDA/ODS-supported workshop.

The second quarterly news update for the CTN was published in October. The quarterly newsletter was distributed to all CTN nodes and posted on the CTN web page.

A revised CTN web page was approved and posted to NIDA's Home Page in December. The new site includes information on the first 11 nodes, patient and clinician information, CTN newsletters, and copies of protocol brochures. Plans are underway to have a Spanish version of this website.

Eight new brochures were published this period. Six of the publications are patient brochures on the current CTN protocols. Two of the brochures are directed towards clinicians. Two of the above patient brochures have been translated into Spanish and have been approved for distribution. Three other Spanish translations are in the process of being approved. Plans have been made to translate the patient brochures into both Chinese and Russian to serve those patient populations.

A weekly CTN Bulletin Board was issued as a result of the CTN communication plan. It is a one-page highlight of CTN weekly activities issued every Tuesday.

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Staff Highlights

Honors and Awards

The following awards were presented at NIDA's 2000 Employee Appreciation Day event held on October 3, 2000:

NIDA Director's Awards

Division of Epidemiology, Services and Prevention Research (DESPR)
James Colliver, Ph.D.
Susan David, M.P.H.
Peter Delany, D.S.W.
Jerry Flanzer, D.S.W.

DESPR Group Award
Elizabeth Robertson, Ph.D.
Kathleen Etz, Ph.D.

Division of Neuroscience & Behavioral Research (DNBR)
Cora Lee Wetherington, Ph.D.

Division of Treatment Research & Development (DTR&D)
Jamie Biswas, Ph.D.
Jim Glass
Harold Gordon, Ph.D.
Joanne Grant
Richard Kline, Ph.D.

Intramural Research Program (IRP)
Jean Lud Cadet, M.D.
Theresa Doged
Morgan Dubrow
Lena Eads

Office of the Director (OD)
Pam Oliver

Office of Extramural Affairs (OEA)
William C. Grace, Ph.D.
Lana Le
Rita Liu, Ph.D.

Office of Planning and Resource Management (OPRM)
Nancy Hurd
Terry King Wheeler
Dinh Mai
Montrue Nelson

Jean Yee
Nikki Zangwill

Office of Science Policy and Communications (OSPC)
Jane Holland
Mary Mayhew
Joan Nolan

Behavioral Science Working Group Award
Lynda Erinoff, Ph.D., DESPR
Kathleen Etz, Ph.D., DESPR
Joseph Frascella, Ph.D., DTR&D
Teresa Levitin, Ph.D., OEA
Minda Lynch, Ph.D., DNBR
Lucinda Miner, Ph.D., OSPC
David Shurtleff, Ph.D., DNBR
Mark Swieter, Ph.D., OEA
Marina Volkov, Ph.D., OEA
Herbert Weingartner, Ph.D., DNBR
Cora Lee Wetherington, Ph.D., DNBR

NIDA EEO Award

Gary Fleming, M.A., J.D., OPRM
John Hamill, OPRM

Commissioned Corps Awards

Captain Robert Adams, (IRP) -- Commendation Medal
Lieutenant Commander Carlo Contoreggi, M.D., (IRP) -- Commendation Medal
Captain Kesinee (Kay) Nimit, M.D., (OEA) -- Commendation Medal

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Length of Service Awards

30 Years of Service
David Conrad, OPRM
Stephen Gane, OPRM
Terry King Wheeler, OPRM
Nancy Soulen, OSPC

40 Years of Service
Joseph Reckley, OPRM

Other Awards

Nancy Hurd of NIDA's Contracts Management Branch, OPRM, as an active member of the NIH team responsible for developing, improving, and maintaining the NIH Contractor Performance System (CPS), received the National Partnership for Reinventing Government's (NPR) Hammer Award on December 5, 2000.

Dr. Leslie Cooper, ERB, DESPR, received a US Public Health Service Commissioned Corps award, the Hildrus A. Poindexter Award for "her untiring leadership, demonstrated excellence, personal dedication, community involvement, and commitment to public health in improving the health of minority and underserved populations," which was presented November 2000.

Dr. Leslie Cooper, ERB, DESPR, received a US Public Health Service Commissioned Corps award in November, 2000, through the Minority Officers Liaison Advisory Committee (MOLC) to the US Surgeon General, as the Minority Officer of the Year. The award was given for "her leadership in representing minority officers; her undying mentoring activities for Commissioned Officers, Civil Servants, and the public; policy development; management; and career

development within the PHS."

Dr. Jean Lud Cadet, IRP, received the 2000 EEO Award in recognition of ongoing commitment and work in support of EEO and affirmative action within NIDA.

Staff Changes

Dr. Jessica Campbell joined CAMCODA's Human Development Program in August 2000. Prior to joining NIDA, Dr. Campbell completed a Postdoctoral Research Fellowship at the National Institute of Child Health and Human Development (NICHD), where she was involved with a longitudinal study of early child-care effects on children's social, emotional, and cognitive development. Dr. Campbell will be focusing on program development in the area of developmental consequences of drug abuse during middle childhood, preadolescence, and adolescence.

Mark Fleming joined OSPC in December 2000 as the webmaster in the Public Information and Liaison Branch. He received a Bachelor of Arts degree in zoology from Miami University in Ohio and a Master of Arts in visual communications from Ohio University. For the past 14 years, he has worked as a NIDA contractor in Baltimore. He established the Visual Media Unit to provide photographic and graphic arts support for NIDA research. In addition, he established the NIDA web site in 1995 and has worked since then to increase its scope and exposure.

Dr. Mark Green joined OEA in December 2000 as Chief of the Clinical, Epidemiological and Applied Sciences Review Branch. Dr. Green brings over 20 years of experience in extramural programs. Prior to joining NIDA he was Chief of the Extramural Project Review Branch at NIAAA, where he directed both grant and contract review committees which evaluated research in the areas of prevention, epidemiology, clinical trials, health services, neuroscience and physiology. Dr. Green has also managed reviews and Center site visits dealing with treatment trials and prevention intervention trials and worked extensively on the CSR integration of prevention and epidemiology sciences and the development of the new services research and other review committees at CSR. Dr. Green received a Ph.D. in pharmacology from New York Medical College.

Dr. Karin Johnson joined CAMCODA in August 2000 as a Society for Research in Child Development/American Association for the Advancement of Science Executive Branch Fellow. Her work at NIDA is focusing on pediatric neuroimaging, health consequences of adolescent substance use, and rural drug abuse/health issues. Dr. Johnson is a certified pediatric nurse practitioner and has a doctorate in Public Health. Most recently, Dr. Johnson was the Assistant to the President of Salisbury State University.

Dr. Suman A. Rao joined the Science Policy Branch in the Office of Science Policy and Communications in December 2000. She received her Ph.D. from the University of Oregon in Clinical Psychology and completed postdoctoral work at the Johns Hopkins University School of Medicine. Dr. Rao's research interests include prevention, law, psychopharmacology, multidisciplinary evaluation, and treatment issues.

Dr. Deborah M. Smith joined CAMCODA in December 2000 as a special expert. She is an obstetrician-gynecologist who received her medical degree from Howard University where she was appointed as an associate professor. Her MPH was obtained at UC Berkeley. Dr. Smith was previously in federal service as the first medical advisor in the Office of Women's Health at the Food and Drug Administration working on issues related to women in clinical trials and gender analysis.

Dr. Yonette Thomas joined the Epidemiologic Research Branch of DESPR as a Health Scientist Administrator in September 2000. Formerly Dr. Thomas was a senior program officer in the National Research Council's Commission on Behavioral and Social Science and Education and served as study director under the Division on Social and Economic Studies. Dr. Thomas will oversee the research program on the social epidemiology of drug abuse which will include issues such as the development of health beliefs and practices, the longitudinal impact of drug use among social and drug-specific cohorts, and the socialization of young people in drug abusing environments. She holds a Ph.D. in medical sociology and demography.

Song Hee (Dianne) Yoo joined DTR&D's Clinical/Medical Branch as an Office Automation Clerk on November 5, 2000.

Dr. Rita Liu was appointed Associate Director for Grants Activities, Office of Extramural Affairs, NIDA, in December 2000. In this role, she is responsible for managing NIDA's Receipt and Referral activities for grant applications, consulting with program divisions, and advising the Director, OEA, on application processing. Dr Liu also continues to serve as the SRA of the Centers Review Committee.

Dr. M. Patricia Needle, Director, NIDA International Program, OSPC, has been named Director, Executive

Secretariat for the 2002 World AIDS Congress to be held in Barcelona, Spain. She assumed that temporary position in January 2001. Dr. Steven W. Gust, Special Assistant to the Director, NIDA, has been named Acting Director for the NIDA International Program.

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

Grantee Honors

Dr. Nora D. Volkow, Associate Laboratory Director for Life Sciences at the U.S. Department of Energy's Brookhaven National Laboratory, has been elected as a member of the Institute of Medicine of the National Academy of Sciences. A board-certified psychiatrist and a world-leader in research on addiction, Dr. Volkow uses positron emission tomography (PET) to understand how addictive drugs affect the brain. She is credited with being one of the first researchers to show the timecourse and distribution of cocaine within the brain, as well as to report that cocaine is toxic to the human brain. She uses PET in pioneering studies of biochemical changes in the brain associated with addiction, and her studies are focused on finding an effective pharmacological treatment for addiction. Dr. Volkow was one of 70 members elected to the institute this* year and is the first member from Brookhaven Lab to be elected in the institute's 30-year history. Members are elected by the current membership on the basis of professional achievement and of demonstrated interest, concern and involvement with problems and critical issues that affect public health.

Dr. Ram Murty of Murty Pharmaceuticals, Inc., Lexington, Kentucky, received the prestigious TIBBETTS award, an initiative of the US Small Business Administration, on October 3, 2000. Dr. Murty is the Principal Investigator of a SBIR Phase II contract and has developed an innovative methodology utilizing supercritical fluid extraction techniques to produce denicotinized tobacco and manufactured standardized placebo and nicotine cigarettes of varying strengths and natural flavors which are used for research in drug abuse and addiction, cancer and related disciplines.

Dr. Peter W. Schiller was awarded the American Association of Pharmaceutical Scientific (AAPS) Research Achievement Award in Medicinal and Natural Products Chemistry. Dr. Schiller is director of the Laboratory of Chemical Biology and Peptide Research at the Clinical Research Institute of Montreal and a professor of pharmacology at the University of Montreal. He received his Ph.D. in chemistry and molecular pharmacology from the Swiss Federal Institute of Technology (ETH) in Zurich, Switzerland. Dr. Schiller is an internationally recognized leader in the field of the medicinal chemistry and molecular pharmacology of peptide hormones and neurotransmitters. He developed novel concepts that provided new insights into peptide-receptor interactions and fundamental aspects of peptide-based drug development.

Dr. Frank Ivy Carroll was elected fellow of the American Association of Pharmaceutical Scientists (AAPS). Dr. Ivy Carroll is Vice President of the Chemistry and Life Sciences Unit and Director of Organic and Medicinal Chemistry at the Research Triangle Institute. Dr. Carroll has varied research interests. Since 1990 the major thrust of his research has been in the synthesis and study of the 3-phenyltropane class of compounds. The compounds developed have had a tremendous impact as tools to assist in establishing the biochemical mechanism of cocaine's pharmacological properties.

Dr. George De Leon, Director of the Center for Therapeutic Community Research at NDRI, was awarded the Governor's Award for Lifetime Service in the field of alcohol and drug abuse in November 2000.

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