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

September, 2001

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

Basic Research

T-Channels on Pain Transmission Fibers Might be Novel Targets for Analgesic Agents

Although T-type calcium channels were first described in sensory neurons, their function in sensory processing has not been clearly established. The authors show that activation of these T-type calcium channels on sensory fibers induces an increased sensitivity to pain. They show that this increased sensitivity to pain is blocked by reducing the activity of these channels with 5,5'-dithio-bis-[2-nitrobenzoic acid] (DTNB). Further, DTNB by itself was able to produce analgesia to both thermal and mechanical (e.g. pinch) stimuli. These data strongly suggest that these channels are critical in the transmission of pain signals to the brain. Modulation of the activity of these channels might provide a novel method of producing analgesia, with broad clinical applications. Todorovic, S.M., Jevtovi-Todorvic, V., Meyenburg, A., Mennerick, S., Perez-Reyes, E., Ramano, C., Olney, J.W., and Zorumski, C.F. Neuron, 31, pp. 75-85, 2001.

Cocaine and Vascular Damage

Cocaine use is associated with a variety of vascular complications, including different forms of vasculitis. In a recent paper published in Life Sciences, Dr. Sulie Chang and her associates examined the actions of cocaine on the microcirculation. They observed that chronic exposure to cocaine resulted in an alteration in the hemodynamics and leukocyte-endothelial interaction in the venules of rats. They postulated that this may occur via modulation of the expression of intercellular adhesion molecule-1 mRNA. Increases in the number of total circulating white blood cells (WBCs) and WBC rolling flux changes in blood cell velocity, and an increase in inflammation-induced leukocyte-endothelial cell adhesion were also seen in animals given cocaine on a chronic basis. Thus, the hemodynamic changes elicited by cocaine may produce a decrease in the effective vessel diameter and an increase in the intravascular resistance. These effects may underlie the progressive vascular damage seen in chronic cocaine-abusing individuals. Chang, S.L., Bersig, J., Felix, B., Fiala, M., and House, S.D., Chronic Cocaine Alters Hemodynamics and Leukocyte-Endothelial Interactions in Rat Mesenteric Venules. Life Sciences, 66(24), pp. 2357-2369, 2000.

Evidence Accumulates Showing that the Mu-Opioid Receptor Plays a More Important Role in Analgesia than the Delta-Opioid Receptor

There is evidence that mu-selective opioid agonists produce less respiratory depression than delta-selective agonists. It is proposed that highly selective mu-opioid agonists may have an advantage over existing opiate analgesics such as morphine. The recent development of mu-selective opioid agonists is based on modifications of the dermorphin sequence. Degradation of dermorphin by tissue peptidases resulted in the N-terminal tetrapeptide H-Tyr-D-Ala-Phe-Gly-OH, which has a mu-selectivity similar to the parent peptide. Amino acid substitutions of this tetrapeptide led to the development of the two most selective mu-opioid agonists, DALDA and {Dmt}-DALDA. Both tetrapeptides display high binding affinity and extraordinary selectivity for the mu-opioid receptor. When administered intrathecally to rats, DALDA and Dmt-DALDA were found in the rat tail-flick test to have an analgesic potency of 14- and 3000-times respectively as compared to morphine. In addition, the duration of analgesia was significantly longer after DALDA and Dmt-DALDA administration when compared at equieffective doses. However, a potential problem with peptide analogs as therapeutic agents is their susceptibility to enzymatic degradation *in vivo* and short elimination half-lives. In this study, the investigators compared in sheep the stability of DAMGO, DALDA and Dmt-DALDA after systematic

administration. Peptide concentrations were measured using high performance liquid-chromatography-mass spectrometry. When incubated in sheep blood at 37 degrees centigrade, all three peptides were stable over a 2-hour period. When given intravenously to sheep, the apparent volume of distribution was 80ml/kg for all three peptides, suggesting that the distribution was limited to blood volume. Plasma clearance of DAMGO was 10-fold faster than DALDA and Dmt-DALDA and their elimination half-lives were 0.24, 1.5 and 1.8 h for DAMGO, DALDA and Dmt-DALDA respectively. The half-lives of DALDA and Dmt-DALDA in sheep are even longer than morphine and meperidine. These favorable pharmcokinetic properties, together with their mu-selectivity, potency, and long duration of action, make them ideal candidates as opioid analgesics. Szeto, H.H., Lovelace, J.L., Fridland, G., Soong, Y., Fasolo, J., Wu, D., Desiderio, D.M. and Schiller, P.W. *in vivo* Pharmacokinetics of Selective mu-Opioid Peptide Agonists. J PET, 298(1), pp. 57-61, 2001.

Structure Activity Relationships at Monoamine Transporters and Muscarinic Receptors for N-Subsituted-3-Alpha-(3'-Chloro-, 4'-Chloro-, and 4', 4"-Dichloro-Substituted-Diphenyl) Methoxytropanes

The design, synthesis, and evaluation of 3 alpha-(diphenylmethoxy) tropane (benztropine) analogs have provided potent and selective probes for the dopamine transporter. Structure activity relationships (SARs) have been developed that contrast with those described for cocaine, despite significant structural similarity. Furthermore, behavioral evaluation of many of the benztropine analogs in animal models of cocaine abuse has suggested that these two classes of tropane-based dopamine uptake inhibitors have distinct pharmacological profiles. The benztropine analogs: in mice do not demonstrate efficacious locomotor stimulation; do not fully substitute for a cocaine discriminative stimulus; and in rhesus monkeys are not appreciably self-administered. These compounds are generally more potent than cocaine as dopamine uptake inhibitors *in vitro*, although their actions *in vivo* are not consistent with this action. These observations suggest that differing binding profiles at the serotonin and norepinephrine transporters as well as muscarinic receptors may have a significant impact on the pharmacological actions of these compounds. In addition, by varying the structures of the parent compounds and thereby modifying their physical properties, pharmacokinetics as well as pharmacodynamics will be directly affected. Therefore, in an attempt to systematically evaluate the impact of chemical modification on these actions, a series of N-substituted analogs of 3'-chloro-, 4'-chloro-, and 4',4"-dichloro-3-alpha-(diphenylmethoxy) tropanes were synthesized. These compounds were evaluated in rat tissue for displacement of [H-3]WIN 35,428 from the dopamine transporter, [H-3]citalopram from the serotonin transporter, [H-3]nisoxetine from the norepinephrine transporter, and [H-3]-pirenzepine from muscarininc mu receptors. SARs were developed and compared to a series of N-substituted-3 alpha-(bis-4'-flurophenyl)methoxytropanes. These present SARs followed previously reported studies with the single exception of the N-butylphenyl substituent, which did not provide high affinity binding in any if these three sets of analogs, as it did in the 4',4"-difluroseries. X-ray crystallographic analyses of these parent ligands were compared to analyses of 3 alpha-(bis-4'-flurophenyl) methoxytropane. The results provided supportive evidence that the N-substituent, in this class of compounds, is not optimal for binding at the dopamine transporter. These studies provide binding profile data that can now be used to correlate with future behavioral analyses of these compounds and may provide insight into the kind of binding profile that might be targeted as a potential treatment for cocaine abuse. Newman, A.H., Robarge, M.J., Howard, I.M., Wjttkopp, S.L., George, C., Kopajtic, T., Izenwasser, S, and Katz, J.L.. J. Med. Chem. 44 (4), pp. 633-640, 2001.

Prenatal Exposure to Methamphetamine Increases the Male Offspring's Vulnerability, When Adults, to Methamphetamine's Neurotoxicity, in Mice

The use of club drugs, such as methamphetamine, by women of childbearing age has become a public health concern. Dr. Alfred Heller and his colleagues at the University of Chicago and Illinois Institute of Technology, modeled this situation in mice. They administered a neurotoxic dose of methamphetamine to pregnant mice during gestational days 7 to 18. Fetal exposure alone did not produce neurotoxicity. The researchers also gave methamphetamine to the offspring after they had become young adults (11 weeks of age), at minimally neurotoxic doses. They observed an enhanced neurotoxicity in the male offspring when they were injected with methamphetamine as adults. The neurotoxicity was evidenced by greater methamphetamine-induced lasting reductions of dopamine and its metabolites in the striatum and of dopamine in the ventral brainstem. Some effects of prenatal methamphetamine exposure were observed in female offspring, but these were much less than those seen in males. The ability of methamphetamine to induce neurotoxicity is associated, in part, with its ability to raise body temperature (hyperthermia). These doses of methamphetamine did not raise the body temperature of the adult female offspring, while the methamphetamine injections did raise the body temperature of the adult males. However, the hyperthermic response to methamphetamine was the same in the adult males whether or not they had been exposed to methamphetamine in utero. These findings raise the concern that male methamphetamine abusers may have an enhanced risk for the neurotoxic effects of the drug if they were previously exposed to it in utero. Furthermore, the

mother's methamphetamine abuse may predispose her male offspring to other neuropathological disorders, such as Parkinson's disease. Heller, A., Bubula, N., Lew, R., Heller, B., and Won, L. Gender-Dependent Enhanced Adult Neurotoxic Response to Methamphetamine Following Fetal Exposure to the Drug. J. Pharmacol. Exp. Ther., 298 (2), pp. 1-11, 2001.

Activation of Nicotine Receptors May Contribute to Cocaine Reinforcement

Dr. Marina Picciotto and her colleagues at Yale University examined the possible role of nicotinic cholinergic receptors (nAChR) in cocaine place preference, a measure of reinforcement, in mice. Nicotine and the psychomotor stimulants are thought to exert their reinforcing properties via an action on the mesolimbic dopamine system. When animals were given both a low dose of cocaine and the nicotinic antagonist mecamylamine, place preference was disrupted. In mice lacking the high affinity nAChR containing the β2 subunit, the researchers also found a diminished place preference to cocaine. By contrast, when a low dose of nicotine was administered, place preference was potentiated to a previously subthreshold dose of cocaine. Measures of dopamine levels and metabolism were decreased in normal mice following cocaine treatment, but mice lacking the β2 subunit showed no such effect. Zachariou, V., Caldarone, B.J., Weathers-Lowin, A., George, T.P., Elsworth, J.D., Roth, R.H., Changeux, J.P., and Picciotto, M.R. Nicotine Receptor Inactivation Decreases Sensitivity to Cocaine. Neuropsychopharmacology, 24(5), pp. 576-89, 2001.

Transport of Opioids from the Brain to the Periphery by P-Glycoprotein: Peripheral Actions of Central Drugs

Many peptides and transmitters found within the brain also have peripheral sites of action. Dr. Pasternak and his research team now demonstrate that the brain releases functionally active neurotransmitters/neuromodulators directly into the blood through a saturable P-glycoprotein (Pgp) transport system. Downregulating Pgp1 expression with antisense reduced the brain-to-blood transport of morphine, β-endorphin and other opioids. Lowering Pgp expression significantly enhanced systemic morphine analgesia and prevented tolerance, but diminished the analgesic activity of centrally administered morphine. This implies that supraspinal analgesia resulted from a combination of central and peripheral mechanisms activated by morphine transported from the brain to the blood. Similarly, mice with a disruption of the multiple drug resistance (Mdr1a) gene were more sensitive to systemic morphine and less sensitive to morphine given centrally. This ability of the Pgp transport system to pump functionally active compounds from the brain to the periphery defines a potentially important mechanism for modulating peripheral systems via the central nervous system. King, M., Su, W., Chang, A., Zukerman, A. and Pasternak, G.W. Nature Neuroscience, 4(3), pp. 268-274, 2001.

Chronic Morphine Induces Concomitant Phosphorylation and Altered Association of Multiple Signaling Proteins: A Novel Mechanism for Modulating Cell Signaling

Traditional mechanisms thought to underlie opioid tolerance include receptor phosphorylation/down-regulation, G-protein uncoupling, and adenylyl cyclase superactivation. A parallel line of investigation indicates that opioid tolerance development results from a switch from predominantly opioid receptor G(i alpha) inhibitory to G(beta gamma) stimulatory signaling. This results, in part, from the increased relative abundance of G(beta gamma)-stimulated adenylyl cyclase isoforms as well as from a profound increase in their phosphorylation. Dr. Gintzler and his group have demonstrated that chronic morphine administration results in the concomitant phosphorylation of three key signaling proteins: G protein receptor kinase (GRK) 2/3; beta-arrestin; and G(beta). These results were obtained using guinea pig longitudinal muscle myenteric plexus tissue. Augmented phosphorylation of all three proteins is evident in immunoprecipitate obtained by using either anti-GRK2/3 or G(beta) antibodies. However, the phosphorylation increment is greater in immunoprecipitate obtained with G(beta) antibodies. Analyses of co-immunoprecipitated proteins indicate that phosphorylation of GRK2/3, beta-arrestin, and G(beta) has varying consequences on their ability to associate. As a result, increased availability of and signaling via G(beta gamma) could occur without compromising the membrane content, and presumably the activity, of GRK2/3. Induction of the concomitant phosphorylation of multiple proteins in a multimolecular complex with attendant modulation of their association represents a novel mechanism for increasing G(beta gamma) signaling and opioid tolerance formation. Chakrabarti, S., Oppermann, M., and Gintzler, A.R. Proc. Natl. Acad. Sci. USA, 98(7), pp. 4209-4214, 2001.

Ascorbic Acid Prevents 3,4-Methylenedioxymethamphetamine (MDMA)-Induced Hydroxyl Radical Formation and the Behavioral and Neurochemical Consequences of the Depletion of Brain 5-HT

MDMA-induced 5-HT neurotoxicity has been proposed to involve oxidative stress due to increased formation of hydroxyl radicals. Recently, MDMA-induced 5-HT neurotoxicity was shown to be accompanied by a suppression of

behavioral and neurochemical responses to a subsequent injection of MDMA. In the present study, Dr. G.A. Gudelsky and his colleagues examined whether suppression of the MDMA-induced formation of hydroxyl radicals by the antioxidant ascorbic acid, attenuates both the MDMA-induced depletion of 5-HT and the functional consequences associated with this depletion. They found that treatment of rats with ascorbic acid suppressed the generation of hydroxyl radicals, as evidenced by the production of 2,3-dihydroxybenzoic acid from salicylic acid, in the striatum during the administration of a neurotoxic regimen of MDMA. Ascorbic acid also attenuated the MDMA-induced depletion of striatal 5-HT content. In rats treated with a neurotoxic regimen of MDMA, the ability of a subsequent injection of MDMA to increase the extracellular concentration of 5-HT in the striatum, elicit the 5-HT behavioral syndrome, and produce hyperthermia was markedly reduced compared to the responses in control rats. The concomitant administration of ascorbic acid with the neurotoxic regimen of MDMA also prevented the diminished neurochemical and behavioral responses to a subsequent injection of MDMA. Finally, a neurotoxic regimen of MDMA produced significant reductions in the concentrations of vitamin E and ascorbic acid in the striatum and hippocampus. Thus, the MDMA-induced depletion of brain 5-HT and the functional consequences thereof appear to involve the induction of oxidative stress resulting from an increased generation of free radicals and a diminished antioxidant capacity in the brain. Shankaran, M., Yamamoto, B.K., and Gudelsky, G.A. Synapse, 40(1), pp. 55-64, 2001.

Modulation of Immune Function by Opioid Systems

Three types of opioid receptors have been characterized, primarily in neural cells. Both the kappa and delta receptors have been studied and are well characterized as reported in the following papers. Most previous studies have utilized macrophages, microglia or complex culture systems to study these effects. Papers reported herein now demonstrate that T-cells alone can modify HIV infection. The first describes more relevant functionality of the delta system in human immune T cells. The paper describes the ability of the delta opioid system to inhibit growth of HIV in thymocyte derived lymphocytes in culture. This study and others demonstrate a clear role for these systems in immune modulation. The delta opioid receptors (DORs) modulate T cell proliferation, IL-2 production, chemotaxis, and intracellular signaling. Moreover, in DOR-transfected Jurkat cells, delta opioids have been shown to suppress HIV-1 p24 antigen (Ag) expression. These observations led investigators to characterize the expression of DORs by human peripheral blood T cells and to determine whether a specific DOR agonist, SNC-80, can suppress p24 Ag expression by HIV-1-infected CD4+ T cells obtained from normal donors. By immunofluorescence flow cytometry, PHA stimulated the expression of DOR in the peripheral blood mononuclear cells (PBMC) population by 48. DOR expression was approximately 40% of both the PHA-stimulated CD4+ and CD8+ T cell subsets, and virtually all DORs were found on these subsets. To determine whether activated DORs suppress HIV-1 expression, PBMC were prestimulated with PHA, and then CD4+ T cells were purified, pretreated with SNC-80, and infected with HIV-1. In a concentration-dependent manner, SNC-80 inhibited production of p24 Ag. SNC-80 10(-10) M maximally suppressed both lymphocytotropic (HIV-1) and monocytotropic (SF162) strains; higher concentrations were less effective. Naltrindole, a selective DOR antagonist, abolished the inhibitory effects of SNC-80. Kinetic studies indicated that 24-h pre- or postincubation with SNC-80, relative to infection with HIV-1, eliminated its suppressive effects. Thus, stimulating the DORs expressed by activated CD4+ T cells significantly suppressed the expression of HIV-1. These findings suggest that opioid immunomodulation directed at host T cells may be adjunctive to standard antiviral approaches to HIV-1 infection. Sharp, B.M., McAllen, K., Gekker, G., Shahabi, N.A., and Peterson, P.K. Immunofluorescence Detection of Delta Opioid Receptors (DOR) on Human Peripheral Blood CD4+ T Cells and DOR-dependent Suppression of HIV-1 Expression. J Immunol, 167(2), pp. 1097-1102, July 15, 2001.

In the second paper, the kappa opioid system is shown to inhibit the growth of HIV in the same human T cell culture system. Thus, both opioid systems may be utilized clinically to combat HIV and other diseases. Further studies are needed to clarify this potential role. Synthetic K-opioid receptor (KOR) agonists have been shown to suppress HIV-1 expression in acutely infected macrophages. In the present study, investigators examined the effects of the KOR ligand (U50,488) on HIV-1 expression in CD4(+) lymphocytes, the main target cell of this virus. When U50,488 was added to activated CD4(+) lymphocytes, HIV-1 expression was inhibited in a concentration- and time-dependent manner with maximal suppression (60%) at 10(-7) M U50,488. The KOR selective antagonist nor-binaltorphimine (nor-BNI) had no effect by itself on viral expression but blocked the antiviral property of U50,488, suggesting that U50,488 was acting via a KOR-related mechanism. Support for the involvement of KOR was provided by the findings that 34% of activated CD4(+) lymphocytes were positive for KOR, using an immunofluorescence technique, and that seven additional synthetic KOR ligands also inhibited HIV-1 expression. The results of this study broaden our understanding of the antiviral properties of KOR ligands to include cells outside of the nervous system and suggest a potential role for these agents in the treatment of HIV-I infection. Peterson, P.K., Gekker, G., Lokensgard, J.R., Bidlack, J.M., Chang, A.C., Fang, X.G., and Portoghese, P.S. Kappa-opioid Receptor Agonist Suppression of HIV-1 Expression in CD4(+) Lymphocytes. Biochem Pharmacology, 61, pp. 1145-1151, 2001.

The third paper describes the role of the mu opioid system. It has not yet been demonstrated to directly inhibit HIV replication. However, it has been demonstrated to inhibit chemokine function, a key system involved in HIV entry into

the cell. The mu opioid system seems to be a major system involved in chemotaxis inhibition. This paper reports a strong action by maturing T-cells. The maturation period of T-cells may be the time when most opioid systems maximally affect immune function. Authors have examined the chemotactic responsiveness of thymocytes to selective mu-, kappa-, and delta -opioid agonists. Results show that developing T cells migrate in response to mu- but not kappa- or delta -opioids. The mu -opioid response appears to be dependent on the classical mu -opioid receptor (MOR-1) since the chemotactic response is blocked by a selective mu-opioid antagonist, and is absent in thymocytes from MOR-l-deficient mice. Flow cytometric analysis of the mu-opioid responsive cells shows that these cells consist predominantly of highly immature CD4(-)CD8(-) T cells. These results represent the first demonstration of the functional expression of mu-opioid receptors by developing T cells. McCarthy, L., Szabo, I., Nitsche, J.F., Pintar, J.E., and Rogers, T.J. Expression of Functional Mu-opioid Receptors during T Cell Development. J Neuroimmunology, 114, pp. 173-180, 2001.

Modulation of Immune Function by Cannabinoid Systems

A more basic understanding of drug actions comes from studies of second messenger systems coupled to the cannabinoid receptors; which may mediate their action. A recent paper demonstrates some involvement of the camp signalling system but these receptors are also linked with map kinases involved in Ca transport in modulating IL-2 activity. Thus, these studies show another receptor-coupled system present in immune cells to elicit their action. Cannabinoid compounds inhibit the cAMP signalling cascade in leukocytes. One of these compounds, cannabinol (CBN has been shown to inhibit interleukin-2 (IL-2) expression and the activation of cAMP response element binding protein (CREB) and nuclear factor for an immunoglobulin chain in B cells (NF-kappaB) following phorbol-12-myristate-13 acetate (PMA) plus ionomycin (Io) treatment of thymocytes. Therefore, the objective of the present studies was to determine the role of cAMP and protein kinase A (PKA) in the CBN-mediated inhibition of IL-2, CREB, and NF-kappaB in PMA/Io-activated thymocytes. The inhibition of CREB/ATF-1 phosphorylation, or cAMP response element (CRE) or KB DNA binding activity produced by CBN in PMA/Io-activated thymocytes, could not be reversed by DBcAMP (brominated camp) costimulation. Furthermore, DBcAMP failed to reverse the concentration-dependent inhibition of IL-2 protein secretion by CBN. Pretreatment of thymocytes with compound H89 produced a modest inhibition of PMA/Io-induced CREB/ATF-1 phosphorylation and CRE DNA binding activity but H89 had no effect on protein binding to a kappaB motif. Additionally, H89 modestly inhibited PMA/Io-induced IL-2 secretion. In light of the modest involvement of the cAMP pathway in CBN-mediated inhibition of CREB and IL-2 in PMA/Io-activated thymocytes, PD098059 (PD), the MEK inhibitor, was utilized to determine the role of ERK MAP kinases in thymocytes. ERKs play a critical role in IL-2 production but not for CREB phosphorylation. Collectively these findings suggest that CBN may modulate several signalling pathways in activated T cells. Herring, A.C., Kaplan, B.L.F., and Kaminski, N.E. Modulation of CREB and NF-kappa B Signal Transduction by Cannabinol in Activated Thymocytes. J Cellular Signalling, 13, pp. 241-250, 2001.

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Research Findings

Behavioral Research

Augmented Levels of Serotonin (5-HT) in the Nucleus Accumbens Decrease Preferences for Cocaine- or Morphine-Associated Environments in Withdrawn Rats

Central serotonergic neurotransmission is known to be increased in nucleus accumbens and other forebrain regions by morphine and cocaine administration. Conversely, it is also known to be depressed during withdrawal from chronic treatment with these drugs. In two recently published studies, Drs. Glenda Harris and Gary Aston-Jones investigated the consequences of experimentally increasing 5-HT transmission by injecting sertaline, (a selective 5-HT reuptake inhibitor), or the 5-HT precursor 5-HTP, directly into the nucleus accumbens. When 5-HT was augmented during acute morphine or cocaine administration, animals showed an increased preference for environments in which they received one of these drugs. This suggested that enhanced serotonergic activity may be important for the learned associations between primary drug reward and exteroceptive stimuli. Dependent animals continue to show a preference for environments previously paired with drug even during a withdrawal period. These investigators found that increasing 5-HT in the nucleus accumbens during withdrawal strongly attenuated the animal's usual preferences for a drug-associated environment. The 5-HT increase also reduced abstinence-induced anxiety as measured by a defensive burying behavior in which rats use their bedding to bury a probe that delivers a mild shock. These findings suggest that increases in accumbal 5-HT levels may reduce cravings elicited by incentive-motivational stimuli in drug-paired environments. Alternatively, increased 5-HT during the withdrawal state may facilitate extinction - that is, the active process whereby animals learn that these environments are no longer associated with positive drug reward. These studies suggest that drugs that augment 5-HT levels may be useful in reducing the desire for morphine or cocaine during withdrawal, and also for ameliorating subjective withdrawal symptoms (e.g., anxiety) that linger long after somatic withdrawal symptoms have dissipated. Harris, G.C, and Aston-Jones, G. Augmented Accumbal Serotonin Levels Decrease the Preference for a Morphine Associated Environment During Withdrawal. Neuropsycho-pharmacology, 24, pp. 75-85, 2001; Harris, G.C., Altomare, K. and Aston-Jones, G. Preference for a Cocaine-Associated Environment is Attenuated by Augmented Accumbal Serotonin in Cocaine Withdrawn Rats. Psychopharmacology, 156(1), pp. 14-22, published online May 9, 2001.

Environmental Enrichment Affects i.v. Self-Administration of d-Amphetamine in an Animal Model

Dr. Mike Bardo at the University of Kentucky is investigating the effects in rats of both environmental enrichment and social enrichment on the reinforcing properties of psychostimulant drugs. In this study, environmental enrichment, EC, is operationally defined as rats in group housing with daily handling and frequently changed novel objects. Social enrichment, SC, is operationally defined as rats in group housing only. He reports EC and SC rats self-administer less d-amphetamine than animals reared in isolated environments (IC=singly housed, with no handling), but only when offered low doses of the drug (0.03 mg/kg/infusion). In fact, when the higher dose of 0.1 mg/kg per infusion was made available, the researchers found no group differences. In addition, using a progressive ratio schedule, the investigators found that EC rats were less willing to 'work' for the drug, (i.e., make responses on an operant lever), than their IC counterparts. The observation that environmental enrichment seems to act as a protective factor for acquiring self-administration of d-amphetamine is interesting in light of previous observations that psychostimulant-induced sensitization is attenuated in EC animals. Collectively, these findings suggest that, under some conditions, environmental enrichment can reduce the motivation to respond for a psychostimulant reinforcer and furthermore

may alter the neural substrate for chronic neuroadaptive processes that underlie sensitization. Thus, environmental enrichment may serve as a protective factor for reducing amphetamine self-administration, and may possibly attenuate the rewarding effects of the drug. Bardo, M.T., Klebaur, J.E., Valone, J.M. and Deaton, C. Psychopharmacology, 155, pp. 278-284, 2001.

Behavioral Requirements Following Drug Ingestion Determine the Reinforcing Effects of Cocaine

Animal and human studies have been unable to completely explain drug reinforcement via the inherent pharmacological properties of the drug or via characteristics of the user. That is, whether or not a drug functions as a reinforcer can be determined by environmental factors such as previous experience with the drug, type of drug, drug dose and response requirements for obtaining the drug. Dr. Roland Griffiths and his collaborators sought to determine whether the reinforcing effects of oral cocaine could be influenced by the behavioral requirements following drug ingestion. Nine adult volunteers with histories of cocaine abuse were trained to discriminate under double-blind conditions between orally administered cocaine (100 mg/70 kg) and placebo capsules. Following the acquisition of discrimination, volunteers could choose to receive either cocaine or placebo prior to performing one of two behavioral activities - a vigilance activity or a relaxation activity. The investigators found that volunteers consistently chose cocaine over placebo with the vigilance activity, and placebo over cocaine with the relaxation condition. Thus, cocaine functioned as a positive reinforcer in the vigilance context, but as a negative reinforcer (i.e., cocaine was avoided) in the relaxation context. These results demonstrate that the behavioral requirements following drug ingestion can be a determinant of whether or not oral cocaine functions as a reinforcer in volunteers with histories of drug abuse and illustrate the malleability of human drug self-administration. These results are also consistent with anecdotal reports that people use stimulant drugs to meet physically or mentally challenging behavioral requirements. Jones, H.E., Garrett, B.E. and Griffiths, R.R. Reinforcing Effects of Oral Cocaine: Contextual Determinants. Psychopharmacology, 154, pp. 143-152, 2001.

Chronic Morphine Enhances the Suppressive Effects of Cocaine on Saccharin Intake

Pairings of a toxic substance (such as LiCl) with a (generally preferred) gustatory cue like saccharin, produce a subsequent aversion to the taste of this flavor. Likewise, when a psychoactive drug such as cocaine, morphine or amphetamine is paired with saccharin, saccharin is subsequently avoided. This phenomenon is known as conditioned taste aversion (CTA). Dr. Patricia Sue Grigson hypothesizes that CTAs that develop to drugs of abuse can be explained by "anticipatory contrast" - thus, avoidance of the flavor results because the soon-to-be-experienced positive drug effects outweigh the appetitive motivation to drink the palatable solution. In other words, the palatable solution becomes devalued by comparison with the rewarding properties of the drug. Dr. Grigson recently reported that a history of morphine treatment augments the CTA that develops via pairing with the drug cocaine, but not with the toxin LiCl, in Sprague-Dawley rats. In particular, she found that 75 mg of subcutaneous morphine per day for 5 days enhanced the saccharin suppressing effects of cocaine, but not of LiCl. These data support the anticipatory contrast hypothesis in that rats appear to avoid tastes conditioned to drugs of abuse because they are anticipating the rewarding properties of the drug, not because of the aversive properties of the drugs (as is the case with toxins such as LiCl). Moreover, these are the first data to show that chronic drug treatment can cross-sensitize CTAs that develop to drugs of abuse, resembling cross-sensitization seen with other behaviors (e.g., psychostimulant-induced hyperlocomotion) after repeated drug administration. Grigson, P.S., Wheeler, R.A., Wheeler, D.S., and Ballard, S.M. Chronic Morphine Treatment Exaggerates the Suppressive Effects of Sucrose and Cocaine, but Not Lithium Chloride, on Saccharin Intake in Sprague-Dawley Rats. Behavioral Neuroscience, 115, pp. 403-416, 2001.

A Single Cocaine Injection Induces LTP-Like Synaptic Changes in Dopamine Neurons of the VTA

Previous studies have implicated increased excitatory input to the midbrain dopamine neurons as a mechanism involved in behavioral sensitization, which is thought to be important for the development of addiction to drugs of abuse. This recent study from the laboratories of Dr. Robert Malenka at Stanford and Dr. Antonello Bonci at the Gallo Research Center, UCSF, showed in both mice and rats that a single injection of cocaine could induce long-term increases in excitatory post synaptic currents in the ventral tegmental area. The increased synaptic currents were measurable for at least 5 days, but not longer than 10 days, and the effect was specific for AMPA-mediated excitatory currents in the dopamine neurons. No effect was observed on hippocampal neurons or on GABAergic neurons in the VTA, although these cells also receive glutamatergic input. The potentiated synaptic currents had many similarities to long-term potentiation (LTP), which is a prominent form of synaptic plasticity involved in learning and memory processes in many areas of the brain. Thus, a single dose of cocaine apparently "usurped" a cellular mechanism involved in a normally adaptive learning process. This rapid and long-lasting change in synaptic transmission in the

VTA may help explain cocaine's ability to take control of incentive-motivational systems to produce compulsive drug seeking behavior. The observed synaptic potentiation may also be important for understanding relapse, where a single exposure to cocaine after a period of abstinence can induce renewed drug-seeking behavior. Ungless, M.A., Whistler, J.L., Malenka, R.C., and Bonci, A. Single Cocaine Exposure *in vivo* Induces Long-Term Potentiation in Dopamine Neurons. Nature, 411, pp. 583-587, 2001.

Estrogen Plays a Role in the Acquisition of i.v. Cocaine Self-Administration in Female Rats

Prior research by Drs. Wendy Lynch and Marilyn Carroll of the University of Minnesota showed that female rats acquire i.v. self-administration of cocaine faster than male rats. To assess the role that estrogen might play in this sex difference, these researchers compared i.v. self-administration in female rats for whom estrogen was blocked, either chemically or surgically, with female rats for whom estrogen was not blocked. Four groups of female rats were studied: ovariectomized (OVX) females treated either with estradiol benzoate (OVX-EB) or vehicle (OVX-VEH), and sham-operated (SH) females treated either with the estrogen blocker tamoxifen (SH-TAM) or vehicle (SH-VEH). In the two groups of female rats for which estrogen was not blocked, the SH-VEH and OVX-EB groups, the percentage of females who acquired cocaine self-administration according to the study criterion (a mean of 100 self-administered infusions over five consecutive 6-hr sessions) was 80% and 70%, respectively. In the two groups in which estrogen was either surgically or chemically blocked, the OVX-VEH and the SH-TAM groups, only 30% and 50%, respectively, met the study criterion for cocaine self-administration. In their prior work, these researchers found that 30% of the intact males met acquisition criterion, which is the same percentage as found for the OVX-VEH females in the present study. Taken together, these studies indicate that estrogen plays a role in the acquisition of i.v. cocaine self-administration among females and also in gender differences seen in the acquisition of i.v. cocaine self-administration. Lynch, W.J., Roth, M.E., Mickelberg, J.L. and Carroll, M.E. Role of Estrogen in the Acquisition of Intravenously Self-Administered Cocaine in Female Rats. Pharmacology, Biochemistry and Behavior, 68, pp. 641-646, 2001.

d-Amphetamine Increases Choice of Cigarette Smoking over Monetary Reinforcement

Dr. Steve Higgins and his colleagues at the University of Vermont report their finding that oral d-amphetamine (0, 7.5 mg/kg, 15 mg/kg) increases ad lib cigarette smoking from 2.8 to 3.8 cigarettes per 3-hr session. This finding is consistent with previously published reports of a relationship between psychostimulant use and cigarette smoking. In a separate study, Dr. Higgins and his colleagues sought to determine whether this relationship is due to non-specific activating effects of psychostimulants or to an increase in the reinforcing effects of cigarette smoking. Ninety minutes after ingesting oral d-amphetamine (0, 7.5, 15 mg/kg) in a 3-hr session, subjects were given 20 opportunities to choose among cigarette smoking (two puffs per choice), money (25 cents per choice), or neither. The authors report that d-amphetamine dose-dependently increased smoking choices from 4.2 to 5.7 cigarettes. While this and other studies have shown d-amphetamine and other psychostimulants increase the frequency of smoking, these findings are the first to provide evidence that d-amphetamine may produce an increase in the reinforcing effectiveness of cigarette smoking. Tidey, J.W., O'Neill, S.C and Higgins, S.T. d-Amphetamine Increases Choice of Cigarette Smoking Over Monetary Reinforcement. Psychopharmacology, 153, pp. 85-92, 2000.

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

Research Findings

Treatment Research and Development

National Costs of Heroin Dependence

The MEDSTAT Group, Inc. in Washington, D.C. evaluated the costs of heroin addiction in the United States, both to the addict and society at large. Using a cost-of-illness approach, costs were estimated in four broad areas: medical care, lost productivity, crime, and social welfare. In 1996 the estimated cost of heroin addiction in the United States was US$21.9 billion. Of these costs, productivity losses accounted for approximately US$11.5 billion (53%), criminal activities US$5.2 billion (24%), medical care US$5.0 billion (23%), and social welfare US$0.1 billion (0.5%). The large economic burden resulting from heroin addiction highlights the importance of investment in prevention and treatment. Mark, T.L., Woody, G.E., Juday, T., and Kleber, H.D. The Economic Costs of Heroin Addiction in the United States. Drug Alcohol Depend, 61, pp. 195-206, 2001.

Treatment Costs with Buprenorphine/Naloxone Combination

Investigators from the Yale University School of Medicine evaluated the potential economic impact of the buprenorphine/naloxone combination in the context of practice in the United States. In comparison to treatment provided through methadone clinics, buprenorphine/naloxone therapy in office practice may be associated with increased medication, physician, and nursing costs, but reduced costs for dispensing, toxicology screens, counseling and administration. It may also result in markedly reduced costs for patients; especially travel costs, resulting in net savings for society as a whole. A review of controlled studies suggests that buprenorphine/naloxone is not likely to be any more or less effective than methadone, but since it will be less expensive in the long run, it may be more cost-effective than methadone when provided to comparable groups of patients. Because of the convenience of office-based treatment, buprenorphine/naloxone may increase access to opiate substitution for some addicts. To the extent that treatment is provided to additional high-cost patients who are involved in extensive criminal activity or who undergo multiple detoxifications each year, net cost savings could be substantial. To the extent that treatment is extended to better adjusted addicts who are employed, married and experience fewer adverse effects from their addiction, costs could increase. The total cost impact will depend on which addict sub-populations make greatest use of the treatment opportunity presented by buprenorphine/naloxone. Rosenheck, R., and Kosten, T. Buprenorphine for Opiate Addiction: Potential Economic Impact. Drug Alcohol Depend., 63, pp. 253-262, 2001.

Bupropion Does Not Alter Subjective Effects of Cocaine

The antidepressant drug bupropion shares some pharmacological features with cocaine and was proposed as a potential medication for the treatment of cocaine dependence. Investigators from Yale University School of Medicine examined interactions between this drug and cocaine in humans. The effects of cocaine were evaluated prior to and during bupropion maintenance in nonopioid-dependent cocaine abusers. Prior to bupropion maintenance, subjects underwent an experimental session during which repeated cocaine doses (0, 50, 100 mg/70 kg) were administered intranasally. Then subjects were maintained on bupropion (150 and 300 mg per day) and underwent experimental sessions as before. Cocaine, regardless of bupropion, produced dose-related increases in several stimulant-like self-reports, performance and cardiovascular measures. Bupropion decreased POMS ratings of friendliness and vigor, regardless of cocaine dose. Bupropion enhanced and attenuated cocaine-induced increases in ratings on the LSD and BG subscales of the ARCI, respectively. These results suggest that bupropion does not alter the acute subjective or

cardiovascular effects of cocaine in a robust manner. Oliveto, A., McCance-Katz, F.E., Singha, A., Petrakis, I., Hameedi, F., and Kosten, T.R. Effects of Cocaine Prior to and During Bupropion Maintenance in Cocaine-Abusing Volunteers. Drug Alcohol Depend, 63, pp. 155-167, 2001.

Pergolide Found Not Useful for Cocaine Dependence

Investigators from the Medical University of South Carolina in Charleston conducted a double blind, multiple dose comparison study of pergolide versus placebo for the treatment of cocaine dependence. The study participants included 255 patients who met criteria for cocaine dependence without comorbid alcohol dependence. The completion rates significantly favored placebo (48.9%) over the low dose (33.3%) and high dose (21.5%) pergolide subjects. Treatment effectiveness scores were significantly higher for the placebo group (31.7) than for the low dose (25.2) and high dose (14.2) pergolide groups. There were no significant differences in side effect profiles after first dose of pergolide or placebo, or at study termination. Results suggest that pergolide is not efficacious in the treatment of cocaine dependence; therefore caution regarding the outpatient use of pergolide in similar populations is warranted. Malcolm, R., Herron, J., Sutherland, S.E., and Brady, K.T. Adverse Outcomes in a Controlled Trial of Pergolide for Cocaine Dependence. J Addict Dis, 20, pp. 81-92, 2001.

Fluoxetine Found Not Effective for Depression and Cocaine Dependence in Addicts

Investigators from the Substance Abuse Research Center, University of Texas Medical School Houston evaluated efficacy of antidepressant fluoxetine in the treatment of depression and cocaine dependence in cocaine addicts. Sixty-eight male and female individuals with both DSM-IV diagnoses of cocaine dependence and major depressive disorder were randomly assigned to one of two medication conditions (placebo vs. 40 mg per day) as part of a double blind, placebo-controlled clinical efficacy trial of fluoxetine for the treatment of this dual diagnosis. During the 12-week outpatient treatment phase all participants also received individual cognitive-behavioral psychotherapy targeting both cocaine use and depression. Depressive symptoms remitted as a function of time in treatment, with no significant medication effects found. Fewer cocaine positive urines were found during the first 6 weeks of treatment in the placebo group compared with the 40-mg group. Cocaine use and depressive symptoms during treatment were significantly correlated. The findings fail to support the role of fluoxetine for treatment of cocaine use and depression in dually diagnosed patients. Schmitz, J.M., Averill, P., Stotts, A.L., Moeller, F.G., Rhoades, H.M., and Grabowski. J. Fluoxetine Treatment of Cocaine-Dependent Patients with Major Depressive Disorder. J. Drug Alcohol Depend, 63, pp. 207-214, 2001.

The D1 Receptor Antagonist Ecopipam Enhanced the Subjective Effects of Cocaine

Investigators from the Columbia University Medical School, NY, examined the efficacy of a dopamine D1 antagonist in the treatment of cocaine dependence, because animal and human studies suggested that drugs from this class decrease cocaine self-administration and block cocaine's discriminative stimulus and subjective effects. The influence of the selective D1 antagonist, ecopipam (SCH 39166), on the reinforcing, cardiovascular, and subjective effects of cocaine in humans was examined. Ten non-treatment-seeking cocaine smokers residing on an inpatient research unit were maintained on placebo and ecopipam (100 mg p.o.) in random order using a within-subjects, crossover design. Cocaine self-administration (0, 12, 25, and 50 mg) was tested beginning on the 5th day of each 8-day maintenance condition. A six-trial choice procedure (cocaine vs. $5 merchandise vouchers) was utilized, with sessions consisting of one sample trial, when participants smoked the cocaine dose available that day, and five choice trials, when participants chose between smoking the available cocaine dose or receiving one merchandise voucher. In the presence of cocaine placebo, ecopipam significantly decreased cocaine craving while increasing alcohol and tobacco craving. In the presence of active cocaine, ecopipam increased cocaine self-administration (12 mg) and increased ratings of "good drug effect," "high," "stimulated," and dose quality (25 and 50 mg). Ecopipam produced small but significant increases in blood pressure, regardless of cocaine dose. Authors concluded that maintenance on the long-acting D1 antagonist enhanced cocaine self-administration and its subjective effects compared to placebo. These data suggest that chronic antagonism of the dopamine D1 receptor may not be a useful approach for the treatment of cocaine abuse. Haney, M., Ward, A.S., Foltin, R.W., and Fischman, M.W. Effects of Ecopipam, a Selective Dopamine D1 Antagonist, on Smoked Cocaine Self-Administration by Humans. Psychopharmacology (Berl), 155, pp. 330-337, 2001.

Naltrexone with Relapse Prevention Therapy Helpful in the Treatment of Cocaine Dependence

Investigators from the University of Texas Medical School-Houston evaluated in a double-blind, placebo-controlled clinical trial the joint action of naltrexone (NTX) in combination with relapse prevention (RP) therapy for the treatment of cocaine dependence. Eighty-five participants who achieved initial abstinence during the intake

evaluation and detoxification phase of the study were randomized into 1 of 4 combined NTX (0 vs. 50 mg) by therapy (RP vs. Drug Counseling) experimental conditions for the 12-week outpatient treatment phase of the study. A random effects regression model to test for group differences on percentage of cocaine-positive urines indicated a significant time by medication by therapy interaction, suggesting less cocaine use over time among subjects receiving RP-50 mg naltrexone than by those in the other conditions. No differences were found for retention or time until first cocaine-positive urine. Naltrexone was well tolerated by participants and medication compliance was satisfactory. These results are consistent with the notion that substance use in dependent patients can be reduced with a combination of coping skills training and pharmacologic treatments. Naltrexone and Relapse Prevention Treatment for Cocaine-Dependent Patients. Schmitz, J.M., Stotts, A.L., Rhoades, H.M., and Grabowski, J. Addict Behav, 26, pp.167-180, 2001.

Psychotherapy for Comorbid Attention-Deficit/Hyperactivity Disorder (ADHD) and Psychoactive Substance Use Disorder (PSUD)

Investigators from Columbia University Medical School suggest that relapse prevention is an appropriate initial treatment for cocaine addicts with ADHD because it is well suited to manage both substance abuse and comorbid symptomatology such as impulsivity, distractibility, and avoidance. ADHD is one of the most common comorbid diagnoses with PSUD, and it is important that efficacious psychotherapies be developed to complement psychopharmacological approaches. Clinicians should consider psychotherapy as part of a multimodal treatment approach that includes medication and perhaps family therapy. Aviram, R.B, Rhum, M., and Levin, F.R. Psychotherapy of Adults with Comorbid Attention-Deficit/Hyperactivity Disorder and Psychoactive Substance Use Disorder. J Psychother Pract Res, 10, pp. 179-186, 2001.

Bupropion Worsens Mood during Marijuana Withdrawal

Investigators from the Columbia University Medical School, NY, examined symptoms of withdrawal after daily marijuana smoking, which include increased irritability and depression. Similar mood symptoms are reported by cigarette smokers during nicotine abstinence. Given the successful use of sustained-release bupropion in treating nicotine dependence, they investigated how maintenance on bupropion influenced symptoms of marijuana withdrawal compared to maintenance on placebo. Ten marijuana smokers were maintained outpatient on active (300 mg/day) or placebo (0 mg/day) bupropion for 11 days, and were then maintained inpatient on the same bupropion dose for 17 days. For the first 4 inpatient days, participants smoked active marijuana [2.8% delta9-tetrahydrocannabinol (THC)] 5 times/day. For the remaining inpatient days, they smoked placebo marijuana (0.0% THC) 5 times/day. Participants were then maintained outpatient on the alternate dose of bupropion for 11 days, followed by a second inpatient residential stay, paralleling the first. Medication administration was double-blind. Mood, psychomotor task performance, food intake, and sleep were measured daily during each inpatient phase. Bupropion had few behavioral effects when participants smoked active marijuana. During marijuana withdrawal, ratings of irritability, restlessness, depression, and trouble sleeping were increased by bupropion compared to placebo maintenance. These data suggest that bupropion does not show promise as a potential treatment medication for marijuana dependence. Haney, M., Ward, A.S., Comer, S.D., Hart, C.L., Foltin, R.W., and Fischman, M.W. Bupropion SR Worsens Mood during Marijuana Withdrawal in Humans. Psychopharmacology (Berl),155, pp. 171-179, 2001.

Cognitive Therapy and Brain Perfusion Deficits

Cognitive behavior therapy is currently a mainstay of treatment for cocaine dependence. It is a complex learning process with a goal of formation of new relationships between mood, thought, and behavior. The capacity to respond to such "psychosocial" intervention is largely dependent on a patient's cognitive flexibility. The investigators from the Yale University Medical School proposed that changes in cognitive function that occur during the period of early recovery from heavy drug abuse are multi-determined, reflecting alterations at many levels of regulation of cerebral function. Previous studies demonstrated deficits in neuropsychological performance and abnormalities in brain perfusion or metabolism in chronic cocaine abusers, which improve during abstinence. Cerebral perfusion was chosen as a marker for recovery from cocaine's complex pharmacological effects, which outlast its serum half-life. Investigators hypothesized that a measure of change in cerebral perfusion during early abstinence from cocaine will correlate with a measure of the capacity to learn new behavior and they presented several cases, which demonstrate an association between the response to cognitive behavior therapy and improvement in cerebral perfusion. This correlation encourages systematic clinical studies of the relationship between cerebral perfusion and the response to cognitive therapy in recovery from cocaine dependence. Gottschalk, C., Beauvais, J., Hart, R., and Kosten, T. Clinical Case Conference Cognitive Function and Cerebral Perfusion During Cocaine Abstinence. Am J Psychiatry, 158, pp. 540-545, 2001.

Propranolol May Reduce Symptoms of Autonomic Arousal Associated with Early Cocaine Abstinence and Improve Treatment Outcome

Investigators from the University of Pennsylvania School of Medicine and the Department of Veterans Affairs Medical Center in Philadelphia evaluated the utility of propranolol in the treatment of cocaine dependence in an 8-week, double-blind, placebo-controlled trial in 108 cocaine dependent subjects. The primary outcome measure was quantitative urinary benzoylecgonine levels. Secondary outcome measures included treatment retention, addiction severity index results, cocaine craving, mood and anxiety symptoms, cocaine withdrawal symptoms, and adverse events. Propranolol treated subjects had lower cocaine withdrawal symptom severity but otherwise did not differ from placebo treated subjects in any outcome measure. However, in a secondary, exploratory analysis, subjects with more severe cocaine withdrawal symptoms responded better to propranolol in comparison to placebo. In these subjects, propranolol treatment was associated with better treatment retention and lower urinary benzoylecgonine levels as compared with the placebo treatment. Propranolol may be useful only for the treatment of cocaine dependent patients with severe cocaine withdrawal symptoms. Kampman, K.M., Volpicelli, J.R., Mulvaney, F., Alterman, A.I., Cornish, J., Gariti, P., Cnaan, A., Poole, S., Muller, E., Acosta, T., Luce, D., and O'Brien, C. Effectiveness of Propranolol for Cocaine Dependence Treatment May Depend on Cocaine Withdrawal Symptom Severity. Drug Alcohol Depend, 63, pp. 69-78, 2001.

The Therapeutic Workplace is an Efficacious and Self-Sustaining Treatment for Heroin and Cocaine Addicts

Dr. Silverman at Johns Hopkins University School of Medicine conducted a study that integrated abstinence reinforcement into a work setting, using salary that drug abusers earn for work to reinforce drug abstinence. Patients are paid to work, but they must provide drug-free urine samples to gain daily access to the workplace. In Phase 1 of this study, each participant's "job" is to work in a job skills training program where they are paid in vouchers exchangeable for goods and services. Results showed that Phase I effectively promoted long-term abstinence from heroin and cocaine in poor, chronically unemployed pregnant and postpartum women. In Phase 2, successful participants were hired as regular employees of a real income-producing business. Participants must still provide drug-free urine samples to maintain access to the workplace each day, but in this phase they earn regular paychecks instead of vouchers. Findings from Phase 2, suggest that the therapeutic workplace business could be financially feasible and self-sustaining. As well as being utilized for unskilled and chronically unemployed people, the therapeutic workplace intervention could be applied to treat drug-addicted individuals who are skilled and already employed. In addition, the therapeutic workplace could be created around different types of jobs and businesses. Silverman, K., Wong, C.J., Svikis, D., Stitzer, M.L., and Bigelow, G.E. The Therapeutic Workplace: A Promising Treatment for Heroin and Cocaine Addiction among the Chronically Unemployed. In Proceedings of 2001 ONDCP International Technology Symposium: Counterdrug Research and Development: Technologies for the Next Decade.

Alcohol Dependence Among Cocaine-Dependent Outpatients: Demographics, Drug Use, Treatment Outcome and Other Characteristics

In this study data were obtained from 302 adults (70% men) enrolled in outpatient treatment for cocaine dependence. Individuals who did and those who did not meet criteria for alcohol dependence were compared on demographics, drug use, treatment outcome and other variables. With regard to cocaine use, alcoholics were more likely than non-alcoholics to report an intranasal route of administration, use of cocaine in social settings, more simultaneous use of cocaine and alcohol, and more adverse consequences of their cocaine use. With regard to alcohol use, alcoholics reported consuming alcohol more frequently and in larger amounts, had longer drinking histories, and were more likely than non-alcoholics to report increases in alcohol consumption when using cocaine. Alcoholics were heavier cigarette smokers than non-alcoholics and reported more severe employment, legal, family, and psychiatric problems. There were overall improvements in both groups from intake through 12 months after treatment. With regard to treatment retention and cocaine abstinence, alcoholics had better outcomes than non-alcoholics when treated with intensive behavioral counseling plus incentives, but the reverse was true when treated with control treatments. Compared with nonalcoholic cocaine dependent subjects, codependent patients exhibit a wider array of problems, many of which merit treatment attention. This study underscores the importance of a comprehensive treatment approach for the significant majority of cocaine dependent patients who are also dependent on alcohol or nicotine. Heil, S.H., Badger, G.J., and Higgins, S.T. Journal of Studies on Alcohol, 62, (1), pp. 14-22, 2001.

The Effectiveness of Incentives in Enhancing Treatment Attendance and Drug Abstinence in Methadone-Maintained Pregnant Women

In this study Dr. Hendree Jones and colleagues at Johns Hopkins University examined the effectiveness of short-term

contingency management for eliminating cocaine use and increasing full day treatment attendance with pregnant methadone-maintained women randomly assigned to either an escalating voucher incentive schedule (n=44) or non-incentive (n=36) condition. Full day treatment attendance and urine toxicologies for cocaine and heroin were assessed for 14 days. The escalating voucher incentive schedule significantly increased full day treatment attendance and drug abstinence compared to the non-incentive schedule. These findings suggest that reinforcing the co-occurrence of two required behaviors (treatment attendance and abstinence from illicit drug use) is effective, and may be an important adjunct to methadone pharmacotherapy for treating pregnant drug dependent women. Jones, H., Haug, N., Silverman, K., Stitzer, M. and Svikis, D. Drug and Alcohol Dependence, 61, pp. 297-306, 2001.

Clinical and Psychosocial Characteristics of Substance-Dependent Pregnant Women with and without PTSD

This study compared psychiatric and psychosocial functioning in 123 pregnant opiate- and/or cocaine-dependent women with and without a comorbid diagnosis of posttraumatic stress disorder (PTSD). Participants were enrolled in a comprehensive perinatal drug treatment program and completed assessments upon admission. Lifetime diagnostic prevalence of PTSD (Structured Clinical Interview for DSM-IV Disorders (SCID) confirmed) among the sample was 19%. Participants with PTSD (n=24) reported greater need for psychiatric treatment, were more likely to report a previous suicide attempt, and had more previous drug treatments than participants without PTSD (n=99). Women with PTSD were twice as likely to have lifetime Axis I and Axis II disorders and had higher rates of abuse than women without PTSD. Lifetime sexual abuse and ASI family/social composite scores were significant predictors of PTSD. The results suggest that pregnant drug-dependent women with comorbid PTSD may benefit from specialized treatment services for trauma and/or abuse issues. Moylan, P., Jones, H., Haug, N., Kissin, W., and Svikis, D. Addictive Behaviors, 26, pp. 469-474, 2001.

Targeting Behavioral Therapies to Enhance Naltrexone Treatment of Opioid Dependence: Efficacy of Contingency Management and Significant Other Involvement

In this study 127 recently-detoxified opioid dependent individuals were randomly assigned to one of three conditions delivered over 12 weeks: 1) Thrice weekly naltrexone plus weekly cognitive-behavioral therapy (CBT); 2) Naltrexone and CBT plus contingency management (CM) with the delivery of vouchers contingent on naltrexone compliance and drug-free urine specimens, or 3) Naltrexone, CBT, CM plus significant other involvement (SO+CM), where a family member was invited to participate in up to six family counseling sessions. Outcomes included retention in treatment, compliance with naltrexone, and the number of drug-free urines. In this study Dr. Carroll and her colleagues at Yale University found that contingency management was associated with significant improvements in retention (7.4 versus 5.6 weeks) and reduction in opioid use (19 versus 14 opioid free urine specimens). Significant effects for the SO condition over CM on retention, compliance and drug use outcomes were seen only for the subgroup that attended at least one family meeting. The significant other condition was associated with improvements in family functioning. Behavioral therapies such as contingency management may enhance compliance with naltrexone maintenance. Carroll, K.M., Ball, S.A., Nich, C., O'Connor, P., Eagan, D.A., Frankforter, T.L., Triffleman, E.G., Shi, J., and Rounsaville, B.J. Targeting Behavioral Therapies to Enhance Naltrexone Treatment of Opioid Dependence. Archives of General Psychiatry, 58, pp. 755-761, August 2001.

Problem Gambling and Cocaine Dependence: Implications for Diagnostic Screening

Dr. Cunningham-Williams presented data from her paper (Cunningham-Williams, et al, 2000) on the risk factors for pathological gambling among drug users, including being male, of African American ethnicity, meeting criteria for Antisocial Personality Disorder, and being dependent on any illicit drug. This presentation was awarded the 2001 Young Investigator Award by the American Society of Addiction Medicine (ASAM) for the best abstract submitted by a young investigator. Cunningham-Williams, R. M., presentation to the American Society of Addiction Medicine, April 2001.

Functional Imaging of Neural Responses to Expectancy and Experience of Monetary Gains and Losses

Dr. Hans Breiter and colleagues at the NMR Center of Massachusetts General Hospital used BOLD fMRI to map the brain areas activated during expectancy and delivery of monetary reward. These regions overlapped with the regions that were activated by cocaine infusions in a prior study by this investigator. Normal subjects viewed one of three stimuli, each of which generated a specific expectancy regarding monetary gains or losses. The stimuli consisted of a circle divided into three equal segments and a spinning arrow. In one stimulus, the 'good' stimulus, two of the three parts denoted a monetary gain, with the third part denoting a zero outcome. A second stimulus was 'bad' in that two

segments predicted a monetary loss, with the third segment again having a zero outcome. The third stimulus had one gain segment, one loss segment, and a zero segment. Brain images were obtained during the expectancy phase while the arrow was spinning and during the outcome phase when the arrow pointed to one of the segments. A widespread brain network was activated during both the expectancy and outcome phases, including regions of the orbitofrontal cortex, ventral striatum, and extended amygdala. In addition, expectancies determined the neural responses to identical outcomes. In the context of the 'good' spinner, an outcome of $0 represented a relative loss (absence of gain), and there was a marked decrease in the BOLD signal to a $0 outcome, similar to an actual monetary loss. But in the context of the 'bad' spinner, a $0 outcome represented a relative gain (absence of loss), and there was a marked increase in the BOLD signal, similar to an actual monetary gain. These data show that the response to reward in these ventral striatal regions are not driven by the presence and absolute magnitude of the reward, but rather by cognitively driven expectancies anticipated outcomes. Breiter, H.C. et al., Functional imaging of neural responses to expectancy and experience of monetary gains and losses. Neuron, 30, pp. 619-639, 2001.

Amygdala Response to both Positively and Negatively Valenced Stimuli

Dr. Hugh Garavan and colleagues at the Medical College of Wisconsin used BOLD fMRI to determine whether the amygdala is differentially tuned to hedonic vs. aversive stimuli. Prior studies have reported activation of the amygdala during drug craving, and so it is important to establish the basic information being processed by the amygdala. The amygdala has long been associated with emotional processing, and a dominant view is that the amygdala responds either exclusively or primarily to negative affective stimuli. In the present study, normal female subjects viewed pictures that varied in emotional content and arousal level selected from a widely used and validated picture set (International Affective Picture System). There was no difference in the amygdala response between negatively and positively valenced pictures, nor were there differences in the laterality of activation. There were differences with respect to interactions with the arousing properties of the pictures. The amygdala response to negatively valenced pictures was influenced by the level of arousal induced, whereas the response to the positive pictures was independent of the level of induced arousal. These results suggest that, at least in female subjects, amygdala activation occurs to both positive and negative emotional stimuli. Garavan et al., Neuroreport, 12, pp. 1-5, 2001.

Neurotoxic Effects in Detoxified Methamphetamine Users

Drs. Volkow, Chang and colleagues at the Brookhaven National Laboratory assessed functional changes in brain regions for 15 detoxified methamphetamine (METH) abusers using positron emission tomography (PET) to determine brain glucose metabolic rate. Twenty-one control subjects were scanned for comparison. Results indicated that whole brain metabolism in the METH abusers was 14% higher than that of the comparison subjects, and this increase was most notable in the parietal cortex. Following normalization for whole brain metabolism, the METH abusers exhibited significantly lower metabolism in the thalamus and striatum. The parietal cortex is a region devoid of any substantial dopaminergic innervation, so the hypermetabolism seen in this region in the METH abusers must be affecting circuits other than those modulated by dopamine. In addition, the researchers suggest the lower metabolism in the striatum and thalamus is likely a reflection of the functional consequence of METH in dopamine circuits. Volkow, N.D., Chang, L., Wang, G.J., Fowler, J.S., Franceschi, D., Sedler, M.J., Gatley, S.J., Hitzemann, R., Ding, Y.S., Wong, C., and Logan, J. Higher Cortical and Lower Subcortical Metabolism in Detoxified Methamphetamine Abusers. American Journal of Psychiatry, 158(3), pp. 383-389, 2001.

Dopamine Transporter Reduction in Detoxified Methamphetamine Users

In a study by Drs. Volkow, Chang and colleagues at the Brookhaven National Laboratory, METH neurotoxicity to dopamine transporter (DAT) was characterized in human METH abusers. Further, this work examined the functional significance of METH's effect on the DAT. Dopamine transporter levels were measured in fifteen detoxified METH abusers, who were evaluated subsequently to determine gross motor and cognitive function. Results indicate that the METH abusers not only showed a significant reduction of dopamine transporter in the striatum relative to the control subjects, but they also displayed substantial memory impairment and motor slowing. Importantly, these data reveal that METH at doses taken by human abusers of the drug leads to significant reductions of DATs that are directly associated with cognitive and motor impairments. Volkow, N.D., Chang, L., Wang, G.J., Fowler, J.S., Leonido-Yee, M., Franceschi, D., Sedler, M.J., Gatley, S.J., Hitzemann, R., Ding, Y.S., Logan, J., Wong, C., and Miller, E.N. Association of Dopamine Transporter Reduction with Psychomotor Impairment in Methamphetamine Abusers. American Journal of Psychiatry, 158(3), pp. 377-382, 2001.

Obesity-Dopamine Link

To better understand the cerebral mechanisms underlying pathological overeating and subsequent obesity, Dr. Gene-Jack Wang and colleagues at the Brookhaven National Laboratory conducted an investigation to assess whether

severely obese individuals had differences in the amount of brain dopamine D2 receptors compared with normal-weight individuals. Ten self-selected males and females meeting all study criteria underwent PET scanning, and results indicated that in obese individuals, there was a significantly lower number of available D2 receptors in brain striatum, and that low amounts of such receptors were negatively correlated with body mass index (BMI). If dopamine deficiency perpetuates pathological eating as a way of compensating the decreased activation of these circuits, strategies aimed at improving dopamine function may be beneficial in the treatment of obese individuals. Wang, G.J., Volkow, N.D., Logan, J., Pappas, N.R., Wong, C.T., Zhu, W., Netusil, N., and Fowler, J.S. Brain Dopamine and Obesity. The Lancet, 357(9253), pp. 354-357, 2001.

Psychiatric Comorbidity of Methamphetamine Dependence in a Forensic Sample

The association between psychiatric symptoms and methamphetamine (METH) dependence was examined. A survey was administered to 1,580 arrestees sampled from the 14 most populous counties in California. The survey included items assessing demographic profile, history of substance dependence, and psychiatric symptomatology. METH-dependent individuals (defined as those having used the drug, unsuccessfully tried to decrease use and/or felt addicted within 12 months of the assessment) were significantly more likely to report depressive symptoms and suicidal ideation than individuals denying METH dependence, even after controlling for demographic profile and dependence on other drugs. METH-dependent individuals also were more likely to report a need for psychiatric assistance at the time of the interview. These findings suggest that METH-dependent individuals are at greater risk to experience particular psychiatric symptoms. There was a significant dependence-by-gender effect, with dependent females reporting significantly more overall symptomatology compared to females reporting no dependence; males significantly differed only with respect to depression. Further study to determine the etiology of these symptoms is warranted. Kalechstein, A.D., Newton, T.F., Longshore, D., Anglin, M.D., van Gorp, W.G., and Gawin, F.H. Psychiatric Comorbidity of Methamphetamine Dependence in a Forensic Sample. Journal of Neuropsychiatry & Clinical Neurosciences, 12(4), pp. 480-484, 2000.

Examination of Cortical Motor Threshold Via Transcranial Magnetic Stimulation in Drug-Free, Cocaine-Dependent Patients

Transcranial magnetic stimulation (TMS) provides a noninvasive method of examining cortical inhibitory and excitatory processes and cortical excitability in awake subjects. Evidence from clinical and electroencephalographic data suggest that cortical excitability may be abnormal in some psychiatric populations. Chronic cocaine abuse influences a number of neurotransmitters that are involved in the excitatory/inhibitory balance of the cerebral cortex; therefore, this pilot study was conducted to ascertain the possible utility of TMS in examining cortical excitability in a population of chronic cocaine abusers. The right and left motor thresholds of 10 cocaine-dependent subjects and 10 normal controls were examined using single pulse TMS. The resting motor thresholds resulting from stimulation of the right or the left motor cortical regions were significantly elevated in cocaine-dependent subjects compared with the controls. These data suggest that chronic cocaine use significantly alters cortical excitability via increased inhibition or decreased excitability. This finding may reflect adaptation to those effects of cocaine intoxication that promote cortical excitability and seizures. Boutros, N.N., Lisanby, S.H., Tokuno, H., Torello, M.W., Campbell, D. Berman, R., Malison, R., Krystal, J.H., and Kosten, T. Elevated Motor Threshold in Drug-free, Cocaine-Dependent Patients Assessed with Transcranial Magnetic Stimulation. Biological Psychiatry, 49(4), pp. 369-373, 2001.

Examination of the Role of Endogenous Brain Dopamine in Methamphetamine-Induced Dopaminergic Neurotoxicity

To evaluate the role of endogenous dopamine (DA) in methamphetamine (METH)-induced neurotoxicity, the neuroprotective effects of reserpine and alpha-methyl-p-tyrosine (AMPT) were examined. Mice pretreated with reserpine developed long-term reductions in striatal DA axonal markers, suggesting that vesicular stores of DA were not crucial for the development of METH neurotoxicity. To test whether cytoplasmic DA might be involved, these DA stores were depleted with AMPT before METH administration. As lower core body temperature is a known neuroprotector and AMPT and reserpine are known to lower body temperature, this study was repeated at both 28ºC and 33ºC. At the lower temperature, complete neuroprotection was observed, but no protection was seen at the increased level. The study demonstrates that when the hypothermic effects of reserpine and AMPT were controlled, METH toxicity was fully expressed, suggesting that endogenous DA plays little if any role in METH-induced neurotoxicity. Yuan, J., Callahan, B.T., McCann, U.D., and Ricaurte, G.A. Evidence Against an Essential Role of Endogenous Brain Dopamine in Methamphetamine-induced Dopaminergic Neurotoxicity, Journal of Neurochemistry, 77(5), pp. 1338-1347, June 2001.

Effects of Methadone Maintenance on Cerebral Metabolism

Regional cerebral metabolic rate for glucose (rCMRglc) was evaluated using the PET [18F] fluorodeoxyglucose method in three groups: four opiate-dependent subjects currently receiving methadone maintenance therapy (MMT), four withdrawn from methadone (MW) and five controls who were without substance abuse disorders (C). Analyses uncovered a significant difference in rCMRglc in the anterior cingulate gyrus between MW and C groups, with the MMT group showing intermediate differences that were not statistically different. These findings suggest that neurobiologic abnormalities can persist in the brain of an opiate user several years after detoxification from methadone. Galynker, I.I., Watras-Ganz, S., Miner, C., Rosenthal, R.N., Des Jarlais, D.C., Richman, B.L., and London, E. Cerebral Metabolism in Opiate Dependent Subjects: Effects of Methadone Maintenance. The Mount Sinai Journal of Medicine, 67(5,6), pp. 381-386, 2000.

Mental Imagery of Personal Drug Use Induced Craving that was Associated with Activations of Specific Areas of Paralimbic and Limbic Systems

Kilts and associates from Emory University composed scripts personalized from interviews with each subject - of cocaine use situations, anger incidences, as well as control (neutral) memories of a beach or forest scene. These were then read to the subjects immediately after which water (O15) PET studies were initiated, followed by questionnaires assessing craving and anger. Compared to the neutral condition, drug use imagery was associated with activation of the amygdala (R>L), the left insula and anterior cingulate gyrus, and the right subcallosal gyrus and nucleus accumbens. There were also some significant decreases in parts of the right frontal and left temporal cortices. When compared to the anger imagery, drug use imagery was associated with activation in limbic and paralimbic brain structures, including the bilateral insula and subcallosal cortices, the left posterior caudate nucleus, and the anterior cingulate. The amount of increase (number of pixels) in these areas was correlated with craving self-reported scores. Conspicuously absent were increases in the prefrontal association cortices suggesting that activation of these areas in other paradigms have a qualitatively different component. These results give insight into which brain areas are involved in what may be characterized as self-generated craving. The caveat is that there are other interpretations as to what the imagery represents in terms of the drug-craving process in the field. Kilts, K.D.,Schwetzer, J.B., Quinn, C.K., Gross, R.E., Faber, T.L., Muhammad, F., Ely, T.D., Hoffman, J.M., and Drexler, K.P.G., Archives of General Psychiatry, 58, pp. 334-341, 2001.

Serotonin Transporters Upregulate with Chronic Cocaine Use

Mash and colleagues examined the status of the serotonin transporter in subgroups of individuals coming to post-mortem with cocaine overdose deaths. Transporter densities were increased in the nucleus accumbens and both the anterior and posterior sectors of the striatum. By contrast, those subjects who had presented with excited delirium did not have the same elevations in the posterior striatum. Also, upregulation was found in the substantia nigra for overdose victims but not for those with delirium. These results suggest that those cocaine abusers experiencing excited delirium may be a different, distinct phenotype than those without this condition. Mash, D.C., Staley, J.K., Izenwasser, S., Basile, M., and Ruttenber, A.J., Journal of Chemical Neuroanatomy, 20, pp. 271-280, 2000.

Reduced Vasoconstriction in Woman Compared to Men and during Different Phases of the Menstrual Cycle after Cocaine May be a Protective Factor

Dr. Marc Kaufman and colleagues studied cerebral blood flow with dynamic susceptibility contrast magnetic resonance imaging in occasional cocaine users: men and woman at different phases of the menstrual cycle. In men, there was a 20% reduction in blood flow, while there was no reduction during the follicular stage of women and a 10% reduction during the luteal phase. It is conceivable that this difference could account in part to the lesser neuronal injury in women and implies that gonadal steroids or the factors they modulate may be therapeutic agents for reducing cocaine-induced cerebrovascular disorders. Kaufman, M.J., Levin, J.M., Maas, L.C., Kudes, T.J., Villafuerte, R.A., Dostal, K., Lukas, S.E., Mendelson, J.H., Cohen, B.M., and Renshaw, P.F., Biological Psychiatry, 49(9), pp. 774-781, 2001.

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

Research Findings

Research on AIDS and Other Medical Consequences of Drug Abuse

Association Between Methamphetamine and High-Risk Behaviors among Gay and Bisexual Men in Los Angeles

This report explored the association between abuse of methamphetamine, high-risk behaviors, and HIV-status among a sample of gay and bisexual men in Los Angeles. Results from a 12-page admission form distributed to 163 gay and bisexual men seeking treatment for methamphetamine abuse indicate that men who reported being HIV-positive were significantly more likely to report that their use of crystal was always associated with sexual behavior (62%) compared to 44% of HIV-negative men indicating that crystal use was always associated with sexual behavior. HIV-positive men were also significantly more likely to report injection as route of administration (48%) compared to 25% of HIV-negative men reporting any injection behaviors. Methamphetamine abuse and its strong association with high-risk sexual and drug use behaviors represent an important public health problem for gay and bisexual men. Hucks-Ortiz, C., Shoptaw, S., and Reback, C.J. Drug and Alcohol Dependence, 63, pp. 1-202, 2001.

HCV Risk Not Limited to Injection Drug Users

A study in New York City examined the prevalence of hepatitis C (HCV) infection among non-injecting drug users residing in East Harlem and the Lower East Side of Manhattan neighborhoods. As many as 17% percent of the subjects who denied a history of injection drug use were found to be infected, compared to a 2% infection rate in the general population. Among women from one of the study sites in East Harlem who reported use of non-injection heroin, the rate of infection was as high as 26%, compared to 14% among women recruited from the Lower East Side. This discrepancy may be attributed at least in part to differences in age between the two study samples. Older women (>35) were found to have a higher anti-HCV prevalence than do younger women (<35). Rates of anti-HCV prevalence were substantially higher for former injectors than for never injectors and, in contrast to never injectors, former injectors exhibited anti-HCV rates that were quite similar across study locations, non-injecting drug use categories, and gender. The researchers posit that the considerable prevalence of HCV among never injectors could be, in part, from some never injectors misrepresenting past injection histories, although study procedures were designed to minimize underreporting. A particular concern is the possibility that the prevalence of HCV among never injectors is related to non-injecting routes of transmission. A pool of HCV-infected non-injecting drug users may be a residual source for the transmission of HCV to other populations. These findings have relevance for HCV testing and treatment policies, as well as for future research focused on the risk factors for HCV transmission among those with no history of injecting drug use. Tortu, S., Neaigus, A., McMahon, J., and Hagen, D. Hepatitis C Among Non-injecting Drug Users: A Report. Substance Use and Misuse, 36(4), pp. 523-534, 2001.

Gender Differences in Condom Usage Among Rural Crack-Using Men and Women

This study explores gender differences in attitudes and motivations to use condoms within a rural, economically disadvantaged sample. Qualitative data analysis identified recurrent themes regarding condom use and assessed how themes varied among men and women. Analyses showed that men and women exhibit different rationales for condom use, while both reported inconsistencies between their knowledge about safe sex, receptivity to condom use, and applications in practice. The findings suggest that prevention programs should be tailored to increase consistent condom use among main partners of crack smokers at risk for HIV. McCoy, H.V. and Wasserman, A. Women and

Health, 33, pp. 1-2, 2001.

HIV-1 Seroconversion in Street-Recruited IDUs is Associated With Sexual Behavior

Many new HIV-1 infections in the U.S. occur among IDUs. HIV-1 seroconversion among IDUs is mainly associated with injection-related risk factors. Harm reduction programs concentrate on injection risk behaviors. In this study, researchers sought to establish whether injection or sexual risk factors, or both, were associated with HIV-1 antibody seroconversion of street-recruited IDUs in San Francisco from 1986 to 1998. IDUs were enrolled every 6 months from four community sites. The researchers used a nested case-control design to compare 58 respondents who seroconverted between visits with 1134 controls who remained seronegative. Controls were matched with cases by sex and date. Adjusted odds ratios and 95% C.I.s were calculated for men and women by use of conditional logistic regression. Men who had sex with men were 8.8 times as likely to seroconvert (95% CI 3.7-20.5) as heterosexual men. Women who reported having traded sex for money in the past year were 5.1 times as likely as others to seroconvert (95% CI 1.9-13.7). Women younger than 40 years were 2.8 times more likely to seroconvert than women 40 years and older (95% CI 1.05-7.6), and women who reported a steady sex partner who injected drugs were 0.32 times less likely to seroconvert than other women (95% CI 0.11-0.92). The researchers conclude that HIV-1 seroconversion among street-recruited IDUs in San Francisco is strongly associated with sexual behavior. HIV-1 risk might be reduced by incorporation of innovative sexual-risk reduction strategies into harm reduction programs. Kral, A.H., Bluthenthal, R.N., Lorvick, J., Gee, L., Bacchetti, P., and Edlin, B. Sexual Transmission of HIV-1 Among IDUs in San Francisco, USA: Risk-Factor Analysis. The Lancet, 357, pp. 1397-1401, 2001.

Factors Associated With Readiness to Change Drug Use Among Needle Exchange Users

In this study, researchers sought to determine if frequent needle exchange program (NEP) use is associated with lower readiness to change drug use. They interviewed 168 NEP clients in Providence, RI regarding drug use, HIV risk, health, and past use of treatment services in 1997 and 1998. Readiness to change was assessed using a 9-step decision ladder. Based on this assessment, 14.3% of the sample were classified as pre-contemplators, 29.2% were in the contemplation stage, and 56.5% were in the determination or readiness to change stage. The researchers found that the mean number of NEP visits was 25.5 among pre-contemplators, 28.7 among contemplators, and 22.5 among those in the determination stage. In multivariate analysis, an inverse relationship between having ever been in alcohol treatment and higher readiness to change drug use was the only significant association. More frequent NEP participation did not impact readiness to change drug use among IDUs. Given the high proportion of NEP clients ready to change drug use, improving linkages between NEP and substance abuse treatment appears warranted. Bluthenthal, R.N., Goginen, A., Longshore, D., and Stein, M. Factors Associated With Readiness to Change Drug Use Among Needle-Exchange Users. Drug and Alcohol Dependence, 62(3), pp. 225-230, 2001.

Longitudinal Study Identifies Sex Differences in HIV Risks Among Injecting Drug Users

Injection drug use directly or indirectly accounts for nearly half the annual HIV infections in the United States today. The changing dynamic of the HIV/AIDS epidemic has also had a significant impact on women and minorities: in 1999, women accounted for 23% of all reported adult AIDS cases in the U.S. and African American and Hispanic ethnic groups accounted for 55% of the cumulative total number of AIDS cases and 77% of AIDS cases in women and girls. Researchers in Baltimore, MD followed a cohort of 1874 IDUs from 1988 to 1998 to investigate drug-related and sexual risk factors for HIV. Participants were 1447 male (77%) and 427 female (23%) HIV-negative IDUs. The median age at enrollment was 35 years; 91% of the participants were African American. Incidence of HIV was 3.14 per 100 person years (95% CI, 2.78-3.53) and did not significantly differ by sex. Younger age independently predicted HIV seroconversion for both men and women. Among men, less than a high school education, recent needle sharing with multiple partners, daily injection, and shooting-gallery attendance independently predicted HIV seroconversion. HIV incidence was double among men who recently engaged in homosexual activity and cocaine injection. Among women, the incidence of HIV was more than double for those recently reporting sexually transmitted diseases. HIV incidence has remained high among IDUs in Baltimore over the past decade. Risk factors for HIV seroconversion differed markedly by sex, with homosexual activity and needle sharing predominant among men and heterosexual activity predominant among women. These findings underscore the importance of interventions for IDUs that are sex-specific and incorporate sexual risk factors. Strathdee, S.A., Galai, N., Safaiean, M., Celentano, D.D., Vlahov, D., Johnson, L., and Nelson, K.E. Sex Differences in Risk Factors for HIV Seroconversion Among Injection Drug Users. Arch Intern Med, 161, pp. 1281-1288, 2001.

Risk Factors Are Compared for Transitions to Injecting In Noninjecting Heroin Users

Researchers sought to compare potential risks for transitioning to injection drug use among noninjecting heroin users with different injecting histories. They recruited 575 noninjecting heroin users for a prospective study on drug use

transitions and conducted baseline interviews between March 1996 and July 1998. Of the 575 heroin users, 385 (67%) had never injected (mean age 33 years), 89 (16%) had injected 1-9 times (mean age 33 years), and 101 (18%) had injected "frequently" or at least 10 or more times (mean age 36 years). To be eligible for the study, none of the former injectors had injected drugs at least 6 months prior to the baseline interview. More African Americans had never injected heroin, and more Latinos had injected 10 or more times in the past. Compared to never injectors and those who injected fewer than 10 times, frequent former injectors were more likely to be homeless, unemployed, to be long-time heroin users, to be younger at first heroin use, to have initiated heroin through injecting drug use, to be unafraid of injecting themselves with needles, to sniff heroin with former IDUs, and to have sex partners who were former IDUs. Frequent and infrequent former injectors were twice as likely as never injectors to perceive that their friends thought that it was "OK" to inject drugs. The data suggest the importance of prevention interventions that target risk factors among never and former noninjectors that may lead to transitions or a resumption of injecting. A significant proportion of such risk factors involve these individuals' peers, their relationships, and their social networks. Neaigus, A., Miller, M., Friedman, S., Hagen, D., et al. Potential Risk Factors for the Transition to Injecting Among Noninjecting Heroin Users: A Comparison of Former Injectors and Never Injectors. Addiction, 96, pp. 847-860, 2001.

Improving the Quality of Life Among Young People Living with HIV

A three-module intervention was designed to address the multiple needs of young persons living with HIV (YPLH): (1) Staying Healthy, (2) Acting Safe, and (3) Being Together. YPLH from three cities were assigned by small cohort to either an Immediate Intervention Condition or a Control Condition. Building on the positive effects of the Staying Healthy and Acting Safe Modules, this paper reports the effects of the Being Together Module, an eight-session cognitive-behavioral intervention aimed at improving YPLHs quality of life. The YPLH (n=104) were aged 14-23 (M=21.03); 73% were male; most were Latino (43%) or African American (24%). YPLH in the Immediate Intervention Condition were significantly less emotionally distressed on multiple indices than those in the Control Condition, and those who attended the intervention showed decreasing emotional distress even when controlling for HIV symptomatology. HIV preventive interventions must promote emotional well-being, as well as reduce risk acts and promote health behaviors. Rotheram-Borus, M.J., Murphy, D.A., Wight, R.G., Lee, M.B., Lightfoot, M., Swendeman, D., Birnbaum, J.M., and Wright, W. Improving the Quality of Life Among Young People Living with HIV. Evaluation and Program Planning, 24, pp. 227-237, 2001.

Drug Use, HIV-related Risk Behaviors and Dropout Status of New Admissions and Re-admissions to Methadone Treatment

New entrants to methadone maintenance treatment programs (MMTP) have been reported to have different drug use patterns than readmissions. This study assesses differences between 211 re-admissions and 128 new admissions to a NYC MMTP. Those new to MMTP were found to be less likely to have ever injected drugs (although those who are injecting appear to be engaging in riskier behaviors than re-admissions who are injectors), have used more types of drugs, and used heroin at higher frequencies in the 30 days prior to admission. Within the first three months of treatment, new admissions dropped out at a higher rate than the re-admissions (31% vs. 20%, $p < 0.05$). The most frequent reasons for dropout, for both groups, included "lost to contact" and incarceration. Further research on strategies to address polydrug use of MMTP admissions is needed. Efforts to identify concerns of new admissions early in treatment, and programs to continue drug treatment services to incarcerated clients, are indicated. Deren, S., Goldstein, M.F., Des Jarlais, D.C., Richman, B.L., Kang, S.Y., and Flom, P.L. Drug Use, HIV-Related Risk Behaviors and Dropout Status of New Admissions and Re-admissions to Methadone Treatment, Journal of Substance Abuse Treatment, 20(2), pp. 185-189, Mar 2001.

Methadone Maintenance as HIV Risk Reduction with Street-Recruited Injecting Drug Users

The objective of this study was to compare changes in HIV risk behaviors between street-recruited opiate injectors who entered and remained in methadone maintenance treatment and those who did not. Three hundred sixteen participants were interviewed at baseline, received outreach interventions, and were interviewed again 6 months later. Significant ($p < .001$) reductions in HIV-related risk behaviors, including frequency of injecting, injecting with used (dirty) needles, and sharing injection paraphernalia, were demonstrated. Participants (31%) who entered and remained in methadone maintenance treatment for at least 90 days before follow-up showed a significantly greater reduction in heroin injections than those who did not. They did not show a greater reduction in using dirty needles or sharing other injection paraphernalia. These findings suggest that although methadone maintenance may reduce injection frequency, it does not reduce other HIV-related risk behaviors beyond what can be accomplished through outreach interventions. Treatment facilities and outreach intervention programs should collaborate to provide a comprehensive approach to reducing HIV risk behaviors among drug injectors both in and out of drug treatment. Kwiatkowski, C.F., and Booth, R.E. Methadone Maintenance as HIV Risk Reduction with Street-Recruited Injecting

Drug Users., J Acquir Immune Defic Syndr., 26(5), pp. 483-489, April 2001.

Regular Outpatient Medical and Drug Abuse Care and Subsequent Hospitalization of Persons Who Use Illicit Drugs

Patients and the public could benefit from identification of factors that prevent drug users' heavy reliance on inpatient care. However, optimal health care delivery models for illicit drug users remain ill defined. This paper reports on an evaluation of associations of outpatient medical and drug abuse care with drug users' subsequent hospitalization rates. A retrospective cohort study of data from longitudinally linked claims for all ambulatory physician/clinic services and drug abuse services covered by the New York State Medicaid program was conducted. Participants totaled 11,556 human immunodeficiency virus positive and 46,687 HIV-negative drug users. The following outcome measures were used: hospitalization in federal fiscal year (FFY) 1997 compared by 4 patterns of care in FFY 1996: regular drug abuse care (>/=6 months in 1 program), regular medical care (>35% of care from 1 clinic, group practice, or individual physician), both, or neither. Data indicated that hospitalization occurred in 55.6% of HIV+ and 37.5% of HIV- drug users, with a mean of 27.5 and 24.5 inpatient days, respectively. In HIV+ drug users, the adjusted odds ratio (AOR) for hospitalization was lowest among those with both regular medical and drug abuse care (AOR, 0.76; 95% confidence interval [CI], 0.67-0.85) followed by those with regular medical care alone (AOR, 0.82; 95% CI, 0.74-0.91) and regular drug abuse care alone (AOR, 0.85; 95% CI, 0.76-0.96) versus those with neither. In HIV- drug users, the AOR of hospitalization was lower for those with regular medical and drug abuse care (AOR, 0.73; 95% CI, 0.68-0.79), regular drug abuse care alone (AOR, 0.71; 95% CI, 0.66-0.76), and regular medical care (AOR, 0.91; 95% CI, 0.86-0.95) versus those with neither. Both types of care showed favorable effects for all but drug abuse-related hospitalizations. Study data suggest that regular drug abuse care with regular medical care is associated with less subsequent hospitalization. Laine, C., Hauck, W.W., Gourevitch, M.N., Rothman, J., Cohen, A., and Turner, B.J. Regular Outpatient Medical and Drug Abuse Care and Subsequent Hospitalization of Persons Who Use Illicit Drugs. JAMA., 285(18), pp. 2355-2362, May 9, 2001.

Social Relationships and Intravenous Drug Use Among Methadone Maintenance Patients

This study examined the extent to which social relationships were associated with continued injection drug use and needle sharing among 252 methadone maintenance patients. Logistic regression analyses indicated that drug use was highest among persons who had a substance using live-in partner and among those with more drug-using social relationships. Among injectors, whites and those who had more people present during IV drug use were more likely to share needles, while those with more emotional support were less likely to do so. These findings suggest that personal relationships strongly influence continued injection drug use and that methadone programs should help patients develop social networks of non-users. In this study of persons on methadone maintenance, findings extend the previous literature by indicating the importance of personal relationships, in particular, live-in partners' and friends' drug use in continued opiate use. Investigators found that the existence of both live-in partners and drug-using social relationships influenced continued drug injection. Furthermore, among persons who continued to inject drugs, social circumstance, such as number of people present during injecting was associated with needle-sharing. Nearly one-third of MMTP patients who received high doses of methadone continued to inject illicit drugs. With nearly one-third of these persons sharing needles, many persons in MMTP are at high risk for HIV infection and transmission of HIV. Gogineni, A., Stein, M.D., and Friedmann, P.D. Social Relationships and Intravenous Drug Use Among Methadone Maintenance Patients. Drug and Alcohol Dependence, 64(1), pp. 47-53, September 1, 2001.

Developing Language Skills of Cocaine-Exposed Infants

In a prospective, longitudinal, quasi-experimental, matched cohort design, Singer et al. assessed the association between level of fetal cocaine exposure and auditory comprehension skills underlying speech-language skills at 1 year corrected age. Maternal self-report and meconium assay were used to define 3 cocaine exposure groups, including nonexposure (n = 131), heavy exposure (n = 66), and light exposure (n = 68). After controlling for drug, medical, and environmental factors, several differences among the exposure groups emerged indicating an association between amount of cocaine exposure and poor infant outcomes. Infants in the heavy exposure group received lower total language scores than infants in the light exposure and nonexposure groups. And, in comparison to infants in the nonexposure group, infants in the heavy exposure group received lower auditory comprehension scores and were more likely to be classified as mildly delayed by total language scores. These findings document significant behavioral teratogenic effects of heavy prenatal exposure to cocaine on developmental precursors of speech-language development. Singer, L.T., Arendt, R., Minnes, S, Salvator, A., Siegel, A.C., and Lewis, B.A. Developing Language Skills of Cocaine-Exposed Infants. Pediatrics, 107, pp. 1057-1064, 2001.

The Search for Congenital Malformations in Newborns With Fetal Cocaine Exposure

Using a prospective longitudinal design, Behnke et al. assessed the association between prenatal cocaine exposure and congenital anomalies in a sample of 272 infants of 154 prenatally identified crack/cocaine users and 154 nonusing matched controls (perinatal deaths and infants not examined within 7 days of birth were not included). Mothers' cocaine use during pregnancy was measured using repeated in-depth histories and urine screens. Measured infant outcomes included 16 anthropometric measurements and a checklist of 180 physical features. In comparison to nonexposed infants, exposed infants were more likely to be born prematurely and to have lower mean birthweights, lengths, and head circumferences. Exposed and nonexposed infants did not differ on remaining anthropometric measurements. Timing and amount of cocaine exposure were not associated with infant outcomes, nor was a consistent pattern of abnormalities associated with prenatal exposure identified. Behnke, M., Eyler, F.D., Garvan, C.W., and Wobie, K. The Search for Congenital Malformations in Newborns with Fetal Cocaine Exposure. Pediatrics, 107, e74, 2001.

Drug Use in One's Social Network and Neighborhood Predicts Use of Heroin and Cocaine

Researchers sought to examine the influence of competing social environmental factors on substance abuse. They conducted a longitudinal study to determine the relative power of social network and neighborhood characteristics in predicting continuing illicit drug use. Adults with a history of injecting drug use (N=342) were followed for one year. Their heroin and cocaine use were assessed semiannually. Multiple logistic regression models were fit to determine the degree to which social network and neighborhood characteristics, assessed at baseline, predicted continuing heroin and/or cocaine use throughout the study period. Of the 342 participants, 236 (69%) reported continuing heroin and/or cocaine use. Drug use by members of the social network was a stronger predictor of participants' continuing drug use (OR=4.31, 95% CI 2.51, 7.40) than was a high level of drug-related arrests in the participant's neighborhood (OR=2.41, 95% CI 1.24, 4.71), after adjusting for drug treatment and demographic variables. Both seemed to have independent effects on study participants' drug use. These findings underscore the importance of breaking social ties with drug-using associates, even for those who reside in high-risk environments. Dissociating from drug-using peers and/or developing relationships with nonusers are generally regarded as important treatment goals and incorporated into drug treatment approaches with demonstrated efficacy. The practical application of these findings is to target the social environment for intervention in the context of drug abuse treatment counseling, but further work will be needed to develop substance abuse treatment and prevention strategies that build coping and social skills to minimize drug abuse in high-risk environments. Schroeder, J.R., Latkin, C.A., Hoover, D.R., Curry, A.D., Knowlton, A.R., and Celantano, D.D. Illicit Drug Use in One's Social Network and in One's Neighborhood Predicts Individual Heroin and Cocaine Use. Ann Epidemiol, 11, pp. 389-394, 2001.

Researchers Identify Predictors of Accidental Fatal Drug Overdose Among IDUs

Researchers sought to evaluate factors associated with accidental fatal overdose among a cohort of 2849 injection drug users in King County, Washington. They used a prospective cohort design and identified 72 deaths by electronically merging subject identifiers with death certificate records. Univariate and multivariate Cox regression analyses were performed to identify predictors of overdose mortality. Thirty-two of the 72 deaths (44%) observed were due to accidental overdose. Independent predictors of overdose mortality were bisexual orientation (relative risk [RR]=4.86; 95% CI=2.30,13.2), homelessness (RR=2.30; 95% CI = 1.06, 5.01), infrequent injection of speedballs (RR=4.84; 95% CI= 1.13, 20.8), and daily use of poppers (RR=22.0; 95% CI=1.74,278). This is consistent with other studies among IDUs, which have found that, even with the competing risk of HIV/AIDS, deaths due to accidental overdose remain a major cause of mortality. Bisexual sexual orientation, homelessness, and drug use, including non-injecting use of powdered cocaine and poppers and recent infrequent injection of speedballs, were found to be important, independent predictors of fatal overdose in this cohort. These characteristics identify high-risk IDUs who may benefit from targeted, educational and risk reduction interventions. Driscoll, P.T., McGough, J., Hagan, H., Thoede, H., Critchlow, C., and Alexander, E.R.. Predictors of Accidental Fatal Drug Overdose Among a Cohort of Injection Drug Users. Am J Public Health, 91, pp. 984-987, 2001.

Study Links Recalled Adolescent Peer Norms About Drug Use With Current Drug Use

Drug use among adolescents is a significant social and public health problem in the U.S. and in many other countries. This study explored the relationship between the drug use norms of young adult peers (recalled from age 15) and subjects' current drug use in the past 12 months. Subjects included two samples of 18-24 year olds from a low income, minority neighborhood in New York City, a probabilistically selected household sample, and a targeted sample of users of cocaine, heroin, crack or injected drugs. Norms varied by drug, and were least for marijuana, and increasingly negative for cocaine, heroin, crack, and injected drugs. There was a strong relationship between recalled norms and current use for both individual drugs and a hierarchically defined level of drug use; this relationship remained significant after controlling for socio-demographics and parental and sibling drug use. Intervention programs for young teens that influence peer selection and norms of groups of adolescents should be developed and

tested. Research is also needed on the social, economic, political, and other determinants of norms in the neighborhood and community context. Flom, P.L., Friedman, S.R., Kottiri, B.J., Neaigus, A., and Curtis, R. Recalled Adolescent Peer Norms Towards Drug Use in Young Adulthood in a Low-Income, Minority Urban Neighborhood. Journal of Drug Issues, pp. 425-444, Spring 2001.

Improved Antioxidant Status Among HIV-infected Injecting Drug Users on Potent Antiretroviral Therapy

Tang and her colleagues from Tufts examined serum antioxidant levels (retinal, alpha-and gamma-tocopherols, alpha-and beta-carotenes, lycopene, lutein/zeanthin, and beta-cryptoxanthin) in 175 HIV-positive and 210 HIV-negative IVDUs in Baltimore, MD. Of these patients, 30 were receiving antiretroviral therapy (ART) including a protease inhibitor (PI), 43 ART without a PI, 22 on montherapies, and 80 were not on any ART. Among HIV+ subjects, there were significant differences in antioxidant levels by ART regimen. In multivariate models adjusting for injecting drug use, dietary intake, supplement intake, gender, and alcohol intake, significant overall differences by ART regimen were observed for alpha-tocopherol, beta-carotene, and beta-cryptoxanthin. Serum levels of these three antioxidants were significantly higher in the PI group than in the other three ART groups combined. These data provide indirect evidence of the effectiveness of PIs in lowering oxidative stress levels in HIV+ IDUs. Tang, A. Smit, E., Semba, R., Shah, N., Lyles, C.M., Li, D., and Vlahov, D. JAIDS, 23 (4), pp. 321-326, 2000.

Study Links Joint Drug Purchases With Drug Preparation Risk Behaviors Among IDUs

In the process of preparing jointly purchased drugs, IDUs may share drug preparation materials and use a single syringe to distribute injectable drugs. The aim of this study was to examine the association of joint drug purchasing with drug preparation risk behaviors among Puerto Rican IDUs. The study sample comprised 555 IDUs from New York City and 297 from Puerto Rico. IDUs reported pooling money for 12% of the injection episodes in New York, and for 14% of the injection episodes in Puerto Rico. In both study sites, correlation coefficients between frequency of pooling money and drug preparation behaviors were .30 or larger. After controlling for sociodemographics, drugs injected, and injection frequency, pooling money was significantly related to all four drug preparation behaviors in both study sites: using rinse water before or after someone else, drawing the drug from the cooker before or after someone else, transferring drugs from one syringe to another, and squirting the drug solution back into the cooker. Results of this study show that during the preparation and division of injectable drugs, IDUs practice other behaviors beyond the shared use of syringes (i.e., needle sharing) that can expose them to infection with HIV and other blood-borne pathogens. HIV prevention interventions need to be cognizant of the joint purchasing of drugs and its relationship to drug preparation risk behaviors. Colon, H.M., Finlinson, H.A., Robles, R.R., Deren, S., Andia, J., K, S.Y., and Oliver-Velez, D. Joint Drug Purchases and Drug Preparation Risk Behaviors Among Puerto Rican Injection Drug Users. AIDS and Behavior, 5(1), pp. 85-96, 2001.

Study Examines Needle Exchange Program Attendance as Correlate of Injection Risk

Needle sharing has long been recognized as a primary route of HIV infection, but research has also shown that HIV antibody is detectable in injection supplies other than needles. In this study, researchers tested the frequency of attendance at a Providence, Rhode Island needle exchange program (NEP) as a correlate of injection risk, including not just sharing needles, but also sharing cookers, cottons filters, cleaning the skin before injecting, and using bleach as a needle disinfectant. Between 1997 and 1998, they asked 354 individuals seen at the NEP to enroll in the study, of which 248 (70%) consented. All of the respondents reporting injecting on a daily basis in the past month, and most were injecting at least three times a day. Most were injecting cocaine only. Over half of the respondents (56%) reported NEP attendance five or more times per month; most of the less frequent attendees (33% of the sample) reported using the NEP two to four times a month; and the remaining 11% attended the NEP not more than once per month. Results showed that drug users who attended the NEP less frequently were more likely to report needle sharing, less likely to report always cleaning their skin, and more likely to report sharing cookers. The Providence NEP is one at which alcohol swabs and cookers are distributed along with clean needles. These findings suggest that, as part of a comprehensive approach to HIV prevention, NEPs represent a valuable and under-exploited opportunity to promote risk reduction efforts beyond the avoidance of needle sharing. In particular, NEPs should be distributing risk reduction supplies in addition to clean needles and educational information about HIV/AIDS. They should also adopt strategies (e.g., outreach and expanded days and hours of operation) to access persons who are hard-to-reach and at highest risk and to encourage more frequent attendance. Longshore, D., Bluthenthal, R.N., and Stein, M.D. Needle Exchange Program Attendance and Injection Risk in Providence, Rhode Island. AIDS Education and Prevention, 13(1), pp. 78-90, 2001.

Patterns of Needle Acquisition and Correlates of NEP Attendance in Baltimore

Researchers examined factors associated with obtaining syringes from a needle exchange program (NEP) and other safer sources in Baltimore, Maryland. They conducted a cross-sectional, face-to-face survey of 741 drug injectors recruited by snowball sampling techniques. They also conducted a brief open-ended interview with a subsample of respondents. Most of the participants (85%) obtained needles from street needle sellers. Only 8% obtained their needles exclusively from safer sources (NEPs, pharmacies, hospitals, or patients with diabetes). Cocaine use was associated with obtaining needles from the NE but not from exclusively safer sources. Obtaining needles from only safer sources was associated with being female and less frequent needle sharing and shooting gallery attendance. Among HIV-seropositive participants, those who were diagnosed before the year that the NEP began were more likely to obtain needles from safer sources. Participants who sold needles reported that it was easy to make used needles appear to be unused and some admitted selling used needles as new. Street needle sellers are an important source of needles for drug injectors and few injectors appear to be able to determine whether these needles are clean. Individual sealing of diabetic syringes may reduce the risk of blood-borne infections by enabling drug injectors and patients with diabetes to better judge the sterility of the needles they purchase. Latkin, C.A. and Forman, V.L.. Patterns of Needle Acquisition and Sociobehavioral Correlates of Needle Exchange Program Attendance in Baltimore, Maryland. J Acquir Immune Defic Syndr, 27(4), pp. 398-404, 2001.

HIV Risks Among IDUs in Low, Medium, and High Seroprevalence Communities

Researchers compared HIV-related risk behaviors for IDUs across communities with low, moderate, and high seroprevalence rates among IDUs. They analyzed interview data collected from 12,072 seronegative IDUs who participated in a large, 22-site HIV prevention program (i.e., NIDA's Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program). The 22 sites were categorized according to seroprevalence among IDUs: sites with seropositive rates of 5% or less were classified as having low seroprevalence, sites with 6%-19% were classified as moderate, and sites with rates of 20% or higher were classified as high seroprevalence; 10 sites were classified as low, 8 sites as moderate, and 4 sites as high. Data on injection risk behaviors showed significantly higher rates of injection in high seroprevalence communities, almost 2.5 times higher than in low and moderate seroprevalence communities (186.0 vs 79.2 [low] and 60.7 [moderate]). Higher percentages of IDUs in low seroprevalence communities reported using other syringes (52%) and paraphernalia (59%) compared with sites having moderate and high seroprevalence levels. IDUs in low seroprevalence sites also reported the highest rate of giving or loaning their used syringes (45% vs 33% in moderate and high seroprevalence level communities). IDUs from high seroprevalence communities were least likely to report engaging in sex in the 30 days prior to the interview (54% vs 75% in the sites with lower seroprevalence levels). Among those who reported engaging in sex, IDUs in lower seroprevalence sites reported the highest rates of having sex with another IDU during the preceding 30 days (51% vs 41% and 30% in moderate and high seroprevalence sites, respectively). Injection- and sex-related risk behaviors were significantly higher in low seroprevalence communities. These differences have implications for developing risk reduction messages and deploying HIV intervention strategies on a continual basis across all IDU communities. Deren, S., Beardsley, M., Coyle, S., Singer, M., and Kang, S. HIV Risk Behaviors Among Injection Drug Users in Low, Medium, and High Seroprevalence Communities. AIDS and Behavior, 5(1), pp. 45-50, 2001.

Concurrence of Drug Users' Self-Reports of Current HIV Status and Serotest Results

This study examined the concurrence of drug users' self-reports of current HIV status with serotest results. The analyses are based on data obtained from face-to-face interviews with 7,256 out-of-treatment injection drug and/or crack users in 10 sites that participated in NIDA's Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program. Although the degree of concurrence between HIV-negative individuals' self-reports of their current HIV status and their serostatus results was high (specificity, 99%), this was not the situation for persons who tested positive for HIV (specificity 44%). Lack of concurrence between self-report of HIV status and serotest results was most pronounced among individuals who tested positive for HIV. HIV-seropositive persons who injected drugs but did not use crack were more likely than crack users to report that they were HIV-positive. In this study, prevalence estimates based on self-report were found to significantly underestimate the number of individuals who were infected with HIV. These results suggest the importance of empirically assessing current HIV status among drug users through biologic testing for the virus. In addition, more attention needs to be given to the placing and wording of questions used to elicit self-report of current HIV status; for example, disclosure of HIV status may be more socially acceptable if questions that elicit HIV status are prefaced with a statement that many individuals in the community have the virus. Strauss, S.M., Rindskopf, D.M., Deren, S., and Falkin, G.P. Concurrence of Drug Users' Self-Report of Current HIV Status and Serotest Results, J Acquir Imm Defic Syndr, 27(3), pp. 301-307, 2001.

Predictors of Condom Use Among Young Adults in High-Risk Neighborhoods

Researchers sought to determine predictors of condom use in the heterosexual non-commercial sexual relationships of young adults who neither inject drugs nor use cocaine, heroin, or crack, in a neighborhood with widespread drug-

use-connected HIV. They analyzed data from a sample of 279 young adults, aged 18-24, who have never injected drugs or used heroin, cocaine, or crack in the last year. The subjects were recruited from the Bushwick neighborhood of New York City from July 1997 to September 1999. A face-to-face interview included items about sociodemographic background, substance use, and sexual networks. The focus of the analysis was on self-reported sexual relationships and consistent (100%) condom use over the prior year with the partner. Subjects had 337 heterosexual non-commercial relationships. Consistent condom use was reported in 32% of the relationships. In multiple logistic regression, consistent condom use was more likely in relationships that were not "very close" (odds ratio[OR]=3.92, 95% CI=2.08, 7.52); and in relationships of subjects whose peer norms support condom use (OR=1.94, 95% CI=1.43, 2.69) and who are not problem drinkers (OR=8.70, 95% CI=2.22, 58.8). Consistent condom use remains uncommon among youth in this high-risk neighborhood. It is important to keep HIV from entering the sexual networks of youth in communities such as this through programs aimed at drug injectors and their sexual partners. Programs to increase condom use among young adults should focus on strengthening norms that promote safer sex to protect oneself and others. In addition, because problem drinking is related to less condom use among young adults in this study, assistance should be given to youth who are problem drinkers. Friedman, S.R., Flom, P.L., Kottiri, B.J., Neaigus, A., Sandoval, M., Curtis, R., Des Jarlais, D.C., and Zenilman, J.M. Consistent Condom Use in the Heterosexual Relationships of Young Adults Who Live in a High-HIV-Risk Neighborhood and Do Not Use "Hard Drugs." AIDS Care, 13(3), pp. 285-296, 2001.

HIV Risk Networks and HIV Transmission Among Injecting Drug Users

This research sought to demonstrate how injecting drug users' HIV risk networks affect their risk for HIV infection and influence their HIV risk behaviors. Concepts utilized in a network approach were specified, including (1) the distinction between risk networks (the people with or among whom IDUs, or others at risk of infection with HIV, engage in HIV risk behaviors) and social influence networks (the people who shape each others behavior), (2) the extent to which risk networks and social influence networks overlap, and (3) three levels of network analysis i.e., the dyad, personal networks, and sociometric networks. The role of IDUs' risk networks in the transmission of HIV and their influence on promoting and preventing HIV risk behaviors have been demonstrated in a number of studies of IDUs in New York City and other locations. By studying IDUs risk networks as conduits of HIV infection, network analysis can help in the identification of network structures that promote HIV transmission, such as bridge populations and concurrent partnerships. Network analysis can also help to identify and locate socially identifiable groups, such as "core groups," that may perpetuate the HIV epidemic among IDUs and may also be a major source for the heterosexual spread of HIV to other populations. The identification of such high-risk groups and network structures can help to target interventions where they have the most effect. Neaigus, A., Friedman, S.R., Kottiri, B.J., and Des Jarlais, D.C. HIV Risk Networks and HIV Transmission Among Injecting Drug Users. Evaluation and Program Planning, 24, p. 226, 2001.

Sexual Transmission of HIV-1 Among Injection Drug Users in San Francisco, USA: Risk Factor Analysis

Many new HIV-1 infections in the USA occur in injection drug users (IDUs). HIV-1 seroconversion of IDUs is mainly associated with injection-related risk factors. Harm reduction programs concentrate on injection-risk behavior. The aim of this study was to establish whether injection or sexual risk factors, or both, were associated with HIV-1 antibody seroconversion of street-recruited IDUs in San Francisco, from 1986 to 1998. IDUs were enrolled every 6 months from four community sites. Investigators did a nested case control study comparing 58 respondents who seroconverted between visits with 1134 controls who remained seronegative. Controls were matched with cases by sex and date. Adjusted odds ratios (AOR) and 95% confidence intervals (CI) were calculated for men and women by use conditional logistic regression. Men who had sex with men were 8.8 times as likely to seroconvert (95% CI = 3.7, 20.5) as heterosexual men. Women who reported having traded sex for money in the past year were 5.1 times as likely as others to seroconvert (95% CI = 1.9, 13.7). Women younger than 40 years were more likely to seroconvert than those 40 years or older (AOR=2.8; 95% CI=1.05, 7.6), and women who reported having a steady sex partner who injected drugs were less likely to seroconvert than other women (AOR=0.32; 95% CI=0.11, 0.92). HIV-1 seroconversion of street-recruited IDUs in San Francisco is strongly associated with sexual behavior. HIV-1 risk might be reduced by incorporation of innovative sexual-risk reduction strategies into harm-reduction programs. Kral, A.H., Bluthenthal, R.N., Lorvick, J., Gee, L., Bacchetti, P., and Edlin, B.R. Sexual Transmission of HIV-1 Among Injection Drug Users in San Francisco, USA: Risk Factor Analysis. Lancet, 357, pp. 397-401, 2001.

Gender Differences in HIV-related Sexual Risk Behavior among Urban African American Youth: a Multivariate Approach

Alcohol and other drug (AOD) use during sexual encounters, sexual partner's age, perceived HIV risk and perceived

condom effectiveness were studied among 388 sexually active African American youth. Cluster analysis of condom use, number of partners, and frequency of sexual intercourse identified four groups: low risk, monogamy strategy, condom strategy, and high risk. Low-risk youth used condoms consistently and had few partners. High-risk youth used condoms inconsistently with many partners. Monogamy strategy youth used condoms inconsistently but had few partners. Condom strategy youth used condoms consistently with a moderate number of partners. The high-risk group included more males and the monogamy group included more females. High-risk males reported more AOD use during sexual activity than all females, and low-risk or condom strategy males. Females had older partners, rated condoms as less effective and perceived lower HIV/AIDS risk than males. Results suggest differential HIV risk mechanisms by gender. Implications for gender-specific HIV prevention are discussed. Newman, P.A., and Zimmerman, M.A. Gender Differences in HIV-related Sexual Risk Behavior among Urban African American Youth: A Multivariate Approach. AIDS Educ Prev,12(4), pp. 308-325, 2000.

Perspectives on Use of Vaginal Microbicides Among Drug-Involved Women

A study was conducted to obtain potential users' perspectives on vaginal microbicides from a population of women at high risk for HIV. Using street outreach sampling techniques, researchers interviewed 743 drug-using women and female sexual partners of male IDUs in Bridgeport, Connecticut, Providence, Rhode Island, and San Juan, Puerto Rico. All of the women were current users of heroin and/or cocaine. Ninety percent of the women said they would be very likely to use micobicides with paying partners (who paid for sex with money or drugs) and 78% with primary partners (p=0.001). Even after potential product characteristics were rated as unacceptable, such as irritation or burning, women expressed a high likelihood of potential use. Latinas had significantly higher predicted likelihood of use with primary (p=0.001) and paying partners (p=0.018) than blacks and whites. Eighty percent of respondents preferred products that provided additional lubrication. More than 80% of respondents said they would want their primary partners to know of their microbicide use and 42% (p=0.001) said that they would want their paying partners to know. Women's concern about a paying partner's violent response to suggested use of risk reduction measures was inversely related to predicted likelihood of microbicide use (p=0.045). Microbicides should be assessed in the context of the potential users' actual relationships and cultures. Achieving broad acceptability among drug-involved women will require a range of products. Hammett, T.M., Norton, G.D., Mason, T.H., Langenbahn, S., Mayer, K.H., Robles, R.R., Feudo, R., and Seage, G. Drug-Involved Women as Potential Users of Vaginal Microbicides for HIV and STD Prevention: A Three-City Survey. Journal of Women's Health and Gender-Based Medicine, 9(10), pp. 1071-1080, 2000.

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

Research Findings

Epidemiology, Etiology and Prevention Research

Predicting Violent Behavior

The social development model seeks to explain human behavior through specification of predictive and mediating development relationships. It incorporates the effects of empirical predictors ("risk factors' and "protective factors) for antisocial behavior and seeks to synthesize the most strongly supported propositions of control theory, social learning theory, and differential association theory. This article examines the fit of the social development model using constructs measured at ages 10, 13, 14, and 16 to predict violent behavior at age 18. The sample of 808 is from the longitudinal panel of the Seattle Social Development Project, which in 1985 surveyed fifth-grade students from schools serving high crime neighborhoods in Seattle, Washington. Structural equation modeling techniques were used to examine the fit of the model to the data. Findings indicate that the social development model adequately predicts violence at age 18 and mediates much of the effect of prior violence. Huang, B., Kosterman R., Catalano, R.F., Hawkins, J.D., and Abbott, R.D. Modeling Mediation in the Etiology of Violent Behavior and Adolescence: A Test of the Social Development Model. Criminology, 39(1), pp. 75-107, 2001.

Timing of Violence Initiation

This study used data from the Seattle Social Development Project (SSDP) to compare social developmental mechanisms predictive of violence at age 18 for youth who initiated violence in childhood compared with those who initiated violence during adolescence. The SSDP is a theory-guided longitudinal study of youth development and behavior that began in 1985 when children were in the fifth grade. A multiple-group structural equation modeling approach was used to test relationships among social development model constructs hypothesized to predict violence and other forms of antisocial behavior. Analyses revealed that socialization pathways leading to violence at age 18 were similar for those who initiated violence in childhood and in adolescence, suggesting that the same preventive interventions may be effective for individuals in both groups. Herrenkohl, T.I., Huang, B., Kosterman, R., Hawkins, J.D., Catalano, R.F., and Smith, B.H. A Comparison of Social Development Processes Leading to Violent Behavior in Late Adolescence for Childhood Initiators and Adolescent Initiators of Violence. Journal Of Research In Crime And Delinquency, 38(1), pp. 45-63, 2001.

Adolescent Problem Behavior by Observed Psychopathology

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

2000.

Session Specific Outcomes

Like their urban counterparts, adolescents from rural areas are at risk for health and behavior problems, including alcohol and other drug use. This study tested the effects of specific sessions of a parent-training intervention on parenting practices. Preparing for the Drug Free Years, an intervention designed to prevent adolescent substance abuse and other problem behaviors was tested with 209 rural families who were randomly assigned to an intervention or a wait-list control condition. Analyses of covariance comparing adjusted post-test scores revealed that parents in the intervention condition reported significant improvements in parenting behaviors targeted in specific sessions when compared with controls. Effects were most pronounced among mothers. No significant effects were found for non-targeted parenting behaviors, and targeted behaviors were most improved among parents attending relevant program sessions. These results strengthen the internal validity of the study and increase the plausibility that reported improvements were due to the intervention. Kosterman, R., Hawkins, J.D., Haggerty, K.P., Spoth, R., and Redmond, C. Preparing for the Drug Free Years: Session-specific Effects of a Universal Parent-training Intervention with Rural Families. Journal of Drug Education, 31(1), pp. 47-68, 2001.

Aggressive Interactions

Results of a seven-session general population intervention for parents and their sixth-grade children were examined to determine the long-term effects of this intervention on aggressive and hostile behaviors during adolescence. Twenty-two public schools were randomly assigned to the Iowa Strengthening Families Program or a control condition. Measures included independent observer ratings of 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-intervention and post-intervention), 7th, 8th, and 10th grades. All measures showed a generally positive trend in intervention-control group differences over time. During 10th grade, significant intervention-control differences were found for adolescent self-report of aggressive and destructive conduct (P=.01),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 (P =.01); differences in family member reports of those behaviors were not significant. Supplemental analyses of both interactional behavior measures, specific to parent sex, indicated significant experimental group differences in interactions with mothers (P=.04 for both measures) but not with fathers. Thus, brief family competency-training interventions designed for general populations can reduce aggressive and hostile behaviors in adolescents' interactions with parents and adolescent aggressive behaviors outside of the home setting. Spoth, R.L., Redmond, C., and Shin, C. Reducing Adolescents' Aggressive And Hostile Behaviors - Randomized Trial Effects of a Brief Family Intervention 4 Years Past Baseline. Archives of Pediatrics & Adolescent Medicine, 154(12), pp. 1248-1257, 2000.

Project EX - Outcomes of a Teen Smoking Cessation Program

Project EX is an eight-session teen school-based clinic tobacco use cessation program that involves the inclusion of enjoyable motivating activities (games, talk show, and alternative medicine-type) to try to enhance quit rates among youth. This clinic program was tested in a three-group experimental design: clinic-only, clinic plus a school-as-community (SAC) component, and standard care control. Eighteen schools were assigned to the three conditions using a randomized block design. A total of 335 smokers participated in the study, making this the largest controlled teen smoking cessation field trial conducted to date. Seventeen percent of the smokers enrolled in the clinics had reports of having quit smoking for at least the last 30 days at 3-month follow-up (5 months after the program quit day), compared to only 8% of the control condition smokers over the same time period. The Project EX clinic component appears to be an effective means of tobacco use cessation among teens. Sussman, S., Dent. C.W., and Lichtman, K.L. Project EX - Outcomes of a Teen Smoking Cessation Program. Addictive Behaviors, 26 (3), pp. 425-438, 2001.

Multimethod Assessment of Psychopathology Among DSM-IV Subtypes of Children with Attention-Deficit/Hyperactivity Disorder

Using data based on self-, parent, and teacher reports, various aspects of psychopathology were assessed in a large sample of control children and those with ADHD. Confirmatory factor analysis was employed to extract response bias from latent constructs of aggression, anxiety, attention problems, depression, conduct disorder, and hyperactivity. These latent constructs were then entered into logistic regression equations to predict membership in control versus ADHD groups, and to discriminate between ADHD subtypes. Results of the regression equations showed that higher levels of attention problems and aggression were the best predictors of membership in the ADHD group relative to

controls. Logistic regression also indicated that a higher degree of aggression was the only significant predictor of membership in the ADHD-Combined group compared to the ADHD-Inattentive group. However, when comorbid diagnoses of Oppositional Defiant Disorder and Conduct Disorder were controlled for in the logistic regression, greater hyperactivity rather than aggression was the sole variable with which to distinguish the ADHD-Combined from the ADHD-Inattentive subtype. Crystal, D.S., Ostrander, R., Chen, R.S., and August, G.J. Multimethod Assessment of Psychopathology Among DSM-IV Subtypes of Children with Attention-Deficit/Hyperactivity Disorder: Self-, Parent, and Teacher Reports. Journal of Abnormal Child Psychology, 29(3), pp. 189-205, 2001.

Replication of a Problem Behavior Model with American Indian, Hispanic, and Caucasian Youth

The replicability of a model of family and peer influences on adolescent problem behavior was evaluated with samples of adolescent boys and girls from three ethnic groups: American Indians, Hispanics, and Caucasians. Participants were 1,450 seventh-grade students from 16 communities. The model included links between three aspects of family functioning and adolescents' association with deviant peers. Those variables were hypothesized predictors of adolescents' problem behavior (antisocial behavior; poor school performance, and frequency of substance use). The resulting cross-sectional model showed good consistency across the three ethnic groups for both genders, but some subgroup differences emerged in the magnitude of relations between monitoring and adolescents' associations with deviant peers and between substance use and the problem behavior construct. With those qualifications, the model was applicable to Hispanic and Native American adolescents in the sample. Barrera, M., Jr., Biglan, A., Ary, D.V., and Li, F. Replication of a Problem Behavior Model with American Indian, Hispanic, and Caucasian Youth. Journal of Early Adolescence, 21 (2), pp. 133-157, 2001.

Further Support for the Developmental Significance of the Quality of the Teacher-Student Relationship

Sociometric nominations and ratings assessed peer's perceptions of supportive and conflicted teacher-student relationships, evaluations of children's positive and negative attributes, and peer-rated liking. Participants were 993 3rd and 4th grade children. Girls obtained higher Teacher Support and lower Teacher Conflict scores, compared to boys. The pattern of correlations between teacher-student relationship scores and other peer evaluations was comparable across genders. Both Teacher Support and Teacher Conflict made independent contributions to peer evaluations of children's competencies and acceptance of children. Teacher Support contributes to the prediction of social preference scores beyond that predicted by peer nominations of aggression. Teacher ratings of aggression were available for a sub-sample of 71 behaviorally at-risk children. For this sub-sample, Teacher Support predicted social preference scores after controlling for both peer nominations of aggression and teacher ratings of aggression. Peer's perceptions of Teacher Support may function as an "affective bias", influencing both perceptions of child competencies and liking for the child. Implications for these findings for classroom-based interventions with peer-rejected children are discussed. Further Support for the Developmental Significance of the Quality of the Teacher-Student Relationship. Hughes, J.N., Cavell, T.A., and Willson, V. Journal of School Psychology, 39(4), pp. 289-301, 2001.

School-based Tobacco Use Prevention and Cessation: Where are We Going?

The objective of this article is to discuss the past, present, and future directions of school-based tobacco use prevention and cessation research. It discusses the origins of tobacco use prevention research; how prevention research advanced with empirical etiologic work; the genesis of comprehensive social influences programming and its contents; multiple modalities of programming beyond the school setting; and the rebirth of teen cessation programming and the issue of dissemination. Results indicate there are many avenues of teen tobacco use prevention and cessation research and practice that need continued exploration, particularly regarding effects on mediation and teen cessation. This discussion provides background to assist health behavior researchers and practitioners to move forward in this area. Sussman, S. School-based Tobacco Use Prevention and Cessation: Where are We Going? American Journal of Health Behavior 20, 25(3), pp. 191-199, 2001.

Predicting Regular Cigarette Use Among Continuation High School Students

This article provides a 1-year prospective examination of social, behavioral, intrapersonal and demographic factors that predict transition from experimental to regular cigarette use among continuation (i.e. alternative) high school students. A cohort of 252 students completed baseline and 1-year follow-up questionnaires on health behaviors. Relatively low smoking prevalence estimates, intention to smoke in the next year, violence perpetration, perceived stress, sensation seeking, and male gender predicted the transition to regular use 1 year later. This implies that

intrapersonal variables may be relatively important in predicting the progression from experimental to regular smoking. Skara, S., Sussman, S., and Dent, C.W. Predicting Regular Cigarette Use Among Continuation High School Students. American Journal of Health Behavior, 25(2), pp. 147-156, 2001.

Concurrent Prediction of Drug Use Among High-risk Youth

Correlates of drug use were examined in a continuation (i.e. alternative) high school sample of 1,315, using canonical correlation analysis. Fourteen demographic, attitudes/belief and psychosocial pressure/anxiety-type variables were included as concurrent predictors. Eight drug-use-related measures were also placed into the analysis as outcome variables. Two factors were revealed. White ethnicity, not being Latino, all attitude/belief measures, and family conflict and depression showed relatively high loadings on the first predictor factor, and were associated with all drug-use measures. Latino, all attitude/belief measures, and family conflict and depression showed relatively high loadings on the first predictor factor, and were associated with all drug-use measures. Latino ethnicity and being relatively unacculturated (i.e., tending to speak Spanish), most of the attitude/belief measures (but not sensation seeking or spirituality), and perceived peer approval to use drugs, trait anxiety, and depression showed relatively high loadings on the second predictor factor, and were associated with the hard-drug-use measures. These results suggest that there is a subgroup of unacculturated Latino youth who are anxious, who perceive they will achieve peer approval by using drugs, and who tend to use hard drugs. Indicated drug abuse prevention strategies may need to be tailored to this subgroup when developing and implementing programming. McCuller, W.J., Sussman, S., Dent, C.W., and Teran, L. Current Prediction of Drug Use Among High-risk Youth. Addictive Behaviors 26 (1), pp. 137-142, 2001.

From Early to Late Adolescence: Alcohol Use and Anger Relationships

The purpose of this article is to evaluate the longitudinal relationship of alcohol use in early adolescent to anger in late adolescence. Data from 1201 students were collected in Indianapolis, Indiana, from 1987 to 1993 as part of a large drug abuse prevention trial. Subjects were asked four anger-related questions: "When I have a problem, I get mad at people," "When I have a problem, I do bad things or cause trouble," and "I am a hotheaded person." Two additional items asked subjects to report the number of alcoholic drinks consumed and frequency of drunkenness in the past 30 days. Odds ratios were used to assess the predictive relationship of alcohol use in early adolescence to anger in late adolescence. Early use of alcohol increased the odds of later anger. Specifically, alcohol use in the past month in grades 6/7 increased the odds in grades 11/12 of saying or doing nasty things, self-reported hotheadedness, and high anger on a composite anger scale. Drunkenness in the past month in grade 6/7 increased the odds of self-reported hotheadedness and high anger on the anger scale in grade 9/10 and doing something bad to cause trouble in grade 11/12. For subjects in grade 9/10, alcohol use in the past month increased the odds in grade 11/12 of doing something bad to cause trouble, saying or doing nasty things, and self-reported hotheadedness. This study showed that alcohol use in early adolescence was associated with increased anger, both in middle and late adolescence, controlling for gender, age, and socioeconomic status. These findings suggest that alcohol and drug prevention programs delivered in early adolescence may have the capacity to prevent risk for later anger and related violent behavior. Weiner, M.D., Pentz, M.A., Turner, G.E., and Dwyer, J.H. From Early to Late Adolescence: Alcohol Use and Anger Relationships. Journal of Adolescent Health, 28(6), pp. 450-457, 2001.

Identifying Trajectories of Adolescent Smoking: An Application of Latent Growth Mixture Modeling

The goal of this study was to identify discrete longitudinal patterns of change in adolescent smoking using latent growth mixture modeling. Five distinct longitudinal patterns were identified. A group of early rapid escalators was characterized by early escalation (at age 13) that rapidly increased to heavy smoking. A pattern characterized by occasional puffing up until age 15, at which time smoking escalated to moderate levels was also identified (late moderate escalators). Another group included adolescents who, after age 15, began to escalate slowly in their smoking to light (0.5 cigarettes per month) levels (late slow escalators). Finally, a group of stable light smokers (those who smoked 1-2 cigarettes per month) and a group of stable puffers (those who smoked only a few puffs per month) were also identified. The stable puffer group was the largest group and represented 25% of smokers. Colder, C.R., Mehta, P., Balanda, K., Campbell, R.T., Mayhew, K., Stanton, W.R., Pentz, M., and Flay, B.R. Identifying Trajectories of Adolescent Smoking: An Application of Latent Growth Mixture Modeling. Health Psychology, 20(2), 2001.

Predictors of Smoking Cessation from Adolescence into Young Adulthood

Although smoking cigarettes is hazardous to health and cessation has positive health benefits, few smokers are able to successfully quit. The purpose of this study was to examine the predictors of smoking cessation in a non-clinical sample of 134 male and 190 female, young adult, regular (daily) smokers within a social learning and maturing-out

framework. Four waves of prospective, longitudinal data from a community sample followed from adolescence into young adulthood were analyzed. Logistic regression analyses were used to test the effects of differential associations, definitions, differential reinforcement, and changes in adult role status on smoking cessation in young adulthood. Becoming married to a nonsmoker and decreases in the proportion of friends who smoked were significant predictors of cessation. Current smokers and stoppers did not differ significantly in terms of prior intensity of cigarette use or alcohol abuse/dependence. They also did not differ in terms of psychological characteristics, including depression and prior coping use of cigarettes. Social networks were more important than social roles for predicting cessation in young adulthood. Thus, smoking cessation programs should focus on social learning processes. Chen, P.H, White, H.R., and Pandina, R.J. Predictors of Smoking Cessation from Adolescence into Young Adulthood. Addict Behav, 26(4), pp. 517-529 2001.

Psychosocial Correlates of Adolescent Smoking Patterns

The purpose of this cross-sectional study of high school students was to examine and to compare the psychosocial characteristics associated with four dimensions of smoking: abstinence (never vs. ever), experimentation, frequency (daily vs. non-daily), and persistence (former vs. current). Six smoking groups were defined: never smokers (n = 862), experimenters (n = 235), former non-daily (n = 80), current non-daily (n = 73), former daily (n = 71), and current daily (n = 110). As found in previous studies, smokers compared to never-smokers had substantially higher scores on most indices of dysfunction. Both frequent and persistent smoking was associated with higher lifetime prevalence of drug abuse/dependence and number of friends who smoke. Smoking persistence was uniquely related to greater conflict with parents and more problematic academic behavior, and smoking frequency was uniquely associated with higher impulsiveness. The associations between smoking status and the psychosocial functioning did not differ by gender. Lewinsohn, P.M., Brown, R.A., Seeley, J.R., and Ramsey, S.E. Psychosocial Correlates of Cigarette Smoking Abstinence, Experimentation, Persistence and Frequency during Adolescence. Nicotine and Tobacco Research, 2(2), pp. 121-131, 2000.

The Association between Inattention and Tobacco Use in Early Adolescence

This longitudinal study examined the relation between distinct dimensions of attention-deficit hyperactivity disorder (ADHD) and substance use among 177 clinic-referred boys (initially between ages 7 and 12) followed thru age 15. The use of tobacco, alcohol, marijuana, or other illicit drugs was reported by 78% of the participants, with 51% reporting any tobacco use. Although the inclusion of conduct disorder (CD) rendered all bivariate relationships with the full diagnosis of ADHD nonsignificant, adolescent inattention, considered independently, was associated with a 2.3 times greater risk for concurrent tobacco use - even after controlling for CD, duration of tobacco use by age 12, poor parental communication in childhood, and ethnicity. These findings highlight the importance of considering the risks for substance use separately by individual dimensions of ADHD. Burke, J.D., Loeber, R., and Lahey, B.B. Which Aspects of ADHD are Associated with Tobacco Use in Early Adolescence? Journal of Child Psychology and Psychiatry, 42(4), pp. 493-502, 2001.

Psychosocial Versus Nicotine-Only Self-Report Measures for Predicting Follow-Up Smoking Status

The most popular measure of tobacco dependence, the Fagerstrom Tolerance Questionnaire (FTQ), measures only tobacco-specific behaviors. In contrast, the most popular assessment of addiction among drug users is the Addiction Severity Index (ASI). Most of the subscales comprising the ASI are psychosocial measures, not drug-specific measures. A study was undertaken to compare the predictive utility of these two contrasting measures. The NAS (adapted from the FTQ) and the Addiction Severity Index (ASI) were used to predict future smoking status in a cohort of polydrug users followed annually for 3 years. The baseline NAS score explained more of the variance in Time 2 and Time 3 smoking status than did the ASI subscales. When previous smoking status was included as a covariate, however, the NAS no longer predicted future smoking status, whereas the ASI Subscales continued to explain significant variance in future smoking status. Results suggest that when past smoking behavior is known, a respondent's legal status and alcohol use may be more useful than a measure of tobacco dependence for predicting future smoking status. McCarthy, W.J., Zhou, Y., and Hser, Y. Psychosocial Versus Nicotine-Only Self-Report Measures for Predicting Follow-up Smoking Status. Journal of Behavioral Medicine, 24(1), pp. 75-91, 2001.

Abuse, Support, and Depression among Homeless and Runaway Adolescents

This study examines the effectiveness of social support networks on psychological well being among 602 homeless and runaway adolescents. The respondents were interviewed in shelters, drop-in centers, and on the streets in cities of four midwestern states (Missouri, Iowa, Nebraska, and Kansas). The path model was used to test the direct effect of family abuse and precocious independence on adolescent depressive symptoms and indirect effects through social

support networks. Results indicate that although abusive family origins contribute directly to depressive symptoms there are indirect effects of family abuse and early independence through social support networks. Family abuse and early independence drive homeless adolescents to rely on peers for social support. While support from friends on the street reduces depression, association with deviant peers increases depression. Bao, W.N., Whitbeck, L.B., Hoyt, D.R. Abuse, Support, and Depression among Homeless and Runaway Adolescents. J Health Soc Behav, 41(4), pp. 408-420 2000.

Influence of Parental Child-rearing Practices and Environment on Adolescent Drug Use

This study examined the relationship between the domains of environmental factors, family illegal drug use, parental child-rearing practices, maternal and adolescent personality attributes, and adolescent illegal drug use. A nonclinical sample of 2,837 Colombian youths and their mothers were interviewed about intrapersonal, interpersonal, and environmental factors in their lives. Results indicated that certain environmental factors (e.g., violence, drug availability, and machismo), family drug use, a distant parent-child relationship, and unconventional behaviors are risk factors for adolescent illegal drug use. As hypothesized, results showed that the adverse effects of family illegal drug use on adolescent drug use can be buffered by protective parental child-rearing practices and environmental factors, leading to less adolescent illegal drug use. Prevention and treatment efforts should incorporate protective environmental, familial, and intrapersonal components in order to reduce adolescent illegal drug use. Brook, J.S., Brook, D.W., De La Rosa, M., Whiteman, M., Johnson, E., and Montoya, I. J. Behav Med, April 24(2), pp. 183-203, 2001.

Association of Maladaptive Parental Behavior with Psychiatric Disorder among Parents and their Offspring

This longitudinal study was conducted to investigate the role of maladaptive parental behavior in the association between parent and offspring psychiatric disorder. Psychosocial and psychiatric interviews were administered to a representative community sample of 593 biological parents and their offspring from 2 counties in the state of New York in 1975, 1983, 1985 to 1986, and 1991 to 1993. In 1975, the offspring were a mean age of 6 years. Maladaptive parental behavior was assessed in 1975, 1983, and 1985 to 1986. Parent and offspring psychiatric symptoms were assessed in 1983, 1985 to 1986, and 1991 to 1993. Maladaptive parental behavior substantially mediated a significant association between parental and offspring psychiatric symptoms. Parents with psychiatric disorders had higher levels of maladaptive behavior in the household than did parents without psychiatric disorders. Maladaptive parental behavior, in turn, was associated with increased offspring risk for psychiatric disorders during adolescence and early adulthood. Most of the youths that experienced high levels of maladaptive parental behavior during childhood had psychiatric disorders during adolescence or early adulthood, whether or not their parents had psychiatric disorders. In contrast, the offspring of parents with psychiatric disorders were not at increased risk for psychiatric disorders unless there was a history of maladaptive parental behavior. Maladaptive parental behavior is associated with increased risk for the development of psychiatric disorders among the offspring of parents with and without psychiatric disorders. Maladaptive parental behavior appears to be an important mediator of the association between parental and offspring psychiatric symptoms. Johnson, J.G., Cohen, P., Kasen, S., Smailes, E., and Brook, J.S. Association of Maladaptive Parental Behavior with Psychiatric Disorder among Parents and their Offspring. Arch Gen Psychiatry, 58(5), pp. 453-460, May 2001.

Childhood Depression and Adult Personality Disorder

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

Tic, Obsessive-Compulsive, and Attention-Deficit/Hyperactivity Disorders

Understanding the interrelatedness of tics, obsessive-compulsive disorder (OCD), and attention-deficit/ hyperactivity disorder (ADHD) has been complicated by studying only cross-sectional samples of clinically referred subjects. The authors report the cross-sectional and longitudinal associations of these disorders in an epidemiological sample of children followed prospectively into early adulthood. Structured diagnostic interview information was acquired on 976 children, aged 1 to 10 years, who were randomly selected from families living in upstate New York in 1975. Reassessments were acquired in 776 of these subjects 8, 10, and 15 years later. Diagnostic prevalences were estimated at each time point. The associations among tics, OCD, and ADHD were assessed within and across time points, as were their associations with comorbid illnesses and demographic risk factors. In temporal cross-section, tics and ADHD symptoms were associated with OCD symptoms in late adolescence and early adulthood after demographic features and comorbid psychiatric symptoms were controlled. In prospective analyses, tics in childhood and early adolescence predicted an increase in OCD symptoms in late adolescence and early adulthood. ADHD symptoms in adolescence predicted more OCD symptoms in early adulthood, and OCD in adolescence predicted more ADHD symptoms in adulthood. The associations of tics with ADHD were unimpressive in temporal cross-section and were not significant in prospective analyses. Tics, OCD, and ADHD shared numerous complex associations with demographic and psychopathological risk factors. ADHD was associated with lower IQ and lower social status, whereas OCD was associated with higher IQ. Tics and OCD were significantly associated in this sample, as were OCD and ADHD. These findings are in general consistent with those from family studies, and they help to define the natural history, comorbid illnesses, and interrelatedness of these conditions. Peterson, B.S., Pine, D.S., Cohen, P., and Brook, J.S. Prospective, Longitudinal Study of Tic, Obsessive-Compulsive, and Attention-Deficit/Hyperactivity Disorders in an Epidemiological Sample. J Am Acad Child Adolesc Psychiatry, 40(6), pp. 685-695, June 2001.

Genetic and Environmental Influences on Antisocial Personality Disorder in Adoptees

This investigation used data from the Iowa Adoption studies to examine the biological and environmental influences and clinical correlates of adult antisocial behavior, a well-established risk factor for drug abuse. We defined three subgroups: antisocials with conduct disorder (n = 30), antisocials without conduct disorder (n = 25), and controls (n = 142). Results demonstrate that having an antisocial biological parent was a specific risk factor for ASPD. In contrast, fetal alcohol exposure, male gender, and adverse environmental factors were associated with the adult antisocial syndrome, regardless of a history of conduct disorder in childhood. The two antisocial groups were similar with respect to clinical characteristics including sociopathy scores, comoribid disorders, and most individual symptoms. Because the phenotypic expression of the potential genetic-risk for ASPD appears to be manifest before adulthood, findings suggest that a history of conduct disorder may be more relevant to the etiological than clinical understanding of adult antisocial behavior. Langbehn, D.R. and Cadoret, R.J. The Adult Antisocial Syndrome with and without Antecedent Conduct Disorder: Comparisons from an Adoption Study. Comprehensive Psychiatry, 42(4), pp. 272-282, 2001.

The Insidious Course of Alcohol Use Disorders from Adolescence to Adulthood

This study investigated whether alcohol use disorder (AUD) in adolescence is a risk factor for AUD and other forms of psychopathology in young adulthood. Nine hundred forty participants from a large community sample in western Oregon were interviewed twice during adolescence (14-18 years of age the first assessment; between 1987 and 1991) and once at age 24 (1993-1999). Participants were classified into non-problematic drinkers, problem drinkers (symptoms of AUD but no diagnosis), and AUD groups. Both problem drinking and AUD significantly predicted adult AUD, substance use disorder, depression, and antisocial personality disorder symptoms. Compared to the problem drinkers, the AUD group had higher rates of adult AUD, more antisocial personality disorder symptoms, and was at risk of borderline personality disorder. Other findings showed that daily smoking and conduct/oppositional defiant disorders predicted future AUD, after controlling for adolescent AUD and other disorders. Paternal, but not maternal, AUD was associated with greater risk of future AUD. In conclusion, findings indicate that AUD and problem drinking in adolescents are not benign conditions that resolve over time. Assessment, treatment, and prevention recommendations are discussed. Rohde, P., Lewinsohn, P.M., Kahler, C.W., Seeley, J.R., and Brown, R.A. Natural Course of Alcohol Use Disorders from Adolescence to Young Adulthood. Journal of the American Academy of Child and Adolescent Psychiatry, 40(1), pp. 83-90, 2001.

Evaluation of a 6-item Self-Report Screener for Conduct Disorder

This study evaluated the ability of a very brief (6-item) self-report screener, the Oregon Adolescent Depression Project Conduct Disorder Screener (OADP-CDS), to identify adolescents with a lifetime diagnosis of conduct disorder and to examine its ability to predict antisocial personality disorder by age 24. Relevant scales from the Youth Self-Report and the Child Behavior Checklist were examined for comparison purposes. A total of 1,709 high school

students completed an initial questionnaire and diagnostic interview assessment (T1); 1,507 participants returned approximately 1 year later for a second assessment (T2). A third (T3) assessment was conducted with selected T2 participants (n = 940) after they had turned 24 years of age. The OADP-CDS demonstrated good internal consistency, test-retest stability, and screening properties. The screening ability of the OADP-CDS did not differ by gender or social desirability, and was as effective as the longer adolescent- and parent-report measures. Perhaps most importantly, the OADP-CDS was able to identify future cases of antisocial personality disorder in young adulthood, thereby underscoring the utility of self-report screening for conduct disorder, a well established risk factor of drug use disorders. Lewinsohn, P.M., Rohde, P., and Farrington, D.P. The OADP-CDS: A Brief Screener for Adolescent Conduct Disorder. Journal of the American Academy of Child and Adolescent Psychiatry, 39(7), pp. 888-895, 2000.

Drug Treatment Careers: Conceptual Overview and Clinical, Research, and Policy Applications

This study illustrates the treatment career perspective as a conceptual framework for consolidating research findings and suggesting research directions that have important policy implications. It presents findings of research by the UCLA Drug Abuse Research Center (DARC) as examples of the products of empirical applications of the concept and discusses related clinical, research, and policy questions. This career concept is valuable in understanding the effects of policy and program practice on treatment outcomes and in suggesting modifications to improve policy and treatment. Although the treatment career approach is in an early stage and needs to be more fully developed with theoretical rigor and research applications, its benefit is significant in matters relevant to drug policy, as indicated by available empirical findings. This conceptual framework will further our understanding of the addiction and treatment career patterns of individuals at treatment entry and the relation of career characteristics and treatment outcomes, particularly within the context of ongoing changes in client service needs and treatment program characteristics. Anglin, M.D., Hser, Y., Grella, C.E., Longshore, D., and Prendergast, P. In J. Platt, C. Leukefeld, and F.M. Tims (Eds.), Drug Treatment Careers: Conceptual Overview and Clinical, Research, and Policy Applications. Relapse and Recovery Processes in the Addictions. Yale University Press, 2001.

Analytic Approaches for Assessing Long-Term Treatment Effects: Examples of Empirical Applications and Findings

Analytic approaches including the structural equation model (autoregressive panel model), hierarchical linear model, latent growth curve model, survival/event history analysis, latent transition model, and time series analysis (interrupted time series, multivariate time series analysis) are discussed for their applicability to data of different structures (panel data, clustered data, duration data for critical events, and time series data) and their utility in evaluating temporal effects of drug and alcohol treatment. Methods are illustrated by presenting applications of the various approaches in previous studies examining temporal patterns of treatment effects. Recent advancements in these longitudinal modeling approaches and the accompanying computer software development offer tremendous flexibility in examining long-term treatment effects through longitudinal data with varying numbers and intervals of assessment, and types of measures. A multi-method assessment will contribute to a more complete understanding of the complex phenomena of the long-term courses of substance use and its treatment. Hser, Y., Shen, H., Chou, C.-P., Messer, S. and Anglin, M.D. Analytic Approaches for Assessing Long-Term Treatment Effects: Examples of Empirical Applications and Findings. Evaluation Review, 25(2), 233-262, 2001.

A 33-Year Follow-Up of Narcotics Addicts

This study examined longitudinal patterns of heroin use, other substance use, health, mental health, employment, criminal involvement, and mortality among heroin addicts. The sample comprised 581 male heroin addicts admitted to the California Civil Addict Program (CAP) during the years 1962 through 1964; CAP was a compulsory drug treatment program for heroin dependent criminal offenders. This 33-year follow-up study updates information previously obtained from admission records and two face-to-face interviews conducted in 1974-75 and 1985-86; in 1996-97, at the latest follow-up, 284 were dead and 242 were interviewed. In 1996-97, the mean age of the 242 interviewed subjects was 57.4 years. Age, disability, years since first heroin use, and heavy alcohol use were significant correlates of mortality. Of the 242 subjects interviewed, 20.7% tested positive for heroin (with additional 9.5% urine refusal and 14.0% incarceration, for whom urinalyses were unavailable), 66.9% reported tobacco use, 22.1% were daily alcohol drinkers, and many reported illicit drug use (e.g., past year heroin use was 40.5%, marijuana 35.5%, cocaine 19.4%, crack 10.3%, amphetamine 11.6%). The group also reported high rates of health problems, mental health problems, and criminal justice system involvement. Long-term heroin abstinence was associated with less criminality, morbidity, psychological distress, and higher employment. While the number of deaths increased steadily over time, heroin use patterns were remarkably stable for the group as a whole. For some,

heroin addiction has been a life-long condition associated with severe health and social consequences. Hser, Y., Hoffman, V., Grella, C.E., and Anglin, M.D. A 33-Year Follow-Up of Narcotics Addicts. Archives of General Psychiatry, 58, pp. 503-508, 2001.

Services Needs of Substance Abusing Women in Jail

While women account for only 11% of the U.S. jail population, the population of women in the nation's jails has increased 7% annually since 1990 (compared to a 4.5% rate of growth among males). Since about two-thirds of female arrestees use illicit drugs, there is a need for substance abuse services and other services for females in jail. But historically programs for substance abusers in jail have focused on males and have not considered the special needs of women. This study compared the self-reported service needs of women requesting drug abuse services with those not in need of substance abuse treatment. Interviews were conducted with 165 women incarcerated in an urban county jail in Ohio. The study population was predominantly African-American (72%), aged 30 to 40, and most women were mothers. Women who reported a need for substance abuse treatment were more likely than those not needing drug abuse treatment to report the need for housing, medical care, education, mental health services, family support, and parenting assistance. Housing was the need most frequently mentioned; more than one quarter of drug abuse treatment-seeking women reported that they did not know where they would live when released from jail as compared to 11% of non-treatment seeking women This study suggests that successful drug treatment of women in jail must consider the multidimensional needs of these women in order to break the cycle of drug use and incarceration. Alemagno, S.A. Women in Jail: Is Substance Abuse Treatment Enough? Amer. J. Pub. Health, 91(5), pp. 798-800, 2001.

Psychiatric Enviromics

Using a selective literature review and synthesis, Dr. James Anthony introduces 'psychiatric enviromics' as a complement to human genomics and proteomics as applied to mental health. He proposes that psychiatric enviromics is the way in which epidemiologists and psychiatrists who study causes of mental and behavioral disturbances and the concomitant prevention strategies, can focus on aspects of environment that affect mental health and behavior. Since "the human genome dwells within environment, determines environment, and its expression is shaped by environment" (p. s9), epidemiological research in general and psychiatric epidemiology in particular can develop a 'human environment project' "that seeks to the total ensemble of environments, both current and in earlier life, that affect the occurrence of mental and behavioral disturbances" (p. s9). The argument here is that "subsets of the psychiatric environment will be discovered to have functional importance precisely because specific environmental conditions or processes will reduce, amplify or otherwise modulate the expression of earlier genes or multiple gene interactions at identifiable periods of life-span development." Needless to say, "other salubrious environmental conditions and processes will have functional importance but lack specificity of action with respect to gene expression" (p. s8). Dr. Anthony advocates an international forum and/or collaboration to assess the evidence. Anthony, J.C. The Promise of Psychiatric Enviromics. British Journal of Psychiatry, 178 (suppl. 40), pp. s8-s11, 2001.

Community Epidemiology Work Group

The 50th meeting of the Community Epidemiology Work Group (CEWG), chaired by Nicolas Kozel, DESPR, was held in Rockville, Maryland on June 12-15, 2001. 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 meeting.

Cocaine/Crack - Cocaine/crack indicators decreased in 10 CEWG areas, increased in 5, and were stable in 6. Since stabilizing in the mid-1990s, cocaine/crack indicators have been decreasing in most CEWG areas. Yet, cocaine/crack remains the major drug problem in most CEWG areas. DAWN Emergency Department (ED) cocaine rates per 100,000 population in the first half of 2000 were especially high in Chicago (121), Miami (110), Philadelphia (105), Baltimore (99), Detroit (94), and Newark (74).

Heroin - Heroin indicators continue an upward trend, increasing in 15 CEWG areas, remaining level or mixed in 5, and decreasing in 1. CEWG members continued to report, as they have since 1994, that heroin abuse is spreading to younger populations and to areas outside the inner cities. Inhaling the drug is increasing in popularity. Several factors

appear related to these patterns and trends, including the availability of different types of heroin from different regions of the world, increases in the purity of heroin, and decreases in the price of the drug. In early 2000, purity levels were very high in Northeast and mid-Atlantic areas such as Newark (77 percent), Philadelphia (73 percent), Boston (66 percent), and New York (60 percent).

Semi-Synthetic Narcotic Prescription Drugs - Indicators continued to increase in urban, suburban, and rural areas. However, the indicator numbers are relatively small compared with other drug categories. Purchased on the street, pharmaceutical narcotics such as hydrocodone and oxycodone (including OxyContin) are being used as a substitute for heroin, and also are being abused by other populations, including long-term prescription drug users and younger populations. Ocycodone/OxyContin are known as "poor man's heroin" in areas such as Philadelphia, St. Louis, and Washington, D.C.

Marijuana - Indicators began leveling off in 1999-2000 in 14 CEWG areas but continued to trend upward in 7. In some areas, substantial and increasing numbers of marijuana abusers are being referred to treatment by the criminal justice system.

Methamphetamine - Indicators varied in the CEWG areas that typically report relatively high levels of methamphetamine abuse. However, in the second half of 1999 and in the first half of 2000, DAWN methamphetamine ED mentions were trending upward in most of these areas. As use of the drug has spread, indicators have increased in areas such as Minneapolis/St. Paul and St. Louis.

"Other" Drugs - Other drugs, including MDMA (ecstasy), gamma hydroxybutyrate (GHB), ketamine, and phencyclidine (PCP), often referred to as "club drugs," are being abused primarily by youth and young adults in many CEWG areas. Ecstasy indicators point to increases in abuse in 13 CEWG areas. CEWG members continue to report use of ecstasy in social settings other than nightclubs and raves, such as house parties and small group gatherings. Reports on GHB indicators show that they increased in nine CEWG areas and decreased in one.

Polydrug Use - Indicators clearly show that multiple drug use is the norm, rather than the exception among drug abusers. Most treatment admissions report current use of at least three drugs, with cocaine frequently being the most commonly reported secondary drug. Medical examiners report the presence of multiple substances in a majority of decedents. Both semi-synthetic narcotics and the so-called "club drugs" are generally used concomitantly or sequentially with other drugs, including alcohol.

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

Research Findings

Services Research

A Comparison of the Predictive Validity of Four Sets of Baseline ASI Summary Indices

This study compared the long-term predictive validity of original and new baseline Addiction Severity Index summary scores in methadone patients. The indices included the original Interviewer Severity Ratings (ISRs) and the new Clinical Indices (CIs), which use both lifetime and recent problem information, and the original Composite Scores (CSs) and Evaluation Indices (EIs), based on recent problems only. Outcomes were medical hospitalization, employment, alcohol intoxication, drug hospitalization, and psychiatric hospitalization in Months 7-24 post study entry and criminal charges in Months 0-24. Hierarchical logistic regression analyses were used in which 1 index was entered first and the other in the 2nd step. The reverse order of entry was used in a 2nd analysis. A final analysis set compared the best predictor from each of the 2 prior analysis sets. The CIs were superior to the other indices in predicting 3 of 6 outcomes (psychiatric hospitalization, drug hospitalization, and criminal charges); the EI was the best predictor of alcohol intoxication, and the CS the best predictor of unemployment. Alterman, A.I., Bovasso, G.B., Cacciola, J.S., and McDermott, P.A. A Comparison of the Predictive Validity of Four Sets of Baseline ASI Summary Indices. Psychol Addict Behav., 15(2), pp. 159-162, June 2001.

Factors Associated with Frequency of 12-Step Attendance by Drug Abuse Clients

Comparison was made of treatment clients attending Narcotics Anonymous and/or Alcoholics Anonymous meetings less than weekly (n = 41) with treatment clients attending meetings at least three times a week (n = 30). The frequent attendees (attending an average of 30.6 meetings monthly) differed from non- and infrequent attendees (attending an average of 0.4 meetings monthly) in terms of histories of greater lifetime drug use, greater incidence of arrests and treatment experiences, and an earlier age of first use of alcohol. Although those who attended more frequently were also older, age was not found to influence the differences found between groups. Measures of religiosity, use of community services, and support from others for recovery and psychological functioning, other than ratings of the helpfulness of 12-Step, were not differentiated among groups. The findings suggest that 12-Step groups are more likely to be selected by clients with more severe histories of drug use and criminal activity, i.e., those most in need of the support to behavior change those groups provide. The role of treatment programs in facilitating the use of 12-Step groups is discussed. Brown, B.S., O'Grady, K.E., Farrell, E.V., Flechner, I.S., and Nurco, D.N. Factors Associated with Frequency of 12-Step Attendance by Drug Abuse Clients. Am J Drug Alcohol Abuse. 27(1), pp. 147-160, Feb 2001.

Initial Validation of a Computer-Administered Addiction Severity Index: The ASI-MV

The Addiction Severity Index--Multimedia Version (ASI-MV) is a CD-ROM-based simulation of the interview-administered Addiction Severity Index (ASI). Clients in treatment (N = 202) self-administered the ASI-MV to examine the test-retest reliability, criterion validity, and convergent-discriminant validity of the ASI-MV. Excellent test-retest reliability was observed for composite scores and severity ratings. Criterion validity, tested against the interviewer-administered ASI, was good for the composite scores. For severity ratings, variable agreement was observed between the ASI-MV and each interviewer, suggesting poor interrater reliability among interviewers. This conclusion was bolstered by a finding of superior convergent-discriminant validity for both composite scores and severity ratings compared to the standard ASI. The ASI-MV is a viable alternative to the expensive and potentially unreliable

interviewer-administered version. Butler, S.F., Budman, S.H., Goldman, R.J., Newman, F.J., Beckley, K.E., Trottier, D., and Cacciola, J.S. Initial Validation of a Computer-Administered Addiction Severity Index: The ASI-MV. Psychology of Addictive Behaviors. 15(1), pp. 4-12, Mar 2001.

The Epidemiology of Physical Attack and Rape Among Crack-Using Women

This prospective study examines the epidemiology of physical attack and rape among a sample of 171 not-in-treatment, crack-cocaine using women. Since initiating crack use, 62% of the women reported suffering a physical attack. The annual rate of victimization by physical attack was 45%. Overall, more than half of the victims sought medical care subsequent to an attack. The prevalence of rape since crack use was initiated was 32%, and the annual rate was 11%. Among those women having been raped since they initiated crack use, 83% reported they were high on crack when the crime occurred as were an estimated 57% of the perpetrators. Logistic regression analyses showed that duration of crack use, arrest for prostitution, and some college education were predictors of having experienced a physical attack. Duration of crack use and a history of prostitution were predictors of suffering a rape. Drug abuse treatment programs must be sensitive to high levels of violence victimization experienced by crack-cocaine using women. Screening women for victimization, and treating the problems that emanate from it, may help make drug abuse treatment more effective. Falck, R.S., Wang, J., Carlson, R.G., and Siegal, H.A. The Epidemiology of Physical Attack and Rape among Crack-Using Women. Violence. Vict.,16(1), pp. 79-89, Feb 2001.

An Evaluation of Drug Treatments for Adolescents in 4 US Cities

Little is known about outcomes of community-based treatment programs for adolescents with drug problems. This study evaluated the treatment outcomes of 1,167 adolescents (age range, 11-18 years; 368 females, 799 males) from 4 US cities (Pittsburgh, Pa; Minneapolis, Minn; Chicago, Ill; and Portland, Ore) using a naturalistic, non-experimental evaluation design. These adolescents were consecutive admissions between 1993 and 1995 in one of 23 community-based treatment programs in the Drug Abuse Treatment Outcome Studies for Adolescents. Included were 418 admissions to 8 residential programs, 292 admissions to 9 outpatient drug-free programs, and 457 admissions to 6 short-term inpatient programs. Adolescents in treatment typically had multiple problems (e.g., 58.4% of them were involved in the legal system, and 63.0% met diagnostic criteria for a mental disorder). Nevertheless, less than half (43.8%) of all patients reported weekly marijuana use in the year following treatment (dropping from 80.4% in the year before admission). Similarly, there were decreases in heavy drinking (dropping from 33.8% to 20.3%), use of other illicit drugs (dropping from 48.0% to 42.2%), and criminal involvement (dropping from 75.6% to 52.8%). Additionally, patients reported better psychological adjustment and school performance after treatment. Longer stays in treatment were positively associated with several favorable outcomes, although length of time in treatment was generally short. These findings suggest that substance abuse treatment for adolescents is effective in achieving many important behavioral and psychological improvements. Strategies specific to adolescents to improve their treatment retention and completion are needed to maximize the therapeutic benefits of drug treatment. Hser, Y.I., Grella, C.E., Hubbard, R.L., Hsieh, S-C., Fletcher, B.W., Brown, B.S., and Anglin, M.D. An Evaluation of Drug Treatments for Adolescents in 4 US Cities. Arch Gen Psychiatry. 58, pp. 689-695, 2001.

Drug Treatment Outcomes for Adolescents with Comorbid Mental and Substance Use Disorders

This study compared the pretreatment characteristics and post treatment outcomes of substance-abusing adolescents with and without comorbid mental disorders in the Drug Abuse Treatment Outcome Studies for Adolescents. Subjects (N = 992) were sampled from 23 adolescent drug treatment programs across three modalities (residential, short-term inpatient, outpatient drug-free). Nearly two thirds (64%) of the sample had at least one comorbid mental disorder, most often conduct disorder. Comorbid youth were more likely to be drug or alcohol dependent and had more problems with family, school, and criminal involvement. Although comorbid youth reduced their drug use and other problem behaviors after treatment, they were more likely to use marijuana and hallucinogens, and to engage in illegal acts in the 12 months after treatment, as compared with the noncomorbid adolescents. Integrated treatment protocols need to be implemented within drug treatment programs in order to improve the outcomes of adolescents with comorbid substance use and mental disorders. Grella, C.E., Hser, Y.I., Joshi, V, and Rounds-Bryant, J. Drug Treatment Outcomes for Adolescents with Comorbid Mental and Substance Use Disorders. J Nerv Ment Dis.,189(6), pp. 384-392, June 2001.

Managed Care and Outpatient Substance Abuse Treatment Intensity

This study examines the extent to which managed care behavioral controls are associated with treatment intensity in outpatient substance abuse treatment facilities. Data are from the 1995 National Drug Abuse Treatment System Survey, a nationally representative survey that includes over 600 provider organizations with a response rate of 86%.

Treatment intensity is measured in three ways: (1) the number of months clients spend in outpatient drug treatment, (2) the number of individual treatment sessions clients receive over the course of treatment, and (3) the number of group treatment sessions clients receive over the course of treatment. After accounting for selection bias and controlling for market, organization, and client characteristics, there was no significant relationship between the scope of managed care oversight and treatment intensity. However, the stringency of managed care oversight activities was negatively associated with the number of individual and group treatment sessions received over the course of treatment. The study provides evidence that managed care influences outpatient substance abuse treatment through the process by which units are selected by managed care firms or choose to participate in managed care programs. The process by which treatment organizations chose to participate or are chosen for managed care programs appears not to be random. Lemak, C.H., and Alexander, J.A. Managed Care and Outpatient Substance Abuse Treatment Intensity. Journal of Behavioral Health Services & Research, 28(1), pp. 12-29, Feb 2001.

Multidimensional Assessment of Perceived Treatment-Entry Pressures Among Substance Abusers

Motivational assessment instruments typically measure clients' attributions about their readiness to change problem behaviors. They do not indicate why a client may be motivated to change, or provide guidance on how to retain an unmotivated client in treatment. The authors interviewed 415 substance abuse clients about their reasons for entering treatment and scored their responses along the dimensions of (a) negative versus positive treatment-entry pressures, (b) internal versus external sources of those pressures, and (c) the life domain from which the pressures emanated. Exploratory cluster analysis yielded 5 types of clients characterized by different profiles of perceived treatment-entry pressures. Cluster membership was predictive of treatment outcomes, and the clusters differed by demographic variables. The results of this study indicate that there are multiple types of pressures on clients to enter treatment. These data support the discriminative and predictive utility of performing a multidimensional assessment of pressures to enter treatment. Marlowe, D.B., Merikle, E.P., Kirby, K.C., Festinger, D.S., and McLellan, A.T. Multidimensional Assessment of Perceived Treatment-Entry Pressures among Substance Abusers. Psychol Addict Behav., 15(2), pp. 97-108, June 2001.

Public Sector Managed Care for Substance Abuse Treatment: Opportunities for Health Services Research

Observations of reduced utilization of alcohol and drug abuse treatment following the introduction of managed behavioral health care suggest that substance abuse services may be especially responsive to managed care restrictions and limits. In publicly funded treatment systems, patient attributes, system and provider characteristics, and financing mechanisms may heighten susceptibility to unintended effects. The State Substance Abuse and Mental Health Treatment Managed Care Evaluation Program reviewed state managed care programs for publicly funded alcohol and drug treatment services and is evaluating programs in Arizona, Iowa, Maryland, and Nebraska. This article describes initiatives and outlines evaluation activities. It discusses the opportunities and challenges of assessing public managed care plans. McCarty, D., Argeriou, M., Denmead, G., and Dilonardo, J. Public Sector Managed Care for Substance Abuse Treatment: Opportunities for Health Services Research. J Behav Health Serv Res., 28(2), pp.143-154, May 2001.

Prevalence of Nonpsychotic Mental Disorders Does Not Affect Treatment Outcome in a Homeless Cocaine-Dependent Sample

This study presents the prevalence and treatment outcome of DUAL diagnoses (psychoactive substance use disorders [PSUD] plus other nonpsychotic mental disorders) among a population of homeless persons participating in a behavioral day treatment and contingency management drug abuse treatment programs. Participants were 128 persons: 76.6% male, 23.4% female; 82.2% African-American, 17.2% Caucasian. There were 46 (35.9%) PSUDs and 82 (64.1%) DUAL participants. Cocaine (96.9%) and alcohol disorders (57.8%) were most prevalent overall, and 60.2% of participants had two or more psychoactive substance use disorders. DUAL participants had significantly more alcohol disorders than PSUDs (62.2% versus 50.0%). The most prevalent mental disorders (other than substance use) for the total and DUAL samples were, respectively, mood (51.6% and 80.5%) and anxiety (35.9% and 56.1%), and 31.3% and 48.8% had more than two mental disorders. The DUAL group had more severe problems than the PSUD group at baseline in alcohol, medical condition, employment/support, and psychiatric status areas on the ASI. Both groups showed treatment improvements at 6-months follow-up with the DUAL group showing greater mean changes than the PSUD group in five of the seven ASI areas. These findings are discussed in terms of effect of dual diagnoses on treatment outcome and study limitations related to a retrospective design and select sample of nonpsychotic mental disorders. McNamara, C., Schumacher, J.E., Milby, J.B., Wallace, D., and Usdan, S. Prevalence of Nonpsychotic Mental Disorders Does Not Affect Treatment Outcome in a Homeless Cocaine-Dependent Sample. Am

J Drug Alcohol Abuse, 27(1), pp. 91-106, Feb 2001.

Benefits in Behavioral Health Carve-Out Plans of Fortune 500 Firms

This study examined the prevalence and nature of behavioral health carve-out contracts among Fortune 500 firms in 1997. A survey was conducted of 498 companies that were listed as Fortune 500 firms in 1994 or 1995. A total of 336 firms (68 percent) responded to the survey. Univariate analyses were used to analyze prevalence, types, and amounts of covered services, cost sharing, and benefit limits. A total of 132 firms reported contracting with managed behavioral health organizations; 124 firms answered benefits questions about covered services, cost-sharing levels, and annual and lifetime limits. Findings indicate that most of the plans covered a broad range of services. Cost sharing was typically required, and for inpatient care it was often substantial. Fifteen percent of the firms offered mental health benefits that were below the limits defined in this study as minimal benefit levels, and 34 percent offered substance abuse treatment benefits that fell below minimal levels. The most generous mental health benefits and substance abuse treatment benefits, defined as no limits or a lifetime limit only of $1 million or more, were offered by 31 percent and 20 percent of the firms, respectively. The carve-out contracts of the Fortune 500 firms in this study typically covered a wide range of services, and the benefits appeared generous relative to those reported for other integrated and carve-out plans. However, these benefits generally did not reach the level of parity with typical medical benefits, nor did they fully protect enrollees from the risk of catastrophic expenditures. Merrick, E.L., Garnick, D.W., Horgan, C.M., Goldin, D., Hodgkin, D., and Sciegaj, M. Benefits in Behavioral Health Carve-Out Plans of Fortune 500 Firms. Psychiatr Serv., 52(7), pp. 943-948, July 2001.

Service Outcomes of Peer Consumer Advocacy for Soup Kitchen Guests

This study determined client outcomes for two "linkage and coordination" models of case management-an individual case manager model and a team model consisting of a case manager and a peer helper-in an inner-city meal program. Soup kitchen guests seeking social services were voluntarily randomly assigned to one of two conditions-linkage and Coordination (WC) plus Peer Consumer Advocacy (PCA) [N = 57] or Linkage and Coordination (L/C) only [N = 53]. The PCAs provided guests with social and instrumental support to help them implement their case plans. Almost all study participants were unemployed and reported drug or alcohol misuse. Participants who received WC plus PCA, compared with those receiving WC only, met more often with the case manager, kept more service referral appointments, and received more entitlements and community services. Other significant predictors of appointments kept were older age and limitations in activities of daily living. The WC plus PCA participants also showed better outcomes for cocaine/crack use, but not for heavy alcohol or other drug use. Nwakeze, P.C., Magura, S., Rosenblum, A., et al. Service Outcomes of Peer Consumer Advocacy for Soup Kitchen Guests. J Soc Serv Res, 27(2), pp. 19-38, 2000.

Association of Outpatient Alcohol and Drug Treatment with Health Care Utilization and Cost: Revisiting the Offset Hypothesis

This study examines the hypothesis that treatment reduces medical utilization and costs of patients with substance use problems. Adult patients (N = 1.011; 67% men) entering the outpatient chemical dependency recovery program at Sacramento Kaiser Permanente over a 2-year period were recruited into the study. Medical utilization and costs were examined for 18 months prior and 18 months after intake. To account for overall changes in utilization and cost, an age, gender and length-of-enrollment matched nonpatient control group (N = 4,925) was selected from health-plan members living in the same service area. Multivariate analyses controlling for age and gender were conducted using generalized estimating equation methods, allowing for correlation between repeated measures and nonnormal distributions of the outcome variable. The treatment cohort was less likely to be hospitalized (odds ratio [OR] = 0.59; $p < .01$) and there was a trend for having spent fewer days (rate ratio [RR] = 0.77; $p < .10$) in the hospital in the post treatment period compared to pretreatment period. These patients were also less likely to visit the emergency room (ER) (OR = 0.64; $p < .01$) and had fewer ER visits (RR = 0.81; $p < .01$) following treatment. Inpatient, ER and total medical costs declined by 35%, 39% and 26%, respectively ($p < .01$). Reductions in cost were greater for the treatment cohort when compared with the matched sample ($p < .05$). Among women, there were significant reductions ($p < .05$) in inpatient, ER and total costs for the study cohort when compared with the matched sample; among men, the reductions in inpatient and ER cost (but not total cost) were significantly larger ($p < .05$) for the study cohort when compared with the matched sample. For the treatment cohort, the change in medical cost was not significantly different by gender. Changes in cost were significantly different across the various age groups ($p < .05$) for the study cohort and the matched sample. Among those in the group aged 40-49 years, the decline in cost for study cohort was significantly larger ($p < .05$) than for the matched sample. For patients with substance use disorders entering treatment, there was a substantial decline in inappropriate utilization and cost (hospital and ER) in the post treatment period. The disaggregated pattern of post treatment decline in utilization and cost is suggestive of

long-term reductions that warrant a longer follow-up. Parthasarathy, S.,Weisner, C., Hu, T.W., and Moore, C. Association of Outpatient Alcohol and Drug Treatment with Health Care Utilization and Cost: Revisiting the Offset Hypothesis. J Stud Alcohol., 62(1), pp. 89-97, Jan 2001.

Association of Outpatient Alcohol and Drug Treatment with Health Care Utilization and Cost: Revisiting the Offset Hypothesis

Individuals with alcohol and drug use problems may receive health care from medical, mental health, and substance abuse providers, or a combination of all three. Systems of care are often distinct and separate, and substantial opportunities for benefit to patient, provider, and payer are missed. In this article, the authors outline (1) the possible benefits of linking primary care, mental health, and substance abuse services from the perspective of the major stakeholders-medical and mental health providers, addiction clinicians, patients, and society-and (2) reasons for sub optimal linkage and opportunities for improving linkage within the current health care system. They also review published models of linked medical and substance abuse services. Given the potential benefits of creating tangible systems in which primary care, mental health, and substance abuse services are meaningfully linked, efforts to implement, examine, and measure the real impact should be a high priority. Samet, J.H., Friedmann, P., Saitz, R. Association of Outpatient Alcohol and Drug Treatment with Health Care Utilization and Cost: Revisiting the Offset Hypothesis. Arch Intern Med., 161, pp. 85-91, 2001.

Treatment Readiness Training and Probationers' Evaluation of Substance Abuse Treatment in a Criminal Justice Setting

Clients who are legally coerced into substance abuse treatment often have low intrinsic motivation to participate, are less ready for treatment, and are consequently more problematic to treat and less satisfied with their treatment than are voluntary clients. A set of readiness training activities, designed to promote early involvement in treatment, was implemented in a 4-month residential criminal justice program. Five hundred probationers were randomly assigned to receive either the readiness training developed by the authors or the approach typically used at the facility. Based on their response to an intake interview, probationers were categorized as having low, medium, or high readiness for treatment. Probationers in the readiness training group rated their counselors, groups, and community meetings higher than did probationers in the standard group. In addition, probationers in the readiness training group rated themselves as "working the program" to a greater extent than did probationers in the standard group. Probationers with higher initial levels of readiness for treatment rated their counselors, sessions, and security staff higher than did probationers with lower levels. The results suggest that the readiness training activities may help probationers become more involved in treatment and that this may lead to greater satisfaction with counselors and sessions. Sia, T.L., Dansereau, D.F., and Czuchry, M.L. Treatment Readiness Training and Probationers' Evaluation of Substance Abuse Treatment in a Criminal Justice Setting. Journal of Substance Abuse Treatment, 19(4), pp. 459-467, Dec 2000.

Are Barriers to Mental Health and Substance Abuse Care Still Rising?

This study estimates unmet need and barriers to alcohol, drug, and mental health (ADM) services in 1997 to 1998 using data from a national household survey (n = 9,585). In 1997 to 1998, 10.9% of the population perceived a need for ADM services, with 15% obtaining no treatment and 11% experiencing delays or obtaining less care than needed. The rate of unmet need due to no treatment is similar to earlier studies, but the group experiencing delays/less care is almost as large. This finding emphasizes the importance of defining access to care more broadly by including timeliness and intensity of care. Economic barriers are highest for the uninsured, but also are high among the privately insured. Individuals with unmet need are significantly more likely to use complementary and alternative medicine (CAM). Those with no conventional mental health care rely on self-administered treatment, while those with delayed/insufficient conventional care use CAM providers and self-administered treatment. Sturm, R., and Sherburne, C.D. Are Barriers to Mental Health and Substance Abuse Care Still Rising? Journal of Behavioral Health Services & Research, 28(1), pp. 81-88, Feb 2001.

The First Week after Drug Treatment: The Influence of Treatment on Drug Use Among Women Offenders

Over the last decade, there has been a dramatic rise in the number of women arrested for drug offenses, and many have serious drug abuse problems. Increasingly, these women have been mandated to drug treatment, often in community-based settings. This article examines the impact of the treatment programs on the short-term post treatment drug use of women offenders (N = 165) leaving two community-based treatment programs in Portland, Oregon. Women who abstained from drug use during the first week after treatment were more likely than those who used drugs during this time to have remained in treatment longer, received a plan to make a successful transition out

of treatment, avoided associations with other drug users after leaving treatment, and obtained encouragement from individuals and groups in support of abstinence. In addition, the research identified the importance of community referrals in the short-term for women to maintain sobriety after leaving treatment. The results suggest that community referrals be provided early in the treatment process since many women offenders do not complete treatment. Strauss, S.M., and Falkin, G.P. The First Week after Drug Treatment: The Influence of Treatment on Drug Use among Women Offenders. Am J Drug Alcohol Abuse, 27(2), pp. 241-264, May 2001.

Treatment Compliance in the Trajectory of Treatment Progress Among Offenders

Research on drug treatment process has been limited, with most studies centering on individual and program factors associated with successful treatment completion. Recent literature has begun highlighting the salience of treatment engagement in reducing drug dependence among criminal offenders. This study descriptively analyzes incidents of treatment noncompliance identified in monthly progress reports for 150 criminal justice-mandated clients in residential treatment. The researchers identify seven problem types and seven dimensions of noncompliance in the trajectory of treatment engagement. The latter are prevalence, frequency, types, specialization, temporal distribution, paths, and correlates. Incidents of rule violations are common among criminal justice participants of residential treatment. Although for most clients these troubles do not appear to evolve into serious obstacles to recovery, a few clients with a high frequency of noncompliant behavior never engage in treatment. Clinical implications for improving treatment engagement and retention are discussed. Sung, H., Belenko, S. and Feng, L. Treatment Compliance in the Trajectory of Treatment Progress Among Offenders. Journal of Substance Abuse Treatment, 20(2), pp. 153-162, March 2001.

Diversity in Relapse Prevention Needs: Gender and Race

Comparisons among Substance Abuse Treatment Patients Attempts to address high relapse rates following substance abuse treatment have focused on identifying relapse prevention needs and development of subsequent relapse prevention programs. Few studies have examined whether women and African-Americans have unique relapse prevention needs. Research in this area could provide an initial basis for the development of alternative relapse prevention approaches that could be more appropriate for this population. This study examined gender and race differences in psychosocial concerns among patients recruited from substance abuse treatment as potential indicators of relapse prevention needs. Participants (N = 331) completed several questionnaires during their first month of substance abuse treatment. Assessment packets included measures of coping, self-efficacy, resource needs, cravings, social influences, exposure, and leisure activities. Analyses focused on gender and race differences in these variables before and after controlling for background characteristics (i.e., age, marital status, income, polysubstance use, treatment type, and problem severity). Gender differences found were that men reported poorer coping skills and more negative social influences and exposure to substances than women; these differences remained significant when controlling for background characteristics. Significant race differences were found on all scales except negative social influences. After controlling for background characteristics, African-Americans reported significantly greater coping skills and self-efficacy than did Caucasians; however, African-Americans also reported greater resource needs in comparison to Caucasians. Results highlight the diversity in psychosocial issues among substance abusers in treatment, particularly between Caucasians and African-Americans. Implications for developing alternative relapse prevention approaches to address this diversity are discussed. Walton, M.A., Blow, F.C., and Booth, B.M. Diversity in Relapse Prevention Needs: Gender and Race Comparisons Among Substance Abuse Treatment Patients. Am J Drug Alcohol Abuse., 27(2), pp. 225-240, May 2001.

Rural-Urban Differences in Substance Use and Treatment Utilization Among Prisoners

Surveys of incarcerated offenders and arrestees consistently report high rates of both drug use and alcohol in this population. This drug-crime connection has highlighted the need to learn more not only about drug treatment effectiveness, but also about drug treatment utilization. While studies have begun to examine drug treatment utilization, most of these studies have been based on urban substance abusers. Little is known about the extent to which urban and rural substance abusers may be different in terms of treatment utilization. This study, therefore, examines differences between urban and rural drug use patterns and treatment utilization among chronic drug abusers to determine whether, and in what ways, rurality may affect substance abuse and treatment seeking. The study examines these issues in a group of chronic drug users who were incarcerated at the time of the study. Findings show significant differences in drug use and treatment utilization of urban and rural offenders. Chronic drug abusers from rural and very rural areas have significantly higher rates of lifetime drug use, as well as higher rates of drug use in the 30 days prior to their current incarceration than chronic drug abusers from urban areas. Nonetheless, being from a very rural area decreased the likelihood of having ever been in treatment after controlling for the number of years using and race. While problem recognition appears to explain much of the effect of very rural residence on treatment utilization for alcohol abuse, the effects of being from a very rural area on seeking treatment

for drug abuse remain statistically significant even after controlling for several other variables. The findings point to the importance of providing culturally appropriate education to very rural communities on the benefits of substance abuse treatment and of providing substance abuse treatment within the criminal justice system. Warner, B.D., and Leukefeld, C.G. Rural-Urban Differences in Substance Use and Treatment Utilization Among Prisoners. Am J Drug Alcohol Abuse., 27(2), pp. 265-280, May 2001.

Factors Affecting the Initiation of Substance Abuse Treatment in Managed Care

A long-standing concern of clinicians in addiction treatment is that a large number of individuals who are admitted to treatment do not return to actually begin the program. Authors of the study identified characteristics that predict treatment initiation. In-person structured interviews were conducted with consecutive admissions to a large outpatient program (N = 1204), and the health plan's automated registration data were used to determine treatment attendance. Those who returned to begin treatment were compared with those who did not. The study was conducted at the Chemical Dependency program of a large group model health maintenance organization (HMO). Study subjects were individuals age 18 or over admitted to the program. Study variables included DSM-IV alcohol and drug dependence and abuse, Addiction Severity Index problem severity, motivation and treatment entry measures. Findings indicate that those who were drug-dependent were less likely to begin treatment than those dependent only on alcohol. Measures of motivation, such as work-place pressures and the patient's perception of the importance of alcohol treatment, predicted starting treatment for individuals who were alcohol-dependent only or alcohol- and drug-dependent. Among patients who were dependent only on alcohol, women were more likely than men to start treatment, and for those who were drug-dependent, being employed and having higher drug severity scores predicted starting treatment. In summary, screening at intake may identify those at risk of not returning after admission to start treatment. Clinicians may consider making additional efforts during the intake process to engage individuals who are unemployed and have drug (as opposed to alcohol) disorders and less motivation. Weisner, C., Mertens, J., Tam, T., and Moore, C. Factors Affecting the Initiation of Substance Abuse Treatment in Managed Care. Addiction., 96(5), pp. 705-716, May 2001.

Gender Differences in Cocaine Craving Among Non-Treatment-Seeking Individuals with Cocaine Dependence

The purpose of this pilot study was to evaluate potential gender differences in cocaine craving among non-treatment seekers with cocaine dependence. Investigators examined 10 female and 11 male individuals matched by demographic characteristics and severity of drug use; we used a multidimensional questionnaire that assesses various aspects of craving: (a) current intensity, (b) projected intensity, (c) resistance to use cocaine, (d) responsiveness to drug-related conditioned stimuli, and (e) imagined likelihood of use if in a setting with access to drugs. Other instruments utilized were the Hamilton Rating Scale for Depression and Addiction Severity Index. Female subjects had higher total craving scores ($p < .05$), with post hoc tests showing more present desire to use cocaine and responsivity to drug-conditioned stimuli, along with lower scores on the desire not to use cocaine. In exploratory analyses, we found greater depressive symptomatology ($p = .02$) and severity of family/social problems ($p = .02$) in females than their males counterparts. These results suggest that gender may influence different aspects of cocaine craving. As estrogen is purported to modulate craving-related dopaminergic systems, further studies will be needed to confirm these observed gender differences and to investigate their possible mechanisms, particularly estrogen-dopamine interactions and their effect on craving and mood. Elman, I., Karlsgodt, K.H., and Gastfriend, D.R. Gender Differences in Cocaine Craving Among Non-Treatment-Seeking Individuals with Cocaine Dependence. Am J Drug Alcohol Abuse, 27(2), pp. 193-202, May 2001.

Can the Treatment Services Review be Used to Estimate the Costs of Addiction and Ancillary Services?

The economic costs of addiction treatment and ancillary services are of great interest to substance abuse treatment providers, researchers, and policymakers. This paper examines whether a widely used treatment evaluation instrument, the Treatment Services Review (TSR), can be used to estimate the costs of addiction and ancillary services. The fifth edition of the TSR (TSR-5) is carefully reviewed and critiqued for cost estimation purposes. Unit cost estimates and sources are presented for most of the service delivery units on the TSR-5, and important missing service measures are identified. A cost analysis method is proposed that is based on data from the TSR. A variety of unit cost estimates are offered so that researchers and practitioners will understand how this financial information is compiled. However, the investigation determined that the TSR-5 is not currently structured for a comprehensive cost analysis of treatment services. The potential benefits and limitations of the TSR-5 as a cost analysis tool are identified and explained. In addition, recommended changes to the TSR-5 are suggested and described. Although not originally developed for economic evaluation purposes, with some modifications and enhancements, the TSR is an instrument

that is capable of facilitating an economic cost analysis of addiction treatment and ancillary services. By combining service utilization information from a revised TSR (i.e., TSR-6) with reliable unit cost estimates for those services, future evaluation studies will be able to provide more standardized estimates of the costs of addiction and ancillary services for different types of treatment clients. When joined with outcome data, the TSR-6, along with the proposed cost module, can also be used to determine cost-effectiveness and benefit-cost ratios for subgroups of patients and treatment components. French, M.T., Roebuck, M.C., McLellan, A.T., and Sindelar, J.L. Can the Treatment Services Review be Used to Estimate the Costs of Addiction and Ancillary Services? J Subst Abuse, 12(4), pp. 341-361, 2000.

The Cost and Cost-Effectiveness of an Enhanced Intervention for People with Substance Abuse Problems at Risk for HIV

This study attempted to estimate the costs, effectiveness, and cost-effectiveness of prevention interventions for out-of-treatment substance abusers at risk for HIV. This is the first cost-effectiveness study of an AIDS intervention that focuses on drug use as an outcome. The researchers examined data from the North Carolina Cooperative Agreement site (NC CoOp). All individuals in the study were given the revised NIDA standard intervention and randomly assigned to either a longer, more personalized enhanced intervention or no additional intervention. The cost of each intervention was estimated and, using simple means analysis and multiple regression models, estimated the incremental effectiveness of the enhanced intervention relative to the standard intervention. Finally, the researchers computed cost-effectiveness ratios for several drug use outcomes and compared them to a "back-of-the-envelope" estimate of the benefit of reducing drug use. The estimated cost of implementing the standard intervention is $187.52, and the additional cost of the enhanced intervention is $124.17. Cost-effectiveness ratios range from $35.68 to $139.52 per reduced day of drug use, which are less than an estimate of the benefit per reduced drug day. The additional cost of implementing the enhanced intervention is relatively small and compares favorably to a rough estimate of the benefits of reduced days of drug use. Thus, the enhanced intervention should be considered an important additional component of an AIDS prevention strategy for out-of-treatment substance abusers. Zarkin, G.A., Lindrooth, R.C., Demiralp, B., and Wechsberg, W. The Cost and Cost-Effectiveness of an Enhanced Intervention for People with Substance Abuse Problems at Risk for HIV. Health Serv Res., 36(2), pp. 335-355, June 2001.

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

Research Findings

Intramural Research

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

Marijuana Craving Questionnaire

The purpose of this study was to develop and validate a multidimensional questionnaire on marijuana craving. Current marijuana smokers (n = 217) not seeking treatment completed a 47-item Marijuana Craving Questionnaire (MCQ) and forms assessing demographics, drug use history, marijuana quit attempts, and current mood. Exploratory and confirmatory factor analyses indicated that a four-factor solution best described the item structure. Factor subscales derived from the 17-items with significant loadings had respectable internal consistencies and were stable across settings and subgroups. The subscales exhibited low to moderate, positive intercorrelations and were significantly correlated with marijuana use history and a wide range of single-item measures of craving. Findings suggested that four specific constructs characterize craving for marijuana: 1) compulsivity, an inability to control marijuana use; 2) emotionality, use of marijuana in anticipation of relief from withdrawal or negative mood; 3) expectancy, anticipation of positive outcomes from smoking marijuana; and 4) purposefulness, intention and planning to use marijuana for positive outcomes. These data indicate that the MCQ is a valid and reliable instrument for assessing marijuana craving in individuals not seeking drug abuse treatment and that marijuana craving can be measured in the absence of withdrawal. Heishman, S.J., Singleton, E.G., and Liguori, A. Addiction, 96, pp. 1023-1034, 2001.

Brain Imaging Section, Neuroimaging Research Branch

Effect of Nicotine on Brain Activation during Performance of a Working Memory Task

Nicotine has been shown to affect cognition and behavior. Using positron emission tomography with O-15 labeled water, we measured cognitive activation during a working memory task (Two-Back task) in 11 smokers who abstained from smoking for 12 h, and 11 ex-smokers. Cerebral blood flow (CBF) was assayed twice, after the administration of placebo gum and that of 4 mg nicotine gum, respectively. Statistical parametric maps were calculated for each group (smokers and ex-smokers) and each condition (placebo and nicotine). Performance on the Two-Back task did not differ between groups in either placebo or nicotine condition. The brain regions activated by the Two-Back task were consistent with those reported in the literature. However, in the placebo condition, CBF activation in the ex-smokers predominated in the left hemisphere, and in smokers in the right hemisphere. When nicotine was administered, CBF activation was reduced in smokers but enhanced in ex-smokers. The lateralization of CBF activation as a function of nicotine dependence suggests that chronic exposure to nicotine or withdrawal from nicotine affects cognitive strategies used to perform the memory task. The lack of enhancement of CBF activation after nicotine administration in smokers, in contrast to ex-smokers, may reflect tolerance. Clarifying the effects of nicotine on brain function can improve our understanding of the mechanisms of nicotine dependence, and provide a basis for novel, rational treatment interventions. Ernst, M., Matochik, J.A., Heishman, S.J., Van Horn, J.D., Jons, P.H., Henningfield, J.E., and London, E.D. Effect of Nicotine on Brain Activation during Performance of a Working Memory Task. Proceedings of the National Academy of Sciences, USA, 98, pp. 4728-4733, 2001.

Cellular Neurophysiology Section, Cellular Neurobiology Research Branch

Methamphetamine Potentiates Ischemia/Reperfusion Insults after Transient Middle Cerebral Artery Ligation

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

Contribution of the Hyperpolarization-Activated Current (Ih) to Membrane Potential and GABA Release in Hippocampal Interneurons

GABAergic interneurons provide inhibitory input to CA1 pyramidal cells of the hippocampus, and thus play a key role in regulating hippocampal activity. The excitability of these interneurons is regulated by various ion channels, including the hyperpolarization-activated current Ih. IRP investigators utilized whole-cell recording techniques in order to determine the role of Ih in regulating the baseline excitability of hippocampal interneurons and the release of GABA onto CA1 pyramidal cells. In current-clamp recordings from hippocampal stratum oriens (s.o.) interneurons at resting membrane potential (-61 ± 1.2 mV), blockade of Ih with the selective inhibitor ZD 7288 (50 mM) resulted in a hyperpolarization of the membrane potential and a decrease in the rate of spontaneous action potentials. A small population of s.o. interneurons that did not express Ih were substantially more hyperpolarized (-73.6 ± 5.5 mV) under baseline conditions, suggesting that Ih contributes significantly to the resting membrane potential of hippocampal interneurons. Voltage-clamp recordings from postsynaptic CA1 pyramidal cells demonstrated that blockade of Ih by ZD 7288 resulted in a significant reduction (~43%) in the frequency of spontaneous, action potential-dependent inhibitory postsynaptic currents (IPSCs). Moreover, miniature, action potential-independent IPSCs were unaffected by ZD7288, confirming the presynaptic site of action of ZD 7288. These data suggest that Ih is active at the resting membrane potential in s.o. interneurons, and thus contributes to the spontaneous activity of these cells and to the tonic inhibition of CA1 pyramidal neurons in the hippocampus. Since Ih is inhibited by both m- and d-opioid receptors, and is activated by serotonin and norepinephrine, this current may represent an important cellular target for drugs of abuse, under either normal or chronic conditions. Lupica, C.R., Bell, J.A., Hoffman, A.F., and Watson, P.L. Journal of Neurophysiology, 86, pp. 261-268, 2001.

Molecular Neuropsychiatry Section, Cellular Neurobiology Research Branch

Methamphetamine Causes Differential Regulation of Pro-Death and Anti-Death Bcl-2 Genes in the Mouse Neocortex

Bcl-2, an inner mitochondrial membrane protein, inhibits apoptotic neuronal cell death. Expression of Bcl-2 inhibits cell death by decreasing the net cellular generation of reactive oxygen species. Studies by different investigators have provided unimpeachable evidence of a role for oxygen-based free radicals in methamphetamine (METH) -induced neurotoxicity. In addition, studies conducted in this laboratory have shown that immortalized rat neuronal cells that overexpress Bcl-2 are protected against METH-induced apoptosis *in vitro*. Moreover, the amphetamines can cause differential changes in the expression of Bcl-X splice variants in primary cortical cell cultures. These observations suggested that METH might also cause perturbations of Bcl-2-related genes when administered to rodents. Thus, the present study was conducted to determine whether the use of METH might indeed be associated with transcriptional and translational changes in the expression of Bcl-2-related genes in the mouse brain. In this paper IRP investigators report that a toxic regimen of METH did cause significant increases in the pro-death Bcl-2 family genes BAD, BAX, and BID. Concomitantly, there were significant decreases in the anti-death genes Bcl-2 and Bcl-X(L.) These results

thus support the notion that injections of toxic doses of METH trigger the activation of the programmed death pathway in the mammalian brain. Jayanthi, S., Deng, X., Bordelon, M., McCoy, M.T., and Cadet, J.L. Methamphetamine Causes Differential Regulation of Pro-Death and Anti-Death Bcl-2 Genes in the Mouse Neocortex. Jayanthi, S., Deng, X., Bordelon, M., McCoy, M.T., and Cadet, J.L. FASEB Journal, 15, pp. 1745-1752, 2001.

Marijuana Abusers are at Increased Risk for Stroke. Preliminary Evidence from Cerebrovascular Perfusion Data

IRP investigators have recorded blood flow velocity in the anterior and middle cerebral arteries by transcranial Doppler sonography in abstinent marijuana abusers (n = 16) and control subjects (n = 19) to assess the effects of prolonged marijuana use of the cerebrovascular system. The pulsatility index, a measure of cerebrovascular resistance, and systolic velocity were significantly ($p < 0.005$) increased in marijuana abusers compared to the control subjects. These findings suggest that cerebral perfusion observed in 18-30 year old marijuana abusers is comparable to that of normal 60 year-olds. Thus, chronic abuse of marijuana might be a risk factor for stroke. Herning, R.I., Better, W.E., Tate, K., and Cadet, J.L. Annals of the New York Academy of Science, 939, pp. 413-415, 2001.

Antiviral Medications Improve Cerebrovascular Perfusion in HIV+ Non-drug Users and HIV+ Cocaine Abusers

Antiviral medications have been useful in delaying the time course of HIV infection. Antiviral medications have also been reported to delay or reduce symptoms associated with AIDS related dementia and to improve cortical perfusion. The mechanism for this improvement is unclear. Thus, this report studies the effects of antiviral medications on cerebral blood flow velocity in HIV+ cocaine abusers, HIV+ control individuals and appropriate control individuals. Thirty-two unmedicated HIV+ individuals (28 cocaine abusers and 4 control individuals), 22 HIV+ individuals using antiviral medications (16 cocaine abusers and 6 HIV+ control individuals), 47 HIV- cocaine abusers, and 27 control HIV- subjects were studied. Blood flow velocities were determined for the anterior and middle cerebral arteries using transcranial Doppler sonography. HIV+ individuals on antiviral medications had lower pulsatility values, suggesting decreased resistance in the cerebral blood vessels, in comparison to HIV+ individuals not taking antiviral medications. HIV+ cocaine abusers and HIV+ control individuals using antiviral medications had pulsatility values similar to HIV- control subjects. Antiviral medications appear to reduce these cerebrovascular perfusion deficits in HIV+ individuals. The antiviral medications appear to have a direct neuroprotective effect in addition to their antiviral effects. The neuroprotective role of antiviral medications requires further investigation. Herning, R.I., Better, W.E., Tate, K., and Cadet, J.L. Annals of the New York Academy of Science, 939, pp. 405-412, 2001.

Fas-induced Apoptosis of Glioma Cells is Associated with Down-regulation of the hSCO1 Protein, A Subunit of Complex IV

ApoI/Fas belongs to the tumor necrosis factor receptor (TNFR) superfamily and mediates cell death in various cell types. Earlier studies from this laboratory have shown that Fas-mediated cell death of glioma cells occur, in part, through the production of reactive oxygen species (ROS). To further dissect the molecular mechanisms that are involved in Fas-induced cell death, IRP investigators compared gene expression between Fas-treated and saline-treated human neuroglioma H4 cells by using the technique of mRNA differential display. This approach led to the identification of hSCO1, a component of the inner mitochondrial membrane, which is required for the correct assembly, and catalytic function of cytochrome-c oxidase, as a Fas down-regulated gene. The decrease in hSCO1 mRNA expression was time-dependent, becoming most prominent after 4 h of Fas-treatment. Morphological changes observed by confocal microscopy revealed that after 4 h of Fas-treatment, the cells undergo membrane blebbing and early formation of apoptotic bodies. These observations are discussed in terms of their support for an important role of mitochondrial events in Fas-induced apoptosis. Jayanthi, S., Lewis, B.D., and Cadet, J.L. Brain Research Molecular Brain Research, 91, pp. 131-136, 2001.

Involvement of Free Radicals in MDMA-induced Neurotoxicity in Mice

3,4-methylenedioxymethamphetamine (MDMA or ecstasy) is a substituted amphetamine with stimulating and hallucinogenic properties. Administration of MDMA leads to the formation of metabolites responsible for its toxic effects on serotonergic neurons in rats and non-human primates and on dopaminergic neurons in mice. IRP investigators' findings indicate that overexpression of the human superoxide dismutase gene (Cu/Zn-SOD) abolishes certain effects of MDMA such as the decreased level of dopamine, DOPAC and 5-HT in the striatum, inactivation of certain antioxidant enzymes (CU/ZN-SPD, catalase or glutathione peroxidase) or peroxidation of lipids. These data are in agreement with the implication of free radicals and consequently of oxidative stress in the mode of action of

MDMA. Cadet, J.L., Thiriet, N., and Subramanian, J. Annals Medicine Interne (Paris), 152, Suppl 3, pp. 57-59, 2001.

Temporal Profiling of Methamphetamine-induced Changes in Gene Expression in the Mouse Brain: Evidence from cDNA Array

Methamphetamine (METH) is a neurodegenerative drug of abuse. Its toxicity is characterized by destruction of monoaminergic terminals and by apoptosis in cortical and striatal cell bodies. Multiple factors appear to control METH neurotoxicity, including free radicals and transcription factors. Here, using cDNA arrays, IRP researchers show the temporal profile of gene expression patterns in the cortex of mice treated with this drug. Two patterns of changes were obtained from 588 genes surveyed. First, an early pattern is characterized by upregulation of transcription factors, including members of the jun family. Second, a delayed pattern includes genes related to cell death and to DNA repair. A number of trophic factors were also activated at the later timepoint. These observations suggest that METH can activate a multigene machinery that participates in the production of its toxic effects. The resulting degenerative effects of the drug are thus the result of a balance between protoxic and anti-apoptotic mechanisms triggered by its administration to these animals. These observations are of clinical relevance because of the recent identification of degenerative changes in the brains of METH abusers. Cadet, J.L., Jayanthi, S., McCoy, M.T., Vawter, M., and Ladenheim, B. Synapse, 41, pp. 40-48, 2001.

Molecular Neurobiology Section, Molecular Neurobiology Research Branch

Defining Molecular Mechanisms of Cocaine Reward

Cocaine blocks uptake by neuronal plasma membrane transporters for dopamine (DAT), serotonin (SERT) and norepinephrine (NET). Cocaine reward/reinforcement has been linked to actions at DAT or to blockade of SERT. However, neither knockouts of DAT, of SERT or of NET reduce cocaine reward/reinforcement, leaving substantial uncertainty about cocaine's molecular mechanisms for reward. Conceivably, the molecular bases of cocaine reward might display sufficient redundancy that either DAT or SERT might be able to mediate cocaine reward in the other's absence. To test this hypothesis, we examined double knockout mice with deletions of one or both copies of both the DAT and SERT genes. These mice display viability, weight gain, histologic features, neurochemical parameters and baseline behavioral features that allow tests of cocaine influences. Mice with even a single wildtype DAT gene copy and no SERT copies retain cocaine reward/reinforcement, as measured by conditioned place preference testing. However, mice with no DAT and either 0 or 1 SERT gene copies display no preference for places where they have previously received cocaine. The serotonin-dependence of cocaine reward in DAT KO mice is thus confirmed by the elimination of cocaine place preference in DAT/SERT double knockout mice. These results provide new insights into the brain molecular targets necessary for cocaine reward in knockout mice that develop in their absence and suggest novel strategies for anti-cocaine medication development. Sora, I., Hall, F.S., Andrews, A.M., Itokawa, M., Li, X-f., Wei, H-b., Wichems, C., Lesch, K-P., Murphy, D.L., and Uhl, G.R. Proceedings of the National Academy of Science USA, 98, pp. 5300-5305, 2001.

Preclinical Pharmacology Section, Behavioral Neuroscience Research Laboratory

Adenosine A2A Agonist CGS 21680 Decreases the Affinity of Dopamine D2 Receptors for Dopamine in Human Striatum

Adenosine A2A receptors (A2AR) and dopamine D2 receptors (D2R) are highly concentrated in the striatum, where they are colocalized and exert reciprocal antagonistic interactions. It has been suggested that the A2R/D2R interactions might provide a therapeutic approach for basal ganglia disorders, such as Parkinson's disease, and schizophrenia. In the present work evidence is presented for the existence of an A2AR/D2R interaction in human brain by using quantitative autoradiography. The areas analyzed were the dorsal caudate nucleus and putamen. Parallel studies were performed in rat striatal sections. The A2AR agonist CGS 21680 was found to significantly increase IC50 values of competitive-inhibition curves of the D2R/D3R antagonist [125I]iodosulpiride versus dopamine both in rat striatal and human striatal brain sections. Diaz-Cabiale, Z., Hurd, Y., Guidolin, D., Finnman, U.-B., Zoli, M., Agnati, L.F., Vanderhaeghen, J.-J., Fuxe, K. and Ferre, S. NeuroReport, 9, pp. 1831-1834, 2001.

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

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

Program Activities

New NIDA PAs and RFAs

On May 21, 2001, NIDA issued a Program Announcement entitled **Drug Abuse Health Services Research (PA-01-097)**. This PA replaces in its entirety PA-94-047 published in the NIH Guide, Vol. 23, No. 10 on March 11, 1994. Through this PA research is sought on the organization, management, and economics of drug abuse treatment and prevention services, and the effects of these factors on the quality, cost, access to, effectiveness and outcomes of care for drug abuse and addictive disorders. Additionally, this announcement seeks studies that examine the impact of the integration of HIV/AIDS and other services on outcomes.

PAs and RFAs Issued With Other NIH Components/Agencies

On May 16, 2001, NIDA, in collaboration with numerous other NIH components issued a Program Announcement entitled **The Zebrafish as an Animal Model for Development and Disease Research (PA-01-095)**. The purpose of this PA is to solicit applications as part of an NIH initiative to increase our support of the zebrafish as an animal model for development, organ formation, behavior, aging, and disease research. This PA is a reissuance of PA-98-074 which was published in the NIH Guide for Grants and Contracts, Vol. 5, No. 22, on May 21, 1998. This effort stems from an NIH initiative with participation of numerous Institutes and Centers working through the Trans-NIH Zebrafish Coordinating Committee under the co-chairmanship of NICHD and NIDDK.

On May 21, 2001, NIDA and several other NIH components issued a Program Announcement entitled **Behavioral, Social, Mental Health, and Substance Abuse Research With Diverse Populations (PA-01-096)**. Through this PA, sponsoring NIH components invite submission of grant applications for behavioral, social, mental health, and substance abuse research with lesbian, gay, bisexual, transgendered, and related populations (LGBT populations). This PA was developed in response to recommendations produced at a workshop on "New Approaches to Research on Sexual Orientation, Mental Health, and Substance Abuse" which took place on September 27-28, 1999, under the co-sponsorship of NIMH, NIDA, OBSSR and ORWH.

On July 31, 2001, NIDA and NIMH jointly issued a Program Announcement entitled **Collaborative R01s for Clinical and Services Studies of Mental Disorders and AIDS (CSMD) (PA-01-123)**. The purpose of this PA is to support collaborative intervention trials and other clinical and services studies at two or more sites. The studies typically share a specific protocol across the sites and are organized in order to increase sample size, accelerate recruitment, or increase sample diversity and representation. Each site has its own PI and the program provides a mechanism for cross-site coordination, quality control, database management, statistical analysis, and reporting. This PA supercedes PAR-98-017 published December 19, 1997.

On June 25, 2001, NIDA, in collaboration with a number of other NIH components, issued an RFA entitled **International Tobacco and Health Research and Capacity Building Program (RFA-TW-02-005)**. This RFA solicits research and capacity building projects that address the burden of tobacco consumption in low- and middle-income nations by 1) pursuing observational, intervention and policy research of local relevance and 2) building capacity in these regions in epidemiological and behavioral research, prevention, treatment, communications, health services and policy research. Letter of Intent Receipt Date for this RFA is September 4, 2001; Application Receipt Date is October 26, 2001.

On July 25, 2001, NIDA in collaboration with a number other NIH components, issued an RFA entitled **Clinical Research Education and Career Development in Minority Institutions (RFA-AR-01-009)**. The purpose of this RFA is to support the development and implementation of curriculum-dependent programs in minority institutions to train selected doctoral and postdoctoral candidates in clinical research leading to a Master of Science in Clinical Research or Master of Public Health in a clinically relevant area. Letter of Intent Receipt Date for this RFA is December 17, 2001; Application Receipt Date is February 15, 2002.

On July 27, 2001, NIDA, in conjunction with several other NIH Institutes, issued an RFA entitled **Cognitive Neuroimaging: Understanding the Link Between Neuronal Activity and Functional Imaging Signals (RFA-NS-02-009)**. This RFA invites research grant applications that offer the promise of exceptional technical and conceptual advances in our understanding of the nature of the signal being recorded in hemodynamic brain imaging techniques. Letter of Intent Receipt Date for this RFA is September 30, 2001; Application Receipt Date is November 28, 2001.

Other Program Activities

The Methamphetamine Clinical Program

To implement the recommendations of the Methamphetamine Addiction Treatment Think Tank (MATTT) meeting held in January, a process was started to establish a group of sites to conduct clinical trials for methamphetamine dependents patients. Five sites have been selected where the epidemic is currently concentrated, two in the Midwest (Des Moines, Iowa, and Kansas City, Kansas), and the other three are Los Angeles, San Diego, CA, and Honolulu, HI. The first study is a behavioral pilot study where three times a week cognitive based group therapy is offered and data on withdrawal symptoms and methamphetamine urine PK data will be obtained. This will be followed by the first medication study protocol that is approved by FDA (ondansetron) and will be sent to local IRBs for review. This study is projected to start in October 2001. Additionally, selegiline and bupropion will be studied first in inpatient clinical pharmacology studies at UCLA, UTSA and UCSF for safety interactions with amphetamine. Following these studies, and if safety is not an issue, selegiline and bupropion will be advanced to outpatient studies. More safety interaction studies are planned for reserpine. Plans are underway to obtain lobeline from a pharmaceutical manufacturer to study its safety profile with amphetamine and ultimately also advance it to outpatient studies.

Clinical Research Efficacy Screening Trial (CREST-II) Study

In April 2001 a group of outside consultants reviewed the data from each NIDA/VA Medications Development Research Unit (MDRU) in their CREST studies (eight medications total and an unmatched placebo). Out of the 8 medications reviewed two medications (tiagabine, a GABA uptake inhibitor, anti-seizure medication, and Sertraline, an SSRI antidepressant) were shown to give trends toward positive signals in these screening pilot studies. The recommendations of the consultants were to follow up with larger phase II studies on these medications.

Cocaine Clinical Trials Operations

This network of four academic clinical sites has been established to replace the old MDRU sites to conduct clinical trials for cocaine addiction. The sites are University of California, Los Angeles, University of Cincinnati, Medical University of South Carolina, and University of Texas at San Antonio. The contract is in place with two other supporting contracts with TRI and KAI for data management. Eight protocols have been submitted for the sites to study, three are phase one interaction studies (Modafinil, Metyrapone, Tolcapone) one is a phase IIa study (Ondansteron) and two are phase IIb studies (reserpine and cabergoline). These studies have been initiated and subject recruitment is underway.

GBR 12909 Study

The study report from the Phase I (healthy volunteer) study is complete and was reviewed by consultants in June 2001 in planning for a cocaine interaction study. The study showed 30-40% dopamine transporter occupancy at the 100mg dose level. Based on primate data showing equivalent levels of occupancy at doses reducing cocaine self-administration, this may be clinically meaningful in cocaine treatment. The consultants' recommendation was to follow up with an ADME study in cocaine dependent patients.

NS2359 Study

The study has started at the Uniformed Services University of the Health Sciences; the first dose cohort will be complete in September 2001 and will be reviewed by DSMB prior to proceeding to the next dose level.

Selegiline Study

The phase III 300 subject, 16 sites Selegiline Transdermal System study started and subject recruitment is underway.

Lofexidine for Heroin Withdrawal Study

This phase III multisite study protocol has started, and subject recruitment is underway.

CTN Protocol Update

For protocol CTN 0001, Buprenorphine/Naloxone for Detoxification in Inpatient Settings, two sites have begun enrollment, four additional sites will start in the next few months.

For protocol CTN 0002, Buprenorphine/Naloxone for Detoxification in Outpatient Settings, all six sites are enrolling patients. Total enrollment has reached about one-third of the total target enrollment.

For protocol CTN 0003, Buprenorphine/Naloxone: Comparison of Three Taper Schedules for Opiate Detoxification, fourteen sites across nine nodes is set to begin enrollment. Enrollment should begin this fall after IRB and other regulatory approvals are complete.

For protocol CTN 0004, Motivational Enhancement Therapy, one site has begun enrolling; five additional sites will be launched soon.

For protocol CTN 0005, Motivational Interviewing, four sites have begun enrollment, one additional site will start shortly.

For protocol CTN 0006, Motivational Incentives in Drug Free Clinics, five sites are currently enrolling patients; two additional sites will be active when fully launched.

For protocol CTN 0007, Motivational Incentives in Methadone Clinics, three sites are enrolling patients, another four sites will begin enrollment shortly.

The CTN nodes submitted 17 new research concepts as the 3rd Wave in March 2001. These concepts were subsequently reviewed by the CTN Concept Review Sub-committee, of the CTN Steering Committee. Nine concepts were selected and presented to the CTN Oversight Board for review on July 31, 2001. Approved Concepts will be further developed into protocols.

QT Prolongation Consultants Meeting

On September 5, the Medications Discovery & Toxicology Branch (MDTB) held a "QT Prolongation Consultants Meeting" at NIDA Headquarters in Rockville. During recent years, drug-induced QT prolongation has surfaced as a major issue in medications development; several drugs have been withdrawn from the market due to QT prolongation and the associated risk of fatal ventricular arrhythmias. As part of a more general effort to identify and drop "problem compounds" early in the preclinical discovery and development process, the MDTB has established subcontracts to conduct two different *in vitro* assays, the "HERG channel assay" and the "Purkinjie fiber action potential duration assay," both of which are claimed to be predictive of clinical QT prolongation problems. NIDA's consultants - Dr. Alan Stuart Bass (Schering Plough), Dr. Anthony Fossa (Pfizer), Dr. Gary Gintant (Abbott), Dr. Dustan (Eli Lilly), Dr. Peter Siegl (Merck) and Dr. Craig January (University of Wisconsin) - assisted NIDA in interpreting the initial data obtained from the two assays, which in several cases yielded conflicting predictions for the same compound. The meeting proved to be mutually beneficial to NIDA, the consultants, and FDA staff (attending in an observer role), all of whom are struggling to deal with the challenge of predicting QT prolongation problems through new, *in vitro* assays. Regulatory guidelines have not been established in this area. The meeting was organized by Drs. Naresh Chand, James Terrill and David McCann.

NIDA/VACSP #1018 Buprenorphine Best Practices Trial

Enrollment for the study closed on January 6, 2001 with a total of 583 patients being enrolled. Patients can participate up to one year from the date of their enrollment. The last patient should complete on February 6, 2002 (assuming 1 year participation and 30 day follow-up). 38 physicians' offices and 33 pharmacies participated.

33.8% of the patients enrolled were female. The mean age at baseline was 35.8 years (36.0 median) with a range of 15 to 66. As of May 21, 2001, 272 patients were still following the protocol. The main reasons for dropout were failure to return to clinic (63%) followed by the patient's request to discontinue (8.6%).

Meetings are currently being held with the data center, to finalize the data analyses to be performed, before the final dataset is obtained, in an effort to decrease the time to a final study report.

NIDA's New and Competing Grants Awarded Since May 2001

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

Akins, Chana K. -- University of Kentucky
A Visual Cue Model To Investigate Cocaine Reward

Andrews, Anthony R. -- Ohio University
High Speed Microscale Drug Screening of Saliva

Anglin, M.D. -- UCLA Drug Abuse Research Training Center
UCLA Integrated Substance Abuse Program

Anokhin, Andrey -- Washington University
Biobehavioral Markers of Risk for Nicotine Addiction

Arfken, Cynthia L. -- Wayne State University
Organizational Processes In Treatment Programs

Barr, Gordon A. -- Research Foundation for Mental Hygiene Inc.
Chronic Opiates During Ontogeny: A Microarray Analysis

Bartus, Raymond T. -- Alkermes, Inc.
Novel, Sustained-Release Naltrexone for Opiate Abuse

Baum, Marianna K. -- Florida International University
Zinc Therapy In Zinc Deficient HIV+ Drug Users

Beaudoin, Alison O. -- Yale University School of Medicine
Behavioral Effects of GHB In Healthy Volunteers

Berke, Joshua D. -- Boston University
Multiple Memory Systems In Action Selection

Bidlack, Jean M. -- University of Rochester
Pharmacology of Drug Abuse

Bigelow, George E. -- Johns Hopkins Bayview Medical Center
Human Behavioral Pharmacology of Substance Abuse

Blanco, Carlos -- Columbia University
Opioid Dependence and Pathological Gambling

Booze, Rosemarie M. -- University of Kentucky Medical Center
HIV/Cocaine Neurotoxicity In Females

Borsook, David -- Massachusetts General Hospital
CNS Reward/Aversion Circuitry Activated By Pain/Opioids

Brown, David R. -- University of Minnesota
Mucosal Defense Mechanisms In Substance Abuse

Brue, Vesta -- Lifetechniques, Inc.
Electronic Smoking Cessation Monitor and Communicator

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

Carelli, Regina M. -- University of North Carolina at Chapel Hill
Neurophysiological Study: Cocaine and Natural Reinforcers

Carlson, Robert G. -- Wright State University
MDMA/Club Drug Use and STD/HIV Sex Risk Behavior In Ohio

Carroll, Frank I. -- Research Triangle Institute
Cocaine: A Study of the Biochemical Mechanism of Action

Catalano, Richard F. -- University of Washington
Reducing Risk and Enhancing Protective Factors In Children

Chiauzzi, Emil -- Inflession, Inc.
Multimedia Smoking Cessation for Alcoholic Clients

Childers, Steven R. -- Wake Forest University
Neuroscience of Drug Abuse Training Program

Clatts, Michael C. -- Columbia University of New York
HIV Risk Among MSM 'Speed' Injectors

Cohen, Mark S. -- UCLA Brain Mapping Center
Enabling Technologies In FMRI and Cigarette Smoking

Commons, Kathryn G. -- Children's Hospital of Philadelphia
Opioids and Stress: The PAG

Corodimas, Keith P. -- Lynchburg College
Adenosinergic Neuromodulation of Emotional Learning

Coscia, Carmine J. -- St. Louis University School of Medicine
Gestational Buprenorphine and Mesolimbic Systems Ontogeny

Crabbe, John C. -- Oregon Health Sciences University
Biological Bases of Drug Seeking Behavior

Dewey, William L. -- Virginia Commonwealth University
Training In the Pharmacology of Abused Drugs

Dishion, Thomas -- University of Oregon
Understanding and Preventing Adolescent Drug Abuse

Eiden, Rina D. -- Research Institute on Addiction
Maternal Substance Use and Toddler Self-Regulation

Ellinwood, Everett H. -- Duke University
Medication Development for Methamphetamine Abuse

Escoffery, Ngoc-Cam T. -- University of Georgia
Smoking Cessation Intervention for College Smokers

Fairbanks, Carolyn A. -- University of Minnesota
Endogenous Agmatine In Glutamatergic Pain Processing

Fals-Stewart, William S. -- Research Institute on Addiction
Brief Couples Therapy In Drug Abuse Treatment

Fiez, Julie A. -- University of Pittsburgh
FMRI Studies of the Neural Basis of Reward Processing

Flanigan, Timothy P. -- Miriam Hospital
HIV and Other Infectious Consequences of Substance Abuse

Flewelling, Robert L. -- Pacific Institute for Research
National Study of Risk Factors for Adolescent Drug Use

Flores, Christopher M. -- University of Texas Health Science Center
Mechanisms of Nicotine-Induced Neurogenic Inflammation

Foster, E. M. -- Oregon Research Institute
School-Wide Prevention of Risk Factors for Drug Abuse

Frost, Douglas O. -- University of Maryland, Baltimore
Effects of M-Amphetamine on Neural Circuit Development

Frost, James J. -- Johns Hopkins University
Brain Opioid Receptors and Cognition In Cocaine Abuse

Gatley, John S. -- Brookhaven National Laboratory
Brain Imaging and Drug Abuse

Gebo, Kelly A. -- Johns Hopkins University School of Medicine
Improving Health Care Utilization In HIV+ Drug Users

Gelberg, Lillian -- UCLA Center for Health Sciences
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Gibb, James W. -- University of Utah
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Girdler, Susan S. -- University of North Carolina at Chapel Hill
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Gollub, Erica L. -- University of Pennsylvania
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Gonzalez-Haddad, Gerardo -- Yale University School of Medicine
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Graham, Camilla S. -- Beth Israel Deacones Medical Center
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Grobe, James E. -- University of Kansas
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Hatsukami, Dorothy K. -- University of Minnesota Medical School
Treatment of Smokeless Tobacco Users

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Voucher-Based Incentives To Treat Pregnant Smokers

Hinkin, Charles H. -- UCLA/NPI
Predictors: Medication Adherence In HIV+ Cocaine Abusers

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Endocannabinoid Mechanisms of Stress-Induced Analgesia

Howell, Leonard L. -- Emory University
PET Imaging and Cocaine Neuropharmacology In Monkeys

Huang, Li-Yen M. -- University of Texas Medical Branch
Opioid Receptor Gene Transfer-Pain and Tolerance

Hunt, Geoffrey P. -- Scientific Analysis Corp.
The Social World of Club Drugs: A Qualitative Study

Javitt, Daniel C. -- Nathan Kline Psychiatric Institute
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Jennings, Peggy J. -- University of Wyoming
Cognitive Consequences of the Stress Response

Kharasch, Evan D. -- University of Washington
Methadone and HIV Drug Interactions

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Kimberg, Daniel Y. -- University of Pennsylvania
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Improving Drug Abuse Treatment By Research and Training

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Cocaine-Induced Disturbances of Mouse Brain Development

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Pharmacotherapy for Opioid and Cocaine Dependence

Kuhar, Michael J. -- Emory University
Cart: A Novel Cocaine Regulated Neurochemical

Landau, Nathaniel R. -- Salk Institute for Biological Studies
Murine Model for HIV-1 Replication

Latimer, William W. -- Johns Hopkins University
Neurobehavioral Model of HIV In Injection Drug Users

Law, Ping-Yee -- University of Minnesota
G Proteins and Opioid Receptor Functions

Levitt, Pat R. -- University of Pittsburgh
Brain Structure and Function After Fetal Cocaine Exposure

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

Ling, Walter -- Friends Medical Research Center
Pain Analgesic Response In Opiate Dependence

Lipsey, Mark W.-- Vanderbilt University
Meta-Analysis of Risk For Substance Use

Lord, Sarah E. -- Innovative Training Systems
Multimedia Addiction Severity Index for Adolescents

Luedtke, Robert R. -- University of North Texas
Mapping the D2/D3 Dopamine Receptor Binding Sites

Lupica, Carl R. -- University of Arizona
The Functional Neurobiology of Cannabinoids In Brain

Macaulay, Araxi -- National Health Promotion Assoc., Inc.
Life Skills Training Parent Component

Mackie, Kenneth P. -- University of Washington
Cannabinoid Modulation of Neuronal Function

Mannuzza, Salvatore -- New York University School of Medicine
Childhood Stimulant Treatment and Adult Substance Abuse

Mao, Jianren -- Massachusetts General Hospital
Cellular Mechanisms of Hyperalgesia and Opioid Tolerance

Martin, Billy R. -- Virginia Commonwealth University
Center for Drug Abuse Research

Mayhan, William G. -- University of Nebraska Medical Center
Nicotine-Induced Cerebrovascular Dysfunction

Meisch, Richard A. -- University of Texas Houston Health Science Center
Drug Reinforcing Effects

Mendelson, Jack H. -- McLean Hospital
Drug Abuse Research Training Program

Miller, Gregory A. -- University of Illinois
Neurocognitive Mechanisms: Appetitive and Aversive Emotion

Molitor, Thomas W. -- University of Minnesota
Training In Neurobehavior/Neuroimmune Addiction Research

Molliver, Mark E. -- Johns Hopkins University School of Medicine
Drug Addiction: Dual 5-HT Innervation of Limbic System

Monterosso, John -- University of Pennsylvania
Brain Substrates of Self-Control In Addiction

Morgan, Michael M. -- Washington State University
Contribution of the PAG To Morphine Tolerance

Morris, Martina W. -- Pennsylvania State University
Modeling HIV and STD In Drug User and Sexual Networks

Morrow, Lisa A. -- Western Psychiatric Institute
WTW Clients: Substance Abuse and Neuropsychiatric Function

Morse, Edward V. -- Tulane University Health Sciences Center
Risk Reduction for Young African American IDUs

Nemoto, Tooru -- University of California, San Francisco
HIV Risk Reduction Among Asian Women

Neumeyer, John L. -- McLean Hospital
Mixed Kappa/MU Opioids: Synthesis and Evaluation

Nunes, Edward V. -- Columbia University
Drug Abuse Pharmacotherapy: Methodologic Initiatives

Odum, Amy -- University of New Hampshire
Effects of Drugs In An Animal Model of Relapse

Orwin, Robert G. -- Westat, Inc.
Specialized Treatment for Women and Children

Perrine, M. W. -- Addiction Research Institute
Drugs, Alcohol, and Driving: Prevalence and Crash Risk

Pickett, Kate E. -- University of Chicago
Patterns of Maternal Smoking During Pregnancy

Polgar, Michael -- Washington University
Families As Partners In Homeless Drug Abuse Services

Porrino, Linda J. -- Wake Forest University School of Medicine
Neurobiological Correlates of Cocaine Abuse

Potts, Geoffrey F. -- Rice University
ERP Studies of Neural Systems of Salience Evaluation

Powell, Jane H. -- Goldsmiths College
Smoking Cessation, Reward Motivation And Impulsivity

Pricheps, Leslie S. -- NYU School of Medicine
Biobehavioral Heterogeneity of Crack Cocaine Dependence

Quick, Michael W. -- FASEB
New Perspectives In Transporter Biology-FASEB Conference

Quick, Michael W. -- University of Alabama at Birmingham
GABA Transporters: Trafficking and Regulation

Richards, Jerry B. -- State University of New York at Buffalo
Drug Abuse and Impulsivity : Tests of Animal Models

Riley, William T. -- Pics, Inc.
Computerized Scheduling of Nicotine Nasal Spray

Risinger, Robert C. -- Medical College of Wisconsin
Neural Substrates of Human Cocaine Self-Administration

Robinson, Terry E. -- University of Michigan
Neural Basis of Behavioral Sensitization

Robinson, Terry E. -- University of Michigan
The Influence of Drugs of Abuse on Neuronal Morphology

Roffman, Roger A. -- University of Washington
Reaching and Motivating - Change In Teen Marijuana Smokers

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Affective and Cognitive Processes In Smoking Craving

Schoffelmeer, Anton N. -- Free University
Gene Expression Patterns During Heroin Seeking Behavior

Schwarzschild, Michael A. -- Massachusetts General Hospital
A2a Adenosine Receptors In Psychostimulant Sensitization

Schweitzer, Paul P. -- Scripps Research Institute
Cannabinoids and Central Neuronal Activity

Sealfon, Stuart C. -- Mount Sinai School of Medicine
Interdisciplinary Training In Drug Abuse Research

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

Segal, David S. -- University of California, San Diego
Behavioral Characterization of Acute and Chronic Amphetamine

Shapshak, Paul -- University of Miami School of Medicine
Gene Expression In HIV Associated Dementia Brain

Shibusawa, Tazuko -- Columbia University
HIV Risk Among Older African American/Latino Drug Users

Shimamura, Arthur P. -- University of California
Role of the Orbitofrontal Cortex In Regulating Emotion

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Associative Contributions To Drug Tolerance

Simon, Eric J. -- New York University
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Sirevaag, Erik J. -- Washington University
Behavioral Genetics of Nicotine Dependence

Slotkin, Theodore A. -- Duke University Medical Center
Fetal and Adolescent Nicotine Effects on CNS 5ht Systems

Smagin, Gennady N. -- Louisiana State University Health Sciences Center
Neurochemistry of Cocaine Reinforcement

Stein, Michael D. -- Rhode Island Hospital
Midcareer Investigator Award In Substance Abuse Research

Stella, Nephi -- University of Washington School of Medicine
Cannabinoid Signaling System In Microglial Cell

Sterk, Claire -- Emory University
Young Adults and Drug Use: Careers and Familiar Factors

Stevens, Craig W. -- Oklahoma State University
Functional Evolution of Opioid Receptors

Stitzel, Jerry A. -- University of Michigan Medical Center
Identification of Functional Nachr Variants In Mice

Striley, Catherine W. -- Washington University
Culture In Congruence and Substance Treatment Access

Tashkin, Donald P. -- University of California, Los Angeles
Pulmonary Effects of Habitual Use of Marijuna

Traynor, John R. -- University of Michigan
Opioid Receptor Mechanisms

Tseng, Leon F. -- Medical College of Wisconsin
Role Of Endogenous Opioid Peptides In Opioid Addiction

Tsibulsky, Vladimir -- University of Cincinnati
Measurement of Priming and Satiety Thresholds In Mice

Wagstaff, John D. -- Cognetix, Inc.
Cgx-1160, A Non-Opioid, Broad-Spectrum Analgesic

Weeks, Margaret R. -- Institute for Community Research
HIV Prevention In High Risk Drug Use Sites: Project Rap

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

Williams, Jill M.-- University of Medicine & Dentistry of New Jersey
Nicotine Dependence Treatment In Psychiatric Comorbidity

Williams, Mark L. -- University of Texas Health Sciences Center, Houston
A Test of Peer Delivered Self-Efficacy Intervention

Winder, Danny G. -- Vanderbilt University Medical Center
Regulation of LTP By GI-Linked Receptors

Wong, Frank Y. -- George Washington University
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Woods, James H. -- University of Michigan Medical School
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Director's Report to the National Advisory Council on Drug Abuse
September, 2001

Extramural Policy and Review Activities

Review Meetings

For this Council cycle, the Office of Extramural Affairs arranged and managed 23 review meetings for 373 applications in its standing committees, applications in conflict-of-interest with standing committees, and RFA submissions. There were an additional 13 reviews held for contract proposals, and one concept was reviewed.

The reviews for NIDA's chartered committees were held. These consist of NIDA-E (Treatment Review Committee), NIDA-F (Health Services Review Committee), NIDA-L (Medications Development Committee), and NIDA-K (Training Committee). Three Special Emphasis Panels were held to review applications in conflict with the chartered committees. Five Special Emphasis Panels were constituted for reviews of specific mechanisms: centers, program projects (two meetings), institutional development programs, and conference grants. Two additional Special Emphasis Panels were required for specific applications. In addition, OEA staff managed the reviews for B/START and Cutting Edge Basic Research Award mechanisms.

The following RFA review meetings were held:

DA 01-004	**The Transition from Drug Use to Addiction: Unearthing the Switch**
DA 01-005	**Health and Developmental Consequences of Prenatal Exposure to Methamphetamine**
DA 01-006	**International Studies of HIV/AIDS**
DA 01-007	**HIV/AIDS and Drug Use Among Adolescents**
DA 01-008	**Health Disparities: Drug Use and Its Adverse Behavioral, Social, and Medical Consequences**
DA 01-009	**The Next Generation of Drug Abuse Prevention Research**
DA 01-010	**Responding to Club Drugs and Other Emerging and Current Drug Abuse Trends**
DA 01-014	**Research on GHB and Its Precursors**
DA 01-015	**Therapeutic Community Research**

The Contracts Review Branch managed the following reviews of proposals:

N44DA-1-5514	**State and Local Epidemiological Planning**
N01DA-1-2200	**Pharmacy and Clinical Support to the Clinical Trials Network**

N01DA-1-2201	**Administrative Support Center to the Clinical Trials Network**
N01DA-1-9902	**Subject Recruitment for NIDA Intramural Research Program**
N44DA-1-5502	**SA Prevention Program - Phase II SBIR**
N01DA-1-1107	**NIDA NOTES**
N44DA-1-7701	**Configure Gene Chips - Phase II SBIR**
N01DA-1-8815	**Synthesis Medicinal Chemistry**
N01DA-1-8817	**Pharmacokinetic Analysis Resource Center**
N44DA-1-7700	**JAVA Tool - MicroArrays**
N01DA-1-1105	**Research Dissemination**
N01DA-1-1106	**NIDA's Science Meetings Logistical Support**
N01DA-1-8818	**Regulatory Affairs Support**

In addition a concept for SBIR contract project N43DA-2-7726, Functional Imaging Agents, was reviewed.

Staff Training and Policy Development

The OEA Symposium Series continued its monthly meetings for staff development. In May 2001, staff raised a number of items for discussion from the scheduled "open floor" forum. In June 2001, Dr. Karin Johnson, of NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA), presented on using the internet to provide ideas for NIDA activities. July 2001's meeting consisted of discussion of case studies, and August's meeting centered on a discussion of bioethics, led by Mr. Noble Jones, CAMCODA. In August 2001, Dr. Mark Swieter, SRA in the Basic Science Review Branch, OEA, assumed responsibility for organization of the OEA Symposium Series.

Dr. Teresa Levitin, Director, OEA, and Ms. Loretta Beuchert, Program Assistant, OEA, are compiling comments reviewers made about their participation in the Cutting-edge Basic Research Award (CEBRA) initiative. These comments will provide guidance as future procedures and policies related to CEBRA are developed.

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Congressional Affairs

(Prepared August 13, 2001)

Fiscal 2002 Budget

Progress on the Labor-HHS Appropriations bill continues, although other pressing legislative concerns took center stage for the Congress before the summer recess. At the time of the recess, scheduled from August 3, 2001 to September 5, 2001 the House had passed nine of the appropriations bills, and the Senate four of the bills.

As a result, by the start of the recess lawmakers in both parties had begun suggesting that the two most expensive of the 13 appropriations bills -- Defense and Labor, Health and Human Services, and Education -- will likely be among the last cleared. There was also speculation that the two measures might be combined into a single piece of legislation, one that would allot more than three-fifths of all discretionary spending in the fiscal year starting October 1, 2001.

President Bush's proposal would spend $115.7 billion in discretionary funds on programs governed by the Labor-HHS bill, a 6.6% increase. That proposal did not assume the additional fiscal year 2002 spending that is likely to be authorized in whatever education bill emerges from conference. The House bill would allow that amount to increase by $4.6 billion, the Senate by $14.4 billion.

Meetings/Briefings

JMay 11, 2001 - Dr. Timothy P. Condon, Associate Director, NIDA and Dr. Jack Blaine, Chief, Medications Research Grants Branch, DTRD, briefed Alan Slobodin, Counsel for the House Energy & Commerce Subcommittee on Oversight and Investigations on prescription drug abuse. The Subcommittee was in preparation for a hearing on the re-importation of pharmaceuticals and sought information on the science of addiction as it related to prescription drugs. Keith Van Wagner, OSPC, accompanied Dr. Condon and Dr. Blaine.

May 14, 2001 - Dr. Alan I. Leshner, Director, NIDA, along with Dr. Ruth Kirschstein, Acting Director, NIH and other members of the NIH community, briefed Rep. Patrick Kennedy (D-RI) on Outreach Programs that are on-going for substance abuse and child health. Dr. Leshner spoke specifically on preventing drug use among children and adolescents. Keith Van Wagner, OSPC, accompanied Dr. Leshner.

June 29, 2001 - Dr. Frank Vocci, Director, DTRD, attended a briefing of Bill Duncan, staffer to Rep. Jim Istook (R-OK). The briefing focused on innovations in substance abuse treatment and was held at NIH. Along with Dr. Vocci, representatives from NIAAA and SAMHSA provided information to Mr. Duncan on the topic. Mary Mayhew, OSPC, accompanied Dr. Vocci.

July 23, 2001 - Susan David, Deputy Director of the Prevention Research Branch, DESPR, briefed Sharon Pinkerton and staff members of the House Government Reform Subcommittee on Criminal Justice, Drug Policy, and Human Resources on the status of NIDA's evaluation of the National Youth Anti-Drug Media Campaign. The Media Campaign is run by the Office of National Drug Control Policy, and was the focus of a hearing before the Subcommittee on August 1, 2001. Mary Mayhew and Keith Van Wagner, OSPC, accompanied Ms. David.

July 26, 2001 - At the request of Tony Haywood, minority staffer for the House Government Reform Subcommittee on Criminal Justice, Drug Policy, and Human Resources, Susan David, Deputy Director of the Prevention Research

Branch in the Division of Epidemiology, Services and Prevention Research, briefed him on NIDA's evaluation of the National Youth Anti-Drug Media Campaign. The Media Campaign is run by the Office of National Drug Control Policy, and was the focus of a hearing before the Subcommittee on August 1, 2001. Mary Mayhew and Keith Van Wagner, OSPC, accompanied Ms. David.

July 31, 2001 - Dr. Glen Hanson, Director, Division of Neuroscience and Behavioral Research, participated in a teleconference on drug abuse that was sponsored by Rep. Sam Graves (R-MO). The panel's discussion was broadcast to the Kansas City area, and focused primarily on the growing use of Club Drugs and their spread into mainstream America. Mary Mayhew, OSPC, accompanied Dr. Hanson.

Hearings

House Energy and Commerce Subcommittee on Oversight and Investigations Hearing - June 7, 2001

Dr. Leshner was invited to testify before the House Energy and Commerce Subcommittee on Oversight and Investigations, chaired by Rep. James Greenwood (R-PA), at a hearing on: "Continuing Concerns Over Imported Pharmaceuticals". The hearing focused on growing concerns that American consumers are not being given adequate protection by the federal government against unsafe pharmaceuticals being imported from abroad. Witnesses included representatives from ONDCP, DEA, US Customs, state and local law enforcement and the pharmaceutical industry.

In his statement before the Subcommittee, Dr. Leshner detailed the latest scientific findings about psychoactive prescription drugs and their potential for abuse. He also informed the members of the recent launch of NIDA's major initiative on prescription drug abuse and misuse. He also discussed efforts to encourage more research into this area and to educate the public about the consequences of abusing prescription drugs. Dr. Leshner stressed that these medications, when taken as directed, can be important life-saving tools, though the public needs to be made aware of the potential dangers posed by misuse.

Senate Governmental Affairs Committee Hearing - July 30, 2001

The Senate Governmental Affairs Committee, chaired by Sen. Joseph Lieberman (D-CT), held a hearing on "The Rising Use of the Drug Ecstasy: Focusing on Ways the Government Can Combat the Problem". Dr. Leshner, along with representatives from ONDCP, DEA, US Customs, and state and local law enforcement, was invited to testify before the Committee. The hearing was convened to learn more about the combined and coordinated efforts on the part of the Federal government to effectively and efficiently combat the threat of Ecstasy. The Committee brought together a broad spectrum of Federal agencies to describe the public health threat of MDMA from the law enforcement, interdiction, education, prevention and research perspectives.

Testifying before the Committee, Dr. Leshner detailed the current state of the science regarding Ecstasy research, as well as what still needs to be discovered in this area. Expounding on some of the potential health consequences of use and abuse, Dr. Leshner told the Committee that in his opinion, the most troubling aspect of MDMA was its impact on the neurotransmitter, serotonin. He also informed the Committee of NIDA's recent National Conference on MDMA Research, which focused on not only on what is known about the drug, but what needs to be emphasized in future investigations. Sen. Lieberman asked Dr. Leshner if there were any legitimate psychoanalytic uses for the drug. Dr. Leshner indicated that there has never been a controlled clinical trial demonstrating MDMA's usefulness for any purpose.

House Government Reform Subcommittee on Criminal Justice, Drug Policy, and Human Resources Subcommittee Hearing - August 1, 2001

Susan David, Deputy Director of the Prevention Research Branch, DESPR, was invited to testify before the House Government Reform Subcommittee on Criminal Justice, Drug Policy, and Human Resources, chaired by Rep. Mark Souder (R-IN) at a hearing on "The National Youth Anti-Drug Media Campaign: How to Ensure the Program Operates Efficiently and Effectively?" The hearing was held to consider how to make sure that the billion dollar Youth Anti-Drug Media Campaign, now in it's fourth year, operates in such a way that it has a meaningful impact to prevent drug abuse among young people. Ms. David testified as to the work being done to successfully complete the Phase III evaluation of the Media Campaign.

Bills of Interest

S. 89 - Drug-Free America Act of 2001 - Sen. Charles Grassley (R-IA) introduced S. 89 on January 22, 2001, a bill that primarily is designed to enhance the illegal narcotics control activities of the US, including provisions relating to enhancing inspection and drug interdiction capabilities of the Customs Service and the National Guard. The bill also authorizes NIDA's Clinical Trials Network to conduct its large-scale treatment studies in community settings. Under the proposed legislation, the authorization would be through Fiscal Year 2007. The bill also includes a 'sense of the Senate' section that encourages NIH to work with experts from private industry to promote research regarding pharmacological options that may be employed to support drug treatment efforts. The bill would also increase the number of residential drug abuse treatment units in Federal prisons and compel the Secretary of HHS to award grants in establishing adolescent therapeutic community treatment programs. In addition, it would have grants awarded by ONDCP to establish the National Community Anti-Drug Coalition, funding up to two million dollars in Fiscal Year 2002. S. 89 was referred to the Senate Judiciary Committee. No further action has been taken.

S. 304 - Drug Abuse Education, Prevention and Treatment Act of 2001 - Citing the need for a more balanced approach to the war on drugs, a bipartisan group of senators introduced S. 304 on February 13, 2001. Sen. Orrin Hatch (R-UT) and four original co-sponsors (2 Republican, 2 Democrat) introduced the bill to reduce illegal drug use and trafficking and to help provide appropriate drug education, prevention, and treatment programs. Along with provisions that would increase penalties for drug-related offenses involving juveniles and reestablish drug courts, S. 304 allows for drug-free prison incentive grants for the creation and expansion of substance abuse treatment programs in correctional settings. Included in the bill is language that encourages an aftercare component in the treatment of prisoners for drug abuse and addiction. Section 308 calls for the expansion of drug abuse prevention and treatment research at NIDA and authorizes an appropriation of $76.4 million for that purpose. The bill also provides for the development of additional school and community-based drug education and prevention programs that are 'researched-based'. In addition, S. 304 contains a section that would include religious organizations as Non-Governmental Organizations that should be considered to provide assistance on the same basis as other such organizations. Upon its introduction, S. 304 was referred to the Senate Committee on the Judiciary. No further action has been taken, though the bill has gained two additional Democrat co-sponsors.

S. 843/H.R. 1896 - Treatment on Demand Assistance Act - These bills, Sen. Barbara Boxer's (D-CA) S. 843, and it's House companion, sponsored by Rep. Calvin Dooley (D-CA), were introduced on May 8th and May 17th of 2001, respectively. The bills would authorize grants for the purpose of increasing the maximum number of individuals to whom public and nonprofit private entities are capable of providing effective treatment for substance abuse, with the goal of ensuring that substance abuse treatment is available for all who seek it. They would set up state grant programs to support: the construction of treatment facilities; payments to treatment centers; drug testing; and counseling, including mental health services. Among the programs proposed under the bills, several would provide substance abuse treatment to convicted criminals. States would be required to match the money with non-federal contributions. S. 843 would authorize $600 million in Fiscal Year 2002, and increase funding by an additional $600 million each year through Fiscal Year 2006 - for a total funding of $3 billion. H.R. 1896 would authorize $250 million each year through 2006. The House version of the bill has 28 co-sponsors (24 Democrats, 3 Republicans, and 1 Independent), while the Senate bill has none. The Treatment on Demand Assistance Act was referred to the Health, Education, Labor and Pensions Committee in the Senate, and both the Energy & Commerce and Judiciary Committees in the House. S. 843 is very similar to S. 160, a bill previously introduced in the 107th Congress by Sen. Boxer.

S. 1208/H.R. 2582 - Ecstasy Prevention Act of 2001 - On July 19, 2001, Sen. Bob Graham (D-FL) and six co-sponsors (five Democrats and 1 Republican) introduced a bill in the Senate that is designed to combat the trafficking, distribution, and abuse of Ecstasy (and other club drugs) in the United States. On July 20, 2001, Rep. John Mica (R-FL) and four co-sponsors (3 Republicans and 1 Democrat) introduced a House companion bill, H.R. 2582. The bills include provisions for new grants for Ecstasy abuse prevention, combating the trafficking of MDMA in areas designated by ONDCP as high intensity drug trafficking areas, and the creation of a drug test for MDMA. They would also direct NIDA to submit a report to Congress by January 1, 2003 on the progress and current findings of the research on the health consequences of Ecstasy abuse. In addition, S. 1208/ H.R. 2582 would establish an interagency Ecstasy/Club Drug Task Force to design, implement, and evaluate the education, prevention, and treatment practices and strategies of the Federal Government with respect to Ecstasy, MDMA, and emerging club drugs. H.R. 2582 differs from S. 1208 only in that it would require NIDA to submit an interim report on MDMA research before the final report. S. 1208 was referred to the Senate Judiciary Committee, while H.R. 2582 has been put before the House Energy & Commerce Committee and the House Judiciary Committee.

H. Con Res. 84 - Sponsored by Rep. Joe Baca (D-CA), this resolution aims to support Red Ribbon Week, which promotes drug-free communities through drug prevention efforts, education, parental involvement, and community-wide support. It also encourages all Americans to promote drug-free communities and to participate in drug

prevention activities to show support for healthy, productive, drug-free lifestyles. On March 27, 2001 H. Con. Res. 84 was referred to the House Committee on Energy and Commerce. On July 18, 2001, the full Committee considered the resolution during a Mark-up session and ordered it to be Reported out by Unanimous Consent.

H.R. 1 - No Child Left Behind Act - Introduced by Rep John Boehner (R-OH), H.R. 1 passed the House on May 23, 2001. The exhaustive bill would amend the Elementary and Secondary Education Act of 1965 (ESEA) to revise, rename, consolidate, and reauthorize certain educational programs and activities. The main component of the bill would require states to test elementary and junior high students in math and reading each year. The bill also would authorize funding for disadvantaged students to meet higher standards, professional development for teachers, funding to states for innovative strategies, safe and drug free schools programs and education technology programs. One amendment to the bill offered and accepted would require the active, written consent of parents before an educational agency or institution can administer any survey to a child concerning "illegal, anti-social, or self-incrementing behavior", which could potentially have an adverse effect on on-going NIDA research, including the Monitoring the Future study. The bill, as of August 1, 2001 is in Conference.

H.R. 162 - Mental Health and Substance Abuse Parity Amendments of 2001 - Introduced by Rep. Marge Roukema (R-NJ) on January 3, 2001, H.R. 162 is identical to legislation sponsored in the 106th Congress by the Representative. The bill would amend the Public Health Service Act, Employee Retirement Income Security Act of 1974, and the Internal Revenue Code of 1986 to prohibit group and individual health plans from imposing treatment limitations or financial requirements on the coverage of mental health benefits and on the coverage of substance abuse and chemical dependency benefits if similar limitations or requirements are not imposed on medical and surgical benefits. H.R. 162 has been referred to the House Education and the Workforce, the House Energy and Commerce, and the House Ways and Means committees. When originally introduced, H.R. 162 had 27 co-sponsors. At present the bill has 155 co-sponsors (131 Democrats, 23 Republicans, and 1 Independent), though no further action has been taken.

H.R. 2291 - reauthorization of the Drug Free Communities Act - On June 21, 2001, Rep. Rob Portman (R-OH) introduced H.R. 2291 that would extend the authorization of the Drug-Free Communities Support program for an additional 5 years, to authorize a National Community Anti-Drug Coalition Institute, and for other purposes. H.R. 2291 has 37 co-sponsors (21 Democrats, 16 Republicans). Included in the bill are provisions to fund the program at just over $50 million for Fiscal Year 2002, with roughly $10 million increases each year through Fiscal Year 2007. Also included are additional grants to foster coalition mentoring activities under the Drug-Free Communities Support Program and an increase of the limit on administrative costs to six percent. In addition, the bill would allow ONDCP to make grants to an organization to provide for the establishment of a National Community Anti-Drug Coalition Institute. The appropriation for this authorization would be $2 million in Fiscal Year 2002. H.R. 2291 was referred to both the House Energy & Commerce and Government Reform Committees. On July 24, 2001 H.R. 2291 was sent to the House Government Reform Subcommittee on Criminal Justice, Drug Policy and Human Resources for Mark-up, and then ordered to be Reported on July 25, 2001 after being forwarded and Marked-up by the full Committee.

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International Activities

Scientists from 25 countries, the World Health Organization, and AIDS 2002 Barcelona participated in the sixth NIDA International Forum, **Building International Research on Drug Abuse: Children and Youth at Risk,** convened from June 14 through 16, 2001, in Scottsdale, Arizona, immediately before the Annual Scientific Meeting of the College on Problems of Drug Dependence. Through plenary sessions, oral and poster presentations, and small group discussions, participants exchanged information about advances in drug abuse research from the fields of basic science, epidemiology and prevention, and pharmacological and behavioral treatment. Presenters included NIDA Director Dr. Alan I. Leshner, Dr. Vincent Smeriglio and Dr. Jagjitsing Khalsa, CAMCODA; Dr. Elizabeth Robertson, DESPR; Dr. Glen Hanson, DNBR; Dr. Frank Vocci, Dr. Joseph Frascella, and Dr. Ivan Montoya, DTRD; Dr. Cindy Miner, OSPC; and Dr. Sharon Hrynkow, NIH Fogarty International Center.

NIDA co-sponsored a symposium at the **9th International Conference on AIDS, Cancer, and Related Problems,** convened from May 27 to June 1, 2001, in St. Petersburg, Russia. The annual meeting is the largest conference in the former Soviet Union dealing with AIDS. The NIDA symposium was co-chaired by Drs. Henry (Skip) Francis and Peter Hartsock, CAMCODA, and featured presentations by Dr. Francis, Dr. Hartsock, Dr. Steven W. Gust, International Program, and Dr. Jerry Flanzer, DESPR. NIDA also supported the participation in the conference of several grantees, including Dr. D. Paltiel from Yale University, Dr. M. Brandeau from Stanford University, Dr. D. Owens from VA Hospital, Stanford University, Dr. A. Wilson from the University of Minnesota, and Dr. G. Zaric from the University of Western Ontario. During the conference, the NIDA representatives also visited research projects in St. Petersburg funded by NIDA under the 1996 Exchange of Letters between NIDA and Pavlov State Medical University, and Dr. Gust began planning a NIDA-funded symposium for 2002 that will be a follow-up to the 1999 bi-national workshop held in St. Petersburg on "Drug Abuse and Infectious Disease Prevention Strategies."

Three scientists have been selected as **INVEST Research Fellows for 2000-2001**: Dr. Zhao Min, China; Dr. Patricia Obando, Costa Rica; and Dr. Tatiana Tsarouk, Russia. Each will spend a year in the United States working with a NIDA-supported scientist and receiving training in U.S. drug abuse research methods and the National Institutes of Health grant application process. Dr. Min will work with Dr. Howard Liddle, University of Miami Center for Treatment Research on Adolescent Drug Abuse, focusing on multidimensional family therapy and research on the relationship of parental psychopathology and treatment outcomes. Dr. Obando will work with Dr. Edward L, Murrelle, Virginia Commonwealth University, Richmond, to study the role of gender in drug abuse, family disintegration, and cognitive dysregulation. Dr. Tsarouk will work with Dr. Elaine Thompson, University of Washington, to examine the effect of adolescent depression on drug abuse; learn advanced methods of data management and analysis; and receive training in the NIDA-supported intervention Reconnecting Youth. INVEST Research Fellows also participate in an orientation program at NIDA and receive travel support to attend scientific meetings. Fellows and their mentors jointly develop a collaborative research proposal for implementation in the Fellows' home country.

The **2000-2001 NIDA Hubert H. Humphrey Drug Abuse Research Fellows** have completed their professional affiliations with NIDA grantees. Ms. Elvia Amesty, Venezuela, was affiliated with Dr. Lana Harrison at the University of Delaware Center for Drug and Alcohol Studies, where she concentrated on improving her data analysis skills by working with the Cross-National Study of Youth Drugs-Violence Nexus and on gaining experience with research on the validity of self-reported drug use in population surveys. Mr. Vedran Mardesic, Croatia, worked with Dr. Martin Y. Igucchi, The RAND Corporation Drug Policy Research Center, Santa Monica, California, focusing on drug policy and trends, prevention, treatment, data systems, and modeling and forecasting. Dr. Olga Vassioutina, Russia, worked with Dr. Sherry Deren, National Development and Research Institutes Center for Drug Use and HIV Research, New York City, participating in training courses, collecting materials on drug use and harm reduction that are suitable for

translation into Russian, and learning how to utilize the findings of statistical analyses to develop meaningful and innovative interventions.

The **2001 WHO/NIDA/CPDD International Traveling Fellows and the 2001-2002 NIDA Hubert H. Humphrey Fellows** were announced. The 2001 WHO/NIDA/CPDD International Traveling Fellows are Dr. Hem Raj Pal, India, and Dr. Fernando Wagner, Mexico. The 2001-2002 NIDA Hubert H. Humphrey fellows are Dr. Monica Beg, Bangladesh; Dr. Petra Exnerova, Czech Republic; Ms. Olga Toussova, Russia; and Dr. Svitlana Pkhidenko, Ukraine.

NIDA supported the participation of three grantees at the **International Society for Neurochemistry and American Society for Neurochemistry Satellite Meeting,** "Cellular and Molecular Mechanisms of Drugs of Abuse: Cocaine, GHB, GBR, Ibogaine, and Substituted Amphetamines," in Mar del Plata, Argentina, August 22-24, 2001. The NIDA grantees were: Dr. Jerry Meyer, Neuroscience and Behavioral Program, Department of Psychology, University of Massachusetts; Dr. Edward French, Department of Pharmacology, University of Arizona College of Medicine; and Dr. Yossef Itzhak, Department of Psychiatry and Behavioral Sciences, University of Miami School of Medicine.

Drs. Steven Gust, Acting Director, International Program, OSPC, and Eve Reider, Prevention Research Branch, DESPR, met with and presented on drug abuse prevention research at NIDA to a delegation from Romania who was visiting NIDA on May 14, 2001 to examine aspects of drug prevention in the United States. The visiting delegation included Ms. Jonela Petrea, Inspector, Health Promotion and Community Health Department, Ministry of Health, Ms. Michaela Julianan Nanu, President, "The Adolescent" Association (NGO), and Mr. Boqdan Korbuly, Health Officer, Health Promotion and Health Education Department, The Public Health Office of Timis Country.

Drs. Steven Gust, Acting Director, International Program, OSPC, and Eve Reider, Prevention Research Branch, DESPR, met with and presented on drug abuse prevention research at NIDA to a delegation from the Vice-Ministry of Drug Prevention and Rehabilitation and the Ministry of Education in Bolivia visiting NIDA on May 16, 2001. The visiting delegation included Ms. Ruth Dora Vilela, Technician, Health and Sexuality Team, School Curriculum Unit, Ministry of Education, Ms. Rosario del Carmen Grandi, Head, Vice-Ministry of Drug Prevention and Rehabilitation, Infrastructure Unit, Ms. Sandra Jessica Kushida, Head, Vice-Ministry of Drug Prevention and Rehabilitation, Social Communication Unit, and Mr. Marcelo Montero, Consultant, Rehabilitation Therapy and Member, Vice-Ministry of Prevention and Rehabilitation, Committee for Special Projects.

On May 18, 2001, Drs. Steven Gust, International Program, OSPC, Jack Stein, Deputy Director, OSPC, Richard Hawks, DTRD, Eve Reider, Prevention Research Branch, and Jacques Normand, Community Research Branch, DESPR, and Ms. Beverly Jackson, Public Information and Liaison Branch, OSPC met with and presented on drug abuse research at NIDA to a United Nations Drug Control Program (UNDCP) delegation from Mexico visiting NIDA. The visiting delegation included Mr. Ketil Karlsen and Mr. Abraham Stein.

On May 23, 2001, Dr. Larry Seitz, Prevention Research Branch, DESPR, and Ms. Beverly Jackson, Public Information and Liaison Branch, OSPC, met with Krzysztof Russ and Justyna Ziembicka from the Polish Association of Students Against Drugs to discuss educating the public on drug abuse prevention and research.

Dr. James Colliver, DESPR, represented NIDA at the Pompidou Group's 31st Meeting of Experts in Epidemiology of Drug Problems in Strasbourg, France held June 7 and 8, 2001. He gave a presentation on epidemiologic trends in the United States and NIDA activities.

Dr. Moira O'Brien, Epidemiology Research Branch, DESPR met with Dr. Neliana Buzi Figlie, from the Alcohol and Drug Research Unit at Sao Paulo University on June 11, 2001 to discuss the work of NIDA in prevention drug abuse and addiction.

On June 12, 2001, Drs. Steven Gust, International Program, OSPC, Ivan Montoya, Clinical Trials Network Branch, DTR&D, and Lisa Onken, Behavioral Treatment Development Branch, DTR&D, met with visitors from the Organization for Combating Drugs from Athens, Greece to discuss and examine the historical and institutional framework of US efforts to deal with illegal drug use. The visitors were: Dr. Olga Auagnostou, Internal Medicine Specialist, Dr. Evgenia Andreou, Psychologist, Dr. Konstantinos Kokkolis, Second in Chard, Okana's Methadone Maintenance Program, Dr. Christos Kokkoris, Neurologist/Psychiatrist, Dr. Chara Spiliopoulou, Associate Professor of Forensic Medicine and Toxicology, Medical School, University of Athens, and Eleni Tsafou, Head of the Department of Education and Human Development.

Drs. Jack Stein, Deputy Director, OSPC, Eve Reider, Prevention Research Branch, DESPR, and Lisa Onken, Behavioral Treatment Development Branch, DTR&D, met with and presented on drug abuse prevention research at NIDA to a Counter-Narcotics Specialist delegation from Thailand visiting NIDA on June 18, 2001. The visiting delegation included Mr. Apinan Patiyanon, Director, Bureau of External Cooperation, Department of Technical and Economic Cooperation (DTEC), Ms. Chittimas Kongpolprom, Chief, North America and Pacific Sub-division, Mr. Pipop

Chamnivikaipong, Plan and Policy Analyst and Director of Survey and Report Unit, Office of Narcotics Control Board (ONCB), Col. Chucheep Srisomboon, Director, Civil Affairs Division (CA), Col. Chanchai Noppawong, Deputy Civil Affairs Director, Ms. Chunsiri Vatahong, Health Coordinator, Royal Project (RP) Foundation, and Mr. JARAE Pokpa. They were escorted by Mr. Vichai Kiyapathya, Foreign Service National from the U.S. Embassy Bangkok's Narcotics Affairs Section (NAS).

On June 26, 2001, the Regional Drug Plan Delegation from Spain visited NIDA. The delegation met with Drs. Elizabeth Robertson, Prevention Research Branch, DESPR, Jerry Flanzer, Services Research Branch, DESPR, and Ms. Beverly Jackson, Public Information and Liaison Branch, OSPC.

On June 27, 2001, Sheryl Massaro, Public Information and Liaison Branch, OSPC, presented an overview of NIDA publications and resources to the Regional Drug Delegation from Spain of drug abuse treatment professionals, as part of the International Visitor Program sponsored by the Department of State.

Ms. Estla Guardia with the Association of Hogares CREA from Panama visited NIDA on July 3, 2001, to discuss drug abuse prevention programs and how NIDA works with non-profits to ensure that the latest research in prevention and treatment is shared. NIDA was represented by Drs. Jack Blaine, Medications Research Grants Branch, DTR&D, Jack Stein, OSPC, and Ms. Jane Holland, Science Policy Branch, OSPC.

Drs. Steven Gust, Acting Director International Program, OSPC, Jack Blaine, Medications Research Grants Branch, DTR&D, and Eve Reider, Prevention Research Branch, DESPR met with and presented on drug abuse prevention research at NIDA to Elisardo Becona, Ph.D., Professor of Clinical Psychology, Universidad de Santiago de Compostela, who was visiting NIDA from Spain on July 11, 2001.

Jag H. Khalsa, Ph.D. of CAMCODA presented NIDA's research efforts in the area of Medical Consequences of Drug Abuse at the **32nd International Narcotics Research Conference**, Helsinki, Finland, July 14-19, 2001. This was an excellent conference where about 300+ nationally and internationally recognized scientists presented some outstanding research findings on opiates. The range of topics included chemistry of opioids, G-protein receptors and pain, opioid modulatory peptides, synthetic ligands, progress in receptor biology, opioid addiction and behavior, opioids and immune function, and finally role of opioid receptors in pleasures of life (opioid receptors in obesity etc.).

On August 2, 2001, Dr. Steven Gust, International Program, OSPC, and Ms. Beverly Jackson, Chief, Publication Information and Liaison Branch, OSPC met with Narcotics Reporter Jailton Marques De Carvalho from the Daily Journal do Brasil to discuss current research on the prevention, effects and treatment of drug abuse and to give an overview of NIDA as part of the International Visitor Program sponsored by the Department of State.

Drs. Alan Leshner, Director, NIDA, Timothy Condon, Associate Director, NIDA, Steven Gust, International Program, OSPC, and Glen Hanson, Director, DNBR, met with visitors from the Institute of Neurosciences, Mental Health and Addiction, Canada to discuss the strategic planning and priority setting process, the structure and programs of extramural research and the peer review process. Visitors included Drs. Remi Quirion and Richard Briere.

Dr. Eve Reider, DESPR, met with and presented on drug abuse prevention research at NIDA to a delegation of fifteen mayors and council members from Chile visiting NIDA on August 7, 2001.

Drs. Frank Vocci and Ahmed Elkashef attended the World Health Organization (WHO) meeting on Amphetamine Type Stimulants in Manila, Philippines, July 16-19, 2001. Presentations at the meeting concentrated on three tracks of studies funded by WHO: the use of Ecstasy in Poland, Estonia, and Russia; "instrumental use" of amphetamines by students, truck drivers, and sex workers; and the use patterns and consequences of methamphetamine use, particularly amphetamine psychosis, in Australia, the Philippines, Japan, and Thailand.

Drs. Frank Vocci and Ahmed Elkashef, accompanied by Dr. Walter Ling of UCLA and Dr. Roger Lauer of the US Embassy, site visited hospitals and clinics treating methamphetamine dependent and methamphetamine psychosis patients in Bangkok, Chiang Mai, and Khon Kaen, Thailand. Methamphetamine abuse is epidemic in Thailand with 5 percent of the population estimated to be current users. Drug treatment centers and psychiatric hospitals in Thailand are admitting an unprecedented number of patients suffering from methamphetamine dependence and psychosis. The Ministry of Public Health in Thailand (the Thai Government entity that coordinates the drug treatment and psychiatric hospitals in Thailand) coordinated the site visits. The group accompanied the Princess of Thailand on visits to treatment centers and psychiatric hospitals in Chiang Mai and Khon Kaen. The purpose of the visit was several-fold: to ascertain the enthusiasm and research capabilities of the investigators at selected sites, the analytic and neuroimaging capabilities available in Thailand, and to determine the feasibility of performing behavioral and pharmacotherapy studies in the treatment of methamphetamine dependence, and the feasibility of performing pharmacotherapy studies in the treatment of methamphetamine psychosis. Dr. Elkashef has recently started a Methamphetamine Clinical Trials Group consisting of five sites in the US. Potential sites in Thailand could form a

parallel network of treatment research sites. The initial study to be performed will be a behavioral therapy study of methamphetamine dependent patients, followed by pharmacotherapy studies. Further discussions with the Ministry of Public Health in Thailand are planned for the fall of this year.

On August 15, 2001, Dr. Frank Vocci presented at an NIH sponsored International Visitor Project for Russia. The NIH project was entitled "Preparing Public Health Campaigns." Dr. Vocci spoke on the development of medications for addictive disorders. Sandy Genser, M.D. of CAMCODA and Jerry Flanzer, DSW of DESPR also presented at this meeting.

Jag H. Khalsa, Ph.D. of CAMCODA in collaboration with Drs. Jonathan Kagan and Karin Klingman of the Division of Therapeutics, National Institute on Allergy and Infectious Diseases (NIAID) presented NIDA's research efforts in the area of Drug-Drug Interactions at the **2nd International Workshop on HIV Pharmacotherapy**, Noordwijk, the Netherlands, April 2-4, 2001. The meeting was sponsored by the Virology Education, the Netherlands, and co-sponsored by the pharmaceutical industry. It was attended by about 160 clinicians/scientists. There were many excellent presentations on various aspects of pharmacokinetic/pharmacodynamics of interactions among the various classes of antiretroviral drugs.

Dr. Jerry Flanzer, DESPR, accompanying a NIDA team led by Drs. Hartsock, Francis, and Gust, presented a paper on Health Services Research: AIDS and Drug Abuse, at the 9th International Conference on AIDS, Cancer and Related Problems. St. Petersburg State University, Russia, May 25-June 2, 2001. While there, he also met with colleagues not only at St. Petersburg State University, and other Eastern European nations attending the conference but also at Pavlov Heath Sciences Campus. In addition, he was invited to teach a seminar on building a practice research curriculum to the faculty of the new School of Social Work.

Ana Anders, SPO, participated in a meeting in Mexico City on June 11-13, 2001 to plan for the Fourth U.S./Mexico Binational Conference that will be held on November 14 to 17, 2001 in Mexico City.

A collaborative study on the interaction between adenosine, dopamine and glutamate receptors in the basal ganglia involves the Preclinical Pharmacology Section, Behavioral Neuroscience Branch at NIDA (Dr. Sergi Ferre, Dr. Steven Goldberg), the Department of Neuroscience at the Karolinska Institute in Sweden (Prof. Kjell Fuxe), the Department of Pharmacology at the Istituto Superiore di Sanita in Rome (Prof. Patrizia Popoli) and the Department of Biochemistry at the Faculty of Chemistry in Barcelona (Prof. Rafael Franco). The main findings include the demonstration of functional heteromeric complexes between specific subtypes of adenosine, dopamine and glutamate receptors.

Dr. David Gorelick presented "Blockade of Cardiovascular Effects of Smoked Marijuana in Humans by the CB1-Selective Cannabinoid Receptor Antagonist SR141716" at the International Cannabinoid Research Society in San Lorenzo de El Escorial, Spain, June 30, 2001.

Dr. Marilyn Huestis presented "Blockade of Subjective Effects of Smoked Marijuana in Humans by the CB1-Selective Cannabinoid Receptor Antagonist SR141716" at the International Cannabinoid Research Society in San Lorenzo de El Escorial, Spain, June 30, 2001.

Dr. Stephen Heishman presented "Marijuana Craving Questionnaire: Development and Validation" at the International Cannabinoid Research Society in San Lorenzo de El Escorial, Spain, June 30, 2001.

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

Meetings/Conferences

A NIDA conference, **MDMA/Ecstasy Research: Advances, Challenges, Future Directions**, filled the Natcher Auditorium July 19-20, 2001. The speakers and poster presenters addressed the scientific research on methylenedioxymethamphetamine (MDMA, "ecstasy"), including its neuropharmacology, addiction liability, MDMA-related risk behaviors, neuropathology and its long-term behavioral consequences, ontogenetic effects, cardiovascular toxicology, drug interactions, patterns of abuse, perceptions of risk, implications for prevention and treatment, and the toxicology of amphetamines replacing MDMA (such as PMA and PMMA). The conference included all NIDA disciplines, preclinical and clinical, and was international in scope. In addition to their findings, speakers commented on the difficulties in conducting and interpreting MDMA-related research, and helped identify research areas requiring special emphasis. The conference was planned by Drs. Jerry Frankenheim (chair), Timothy P. Condon, Dorynne Czechowicz, Joseph Frascella, Steven Grant, Glen Hanson, Elizabeth Lambert, Rita Liu, Minda Lynch, Dorota Majewska, Angela Martinelli, Cindy Miner, Ro Nemeth-Coslett, Moira O'Brien, Eve Reider, and Jack Stein.

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

On July 10, 2001, NIDA sponsored a workshop entitled **The Hypothalamus and Addiction**, co-chaired by Drs. Karen Skinner, Deputy Director for Science and Technology Development, DNBR, and Jonathan Pollock, Chief, Genetics and Molecular Neurobiology Research Branch, DNBR. The purpose of the meeting was to discuss the extent to which gene expression studies in the hypothalamus may inform biological studies on the anatomy and function of the hypothalamus in varying "states" including addiction. The workshop brought together leading experts interested in the hypothalamus from a variety of research perspectives. Their expertise included molecular biology, the anatomy and development of the hypothalamus, and the role of the hypothalamus in sleep, appetite, addiction, and mental health. The workshop's agenda included a few brief presentations to stimulate discussion. They covered a range of topics including: (1) the functional significance of the hypothalamus from an evolutionary perspective; (2) the utility of studying gene expression in the hypothalamus to identify neuronal cell types and their interactions; (3) current perspectives and hypotheses regarding the role of the hypothalamus in addiction; (4) applications of molecular biology to specific neuronal tracing; (5) identification and quantification of low expression genes; (6) acquisition of spatial information about gene expression; (7) advances in understanding the complexity of hypothalamic connections and gene expression; and (8) the extensive challenges associated with high throughput transfer of gene expression data to a 3-dimensional atlas in a practical, informative and correct manner.

Drs. Bill Bukoski, DESPR and Minda Lynch, Chief Behavioral and Cognitive Science Research Branch, DNBR co-organized a one-day workshop entitled **Bridging Neurobiological, Behavioral, and Prevention Sciences** in conjunction with the June 2001 meeting of the Society for Prevention Research in Washington, D.C. The event brought together senior scientists and early career investigators in an interactive forum to discuss training and research issues at the intersection of basic and prevention sciences. Junior investigators in cross-cutting areas that span basic biobehavioral investigation and prevention research (e.g., parenting influences, stress and environmental enrichment) were invited to present research findings and discuss shared research perspectives. The workshop included a grants writing tutorial and topics tables (e.g., gender issues, cognitive science in prevention, neurobiological influences, etc.) staffed by the senior scientists, with NIDA staff participation.

A workshop entitled **The Development and Functions of the Frontal/Prefrontal Lobes: Role in Drug Abuse** was held on June 11-12, 2001. The aims of this meeting were to review what we know about the development and expression of frontal/prefrontal lobe functions and to make recommendations about how this knowledge can be used in the study of drug abuse. Participants included: Drs. Adriana Alcantara (University of Texas at Austin); Russell Barkley (University of Massachusetts); Joshua Berke (Boston University); Martha Denkla (Johns Hopkins University); Jordan Grafman (National Institute on Neurological Disorders and Stroke); Marc Hauser (Harvard University); Bill Overman (University of North Carolina); Linda Porrino (Wake Forest University); Michael Posner (Cornell University); Tony Simon (University of Pennsylvania); and Linda Spear (State University of New York at Stony Brook). Two of the research areas targeted for further development were decision processes/choice, and the role of the reward system and emotion in controlled and automatic cognitive processes. The workshop was planned and chaired by, Drs. Herb Weingartner, Glen Hanson, David Shurtleff, Lisa Onken, Meyer Glantz and Richard Millstein.

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

Drs. Susan Volman and Minda Lynch, BCSRB/DNBR, along with co-chair Dr. Patricia Grigson from Hershey Medical Center, organized a symposium at this year's Society for the Study of Ingestive Behavior meeting in June, 2001. This session, entitled **Like Drugs for Chocolate: Separate Rewards Modulated by Common Mechanisms?** addressed overlapping neurocircuitry for natural and drug rewards in the context of appetitive and consumatory behaviors. Presentations were given by Dr. Marci Pelchat (Monell Chemical Senses Ctr.) entitled "Of Human Bondage: Craving, Obsession, Compulsion and Addiction", Dr. Regina Carelli (UNC) on "Neurophysiological Analysis of Cocaine Self-Administration vs. Natural Reinforcement", Dr. Ann Kelley (University of Wisconsin-Madison) on "Opioid Modulation of Taste Hedonics within the Ventral Striatum", and Dr. Kenneth Carr (NY School of Medicine) on "Augmentation of Drug Reward by Chronic Food Restriction: Behavioral Evidence and Underlying Mechanisms". Dr. Grigson also served as discussant for the symposium.

Drs. Minda Lynch, DNBR, Steve Gust, OD, and Katherine Davenny, CAMCODA, served as NIDA representatives to the planning committee for a trans-NIH, international meeting on **Stigma**, sponsored by the Fogerty Institute at the Pooks Hill Marriott in Bethesda, MD, September 5-7, 2001. Aspects of stigma and stigmatization of individuals and groups were addressed in regard to the epidemiology of stigma, theoretical perspectives, methodological considerations, interventions, ethical and legal aspects. In addition to presentations by internationally known researchers studying the effects of stigma, break-out groups run by NIH staff discussed exemplars of disease-associated stigma, including drug abuse and alcoholism disorders.

Dr. Bill Bukoski, OD, DESPR, Dr. Minda Lynch, BCSRB, DNBR, and Dr. David Shurtleff, OD, DNBR coordinated a NIDA-sponsored workshop at the CPDD meeting in June, 2001 in Scottsdale, AZ. The workshop, entitled **Bridging Biological, Behavioral Science and Drug Abuse Prevention: Intervention and Insult Along a Developmental Continuum** addressed developmental issues in the malleable trajectory to drug abuse behaviors in youth. Dr. Stephen Suomi from NICHD presented recent findings on complex interactions between parenting style and genetic markers for central neurotransmitter activity. Dr. Barry Kosofsky and Dr. Joseph Biederman from Harvard Medical School presented, respectively, on prenatal drug effects in cocaine-treated rats and ADHD/co-morbid disorders as a risk for subsequent drug abuse in adolescents.

Dr. Frank Vocci, director, DTR&D, NIDA, and Dr. Scott Leischow of NCI co-chaired a locally held joint NCI-NIDA working group meeting on pharmacological approaches to nicotine addiction on May 17-18, 2001. The goal of the meeting was to define the needs and challenges associated with the development of new agents for the treatment of nicotine addiction and to propose strategies for their resolution, with a particular focus on the more rapid testing of promising new agents. Dr. Richard Klausner, Director, NCI and Dr. Alan Leshner gave their perspectives on this issue. NCI (Dr. Leischow and others) and NIDA (Drs. Aigner, Hanson, and Vocci) met subsequently and will follow up on a list of potential activities that arose from the meeting.

A workshop on **Clinical Consequences of Marijuana**, planned, organized, and conducted by Jag H. Khalsa, Ph.D., CAMCODA, and Rao Rapaka, Ph.D., DNBR, was held on August 13-14, 2001. A group of nationally and internationally recognized clinicians and scientists (Martin, Mechoulam, Fried, Tashkin, and many others) discussed the available published and/or unpublished data on clinical consequences of marijuana. The topics included: general health, brain, cardiovascular, pulmonary/respiratory, endocrine, reproductive/developmental, and immune consequences of

marijuana, and finally, treatment of clinical consequences of marijuana use. Speakers also discussed the issues of translating/extrapolating basic research to clinical consequences. Finally, they made excellent recommendations for future research. The recommendations included the study of: (a) neurocognitive effects of chronic marijuana use by adolescents and young adults; develop animal models for studying marijuana dependence in humans; marijuana effects in various human diseases (cardiovascular, endocrine, pulmonary/respiratory diseases; immune dysfunction-related infections); chronic effects of marijuana on sleep disorders; drug-drug interactions between marijuana and those used in the treatment of mental disorders or other diseases; develop functional assays to study neuro-psychiatric/behavioral deficits; (b) effects of chronic marijuana use on atherosclerotic events (clotting mechanisms; lipid metabolism) and endothelial function; arrhythmic effects of chronic marijuana use; plasma fluid changes (i.e., renal effects via renin-angiotensin-aldosterone system); long-term effects on coronary output by using non-invasive techniques; (c) lung immunity among chronic marijuana smokers; incidence, prevalence and underlying pathophysiology (molecular/genetic basis) of head and neck cancer and other cancers (cervix, prostate) associated with chronic marijuana use; conduct population-based epidemiologic studies, and determine if chronic marijuana smoking is associated with cancer by using tumor registries. The speakers recommended that NIDA should train and encourage investigators from other disciplines to conduct research on clinical consequences of marijuana. It was also agreed that the proceedings should be published in a scientific journal. An executive summary is being prepared for publication that will identify the research priorities for the future. In addition, a brief summary of the workshop, the agenda, abstracts, and recommendations for future research will be placed on the NIDA website.

The Clinical Trials Network and the Women and Gender Research Group co-sponsored a meeting entitled **Research Opportunities for Gender Issues in the Clinical Trials Network**, held in Bethesda, MD, May 14-15, 2001. This meeting has led to the establishment of the Gender Issues Group within the CTN.

The Women and Gender Research Group sponsored a seminar by Dr. Heidi Resnick of the Medical University of South Carolina entitled, **Prevention of Post-Rape Psychopathology and Drug Abuse**, May 24, 2001. The seminar was organized by Drs. Eve Reider and Coryl Jones, DESPR.

Drs. Lisa Onken and David Shurtleff organized and co-chaired a symposium entitled **Treatment Strategies for Smoking Cessation** at the annual meeting of the American Psychological Association, August 24-27, 2001, San Francisco, CA. The session speakers were Drs. Sharon Hall, David Wetter, Timothy Baker and Stephanie O'Malley.

NIDA sponsored 30 Junior Investigator Travel Awards for **Research on Women and Gender Differences** for the June 17-21, 2001 College on Problems of Drug Dependence, Scottsdale, AZ meeting in Scottsdale, AZ. These awards are designed to promote entry of junior investigators into drug abuse research on women and gender differences.

NIDA was a co-sponsor of the **Third SAMHSA National Conference on Women**, held in Orlando, FL, June 18-21, 2001.

NIDA's Special Populations Office convened a meeting of its **Native American/Alaskan Native Work Group** on May 22-23, 2001.

A **CTN National Steering Committee Meeting** was held July 16-18, 2001, in Denver, Colorado. The members met to review and discuss 13 new protocol concepts for further development in the Network. The Lead Investigators for the current 7 CTN protocols gave updates on their enrollment status. All CTN subcommittees and interest work groups presented reports as well.

The **NIDA CTN Ad Hoc Oversight Board**, chaired by Dr. Leshner, convened on July 31, 2001, at NIDA Headquarters. The members reviewed the next round of research concepts for implementation in the Clinical Trials Network.

The **CTN Data and Safety Monitoring Board** met on June 25, 2001. The group reviewed the status of the CTN protocols, data from CTN-0001, 0002, 0004, 0005, 0006, 0007 including any serious adverse events in the current protocols.

The **CTN Annual Kick Off Meeting** was held September 10-11, 2001, in Washington, D.C.

Mr. Richard A. Millstein, NIDA Deputy Director, spoke to the Native American Researchers and Scholars Workgroup on NIDA's Health Disparities Plans, May 22, 2001, Rockville, Maryland.

Mr. Richard A. Millstein, as Acting Director of NIDA's Division of Epidemiology, Services and Prevention Research, met with the Board of Directors and engaged with the membership of the Society for Prevention Research on current and future prevention program planning, May 31 - June 1, 2001, Washington, D.C.

Mr. Richard A. Millstein, NIDA Deputy Director, spoke on NIDA's health disparities plan and opportunities for minority

researchers at the Boston University School of Social Work Faculty Institute on Substance Abuse Research and Communities of Color, June 4, 2001, Boston, MA.

Mr. Millstein presented welcoming remarks at the NIDA Symposium "Frontal Lobe Functions: Applying what we Know to Prevention of Drug Abuse," June 11, 2001, Rockville, M.D.

Mr. Millstein moderated a panel, "Observations and Perspectives: NIDA's Community Epidemiology Workgroup at 25: Where We've Been and Where we Should be Going," at the 50th meeting of the CEWG, June 14, 2001, Rockville, MD. Panelists included Drs. David Musto, Robert DuPont, Richard Clayton, and Zili Sloboda.

Mr. Millstein presented on Understanding and Treating Drug Abuse and Addiction and Addiction is a Brain Disease, at the Parole Board of Georgia Training Conference, "Improving Public Safety Through Quality Programming," August 1, 2001, Jekyll Island, GA.

Mr. Millstein participated as a discussant and as a moderator in the U.S.-Netherlands Workshop on Bi-National Research Collaboration on Drug Abuse and Drug Addiction, September 6 - 7, Cumberland, MD.

Dr. Timothy P. Condon, Associate Director, NIDA, presented a plenary address entitled "Prevention and Treatment of Drug Abuse: What We Have Learned From Research?" at the Northwest Substance Abuse Prevention Conference in Portland, OR on May 4, 2001.

Dr. Timothy P. Condon gave the keynote address entitled "Addiction is a Brain Disease: New Implications for Research and Practice" at the National Council on Alcoholism and Drug Dependence - Rochester Area meeting in Rochester, NY on May 18, 2001.

Dr. Timothy P. Condon presented NIDA's third Annual Leadership in Research Award to Steven L. Gallon, Ph.D. in recognition for his outstanding leadership in applying research on drug abuse and addiction. The award was presented at the National Association of Alcoholism and Drug Abuse Counselors' Annual Conference in Portland, OR on May 24, 2001.

Dr. Timothy P. Condon presented "Community Impact of Designer Drugs" at the Law Enforcement and Educator's Response to Ecstasy and Party Drugs Conference in Albuquerque, NM on May 30, 2001.

Dr. Timothy P. Condon presented the keynote address at the Parsons Oklahoma Summer Institute on Substance Abuse entitled "Research Advances in Drug Abuse and Addiction: Implications for Blending Research and Practice" in Oklahoma City, OK on June 11, 2001.

Dr. Timothy P. Condon presented "Addiction is a Brain Disease: New Implications for Research and Practice" at a plenary session at the Connecticut Alcohol & Drug Policy Council Conference on Prevention, Treatment, Criminal Justice, Forging Partnerships for Substance Abuse Services in Middletown, CT on June 13, 2001.

Dr. Timothy P. Condon spoke at the Early Career Investigator Luncheon at the annual College on Problems in Drug Dependence meeting in Scottsdale, AZ on June 19, 2001.

Dr. Timothy P. Condon was the keynote speaker at the Summer Institute on Addiction Treatment and Prevention entitled "Principles of Effective Treatment: Blending Research and Practice" in Reno, NV on July 18, 2001.

Dr. Timothy P. Condon served as a judge at the Palm Springs International Short Film Festival in Palm Springs, CA on August 12, 2001.

Dr. Jack Stein, Deputy Director, OSPC, presented a "NIDA Research Update" at the Johnson Institute Foundation National Leadership Forum Meeting in Washington, D.C. on May 11, 2001.

Dr. Jack Stein presented an "Overview of Club Drugs" for Naval officers at the Washington Navy Yard, Washington, DC on July 11, 2001.

Dr. Jack Stein participated in a panel discussion on "Substance Abuse Clinical and Policy Advances: What is Needed for Welfare and Medicaid?" at the Physician Leadership on National Drug Policy Forum Meeting in Queenstown, Maryland on July 17, 2001.

Dr. Jack Stein participated in a plenary session "Federal Perspectives on Research to Practice, What NIDA is Doing" at the Summer Institute for Arizona Substance Abuse Consortium in HonDah, Arizona on August 2, 2001.

On July 11-13, 2001, Dr. Timothy P. Condon and Beverly Jackson, Chief, Public Information and Liaison Branch, OSPC, participated in the Transdisciplinary Tobacco Use Research Center (TTURC) Meeting in Chicago, IL. Ms. Jackson

participated in a communications training session for TTURC information and press officers.

Drs. Cindy Miner and Angela Martinelli of the Science Policy Branch, OSPC, organized and hosted, "NIDA Tutorials", Saturday, June 16, 2001, at the annual College on Problems in Drug Dependence meeting in Scottsdale, Arizona. This workshop featured several NIDA training grant directors presenting overviews on both fundamental and emerging issues in drug abuse research to NIDA supported pre and post doctoral trainees and fellows.

Drs. Cindy Miner, Mark Swieter, David Shurtleff and Angela Martinelli organized and presented the NIDA/CPDD Grant writing workshop at the annual College on Problems in Drug Dependence meeting, Tuesday, June 19, 2001.

Dr. Cindy Miner, Chief Science Policy Branch presented "Addiction is a Brain Disease" for the Summer Program in Neuroscience, Ethics, and Survival" (SPINES) program at the Marine Biological Laboratory, June 28, 2001, in Woods Hole, Massachusetts.

Dr. Angela Martinelli, Science Policy Branch, OSPC visited the Georgian Forest Elementary School, Silver Spring, MD on February 23, 2001. She discussed the role of elementary education in preparing her for a career in nursing and science and how her education prepared her for her current responsibilities at NIDA and NIH.

On June 23, 2001, Dr. Angela Martinelli, Science Policy Branch, OSPC represented NIDA at a program entitled "Education Excellence through Prevention, Montgomery County Public Schools, Safe and Drug-Free Schools." Participants of this program included Montgomery School system teachers, counselors, security officers and parents.

Dr. Cathrine Sasek, Science Policy Branch, OSPC, participated in a conference entitled 'Ethics in the Science Classroom", July 23-27, 2001. Much of the conference focused on issues related to drug abuse research and the use of animals in research. High school science teachers had the opportunity to try some of the activities in the high school curriculum "The Brain: Understanding Neurobiology Through the Study of Addiction" that is scheduled to be released this fall.

Drs. Jack Blaine and Frank Vocci, DTR&D, co-chaired a panel on Pharmacotherapies for Cocaine Dependence on May 30, 2001, at the NCDEU meeting in Phoenix, Arizona. At this panel Dr. Thomas Kosten spoke on the efficacy of disulfiram in several studies, Dr. Kyle Kampman spoke on the efficacy of amantadine and propranolol in patients with severe cocaine withdrawal symptoms, Dr. Paul Fudala spoke about the evaluation of selegiline, and Dr. Ed Nunes spoke about antidepressant medications treatment for comorbid cocaine dependence and depression.

Dr. Frank Vocci, Director, DTR&D, spoke on The Development History of Buprenorphine at a symposium titled: Ready, Set, Go: Bringing Buprenorphine to the U.S. Market at the CPDD meeting on June 18, 2001, in Scottsdale, Arizona.

In June 2001, Dorynne Czechowicz, M.D., DTR&D, represented the National Institute on Drug Abuse, at the CSAT sponsored meeting of the Federation of State Medical Boards in Dallas, Texas. The purpose of this meeting was to develop model guidelines for State medical boards regarding the use of buprenorphine in medical practice.

On July 25, 2001, Dorynne Czechowicz, M.D., DTR&R, represented NIDA at a CSAT sponsored meeting on LAAM and its cardiac effects. The purpose of this meeting was to develop guidance for drug treatment programs.

Dr. Steven Grant, DTR&D, was a discussant at a symposium entitled "Risky Business: Pathological Gambling and Drug Use Disorders" at the 63rd Annual Meeting of the College on Drug Dependence in Scottsdale, AZ, June 16-21, 2001.

Dr. Steven Grant, DTR&D, represented NIDA at the Office of National Drug Control Policy International Technology Conference in San Diego, California, June 25-28, 2001.

Dr. Steven Grant, DTR&D, was a discussant at the "Current Neuroimaging Studies" and "Co-Morbid Psychiatric Disorders" sessions at the workshop on "Chromosome 18: The Current State of the Science" held at the Natcher Auditorium on the NIH Campus, Bethesda, MD in July 9 - 10, 2001.

Dr. Steven Grant, DTR&D, gave a talk entitled "Consumer's Guide to Functional Imaging" in the symposium "Integrating Neuroimaging and Neuropsychology: An Interdisciplinary Approach to Substance Abuse" at the 109th Annual Meeting of the American Psychological Association in San Francisco, California, August 24-26, 2001.

Drs. Steven Grant and Joseph Frascella, DTR&D, represented NIDA at the HIRES2001 "High Resolution Imaging in Small Animals with PET, MR and Other Modalities: Instrumentation, Applications and Animal Handling" conference held in Rockville MD, September 9-11, 2001.

Dr. Joseph Frascella and Dr. Ahmed Elkashef, DTR&D, co-chaired a symposium (Dr. Frank Vocci was a discussant) at

the CPDD meeting entitled Biomarkers in Cocaine Addiction: Implications for Drug Development, Scottsdale, AZ, June 20, 2001.

Dr. Joseph Frascella, DTR&D, participated with Dr. Scott Lukas of McLean Hospital in a grant-writing workshop at the Brookhaven National Laboratory in Upton, New York, June 28, 2001.

The Regulatory Affairs Branch, DTR&D, held a workshop at the annual meeting of the College on Problems of Drug Dependence (CPDD) on Monday, June 18, 2001 entitled "Regulatory and Human Protections Issues for Running Clinical Trials in Drug Dependent Populations." Robert Walsh, RAC and Frank Vocci, Ph.D. co-chaired the workshop, which was intended to help PIs become more familiar with Human Subjects Protections, Investigational New Drug (IND) submissions, and new NIH regulations that are targeted towards clinical trials.

Robert Walsh, RAC, Frank Vocci, Ph.D., Ahmed Elkashef, M.D., Richard Hawks, Ph.D., and Nora Chiang, Ph.D., all of DTR&D, participated in a series of meetings with the Food and Drug Administration's Division of Anesthetic, Critical Care and Abused Drug Products staff to discuss "Phase II medications trial issues relating to cocaine and methamphetamine dependent populations; and safety issues related to Research INDs." The purpose of the meetings was to: 1) identify safety information that would be necessary for researchers to have when doing clinical studies in these populations, and 2) identify common deficiencies in sponsor-investigator INDs and how best to help researchers in the field avoid them.

Debra Grossman, DTR&D, participated in a CSAT sponsored Federal Resource Panel Meeting focused on Guidelines on Acupuncture Incorporation in Addiction Treatment Programs (GAIATP) on August 2, 2001.

Dr. Lisa Onken, DTR&D, chaired a symposium at the American Psychological Association annual meeting in August on "Innovative Behavioral Treatment Development Research: Highlights of NIDA's Stage I Program." At this symposium, Drs. Varda Shoham & Michael J. Rohrbaugh presented their research on a family treatment for change-resistant smokers. Dr. Marsha Linehan talked about treating women with drug dependence and borderline personality disorder.

Dr. Thomas Brandon spoke on the development of a new treatment strategy for smokers involving enhancing task persistence. NIDA Council member Dr. Steven Hayes served as a Discussant for the panel.

Dr. Betty Tai, DTR&D, gave a presentation on the CTN: What's In It for You at the annual NAADAC Meeting on May 23-26, 2001, held in Portland, Oregon.

Dr. Betty Tai, DTR&D, gave a presentation on the CTN at the CPDD CTN symposium "CTN Challenges and Opportunities" in Scottsdale, AZ. Dr. Leshner and several CTN researchers and community treatment providers also spoke.

Dr. Jerry Frankenheim, DNBR, presented "NIDA's Club Drugs Initiative" at the American Society of Addiction Medicine Annual Medical-Scientific Conference, in Los Angeles, April 21, 2001.

Dr. Frankenheim, DNBR, presented "GHB Abuse - Pharmacology, Sociology, and Withdrawal" at an American Academy of Sleep Medicine satellite symposium, "Sodium Oxybate and Narcolepsy: Basic and Clinical Aspects," at the Association of Professional Sleep Societies Annual Meeting, in Chicago, June 7, 2001.

Dr. Cora Lee Wetherington, DNBR, and NIDA's Women and Gender Research Coordinator, hosted the "Gender Issues" roundtable in the "Roundtable Discussions: Hot Topics in Drug Abuse Research". The event was sponsored by NIDA's Child and Adolescent Workgroup and was held at the annual meeting of the Society for Research on Child Development, Minneapolis, April 18-22, 2001.

Dr. Cora Lee Wetherington, DNBR, and NIDA's Women and Gender Research Coordinator, gave a talk, "Gender Differences in Drug Abuse" at the meeting, "Research Opportunities for Gender Issues in the Clinical Trials Network," May 14-15, 2001, Bethesda, MD.

Dr. Cora Lee Wetherington, DNBR, and NIDA's Women and Gender Research Coordinator, hosted the roundtable "Gender: How Does It Matter for Prevention Science?" at the NIDA meeting, "Bridging Neurobiological, Behavioral, and Prevention Science Workshop," May 29, 2001, Washington, DC.

Dr. Cora Lee Wetherington, DNBR, and NIDA's Women and Gender Research Coordinator, served as the discussant in the symposium, "When Mars Meets Venus: Gender Differences in Drug Dependence," at the annual meeting the College on Problems of Drug Dependence, June 16-21, 2001, in Scottsdale, AZ. The symposium was co-chaired by Drs. Dace Svikis and Loretta Finnegan and the speakers were Drs. Howard Chilcoat, Donna Miles, Scott Lukas, Karol Kaltenbach, and Kathleen Brady.

Dr. Cora Lee Wetherington, DNBR, and NIDA's Women and Gender Research Coordinator, served as the discussant in the session, "Gender Specific Issues in the Addictions" at the annual meeting of the American Psychological Association, August 24-27, 2001, San Francisco, CA. The session speakers were Drs. Rebecca Craft, Nancy Petry, Hendree Jones, Christine Grella, Lisa Marsch, and Warren Bickel.

Dr. Dionne J. Jones, CAMCODA, represented NIDA at the AIDS IMPACT: Biopsychosocial Aspects of HIV Infection Fifth International Conference in Brighton, England, July 8-11, 2001.

Dr. Dionne J. Jones, CAMCODA, represented NIDA at the Research Ethics for Mental Health Science Involving Ethnic Minority Children and Youth Conference sponsored by Fordham University Center for Ethics Education in New York, July 16-17, 2001.

Dr. Dionne J. Jones, CAMCODA, represented NIDA at the 7th Annual Summer Public Health Research Videoconference on Minority Health, University of North Carolina, Chapel Hill, June 20-22, 2000.

Dr. Lula Beatty, Special Populations Office (SPO), presented a talk entitled "Women in Cultural Context: The Hope of the CTN" at NIDA's CTN meeting on gender on May 15, 2001 in Bethesda, MD.

Dr. Lula Beatty, SPO, presented a session entitled "Grant Writing: Obtaining Support for Outstanding Ideas" at the 4th Annual Conference on Counseling African American Families on April 27, 2001 in Houston, TX.

Dr. Lula Beatty met with participants in a summer institute for minority doctoral students at Boston University on June 7, 2001 to discuss drug abuse research in minority communities and research training opportunities.

Dr. Lula Beatty attended the CPDD meeting June 17-19, 2001, and met with the underrepresented populations committee to discuss research development and training needs.

Dr. Lula Beatty met with participants in NIH's Extramural Associates Program on July 19, 2001, to discuss research needs and opportunities at NIDA.

Dr. Lula Beatty presented a faculty development seminar at Hampton University on August 6, 2001, to discuss funding opportunities at NIDA.

Dr. Lula Beatty participated in several events at the annual convention of the American Psychological Association, August 23-27, 2001 in San Francisco. They include: organizing a symposium on drug abuse research and careers for Diversity 2000, a leadership development program for minority community college students; hosting a session on NIH funding opportunities for the Public Interest Directorate; and participating in the Executive Committee meeting of Division 35 (Psychology of Women).

Ana Anders, SPO, opened the Hispanic Cluster Conference in San Diego on August 6, 2001.

Ana Anders attended the Substance Abuse Treatment in Women Workshop sponsored by CSAT on June 22, 2001.

Ana Anders attended the NIH Diversity Council meeting representing the Hispanic Employees organization on July 18, 2001.

Dr. Teresa Levitin, Director, OEA made a presentation on the NIH grant review process and procedures at the Joint Statistical Meeting, Atlanta Georgia in August 2001.

Dr. Mark Green, Chief, Clinical, Epidemiological, and Applied Sciences Review Branch, OEA, and Dr. Swieter presented an OEA workshop entitled, "What's New at NIH: How Will it Affect You?" at CPDD.

Mr. Richard Harrison, Chief, Contracts Review Branch, OEA, served as consultant and panelist on the "Traditional Teaching of our Sons" panel at the Phoenix Area Indian Health Service Women's Leadership Conference III held in Scottsdale, Arizona, May 22-23, 2001.

Dr. Marina Volkov, Clinical, Epidemiological, and Applied Sciences Review Branch, OEA, presented on grants and NIDA funding at a workshop at Iowa State University on June 12, 2001.

Dr. Elizabeth Robertson, DESPR, presented a two-day workshop on funding opportunities and grant writing at the University of Alabama on May 14 and 15, 2001.

Ms. Susan David, DESPR, moderated two panels on persuasive communications research and presented on a panel on the evaluation of the ONDCP media campaign at the International Communications Association Meeting, May 24-28, 2001, Washington, DC.

The Society for Prevention Research met in Washington, D.C. from May 29 to June 2, 2001. Stff from NIDA's Prevention Research Branch were involved in a variety of activities. Dr. Elizabeth Robertson consulted with early career at the Early Career Preventionist Network luncheon and presented at a symposium titled Prevention Science Priorities at NIH. Ms. Susan David moderated a panel on persuasive communications research. Dr. Eve Reider participated in the Bridging Neurobiological, Behavioral, and Prevention Science Workshop held before the conference. She participated in the NIDA Grants-Writing Workshop and Topics Roundtable on Gender: How Does it Matter for Prevention Science?

On June 6-8, 2001, Ms. Susan David, DESPR, represented NIDA at a National Cancer Institute-sponsored meeting, "Tobacco Use Among Youth-Research Investigators Meeting in Park City, Utah.

On June 16, 2001, Dr. Elizabeth Robertson, DESPR, presented "An Update on Prevention Research" at the CPDD international pre-conference meeting. On August 15, Dr. Elizabeth Robertson, DESPR, presented a briefing on the 2nd National Prevention Conference to the Prevention Round Table.

Dr. Eve Reider, DESPR, presented on April 25, 2001 at grand rounds, Department of Psychiatry, Washington University, St. Louis, MO on "The Science of Drug Abuse Prevention: Meeting the Challenge in the 21st Century."

Dr. Eve Reider, DESPR, represented the Prevention Research Branch at NIDA at the Drug Abuse Prevention Summit Conference held in Snowbird, Utah on April 26-27, 2001.

Dr. Eve Reider, DESPR, presented at the Grantsmanship Workshop for Social Scientists, held June 12-13, 2001, Institute for Social and Behavioral Research, Iowa State University, Ames, Iowa. Her presentations included "Current Funding Priorities at NIDA" and "Effective Consultation with Agency Staff and Identifying the Right Grant Mechanism."

Dr. Eve Reider, DESPR, presented a poster at the 2001 National HIV Prevention Conference on August 14, 2001 in Atlanta, Georgia at the Hyatt Regency Atlanta Hotel. The poster is entitled "NIDA Funded HIV and Drug Abuse Prevention Programs in At-Risk Populations."

Dr. Jacques Normand, DESPR, participated in the NIDA, NCI, and RWJF TTURC/Partners Summer Retreat 2001 meeting in Chicago, IL July 11-13, 2001.

Dr. Lynda Erinoff, DESPR, represented NIDA at the University of Rochester Center for the Study and Prevention of Suicide Scientific Consensus Meeting held in Bethesda on June 13-14, 2001.

Dr. William Cartwright, DESPR, participated in the Workshop on Estimating Costs of Parity, sponsored by the Robert Wood Johnson Foundation in Washington, DC, April 30-May 1, 2001.

Dr. William Cartwright, DESPR was the chair and discussant at a session on the Economic Evaluation of Drug Abuse Treatment at the International Health Economics Association biannual meeting in York, England, July 22-26, 2001.

Dr. Jerry Flanzer, DESPR, conducted a grants workshop with the Faculty of the School of Social Work of Gallaudet University, Washington, DC on April 10, 2001.

Drs. Flanzer, Fletcher and Hilton, DESPR, met with county executives of Riverside, Tri-Cities (E. LA) and Imperial County California April 29-30, 2001 to discuss the developing urgency and opportunity for research between the public health and public safety systems due to the passing of California's Proposition 36. This resulted in a "blending science-community" meeting held July 15-16, 2001, hosted by the ten Southern California County substance abuse administrators and NIDA, with invited California oriented investigators exploring ways to "jump start" significant organizational, financial and other forms of health services research. Dr. Flanzer, NIDA, and Mr. John Ryan, County Administrator Association, chaired the sessions. Drs. Cartwright, Hilton and Delany contributed significantly with presentation highlighting the organizational, economic and service delivery outcomes science needs and directions.

Dr. Jerry Flanzer, DESPR, led a panel on the state of the art of NIDA sponsored adolescent services research at the CPDD conference, Scottsdale, Arizona, June 21, 2001.

Dr. Thomas Hilton, DESPR, participated in and presented a paper entitled: "New Funding Opportunities in Organizational and Management Science at NIDA" at the annual conference of the Society of Industrial/Organizational Psychology (SIOP) in San Diego, CA. June 25-30, 2001.

Dr. Thomas Hilton, DESPR, presented a paper entitled: "New NIDA Funding Opportunities in Health Services Research" at the annual conference of the Academy for Health Sciences Research and Health Policy (AHSRHP) in Atlanta, GA, held July 8-10, 2001.

Dr. William J. Freed, IRP, presented "Human Midbrain and Medulla Progenitor Cell Cultures" at the American Society for Neural Transplantation & Repair Eight Annual Conference, May 3-6, 2001, Clearwater, FL.

Dr. Cesar Borlongan, IRP, presented "Bradykinin B2 Receptor Agonist, Cereport, Facilitates Neuroprotective Effects of Cyclopsorine-a in an Animal Model of Parkinsonism" at the American Society for Neural Transplantation & Repair Eight Annual Conference, May 3-6, 2001, Clearwater, FL.

Dr. Rowena Johnston, IRP, presented "Analysis of Six Kidney Cell Lines for Transplantation" at the American Society for Neural Transplantation & Repair Eight Annual Conference, May 3-6, 2001, Clearwater, FL.

Dr. William J. Freed, IRP, chaired and presented a session entitled "Brain Imaging Tools for Drug Abuse Research" at the 2001 ONDCP International Technology Symposium entitled "Counterdrug Research and Development: Technologies for the Next Decade", June 24-28, 2001, San Diego, CA.

Dr. Jean Lud Cadet, IRP, presented at Grand Rounds at Howard University Department of Psychiatry in Washington, D.C. on June 28, 2001.

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

Media and Education Activities

Awards

On May 21, 2001, NIDA received the National Association of Addiction Treatment Providers' (NAATP) Michael Q. Ford Journalism Award. The award recognized NIDA's creative and effective "Addiction is a Brain Disease" public service announcements. Created in honor of Michael Q. Ford, first President and CEO of NAATP, the award is presented each year to an organization or individual whose efforts help promote addiction treatment. Dr. Timothy P. Condon, Associate Director, NIDA accepted the award on NIDA's behalf.

Press Releases

April 12, 2001 - **Potential Medication Can Reduce Effects of Smoked Marijuana in Humans.** Scientists at the National Institute on Drug Abuse's (NIDA) Intramural Research Program in Baltimore, MD, have confirmed for the first time in humans that chemically blocking the body's cannabinoid receptors can significantly reduce the effects of smoked marijuana. The study appeared in the April 14th issue of the *Archives of General Psychiatry.* Coverage of this publication appeared in *The Washington Post, Alcoholism & Drug Abuse Weekly, United Press International, The New York Times, HealthScout.com, Join Together Online, and Substance Abuse Letter.*

April 18, 2001 - **New Brochure Helps Spanish-Speaking Families Discuss Drug Abuse and Related Health Risks.** Juventud Latina-Hable con Sus Hijos Sobre las Drogas y sus Peligros (Latino Youth-Speak to Your Children About Drugs and Their Dangers) provides a science-based discussion tool for Hispanic/Latino families. It includes the latest information on the health effects of inhalants, marijuana, cocaine, methamphetamine, and heroin, in addition to information on drug abuse prevention and treatment strategies. Coverage of this publication release appeared in *The Washington Post and Alcoholism & Drug Abuse Weekly.*

May 1, 2001 - **Researchers Find Evidence That Prenatal Use of Ecstasy Can Cause Long-Term Memory Loss and Other Impairments in Offspring.** Scientists from Children's Hospital Research Foundation and the University of Cincinnati College of Medicine reported the first evidence that a mother's use of MDMA (ecstasy) during pregnancy may result in specific types of long-term learning and memory impairments in her offspring. The research was published in the May 1, 2001, issue of the Journal of Neuroscience. Coverage of this paper appeared in *The New York Times, Associated Press Online, Milwaukee Journal Sentinel, Reuters Health Information, Join Together Online, and Alcoholism & Drug Abuse Weekly.*

May 1, 2001 - **Quitting Smoking Harder for Women than for Men. Review of Research Finds Variety of Reasons for Why It Is Harder for Women to Break Free of Nicotine Addiction.** A review of numerous research studies focusing on smoking cessation has concluded that while women may suffer greater relative risks of smoking-related diseases than do men, they tend to have less success than men in quitting smoking. Dr. Kenneth A. Perkins from the University of Pittsburgh School of Medicine who conducted the review offered several reasons for this disparity in a paper published in the May 2001 issue of CNS Drugs. Coverage of this publication appeared in *Newsweek, Join Together Online, Alcoholism & Drug Abuse Weekly, Reuters Health Information, and HealthScout.com.*

May 4, 2001 - **NIDA NewsScan**

- Studies Shed New Light on HIV Risk-Taking Behavior Among Intravenous Drug UsersUnderstanding the Behavior

that Forges the Link Between Drug Use and HIV

- Study Finds Drug Users in Communities with Low HIV Rates More Likely to Engage in High-Risk Behaviors
- 90-Minute Counseling Session Reduces High-Risk Behaviors: Needle Use Behavior More Resistant to Change than Risky Sexual Practices
- Methods Based on Street "Myths" Not Effective Prevention Against HIV

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

May 7, 2001 - **Hepatitis C Risk Not Limited to Injection Drug Users.** A study in New York City has found a higher than expected prevalence of Hepatitis C infection among non-injecting drug users. In this study, as many as 17 percent of the subjects who denied a history of injection drug use were found to be infected, compared to a 2 percent infection rate in the general population. Among women from one of the study sites in East Harlem who reported use of non-injection heroin, the rate of infection was as high as 26 percent. Coverage of this publication appeared in *Join Together Online and Alcoholism & Drug Abuse Weekly.*

May 14, 2001 - **33-Year Study Emphasizes Lethal Consequences of Heroin Addiction.** After following a cohort of heroin addicts for more than 33 years, researchers from the UCLA Drug Abuse Research Center found that nearly half of the original group of 581 men first interviewed in 1964 had died by 1997, when they would have been between 50 and 60 years of age. The study also found that about 40 percent of the 242 survivors reported past year heroin use and many reported other illicit drug use. The study was published in the May 14, 2001, issue of the *Archives of General Psychiatry. Coverage of this publication appeared in Workplace Substance Abuse Advisor, The New York Times, Alcoholism & Drug Abuse Weekly, The Houston Chronicle, Join Together Online, Reuters Health Information, United Press International, and Ascribe Newswire.*

May 21, 2001 - **NIDA NewsScan**

- Progress Made in Understanding Neurobiological Basis for Relapse to Cocaine Abuse
- Study of Nearly 60,000 Drug Users Shows that Regular Drug Abuse Treatment Coupled with Outpatient Medical Care Helps Cut Hospitalization

As a result of NewsScan promotion, coverage appeared in *Boston Globe, Join Together Online, and Reuters Health Information.*

May 23, 2001 - **Researchers Localize the Brain Circuitry Anticipating Monetary Gains.** Using money as an incentive, researchers from Massachusetts General Hospital (MGH) and two other institutions found that human neural responses accompanying the anticipation and experience of winning and loosing in a laboratory gaming situation were similar to those noted in animals responding to tactile or gustatory stimuli or to euphoria-inducing drugs. This suggests that the same neural circuitry is involved in the highs and lows of winning money, abusing drugs, or anticipating a gastronomical treat. The findings were published in the May 24, 2001, issue of Neuron. Coverage of this publication appeared in *The Seattle Times, Newsweek, Alcoholism & Drug Abuse Weekly, The Advocate, Join Together Online, Newsday, Associated Press Online, The Washington Times, The Washington Post, Boston Globe, and Reuters Health Information.*

May 27, 2001 - **Study Sheds Light on Role of Gender Differences in the Risk of HIV Infection Among Injection Drug Users.** *High-risk Sexual Activity Plays Key Role.* HIV risk factors among drug users differ markedly by gender, according to a 10-year study funded by the National Institute on Drug Abuse. A recent study by researchers at the Johns Hopkins University reported that while drug-related risk behaviors and homosexual activity are the most important predictors of HIV seroconversion among males, factors consistent with high-risk heterosexual activities are the main predictors among females. The findings, reported in the May 28, 2001, issue of the *Archives of Internal Medicine,* provide insight into the relationship between gender and high-risk sexual behaviors in the development of HIV infection.

May 30, 2001 - **New Research Shows Even a Single Drug Exposure Can Alter Brain Function.** Researchers from the University of California San Francisco have found that a single use of cocaine can modify neural connections in the brain, and this may help explain at the cellular level how occasional drug use can progress into a compulsion. The findings are reported in the May 31, 2001, issue of *Nature.* Coverage of this publication appeared in *The Washington Times, The Washington Post, Join Together Online, Yourhealthdaily.com, HealthScout.com, San Francisco*

Chronicle, CNN.com, and Wired.com.

June 8, 2001 - **Researchers on the Frontline of Tracking Drug Use to Hold 50th Biannual Meeting June 12-15. *Reports Have Given Early Warning of National Trends.*** For the past 25 years, drug abuse researchers and public health officials from across the country have been ahead of the curve when it comes to identifying trends such as the surge in heroin use, the emergence of crack, and the increase in methamphetamine use across the United States. The Community Epidemiology Work Group, established by the National Institute on Drug Abuse in 1976 meets twice a year to assess local drug use trends and how they may affect the nation.

July 11, 2001 - **Researchers Find That After Stopping Cocaine Use, Drug Craving Gets Stronger Over Time.** Using an animal model of drug craving in laboratory rats, researchers at the Intramural Research Program of the National Institute on Drug Abuse have found that craving for cocaine seems to increase, rather than decrease, in the days and months after drug use has stopped. The research team published its findings in the July 12, 2001, issue of *Nature.* Coverage of this publication appeared in A*lcoholism & Drug Abuse Weekly.*

July 12, 2001 - **Study of Teens in Four Cities Finds Drug Treatment Effective. *Drug and Alcohol Use Dropped, School Performance Improved.*** The first large-scale study specifically to evaluate drug abuse treatment outcomes among adolescents found that community-based programs can reduce drug and alcohol use, improve school performance, and lower involvement with the criminal justice system. The study published in the July 2001, issue of the *Archives of General Psychiatry,* evaluated the treatment outcomes for nearly 1,200 adolescents, ranging in age from 11 to 18, who were enrolled in one of 23 community-based treatment programs in four cities. Coverage of this publication appeared in *Alcoholism & Drug Abuse Weekly, United Press International, Tribune-Review, and The Washington Times.*

July 19, 2001 - **Scientific Conference on Ecstasy (MDMA). *International Experts Meet to Discuss the Latest Research and Emerging Trends.*** Scientists from around the world met at the National Institutes of Heath (NIH) in Bethesda, MD, July 19-20, 2001, to discuss the latest research about the drug Ecstasy (methylenedioxymethamphetamine (MDMA)) and its diverse effects on the brain and behavior. Coverage of this NIDA sponsored event appeared in *USA Today and United Press International.*

Opinion Pieces

Spring 2001, *Issues in Science and Technology, Volume XVII, Number 3* - Article by Alan I. Leshner, Ph.D. - "Addiction Is a Brain Disease"

Articles of Interest

April 19, 2001, *The News and Observer* (Raleigh, NC) - Interview with Alan I. Leshner, Ph.D. - "The Agony of Ecstasy"

April 26, 2001, *USA Today* - Interview of Alan I. Leshner Ph.D. - "Don't Write Off the Addict, Experts Advise"

April 26, 2001, *NBC News, Today Show* - Interview with Alan I. Leshner, Ph.D. - "Dr. Alan Leshner, National Institute on Drug Abuse, Discusses Drug Addiction"

April 29, 2001, *Ventura County Star* - Interview with Alan I. Leshner, Ph.D. - "Addiction a Brain Disease, Doctors Say"

April 30, 2001, *Alcoholism & Drug Abuse Weekly* - Interview with Alan I. Leshner, Ph.D. - "NIDA Announces Progress in Blocking Two Drugs' Effects"

May 2, 2001, *HealthScout.com* - Interview with George Uhl, M.D., Ph.D. - "Missing Clue to Cocaine Addiction Found"

May 3, 2001, *Reuters Health Information* - Interview with Charles Vorhees, Ph.D. - "Ecstasy May Cause Permanent Damage in Fetus"

May 2001, *Focus Magazine* (German) - Interview with Alan I. Leshner Ph.D. - "Teuflische Erinnerungen"

May 17, 2001, *The Boston Globe* - Interview with Glen Hanson D.D.S., Ph.D. - "Hospital Uses MRI to Probe Substance Abuse"

May 22, 2001, *The New York Times* - Interview with Yih-Ing Hser, Ph.D. - "For Users of Heroin, Decades of Despair"

May 24, 2001, *Associated Press Online* - Interview with Alan I. Leshner Ph.D. - "Brain Activity Links Gambling, Drugs"

June 11, 2001, *Physician's Weekly* - Point/counterpoint column with Alan I. Leshner, Ph.D. and Sally Satel, M.D. - "Is Drug Addiction a Brain Disease?"

July 16, 2001, *Los Angeles Times* - Interview with Alan I. Leshner, Ph.D. - "The Highs and Lows of Ecstasy"

July 17, 2001, *Wyoming Tribune* - Eagle-Interview with Glen Hanson, D.D.S., Ph.D. - "In a State of Ecstasy"

July 20, 2001, *USA Today* - Coverage of MDMA Conference, interview with Alan I. Leshner, Ph.D., and Glen Hanson D.D.S., Ph.D. - "Studies Show Ecstasy Can Damage Brain"

July 22, 2001, *The Record* (NJ) - Coverage of MDMA Conference, interview with Alan I. Leshner, Ph.D. - "Harmful Effects of Ecstasy Aren't Fully Known, Most Users Are Teens Who Don't Worry"

Dr. Steven Grant, DTR&D, was interviewed for the article "Cognition is Central to Drug Addiction" appearing in a special issue of the APA journal Monitor on Psychology dedicated to substance abuse published in June 2001.

NIDA Exhibits Program

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

June 2-6, 2001	National Association of State Alcohol and Drug Abuse Directors and National Prevention Network
June 14-17, 200	American Psychological Society
June 16-21, 2001	63rd Annual Scientific Meeting of the College on Problems of Drug Dependence
June 23-26, 2001	105th Annual National Congress of Parents and Teachers Association
July 11-15, 2001	National Alliance for the Mentally Ill
July 14-18, 2001	National Council of La Raza Conference
July 19-20, 2001	MDMA/Ecstasy Research: Advances, Challenges, Future Directions
July 24-28, 2001	24th Annual Meeting of the Association on Higher Education and Disability
August 9-10, 2001	National Conference on Drug Abuse Prevention Research: A Progress Update
August 24-28, 2001	American Psychological Association
September 10-11, 2001	NIDA CTN Annual Meeting

Educational Activities

NIDA's latest slide teaching packet is now available on NIDA's Web site. The teaching packet, "The Neurobiology of Ecstasy", was developed for use by teachers and researchers who might wish to make presentations to high school or other students. The packet, which contains 20 downloadable slides, was developed through NIDA's Science Education Program in the Science Policy Branch, OSPC.

Training was held for ASI - Lite: Train the Trainer on July 23-24, 2001, in Miami, Florida. Representatives from 7 CTN nodes attended the program.

The CTN was featured in the June 2001 edition of APA's Monitor on Psychology. An article entitled "Real-world Research: the Clinical Trials Network" was included and the CTN was the subject of the magazine's President's Column.

A one-day training was held on Good Research Practices, May 1, 2001, in Gaithersburg, MD. Members from all fourteen nodes attended the session.

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Planned Meetings

On September 23-26, 2001, NIDA will sponsor a science-based institute in Denver, CO. The **Demand Treatment Leadership Institute II** will target community-based teams involved in Join Together's Demand Treatment! initiative.

As part of its Health Disparities Strategic Plan, NIDA will convene a national conference on drug abuse research in minority populations entitled **Bridging Science and Culture to Improve Drug Abuse Research in Minority Communities** on September 24-26, 2001 in Philadelphia.

Ana Anders, as President of the NIH/Hispanic Employee Organization (HEO), is planning the **Hispanic Heritage Month Celebration for NIH** that will be held September 19 and October 1, 2001.

The American Psychological Association will hold a conference **Enhancing Outcomes in Women's Health: Translating Psychosocial and Behavioral Research Into Primary Care, Community Interventions and Health Policy - An Interdisciplinary Conference** in Washington, DC, October 4-6, 2001. This conference, which is co-funded by NIDA, will include three NIDA sponsored symposia. The first, "The Convergence of Drug Abuse, Sex, and Violence," co-organized by Helen Cesari and Elizabeth Lambert, will be chaired by Elizabeth Lambert, and will feature Claire E. Sterk, Ph.D., (Emory University), Stephanie Tortu, Ph.D., (Tulane University), Nabila El-Bassel, Ph.D., (Columbia University), and Patricia Case, Ph.D. (Harvard Medical School) as presenters, with Deborah Smith, M.D. in the role of discussant. The second symposium, organized by Dionne Jones, Ph.D. will feature Sally J. Stephens, Ph.D. (University of Arizona), Murelle G. Harrison, Ph.D. (Southern University, Baton Rogue, LA), Suzanne Montgomery, Ph.D. (Loma Linda University), and M. Bahati Kuumba, Ph.D. (Spelman College) as presenters, with Dionne Jones, Ph.D. in the role of chairperson and discussant. The third symposium, co-organized by Dorynne Czechowicz, M.D. and Adele Roman will be chaired by Cora Lee Wetherington, Ph.D. and will feature Wendee M. Wechsberg, Ph.D. (Research Triangle Institute), Karla Moras, Ph.D. (University of Pennsylvania), Lisa M. Najavits, Ph.D. (Harvard Medical School), and Heidi Resnick, Ph.D. (National Crime Victims Research and Treatment Center) as presenters, with Mary E. McCaul Ph.D. (Johns Hopkins University) in the role of discussant.

A NIDA sponsored Workshop **Using Buprenorphine in Office-Based Practice** will be held on Monday, October 8, 2001, at the American Methadone Treatment Association Meeting in St. Louis, Missouri. Dr. Czechowicz, Robert Walsh and Dr. Frank Vocci, DTR&D organized this session.

The **4th Annual Meeting of the Global Research Network (GRN) on HIV Prevention in Drug-Using Populations** will be held October 11- 12, 2001 in Melbourne, Australia, immediately following the 6th International Congress on AIDS in Asia and the Pacific (ICAAP) on October 5-10. Three symposia in the 6th ICAAP meeting are sponsored by the GRN, in addition to a roundtable and a workshop on research and training opportunities at the NIH. The GRN meeting will include four major sessions, on the research implications of IDUs as multipliers of HIV to the general population, on challenges for HIV prevention in Asia and the Pacific Islands, on the GRN's indicators database on HIV prevention in drug users, and on the GRN's mission and future plans. In addition to NIDA, the GRN's co-sponsoring organizations are the Joint U.N. Programme on HIV/AIDS, Health Canada, the WHO, the U.N. Office of Drug Control and Crime Prevention, CDC, and the NIH's Office of AIDS Research and the Fogarty International Center. Henry I. Francis, M.D., Director of NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA) and Helen Cesari, M.Sc., Chief of CAMCODA's Population-Based Health Intervention, will be participating in both the ICAAP and GRN meetings.

NIDA will host its **Seventh Constituent Conference** at the Westfields Marriott in Chantilly, Virginia, December 3-4,

2001. This conference provides NIDA and constituent organization leaders with the opportunity for dialog and gives NIDA the chance to receive and respond to the concerns and research recommendations from the field. NIDA also uses this setting to present the field with its latest research findings.

Dr. Steven Grant, DTR&D, will be co-chairing a symposium entitled **Transition to Addiction: Does Pushing the Lever Pull the Switch?** at the upcoming annual meeting of the American College for Neuropsychopharmacology in December 2001. Speakers at the symposium are James Anthony, Johns Hopkins University, Elliot Stein, Medical College of Wisconsin, Linda Porrino, Wake Forrest University, Barry Everitt, Cambridge University.

National CTN Steering Committee Meetings are planned for the follow dates and locations: October 22-24, 2001, in Bethesda, MD, January 28-30, 2002, in Charleston, South Carolina, and March 13, 2002, in New York City.

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

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Publications

Epidemiologic Trends in Drug Abuse - Community Epidemiology Work Group, Volume I- December 2000
NIH Pub. No. 01-4916

This report provides an ongoing assessment of drug abuse in major metropolitan areas of the United States with the purpose of keeping both public and private sector policymakers and researchers informed with current and accurate data.

Monitoring the Future National Survey Results on Adolescent Drug Use - Overview of Key Findings, 2000
NIH Pub. No. 01-4923

This report will provide systematically recurring annual estimates of drug use among students. The trends are useful for understanding the changing drug abuse problems and for formulating the appropriate intervention (both prevention/treatment) policies.

Monitoring the Future National Survey Results on Drug Use, 1975-2000, Volume I: Secondary School Students, 2000
NIH Pub. No. 01-4924

This annual monograph reports the prevalence of drug use among American secondary students (specifically 8th, 10th & 12th graders). The trends are used for understanding the changing drug abuse problems and for formulating the appropriate intervention (prevention/treatment) policies.

Monitoring the Future National Survey Results on Drug Use, 1975-2000, Volume II: College Students and Young Adults, 2000
NIH Pub. No. 01-4925

This annual monograph reports trends in drug use by populations based on gender, college plans, regions of the country, population density, race/ethnicity, and parents' education. The trends are used for understanding the changing drug abuse problems and for formulating the appropriate intervention (prevention/treatment) policies.

Native American/Alaska Natives Calendar 2002
NIH Pub. No. 01-499

This calendar encourages Native Americans/Alaska Natives to reject illicit drugs; the purpose of the material is to increase the audience's knowledge and awareness of the signs, symptoms and physiological effects of various drugs. To ensure cultural relevancy of the material, the calendar will integrate images and quotations that convey and reinforce Indian pride with its drug education messages.

Brain Power: Student Magazine; Teacher's Guide; Parent's Guide and Video (Grades 2-3)
NIH Pub. No. 01-4575

These materials are designed to interest and educate students in an age appropriate manner about their brain, why they should protect it, and how drugs such as nicotine and inhalants can hurt their brain. The materials are designed to accompany a short video on these topics. The teacher's guide will provide more in depth information, suggestions for activities that can be done in the classroom and a listing of resources. The parent's guide will include activities that can be done with the whole family and a listing of resources.

NIDA NOTES

NIDA NOTES, Volume 16, Issue 3
NIH 01-3478

The lead story in this issue reports on NIDA's prescription drug abuse initiative and the information presented by the scientific panel at the kickoff event. In a Director's Column titled "Understanding the Risks of Prescription Drug Abuse," Dr. Leshner describes this problem, as well as NIDA's efforts to address it. Other stories report on the negative effect of nicotine on the brains of rat pups and how this might translate to prenatal nicotine exposure of fetuses by mothers who smoke during pregnancy; injection drug users' risks of acquiring hepatitis C through sharing cookers and filtration along with information on the prevalence of hepatitis C; and how the brain chemical agmatine may offer promise for treatment of chronic pain. Other stories highlight NIDA's newly designed Web site and this year's PRISM award winners. The Tearoff describes NIDA's new *Research Report* on prescription drug abuse. The Bulletin Board reports on an addiction studies program at Wake Forest University for journalists who cover drug abuse and addiction issues.

Other Publications

United States-Eastern Europe Regional Meeting on Methamphetamine and Ecstasy Research

This volume summarizes the oral presentations and includes the agenda and participant list from the March 2000 meeting cosponsored by NIDA and the Hungarian Ministry of Youth and Sports to exchange information about the growing abuse of methamphetamine and MDMA (Ecstasy) by young people and the potential for research cooperation in this area.

Street Children and Drug Abuse: Social and Health Consequences

This volume provides summaries of oral presentations, panel discussions, and workgroup reports; participant recommendations; the agenda; and the participant list from the September 2000 meeting cosponsored by NIDA and the World Health Organization to discuss the numerous challenges, including substance abuse, that face the world's vulnerable children and youth.

Vaccines Against Nicotine: How Effective are They Likely to Be in Preventing Smoking? Vocci, F.J. and Chiang, N. CNS Drugs, 15(7), pp. 505-514, 2001.

Elkashef, A., Doudet, D., Bryant, T.,Cohen, R., Li, S. and Wyatt, R.J. 6-18F-DOPA PET Study in Patients with Schizophrenia. Psychiatry Research: Neuroimaging, 100, pp. 1-11, 2000.

Ten editions of the CTN Bulletin Board were distributed this period. The Bulletin Board is an electronic report on the activities of the various protocol teams and subcommittees of the CTN. Patient and clinician brochures for the protocol entitled "Buprenorphine/Naloxone: Comparison of Three Taper Schedules for Opiate Detoxification" were approved and published this period. Copies were distributed to all community treatment sites participating in that study.

Tai, B. NIDA's Clinical Trials Network: Overview and Challenges. In Sorensen, J.L., Rawson, R.A., Guydish, J. and Zweben, J.E. (Eds.), Research to Practice, Practice to Research: Promoting Scientific-Clinical Interchange in Drug Abuse Treatment. Washington, DC: American Psychological Association, 2001.

Cadet, J.L., Jayanthi, S., McCoy, M.T., Vawter, M., and Ladenheim, B. Temporal Profiling of Methamphetamine-induced Changes in Gene Expression in the Mouse Brain: Evidence from cDNA Array. Synapse. 41(1), pp. 40-48, 2001.

Herning, R.I., Better, W.E., Tate, K., and Cadet, J.L. Marijuana Abusers are at Increased Risk for Stroke. Preliminary

Evidence from Cerebrovascular Perfusion Data. Ann N Y Acad Sci. 939, pp. 413-415, 2001.

Herning, R.I., Better, W.E., Tate, K., and Cadet, J.L. Antiviral Medications Improve Cerebrovascular Perfusion in HIV+ Non-drug Users and HIV+ Cocaine Abusers. Ann N Y Acad Sci., 939, pp. 405-412, 2001.

Imam, S.Z., Itzhak, Y., Cadet, J.L., Islam, F., Slikker, W., and Ali, S.F. Methamphetamine-induced Alteration in Striatal p53 and bcl-2 Expressions in Mice. Brain Res Mol Brain Res. 13,91(1-2), pp. 174-178, 2001.

Imam, S.Z., el-Yazal, J., Newport, G.D., Itzhak, Y., Cadet, J.L., Slikker, W. Jr., and Ali, S.F. Methamphetamine-induced Dopaminergic Neurotoxicity: Role of Peroxynitrite and Neuroprotective Role of Antioxidants and Peroxynitrite Decomposition Catalysts. Ann N Y Acad Sci., 939, pp. 366-380, 2001.

Jayanthi, S., Deng, X., Bordelon, M., McCoy, M.T., and Cadet, J.L. Methamphetamine Causes Differential Regulation of Pro-death and Anti-death Bcl-2 Genes in the Mouse Neocortex. FASEB J., 15(10), pp. 1745-1752, 2001.

Jayanthi, S., Lewis, B.D., and Cadet, J.L. Fas-induced Apoptosis of Glioma Cells is Associated with Down-Regulation of the hSCO1 Protein, a Subunit of Complex IV. Vol Brain Res., 13, 91(1-2), pp. 131-136, 2001.

Thiriet, N., and Subramanian, J. Involvement of Free Radicals in MDMA-induced Neurotoxicity in Mice. Ann Med Interne (Paris), 152 Suppl 3, pp. 57-59, 2001.

Ernst, M., Matochik, J.A., Heishman, S.J., Van Horn, J.D., Jons, P.H., Henningfield, J.E., and London, E.D. Effect of Nicotine on Brain Activation during Performance of a Working Memory Task. Proceedings of the National Academy of Sciences, USA, 98, pp. 4728-4733, 2001.

Radzius, A., Moolchan, E.T., Henningfield, J.E., Heishman, S.J., and Gallo, J.J. A Factor Analysis of the Fagerstršm Tolerance Questionnaire. Addictive Behaviors, 26, pp. 303-310, 2001.

Heishman, S.J., Singleton, E.G., and Liguori, A. Marijuana Craving Questionnaire: Development and Initial Validation of a Self-report Instrument. Addiction, 96, pp. 1023-1034, 2001.

Witt, L.A., Hilton, T.F., and Hochwarter, W.A. Addressing Politics in Matrix Teams. Group and Organization Management, 26(2), pp. 230-247, 2001.

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Staff Highlights

Honors and Awards

NIDA Director's Awards

Dionne Jones, Ph.D., CAMCODA
Noble Jones, CAMCODA
William S. Cartwright, Ph.D., DESPR
James Colliver, Ph.D., DESPR
Lynda Erinoff, Ph.D, J.D., DESPR
Christie Baxter, DNBR
Jerry M. Frankenheim, Ph.D., DNBR
Minda Lynch, Ph.D., DNBR
Herb Weingartner, Ph.D., DNBR
Catherine Mills, OPRM
Donna Tolson, OPRM
Robin Mackar, OSPC
Michelle Muth, OSPC

Genetics Consortium Steering Committee Group Award:

Rebekah Rasooly, Ph.D., DNBR
Harold Gordon, Ph.D., DTR&D
Naimah Weinberg, M.D., DESPR
Jonathan Pollock, Ph.D., DNBR
Robert Walsh, DTR&D
Joseph Frascella, Ph.D., DTR&D

The Neurosearch Team Group Award (DTR&D):

Ann Anderson, M.D.
Lee Cummings, J.D.
Ahmed Elkashef, M.D.
Richard Hawks Ph.D.
Aida Klun, M.B.A.
Jurij Mojsiak, M.S.
Jahnavi Kharidia, Ph.D.
Moo Park, Ph.D.
Amrat Patel, Ph.D.
James Terrill, Ph.D.
Frank Vocci, Ph.D.
Robert Walsh, B.S.
Nora Chiang, Ph.D.

Yavin Shaham, Ph.D.

The Procurement Section Group Award (IRP):

Tonya D. Anderson
Lesley W. Johnson
Mary G. Mancuso
Roger W. Remsburg
Iris M. Johnson

NIDA's Health Disparities Plan Group Award:

Ana Anders, SPO
Flair Lindsey, SPO
Ann Anderson, DTR&D
Henry Francis, CAMCODA
Arnold Mills, DESPR
Jean Lud Cadet, IRP
Cindy Miner, OSPC
Joseph Frascella, DTR&D
David Conrad, OPRM
Leslie Cooper, DESPR
David Shurtleff, DNBR
Lula Beatty, SPO
Dionne Jones, CAMCODA
Pamela Goodlow, SPO
Dorynne Czechowicz, DTR&D
Richard Harrison, OEA
Angela Benjamin, OEA
Jacqueline Porter, OEA
Pamela Stokes, OEA

MASB/OPRM Group Award:

Chanvadey Nhim
Traci Pelan
Maryann Postorino
Earle Stalfort
Terry Wheeler
Jean Yee

Prescription Drug Abuse Initiative Group Award:

Joan Nolan
Lucinda Miner, Ph.D.
Jack Stein, Ph.D.
Pat Thomas
Michelle Muth
Sheryl Massaro
Mark Fleming
Blair Gately
Jan Lipkin
Catherine Law
Robin Mackar
Monica Jones
Beverly Jackson

Equal Employment Office, Diversity and Quality of Worklife Awards

David Anderson, OSPC
Susan Volman, DNBR

Commissioned Corps Awards

LTCDR Carlo S. Contoreggi, IRP -- Public Health Service Citation Medal
LTCDR Ann Anderson, DTR&D -- Public Health Service Achievement Medal
CAPT Leslie Cooper, DESPR -- Public Health Service Achievement Medal
CAPT Dorynne Czechowicz, DTR&D -- Public Health Service Achievement Medal
LTCDR Paul Na, IRP -- Public Health Service Achievement Medal
CAPT Anthony Brooks, IRP -- Public Health Service Commendation Medal
Peter J. Delany, Ph.D.-- PHS Outstanding Service Medal

Length of Service Awards

20 Years of Service
Alan Leshner

30 Years of Service
Beverly Cepl
Carol Cowell
Anner Grantham
Jacqueline Porter
Celestine Proctor
Nikki Zangwill

40 Years of Service
Ana Anders

Employee of the Month Awards

September 2000	Berhane Yitbarek, Theresa Doged
October 2000	Camilla Holland, Janice Carico
November 2000	James Terrill, Beverly Cepl
December 2000	Diana Haikalis, Cindy Ambriz
January 2001	Janice Walden, Ora Dillon-Carter
February 2001	Celeste Proctor, Anne Gupman
March 2001	Veronica Lawrence, Nicole Jones
April 2001	Christie Baxter, Iris Johnson
May 2001	Davey Jones, Christie Brannock
June 2001	Angela Benjamin, Beverly Beall

NIH Director's Awards

David Shurtleff, Ph.D, DNBR

Minority Recruitment Training Program Team Group Award:

Mary Affeldt
Christie Brannock
Jean L. Cadet, M.D.
Lena Eads

Prevention Science Resource Workgroup:

Susan David, M.P.H.
Elizabeth Robertson, Ph.D.

Special Pops Educational Outreach Workgroup:

Ana Anders, M.S.W.
David Anderson
Niki Andrews
Linda Barber
Lula Beatty, Ph.D.
Garveyette Brown
Timothy Condon, Ph.D.
Audrey Cooke
Mark Fleming
Brenda Fogel
Pamela Goodlow
Jane Holland
Beverly Jackson
Anne Jarrett
Monica Jones
Catherine Law
Flair Lindsey
Jan Lipkin
Robin Mackar, M.P.H.
Angela Martinelli, RN, DN.Sc.
Sheryl Massaro
Mary Mayhew
Geraldine McCarthy
Cindy Miner, Ph.D
Michelle Muth
John Nagy
Patricia Needle, Ph.D.
Juanita Nelson
Joan Nolan
Lanette Palmquist
Suman Rao, Ph.D.
Cathrine Sasek, Ph.D.
Margaret W. Scofield
Nancy Soulen
Jack Stein, Ph.D.
Patricia Thomas
Keith Van Wagner

Other Honors and Awards

This year's J. Michael Morrison award from the College on Problems of Drug Dependence (CPDD) went to **Dr. Roger Brown**, Associate Director for Neuroscience Coordination, DNBR. The award consists of a monetary award and a plaque, and it is given to outstanding people within NIDA who facilitate research. Over the course of the past 20 years, Dr. Roger Brown has been instrumental in building the brain reward program and in getting many young investigators on their feet --many of whom are our finest researchers today. The award was presented to him at the Sixty-Third Annual Scientific Meeting of the CPDD on June 16, 2001 in Scottsdale, Arizona.

Dr. Thomas G. Aigner, DNBR received two NIH Director's Awards on August 1, 2001. The NIH Bioengineering Consortium (BECON), of which he is the NIDA representative, and the 2000 BECON Symposium Coordinating Committee for the meeting "Nanoscience and Nanotechnology: Shaping Biomedical Research" were recognized for their work in furthering biomedical engineering research at the NIH.

Dr. Cora Lee Wetherington, DNBR and NIDA's Women and Gender Research Coordinator was elected member-at-large for Division 28, Psychopharmacology and Substance Abuse, of the American Psychological Association.

Dr. Lula Beatty, SPO, received a Distinguished Career Award from Division 45 (Ethnic Minority Affairs), American Psychological Association, at the annual convention on August 25, 2001 in San Francisco.

Dr. Peter I. Hartsock, CAMCODA, was presented with the University of St. Petersburg Medal on May 30, 2001 in recognition of his vision and vital contributions to Russian and American cooperation in HIV/AIDS research.

Dr. Jean Lud Cadet, IRP, received the NIH Director's Award for the Minority Recruitment and Training Program (MRTP).

Dr. Jean Lud Cadet, IRP, received the AMS Award (Associated Medical Schools of New York) for service and dedication to the promotion of Science and Health education among minority youth.

Lee Cummings, J.D., DTR&D, received a Federal Technology Transfer Act Award from the National Cancer Institute for recognition of his contributions to the planning and implementation of a national forum on NIH Cooperative Research and Development Agreements.

Joann Grant, Technology Transfer Specialist in the Regulatory Affairs Branch, DTR&D, received a Special Recognition Award for managing technology transfer activities within the division, and for being instrumental in coordinating and assisting with various functions such as personnel, regulatory affairs and administrative management.

Staff Changes

Holly Buchanan joined OSPC in May 2001 as the Secretary to the Deputy Director, OSPC. Prior to joining NIDA, Ms. Buchanan worked at the National Naval Medical Center in the Orthopedic Department, scheduling patients, doctors and serving as the point of contact for the Department.

Kevin P. Conway, Ph.D. joined NIDA's Division of Epidemiology, Services, and Research Branch on July 1, 2001. Most recently, Dr. Conway was an Associate Research Scientist in the Department of Epidemiology and Public Health at Yale University School of Medicine, where he worked with Professor Kathleen Merikangas at the Genetic Epidemiology Research Unit. Dr. Conway's research focuses on the genetic epidemiology and etiology of drug use disorders, psychopathology, personality, crime and violence, and cultural influences on patterns of comorbidity among drug abusers.

Suzanne Dawkins joined NIDA's Office of Planning and Resource Management (OPRM) as a Constract Specialist in the Contracts Management Branch on July 15, 2001. Prior to coming to NIDA Ms. Dawkins was with the National Heart, Lung and Blood Institute.

Amira Debbas joined NIDA's Division of Neuroscience and Behavioral Research as the Division's Secretary on May 21, 2001. Prior to coming to NIDA, Ms. Debbas worked for the Louis Dreyfus Corporation's Washington DC office.

Roberta C. Kahn, M.D. joined NIDA's Division of Treatment Research and Development (DTR&D) as a Medical Officer on July 1, 2001. Prior to coming to NIDA, Dr. Kahn served as a Medical Officer in the FDA's Center for Drug Evaluation and Research, Division of Anesthesia, Critical Care and Addictive Drug Products. Following extensive postgraduate training in Internal Medicine, Anesthesiology, and Critical Care Medicine, Dr. Kahn served consecutive appointments as Assistant Clinical Professor of Anesthesiology at Cornell Medical Center-New York Hospital and Associate Professor of Anesthesiology at New York University Medical Center.

Annie Mathew joined NIDA's Office of Extramural Affairs as a Grants Technical Assistant on June 3, 2001. Ms. Mathew comes to NIDA from the NIH's Center for Scientific Review.

Michael Wright joined NIDA's Office of Planning and Resource Management as a Computer Specialist in the Information Resources Management Branch on July 15, 2001.

CDR Peter J. Delany, D.S.W., DESPR, was appointed as the Deputy Director of the Division of Epidemiology, Services and Prevention Research (DESPR). Since joining NIDA in 1992, he has worked primarily in the Services Research Branch focusing on the development of research with criminal justice-involved populations, the organization and management of treatment, and health services research with underserved populations. He held the position of Acting Deputy Director first in the Division of Clinical and Services Research and since January 2000 in DESPR.

Dr. Ann Anderson, Medical Officer, transferred from the DTR&D's Medications Research Grants Branch to the Clinical Trials Network Branch.

Meg Scofield left NIDA to pursue a Master's Degree in Library Science at the University of Maryland College Park (UMD) and is currently working as a graduate assistant in the UMD libraries' grants office. She had been with NIDA since December 1999 when she joined the Public Information and Liaison Branch, OSPC as a Writer-Editor.

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Grantee Honors

Dr. Thomas Dishion recently founded the Child and Family Center in the Department of Psychology at the University of Oregon where he serves as the Science Coordinator. The Center is a nonprofit center dedicated to understanding and promoting mental health and resilience within families across cultural communities. The Center emphasizes research on social emotional development from infancy through adolescence, as well as innovation in assessment, prevention, and intervention services for children and families.

Dr. Brian R. Flay, Professor of Community Health Sciences, School of Public Health, and Director Emeritus of the Health Research and Policy Centers, University of Illinois at Chicago, was appointed Distinguished Professor.

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