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

February, 2002

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

Basic Research

Separate Neural Pathways Mediate the Rewarding Effects of Cocaine and Reinstatement of Cocaine-Taking Behavior

Although the acute pharmacological effects of psychostimulants is mediated by changes in dopamine transmission, it is becoming increasingly apparent that addiction is associated with long-term changes in the cortical and allocortical circuitry. The mesolimbic dopamine system, originating in the VTA, projects to the nucleus accumbens, the amygdala, the prefrontal cortex, and the ventral pallidum. However, this system can be divided into two sub-circuits, the limbic circuit comprised of the ventral prefrontal cortex, the shell of the accumbens, the medial ventral pallidum, amygdala, and the VTA and the other primarily a motor circuit, comprised of the dorsal prefrontal cortex, the core of the accumbens, the dorsolateral ventral pallidum, and the substantia nigra. Most research suggests that the limbic circuit is intimately involved with the rewarding effects of abused drugs. By microinjecting GABA-A and GABA-B agonists to limit the activity of dopamine within specific nuclei of the motor sub-circuit, researchers in South Carolina were able to block the cocaine-primed reinstatement of responding for cocaine in animals in whom drug-seeking behaviors had been extinguished. Although dopamine projections from the VTA project to accumbens core, the ventral pallidum, and the dorsal prefrontal cortex, only the blockade of dopamine receptors in the dorsal prefrontal cortex antagonized the cocaine-induced reinstatement; furthermore, microinjection of dopamine in the same area elicited a reinstatement in drug-primed responding. These data showing that brain nuclei subserving motor functions, with limited limbic involvement, are important for inducing reinstatement of drug-taking behavior in drug-experienced subjects may be part of the substrate underlying the compulsive behavior associated with drug addiction. McFarland, K. and Kalivas, P.W., J. Neuroscience, 21, pp. 8655-8663, 2001.

Regulation of the Vesicular Monoamine Transporter-2

The plasmalemmal dopamine (DA) transporter (DAT) is a principal site of action for cocaine. Dr. Annette Fleckenstein of University of Utah and her research team reported the novel finding that in addition to inhibiting DAT function, cocaine administration rapidly alters vesicular DA transport. Specifically, cocaine treatment abruptly and reversibly increased both the Vmax of DA uptake and the Bmax of vesicular monoamine transporter-2 (VMAT-2) ligand (dihydrotetrabenazine) binding, as assessed ex vivo in purified rat striatal synaptic vesicles. Selective inhibitors of the DAT (amfonelic acid and GBR12935), but not the plasmalemmal serotonin transporter (fluoxetine), also increased vesicular DA uptake. Moreover, DA depletion resulting from administration of the tyrosine hydroxylase inhibitor alpha-methyl-p-tyrosine had cocaine-like effects. Conversely, administration of the DA-releasing agent methamphetamine rapidly decreased vesicular uptake. Taken together, these data demonstrate for the first time ex vivo that cocaine treatment rapidly alters vesicular monoamine transport, and suggest that alterations in cytoplasmic DA concentrations contribute to stimulant-induced changes in vesicular DA uptake. Hence, VMAT-2 may be an important target for developing strategies to treat not only cocaine addiction but also other disorders involving alterations in neuronal DA disposition, including Parkinson's disease. Brown, J.M., Hanson, G.R., and Fleckenstein, A.E. Regulation of the Vesicular Monoamine Transporter-2: A Novel Mechanism for Cocaine and Other Psychostimulants. J Pharmacol Exp Ther, 296(3), pp. 762-767, 2001.

New Family of Receptors that Binds Amphetamine, MDMA and LSD Cloned

The roles of the transporters and receptors of the biogenic amines, especially dopamine and serotonin, are well appreciated with regard to their importance in mediating the effects of psychostimulants such as cocaine and the amphetamines. However, antagonism of these proteins has often led to mixed results in the search for a medication that would limit their psychoactive effects. Researchers in Portland, OR, have recently cloned a trace amine receptor. These receptors bind to the major meta-O-methyl metabolites of the biogenic amines and trace amines such as tyramine, tryptamine, and _-_phenylethylamine, but not the classical neurotransmitters such as dopamine or serotonin, and then activate specific G-protein coupled receptors with nanomolar potency in pre- and post-synaptic membranes of target neurons. Importantly, these receptors also bind amphetamine, MDMA ("ecstasy") and LSD with high affinity, suggesting that the action of these widely used drugs of abuse may be mediated in part by these novel receptors. The trace amine receptor may be a new target for the development of anti-stimulant medications. Bunzow, J.R., Sonders, M.S., Arttamangkul, S., Harrison, L.M., Zhang, G., Quigley, D.I., Darland, T., Suchland, K.L., Pasumamula, S., Kennedy, J.L., Olson, S.B., Magenis, R.E., Amara, S.G. and Grandy, D.K. Molecular Pharmacology, 60, pp. 1181-1188, 2001.

Endogenous Nicotinic Cholinergic Activity Regulates Dopamine Release in the Striatum

Dr. John Dani of Baylor College of Medicine and his co-workers Drs. Fu-Ming Zhou and Yong Liang recently showed that the neurotransmitter acetylcholine is important for controlling the release of dopamine in the target. Dopamine has long been known to be important for movement and in the learning process that enables us to adapt to our environment. It is now also widely regarded as playing a critical role in the rewarding properties of addictive drugs such as cocaine, amphetamines, and nicotine. Dr. Dani and his colleagues found that nicotinic receptors, responding to the neurotransmitter acetylcholine, control the release of dopamine in the target regions of the forebrain responsible for many of these behaviors. These findings have important implications for addiction in general, and for nicotine dependence in particular. In addition, his findings may also be important for other disorders that involve dopamine, such as Parkinson's disease and schizophrenia. Zhou, F.M., Liang, Y., and Dani, J.A. Endogenous Nicotinic Cholinergic Activity Regulates Dopamine Release in the Striatum. Nature Neuroscience, 4, 1224–1229, 2001.

Marijuana and Lung Cell Death Pathways

In a recent paper, NIDA supported researchers demonstrate that the delta-9-THC contained in marijuana smoke disrupts elements of the apoptotic pathway, thereby shifting the balance between apoptotic (preprogrammed) and necrotic (gross tissue damage) cell death. They noted that exposure to whole marijuana and tobacco smoke blocked the induction of caspase-3 (a key regulatory enzyme in the apoptotic process) in A549 lung tumor cells. In contrast, gas-phase smoke, which generates high levels of intracellular reactive oxygen species, had no effect on caspase-3 activity. Exposure to marijuana or tobacco smoke is known to be toxic to respiratory epithelium. However, the researchers also observed that the balance between apoptotic and necrotic cell death may play a key role in determining host response to injury. These findings are important because they demonstrate that the observed shift in the two cell death pathways may very well affect both the carcinogenic and immunologic consequences of marijuana smoke exposure. Sarafian, T.A., Tashkin, D.P. and Roth, M.D. Marijuana Smoke and Delta-9 Tetrahydrocannabinol Promote Necrotic Cell Death But Inhibit Fas-Mediated Apoptosis. Toxicology and Applied Pharmacology, 174, pp. 264-272, 2001.

Endocannabinoid Synthesis

The endocannabinoids are a family of endogenous lipids, which include N-acylethanolamines such as anandamide and palmitoylethanolamine, and 2-monoacylglycerols such as 2-arachidonylglycerol (2-AG). Anandamide and 2-AG bind to both the CB1 and CB2 cannabinoid receptors, while palmitoylethanolamine (pamitylethanolamide) does not. Endocannabinoids are produced from cell membrane lipid precursors via several enzyme-catalyzed biosynthetic pathways. The enzymes are stimulated by an increase in cellular calcium ion concentration, which can occur during neuronal injury or insult. This has suggested a "neuroprotective" role for endocannabinoids. Some examples of this include increased anandamide by direct NMDA injection (NMDA is released naturally during brain injury) into the brain, increased anandamide levels found in post-mortem brain, elevation of both anandamide and 2-AG levels in endotoxic shock, and formation of 2-AG in animal models of head injury. It has been proposed that endocannabinoids may play a role as "reverse" or feedback signaling molecules, in which increases in postsynaptic neuronal calcium levels first trigger synthesis and release of endocannabinoids. These then reach (by an unknown mechanism) and activate presynaptic CB1 receptors. This leads to an inhibition of calcium channels, and a decrease in neurotransmitter release. This phenomenon is observed in-vitro by the reduction of GABA release from hippocampal neurons following depolarizing suppression of synaptic current, and in Purkinje cells, where elevation of postsynaptic calcium levels suppresses both excitatory and inhibitory inputs. The phenomenon is absent in knockout mice lacking the CB1 receptor. The production of endocannabinoids might be due to the stimulation of electrical potentials in the cells, or to receptor activation, or both. Recently, Dr. Daniele Piomelli and colleagues found that receptor activation is

a requirement for endocannabinoid formation in cortical neurons. The researchers found that the coactivation of NMDA receptors (using NMDA) and cholinergic receptors (using carbachol) stimulates the production of the endogenous cannabinoids palmitylethanolamide and oleylethanolamide. They found that this process is inhibited by intracellular calcium chelation, and by the cholinergic antagonist atropine. Activation of NMDA receptors alone (by glutamate or NMDA) caused a substantial increase in 2-AG formation, which was blocked by application of an external cellular calcium chelator, which reduces the concentration of extracellular calcium available to activate the NMDA receptors. Anandamide formation required activation by both glutamate and carbachol, but in this case antagonism was found with the alpha 7 nicotinic acetylcholine antagonist methyllycaconitine. Anandamide formation was also blocked by an intracellular chelation of calcium ions. This work suggests that endocannabinoid synthesis may be a response modulating the effects of the neurotransmitters glutamate and/or acetylcholine in primary rat cortical neurons, and that the type of endocannabinoid released depends on the type of receptor activated. Stella, N. and Piomelli, D. European Journal of Pharmacology, 425, pp. 189-196, 2001.

Cannabinoids Prevent Formation of Synapses between Hippocampal Neurons in Culture

Marijuana (cannabis) is well known to impair the formation of memories in humans and animal models. However, the mechanisms by which the active constituents of marijuana, principally _9-tetrahydrocannabinol (_9-THC), bring about this memory impairment are not known. Drs. Daniel Kim and Stanley Thayer, University of Minnesota Medical School, grew rat hippocampal neurons in culture, and induced synapse formation between these neurons in culture by elevating cAMP with an agent called forskolin. The forskolin-induced formation of new synapses was prevented by the cannabinoids Win55212-2, _9-THC, and anandamide (an endogenous cannabinoid). The cannabinoids did not prevent the formation of synapses induced directly by a cAMP analog, indicating that they act by inhibiting the formation of cAMP. A cannabinoid CB1 receptor antagonist blocked the cannabinoid action, indicating that this action is CB1 receptor-mediated. These researchers concluded that preventing the formation of new synapses might contribute to the impairment of memory produced by cannabinoids. Kim, D., and Thayer, S.A. Cannabinoids Inhibit the Formation of New Synapses between Hippocampal Neurons in Culture. J. Neurosci., 21:RC146, pp. 1-5, 2001.

Interaction of Co-expressed Mu- and Delta-Opioid Receptors

Mu- and delta-opioid agonists interact in a synergistic manner to produce analgesia in several animal models. Additionally, receptor binding studies using membranes derived from brain tissue indicate that interactions between mu- and delta-opioid receptors might be responsible for the observation of multiple opioid receptor subtypes. To examine potential interactions between mu- and delta-opioid receptors, Dr. Paul Prather and his colleagues at University of Arkansas for Medical Sciences examined receptor binding and functional characteristics of mu-, delta-, or both mu- and delta-opioid receptors stably transfected in rat pituitary GH3 cells [GH3MOR, GH3DOR, and GH3MORDOR, respectively]. Saturation and competition binding experiments revealed that co-expression of mu- and delta-opioid receptors resulted in the appearance of multiple affinity states for mu- but not delta-opioid receptors. Additionally, coadministration of selective mu- and delta-opioid agonists in GH3MORDOR cells resulted in a synergistic competition with [3H][D-Pen2,5]enkephalin (DPDPE) for delta-opioid receptors. Finally, when equally effective concentrations of [D-Ala2, N-MePhe4, Gly-ol5]enkephalin (DAMGO) and two different delta-opioid agonists (DPDPE or 2-methyl-4a-(3-hydroxyphenyl)-1,2,3,4,4a,5,12,12aa-octahydroquinolino-[2,3,3-g]-isoquinoline; TAN67) were coadministered in GH3MORDOR cells, a synergistic inhibition of adenylyl cyclase activity was observed. These results strongly suggest that cotransfection of mu- and delta-opioid receptors alters the binding and functional characteristics of the receptors. Therefore, they propose that the simultaneous exposure of GH3MORDOR cells to selective mu- and delta-opioid agonists produces an interaction between receptors resulting in enhanced receptor binding. This effect is translated into an augmented ability of these agonists to inhibit adenylyl cyclase activity. Similar interactions occurring in neurons that express both mu- and delta-opioid receptors could explain observations of multiple opioid receptor subtypes in receptor binding studies and the synergistic interaction of mu- and delta-opioids in analgesic assays. Martin, N.A., and Prather, P.L. Interaction of Co-Expressed Mu- and Delta-Opioid Receptors in Transfected Rat Pituitary GH3 cells. Mol. Pharmacol., 59(4), pp. 74-83, 2001.

Identification of a New Class of Molecules Involved in Pain Transmission

Dr. J. Michael Walker of Brown University and his colleagues have identified the existence of lipoamino acids in mammals. Lipoamino acids are conjugates of lipids and amino acids, and have previously been found to have biological activity in bacteria. Dr. Walker and his colleagues have found three examples of one class of lipoamino acid, the arachidonyl amino acids, in bovine brain. One of these, N-arachidonylglycine (NAGly), was also present in rat brain and other tissues. While the biological role of NAGly needs clarification, it was found that NAGly inhibited tonic inflammation pain in the rat. These data suggest a novel class of molecules that might be involved in pain processing, and may ultimately lead to novel pain treatments. Huang, L.-Y. et al., Identification of a New Class of Molecules, the Arachidonyl Amino Acids, and Characterization if One Member That Inhibits Pain, The Journal of Biological Chemistry,

276 (46), pp. 42639-42644, 2001.

Candidate Molecules Involved in Mechanisms of Chronic Cocaine-Mediated Changes are Identified Using Microarray Technology

The molecular composition of a cell is altered when receptors on that cell come in contact with molecules that the receptor recognizes and responds to. The response will often take the form of a change in the expression of various genes and production of proteins. In this study, the investigators used microarray technology to identify molecules involved in chronic cocaine-mediated changes in cells of the nucleus accumbens. They studied these cells in a non-human primate model, the cynomolgus macaque. Using a microarray with a limited number of genes, Freeman and associates identified 18 genes with significant changes in expression. The protein production for 8 of the 18 genes was examined to determine whether the mRNA levels measured with the microarray were consistent with levels of corresponding protein produced. They confirmed that, in their model system, chronic cocaine use (with increasing doses over the period of one year) lead to a statistically significant increase in the following proteins in the cells of the nucleus accumbens: protein kinase A _ _ catalytic subunit, cell adhesion tyrosine kinase __ (PYK2), mitogen activated protein kinase 1 (MEK1), and __-catenin. In the case of PKA_ _ catalytic subunit and MEK1, these results correlated with cocaine-induced changes in gene expression observed in other model systems. All four proteins are members of a common regulatory pathway that affects downstream molecules that have implications for drug addiction. Freeman, W.M., Nader, M.A., Nader, S.H., Robertson, D.J., Gioia, L., Mitchell, S.M., Daunais, J.B., Porrino, L.J., Friedman, D.P., and Vrana, K.E. Chronic Cocaine-Mediated Changes in Non-Human Primate Nucleus Accumbens Gene Expression. J. Neurochem., 77, pp. 542-549, 2001.

Rats Exposed to Methylphenidate during Development Respond Differently to Cocaine as Adults

Previous research had suggested that children with attention-deficit hyperactivity disorder who are treated with Ritalin (methylphenidate) are less likely to become substance abusers later in life than similar children who do not receive such treatment (Biederman et al, 1999). NIDA-supported researchers in Boston recently reported that the administration of methylphenidate to pre-adolescent rats results in behavioral and molecular adaptations that persist into adulthood and that the same treatment in adult rats results in different patterns of behavior and molecular adaptations. Rats were given a clinically relevant dose of methylphenidate or vehicle daily from postnatal days 20-35 or from days 50-65 and were studied 25 days later. Cocaine reward was assessed using a conditioned place preference procedure at a low and a high dose of cocaine. Rats treated in the earlier developmental period with vehicle showed the expected preference for cocaine in this test whereas those treated with the methylphenidate failed to establish a place preference to cocaine, suggesting that cocaine was less rewarding or aversive in these animals. Animals treated and tested as adults consistently demonstrated a preference for cocaine. Numerous neuroadaptations have been described in adult rats after treatment with cocaine, including increases in CREB (cAMP response element binding protein) and changes in NMDA receptors (GluR1, GluR2, NMDAR1). When the brains of the animals treated as juveniles were examined, CREB had increased as much as in animals treated as adults. However, there was no corresponding increase in GluR2, as there was in the animals treated as adults. These results show that neurobiological adaptations persist after treatment with methylphenidate and that the adaptive responses are different, depending on the age at which treatment occurred. Furthermore, they may represent neurobiological substrates that mediate the rewarding and aversive properties of stimulants. These findings suggest that the neurobiological impact of methylphenidate depends critically on the developmental stage during which it is administered. Andersen, S.L., Aravanitogiannis, A., Pliakas, A.M., LeBlanc, C. and Carlezon, Jr., W.A., Altered Responsiveness to Cocaine in Rats Exposed to Methylphenidate during Development. Nature Neuroscience, 5, pp. 13-14, 2002.

Studies of Opiate-Systems Regulation of Immune Function

Previously, it has been observed that opiates potently inhibit chemotaxis in phagocytic type cells such as macrophages. Thus, opiates diminish the capacity of these cells to reach and engulf foreign bodies in humans. This study explores this feature of other non-phagocytic immune cells and elaborates on the mechanism of cross sensitivity of opiates and chemotaxic peptides involved in this process. Opioids are known to suppress a number of elements of the immune response, including antimicrobial resistance, antibody production, and delayed-type hypersensitivity. Phagocytic cells may be particularly susceptible to opioid administration, since reduced production of the cytokines IL-1, IL-6 and TNF-alpha, monocyte-mediated phagocytosis, and both neutrophil and monocyte chemotaxis have all been well established. Earlier studies have shown that both mu- and delta -opioid agonists induce a chemotactic response in monocytes and neutrophils. In addition, mu- and delta -opioid administration inhibited the chemotactic response of these cell populations to a number of chemokines through a process of

heterologous desensitization. Authors report here that mu-, delta-, and kappa-opioid agonists also induce a chemotactic response in T lymphocytes. Using the human T-cell line Jurkat, they confirmed previous observations that pre-incubation with met-enkephalin (MetEnk), an endogenous opioid agonist, prevents the subsequent chemotactic response to the chemokine RANTES. On the other hand, treatment with MetEnk does not alter the response to the chemokine SDF-1 alpha. Moreover, they found that pretreatment with RANTES prevented a subsequent response of monocytes to the mu-opioid agonist DAMGO. These results suggest that activation of members of the opioid and chemokine receptor families leads to downregulation of each other's leukocyte migratory activities. Rogers, T.J., Steele, A.D., Howard, O.M.Z., and Oppenheim, J.J. Bidirectional Heterologous Desensitization of Opioid and Chemokine Receptors. Neuroimmunomodulation: Annals NY Acad. Sci., 917, pp. 19-28, 2000.

There is considerable controversy about whether opioids modulate immunity centrally or in the periphery. Opioid receptors are present in lower quantities on T-cells or macrophages in comparison to the neural cells but the opiates have a higher affinity for immune cells. This paper clarifies the role of these systems in immunomodulation. Administration of morphine to rats was found to decrease the proliferative potential of blood lymphocytes by 60-80% and concurrently elevate circulating levels of the cytokine, interleukin-6 (IL-6), 2- to 4-fold. Both parameters were similarly altered upon the central administration of morphine and were blocked upon pretreatment of animals with the opioid receptor antagonist, naltrexone. These results suggest that the activation of central opioid receptors is involved in morphine-induced inhibition of lymphocyte proliferation as well as increases in circulating levels of IL-6. Studies addressing the potential peripheral mechanisms demonstrated that intact ganglionic transmission was required for both effects of morphine. Although the suppression by morphine of lymphocyte proliferation appeared to be largely independent of stimulation of the hypothalamic-pituitary-adrenal axis, the elevation of IL-6 was completely abolished in adrenalectomized animals. Collectively, these results suggest that central opioid receptor activation results in changes in different immune parameters that can be mediated through distinct peripheral mechanisms. Houghtling, R.A., Mellon, R.D., Tan, R.J., and Bayer, B.M. Acute Effects of Morphine on Blood Lymphocyte Proliferation and Plasma IL-6 Levels. Annals NY Acad. Sci., 917, pp. 771-777, 2000.

Cholecystokinin (CCK) Gene Polymorphism is Significantly More Prevalent in Two Independent Samples of Smokers

Two independent samples, one from Dr. Comings at the City of Hope, selected from women seeking treatment for obesity, and the other from parents of twins studied by Drs. Iacono, McGue and colleagues at the University of Minnesota were assessed for prevalence of the polymorphic SNP, C-45T, in relation to smoking history. The allele was 4 times more prevalent in smokers compared to never smokers of the obesity sample and nearly twice as prevalent in those diagnosed with nicotine dependence in the second sample. Even though CCK is considered a satiety gene, the polymorphism was not associated with obesity. It is concluded that there may be a role for the CCK gene to be a risk factor for
smoking. Comings, D.E., Wu, S., Gonzalez, N., Iacono, W.G., McGue, M., Peters, W.W., and MacMurray, J.P., Mol Genet Metab, 73, pp. 349-353, 2001.

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Research Findings

Behavioral Research

Benzodiazepines Facilitate Heroin Reward

Few studies have been conducted on drug-interactions although polydrug use is common among drug abusers. Popular drug combinations are ethanol plus cocaine (cocaethylene), heroin plus cocaine (speedball), and heroin plus a benzodiazepine. Dr. Aaron Ettenberg completed a study of heroin plus alprazolam (a benzodiazepine) in which the conditioned place preference was used as a measure of drug reward. It was demonstrated that subcutaneously-applied alprazolam, at low doses, produced a leftward shift in the heroin dose-response curve. That is, small non-rewarding dose of benzodiazepine was seen to reliably increase the conditioned place preference produced by a non-rewarding dose of heroin. This confirms the clinical and case reports of human heroin users who pretreat themselves with benzodiazepines as a means of enhancing the rewarding effect of heroin and/or extending their supply of narcotic. Walker, B.M. and Ettenberg, A. Benzodiazepine Modulation of Opiate Reward. Experimental and Clinical Psychopharmacology, 9, pp. 191-197, 2001.

Beyond the Nucleus Accumbens: the Ventral Pallidum

Dopamine innervation of the nucleus accumbens is thought to have a major role in the biological processes underlying the self-administration of many drugs of abuse. Recent data has also suggested that the dopamine innervation of the ventral pallidum may also play an important role. A microdialysis study was done using rats self-administering cocaine. The animals had intravenous jugular catheters for drug self-administration and microdialysis probes aimed into the ventral pallidum. Controls were yoked; that is, they were surgically prepared in an identical fashion but received vehicle infusions when the experimental animals received cocaine. In the self-administering animals, extracellular fluid levels of dopamine and serotonin were elevated throughout the session and the increase was cocaine dose dependent. Extracellular fluid levels of other transmitters were only slightly increased or not at all (GABA, glutamate). The data and other studies from this laboratory indicate that the ventral pallidum plays an important role in psychomotor stimulant self-administration. Sizemore, G.M., Co, C., and Smith, J.E. Ventral Pallidal Extracellular Fluid Levels of Dopamine, Serotonin, Gamma Amino Butyric Acid, and Glutamate During Cocaine Self-Administration in Rats. Psychopharmacology, 150, pp. 391-398, 2000.

Inhalant Effects on Attention and Information Processing.

Epidemiologic tracking systems have detected alarming trends in the abuse of volatile inhalants, especially among adolescents and young adults. In light of this trend, there is increasing concern about the cognitive deficits that have been observed with chronic abuse of these substances. In particular, pronounced negative effects on attentional processes and short-term memory have been reported following repeated intoxication in human abusers and under conditions of occupational exposure. Dr. Jenny Wiley and colleagues at the Medical College of Virginia have been studying the behavioral, cognitive and neurotoxicologal effects of solvent exposure in preclinical models. Recently they exposed rats to vapors of toluene, 1,1,1-tricholorethane, methoxyflurane or flurothyl-m-xylene and measured their behavioral reactions in a pre-pulse inhibition procedure. Normally, animals react with a startle response to the presentation of a loud auditory stimulus. However, when preceded by an initial “pre-pulse”, this behavioral reaction is inhibited, or “gated”. In the pre-pulse inhibition paradigm, a low-intensity auditory stimulus is presented just prior to a second, higher intensity tone, and startle responses are measured to the second tone. The paradigm is routinely

used as an assessment of pre-attentional processes in both human and animal studies. None of the vapors tested affected pre-pulse inhibition in this model. Thus, the findings suggest that these volatile solvents do not disrupt cognitive processes by virtue of interfering with attentional stages of information processing. Future studies using repeated exposures are needed to more closely model patterns of human abuse and identify the cognitive mechanisms that are disrupted by inhalants. Wiley J.L., Bowen, S.E., and Balster R.L. Effects of Volatile Inhalants on Sensorimotor Reactivity in Rats. Addiction Biol., 6, pp. 35-43, 2001.

Multi-Dimensional Analysis of Cue-Elicited Craving

Although “craving” is often considered to be a core component of drug addiction, its nature and assessment remain in dispute. The present study examined several new measures of craving, including a behavioral choice measure, a reaction time (RT) measure of cognitive resource allocation, two judgment measures and a novel measure of self-reported urge. Four groups of subjects, predicted to vary in the strength of their cravings, were assessed on these measures. Heavy smokers (HS: at least 21 or more cigarettes/day for 2 years, n=67) and tobacco chippers (TC: 1-5 cigarettes/day on at least 2 days/week for 2 years, n=60), who were either deprived (for at least 7 hours) or minimally deprived (20-25 min) of nicotine, were exposed to smoking cues and control cues. The smoking cue involved holding a lit cigarette. As expected, results indicated that both deprivation state and smoker type tended to affect responses across the multiple measurement domains. For example, deprived smokers reported higher urge scores than minimally deprived smokers, HSs reported higher scores than TCs and deprived HSs reported especially high urge scores relative to the other groups. In addition, TCs reported more positive mood than HSs and minimally deprived smokers reported more positive mood than did deprived smokers. On the choice measure, HSs demanded more money to delay smoking (for 5 min) than did TCs and deprived smokers demanded more money than did minimally deprived smokers. Moreover, deprived HSs demanded the most money, followed by minimally deprived HSs, deprived TCs and minimally deprived TCs. Both HSs and TCs responded slower in the presence of cigarette cues than in the presence of control cues. These findings support the use of several new measures for measuring craving-related processes. Behavioral choice was an especially sensitive measure in this study. Furthermore, magnitude estimation and a composite urge measure were found to be useful approaches when initial deprivation produces ceiling effects. Finally, judgment measures that are sensitive to assessing how craving alters reasoning provide promising tools for examining cognitive dimensions of craving. Sayette, M.A., Martin, C.S., Wertz, J.M., Shiffman, S., and Perrott, M.A. A Multi-dimensional Analysis of Cue-elicited Craving in Heavy Smokers and Tobacco Chippers. Addiction, 96, pp. 1419-1432, 2001.

Effects of d-Amphetamine and Alcohol on Behavioral Inhibition

Drs. Harriet de Wit, Jerry Richards and colleagues have been investigating the effects of drugs of abuse on cognitive inhibitory processes in parallel studies with human and animal subjects. These studies are of interest because drug abuse and addiction have long been associated with “impulsive” behavior patterns. Indeed, impulsive individuals are hypothesized to be predisposed to use drugs. Little is known, however, about the acute effects of psychoactive drugs on impulsive behavior. One factor that has hampered progress in this area is the lack of an agreed upon definition of impulsivity. These studies investigated the acute effects of drugs on one operationally defined measure of impulsivity in humans and the companion study investigated the effects of the same drugs in a parallel procedure in rats. Human subjects with a history of psychostimulant or alcohol abuse were treated with d-amphetamine (AMP: 10 and 20 mg, n=20) or ethanol (EtOH: 0.2, 0.4, and 0.8 g/kg, n=17) and assessed on a computerized “stop” task, a putative measure of behavioral inhibition and impulsivity. The stop task provides a measure of the reaction time (RT) needed to inhibit a response (Stop RT) relative to the time taken to execute a simple response (Go RT). Subjects performed the stop task before and after receiving one of the drugs. AMP decreased Stop RT (i.e., facilitated inhibition) but only among participants with relatively slow Stop RT baselines. EtOH increased Stop RT (i.e., impaired inhibition) at doses that did not affect Go RTs. These results suggest that AMP and EtOH have specific and opposite effects on the ability to inhibit responses. de Wit, H., Green, J., and Richards, J.B. Effects of d-Amphetamine and Ethanol on a Measure of Behavioral Inhibition in Humans. Behavioral Neuroscience, 114 (4), pp. 830-837, 2000.

In a parallel preclinical study, the researchers developed a stop task procedure for use in rats and assessed the effects of AMP and EtOH on behavioral inhibition. This task provides a quantitative index of the ability to inhibit a response that has been initiated. Rats were tested after intraperitoneal injections of AMP (0.125, 0.25, 0.5, 1.0 mg/kg) and EtOH (250, 500, 750 mg/kg). As in humans, AMP improved the ability to inhibit responses only in rats with relatively poor inhibitory performance at baseline, whereas EtOH impaired inhibition at doses that did not affect simple RT. These results support the sensitivity, reliability, and validity of the procedure as a measure of behavioral inhibition in rats and they are highly concordant with the parallel study conducted with humans. The establishment of the stop task in rats provides an important approach for studying neurobiological processes that mediate behavioral inhibition and substrate changes responsible for drug effects on these cognitive mechanisms. Feola, T.W., de Wit, H.,

and Richards, J.B. Effects of d-Amphetamine and Alcohol on a Measure of Behavioral Inhibition in Rats. Behavioral Neuroscience, 114 (4), pp. 838-848, 2000.

Triazolam Improves Memory Through Effects on Automatic Processes

In addition to their well-known amnestic effects, benzodiazepines (BZPs) have been shown to improve memory. Thus, memory enhancement might contribute to the motivation for BZP abuse. It is important, therefore, to understand the mechanisms responsible for these BZP effects. If subjects receive a BZP immediately after studying to-be-remembered material, memory for the information is improved (retrograde facilitation) when tested in the drug state. This is an important finding because it demonstrates, (contrary to so-called 'state-dependent' learning), that a drug can be used after the fact to enhance memory even when the original learning occurred in the drug-free state. Previous research has shown that this retrograde facilitation of memory is not due to suppression of new learning that might interfere retroactively with recall. Rather the facilitation affects some aspect of memory retrieval. The present study tested the degree to which BZP-induced retrograde facilitation of recall is due to enhancement of an automatic (nonconscious, unintentional), as opposed to a controlled (conscious, intentional), retrieval processes. Forty healthy adults were randomly assigned to one of three dose conditions (double-blind), under which they received 0 mg (placebo), 0.125 mg, or 0.25 mg of the short-acting BZP, triazolam. Subjects studied a list of words just prior to drug administration. One hour later, subjects were tested using a word-stem completion task. This commonly used test of implicit memory involves studying a list of nouns (e.g., motel), followed by a test in which the subjects are cued with a word stem (e.g. mot--) which can be completed in one of several ways (e.g., motel, motor, motif or motto). Automatic influences on memory are inferred when there is a greater probability of completing a stem with a previously studied word than with an unstudied word. In this study, the investigators estimated the degree to which retrieval was under the influence of memory processes that were automatic versus controlled. Results revealed that those who received active doses of triazolam had a higher probability of using studied words as stem completions, implicating greater use of automatic influences during memory retrieval under triazolam. These findings indicate that retrograde facilitation of memory following BZP administration does not necessarily reflect an improved ability to intentionally retrieve information but could instead reflect increased responsiveness to cues that automatically elicit retrieval of pre-drug information. Fillmore, M.T., Kelly, T.H., Rush, C.R., and Hays, L. Retrograde Facilitation of Memory by Triazolam: Effects on Automatic Processes. Psychopharmacology, 158, pp. 314-321, 2001.

Methylphenidate Treatment of Adolescent Rats Enhances Behavioral Reactivity and Vulnerability to Self-Administer Cocaine as Adults

The recent dramatic increase in the use of methylphenidate (MP; Ritalin') to treat attention deficit hyperactivity disorder (ADHD) in children and adolescents has raised the question of whether long-term exposure to this psychostimulant might lead to increased vulnerability for drug abuse disorders. Epidemiological studies have yielded conflicting answers to this important question, and previous studies in animal models have also been inconclusive, in part because of controversy about whether the MP dosages tested in rats have replicated therapeutic levels in humans. In a recent study, Dr. Cindy Brandon, a NIDA NRSA postdoctoral fellow in Dr. Frank White's laboratory, developed an animal model to assess whether repeated exposure to MP during adolescence enhances locomotor stimulant effects of cocaine and increases vulnerability to self administer this drug in adulthood. Adolescent rats (5-weeks old – age equivalent to the beginning of adolescence) received seven daily injections of moderate doses (10 mg/kg or 5 mg/kg) of MP and were then tested as adults (8-weeks old) for their response to a single dose of cocaine. The pre-exposure to MP significantly increased sensitivity to the locomotor activating effects of the cocaine, a phenomenon known as cross sensitization. In a separate experiment intended to emulate more closely dosing regimens in humans and associated plasma drug concentrations, the investigators pretreated adolescent rats with a low dose of MP (2 mg/kg) and challenged them with various doses of cocaine. The rats showed no cross sensitization at any of the cocaine doses, but when they were tested in a self-administration (SA) protocol, they acquired SA at the low cocaine dose of 75 mg/kg and showed enhanced intake of cocaine compared to control animals pretreated with saline. Thus, animals exposed to the low dose of MP during adolescence appeared considerably more vulnerable to the reinforcing effects of cocaine as adults even though they did not show locomotor cross sensitization. The results of this study suggest that known neuroadaptations produced by therapeutic treatment with MP, such as decreased dopamine transporter binding, may increase drug abuse vulnerability. Brandon, C.L., Marinelli, M., Baker, L.K. and White, F.J. Enhanced Reactivity and Vulnerability to Cocaine following Methylphenidate Treatment in Adolescent Rats. Neuropsychopharmacology, 25, pp. 651-661, 2001.

Sexual Experience Activates Neurons in the Nucleus Accumbens and Cross Sensitizes Female Hamsters to the Behavioral Effects of Amphetamine

Dopamine transmission in the nucleus accumbens from neurons originating in the midbrain ventral tegmental area is

important both for the regulation of appetitive behaviors and for self-administration of drugs of abuse. Dr. Robert Meisel and his graduate student Katherine Bradley recently carried out a study to examine the effects of female sexual experience on cellular activity in the nucleus accumbens and to determine whether previous sexual experience could sensitize animals to the behavioral effects of amphetamine. They found that sexual activity elevated c-Fos induction (a measure of neuronal activity) in the core, but not the shell, of nucleus accumbens. Drugs of abuse have most often been observed to activate neurons in the shell of nucleus accumbens. Nevertheless, the investigators were able to demonstrate that prior sexual activity made female hamsters more sensitive to the locomotor effects of amphetamine. These experiments in female animals join a growing list of studies indicating that the prior experiences of an animal -- such as exposure to mild stress, environmental novelty, or highly palatable food, and male sexual behavior -- can sensitize the responsiveness of the mesolimbic dopamine pathway to the effects of drugs of abuse. Research on cross-sensitization between experience and drug effects may shed light on the neural mechanisms underlying individual vulnerability to the effects of drugs. Bradley, K.C. and Meisel, R.L. Sexual Behavior Induction of c-Fos in the Nucleus Accumbens and Amphetamine-stimulated Locomotor Activity are Sensitized by Previous Sexual Experience in Female Syrian Hamsters. Journal of Neuroscience, 21, pp. 2123-2130, 2001.

Common Areas of Prefrontal Cortex are Activated by Environments Associated with Either Nicotine or Chocolate

In humans, a specific environment or the sight of objects associated with prior drug use can trigger craving and relapse. Corollary responses to drug-associated cues have also been demonstrated in animals. Such reactions to drug-associated environments may be maladaptive, but the general phenomenon of learning about environmental cues that predict the availability of, for example, a food source, and the activation of appetitive behaviors in the presence of such cues, has an obvious adaptive value for an organism. In a recent study, Dr. Anne Kelley and her colleagues sought to determine whether similar neural circuits would be activated by cues associated with nicotine and a naturally rewarding palatable food, chocolate. In the first experiment, rats were treated with either nicotine (0.4 mg/ml/kg) or saline once per day for 10 days in a test environment distinct from their home cages. In the second experiment rats were given access to either a bowl of chocolate chips or an empty bowl in the distinct environment for 10 days. After a 4-day interval, rats were re-introduced to the environment where they previously received either nicotine treatment or chocolate access. Nicotine-associated sensory cues elicited marked and specific activation of Fos (an “immediate early gene” that serves as a marker for neural activation) expression in prefrontal cortical and limbic regions. Exposure to cues associated with the chocolate induced a pattern of gene expression that showed similarities with that elicited by the drug cues, particularly in the ventrolateral orbital area, and other areas, of the prefrontal cortex. Previous experiments have shown an overlapping pattern of neural activation in morphine- and cocaine-associated environments. Taken together, the previous results and those of the current experiment, in which nicotine and chocolate were explicitly compared, support the hypothesis that addictive drugs induce long-term changes in brain regions that subserve normal learning and memory for motivationally salient stimuli, especially within the prefrontal cortex. Schroeder, B.E., Binzak, J.M., and Kelley, A.E. A Common Profile of Prefrontal Cortical Activation following Exposure to Nicotine- or Chocolate-associated Contextual Cues. Neuroscience, 105, pp. 535-545, 2001.

Selective Disruptions of Serotonergic (5-HT) Function May Produce Mood Disruptions seen During Abstinence from Chronic Cocaine

Abstinence from chronic cocaine abuse in human addicts has been associated with a range of mood disturbances, including increased depression, anxiety and irritability. While cocaine induces its subjective and behavioral effects via inhibition of monoamine reuptake in central dopaminergic (DA) and serotonergic (5-HT) systems, little is known about the neurochemical changes in abstinence giving rise to these mood disturbances. Preclinical studies have revealed reductions in central DA and 5-HT levels following chronic cocaine exposure in the rat. Dr. M. Haney and her colleagues recently used an indirect measure of central 5-HT and DA activity to study neurochemical perturbations during abstinence from cocaine in human addicts. These researchers assessed prolactin and cortisol release in response to challenge with the 5-HT releaser and reuptake inhibitor, d-fenfluramine (d-FEN). Previous research has demonstrated that neuroendocrine response to 5-HT agonists such as d-FEN are blunted in clinically depressed populations, suggesting that this challenge is potentially useful for assessing the neurochemical substrate changes giving rise to mood disturbances during abstinence. In this study, cocaine-dependent subjects who were not seeking drug abuse treatment were allowed to self-administer “crack” cocaine in an inpatient setting over a three day bout. Neuroendocrine challenges with d-FEN were performed during 2-weeks of abstinence following this three day bout. A separate group of addicts was challenged with the DA agonist, bromocriptine, to assess sensitivity of the central DA system (which regulates prolactin release), during abstinence. Results show that abstinent cocaine addicts had a similar stimulation of prolactin upon DA stimulation as non-addicted control subjects. However, while d-FEN administration to non-addicts induced profound increases in both prolactin and cortisol, abstinent addicts showed a

blunted response to 5-HT agonist challenge on both neuroendocrine measures. These observations suggest that central DA systems in cocaine addicts appear normal over 2 weeks following cessation of a cocaine binge. However, the central 5-HT systems regulating neuroendocrine activity appear to be suppressed for at least 14 days after drug cessation. The authors conclude that hypoactivity of central 5-HT systems may underlie the mood disturbances seen in abstinent cocaine addicts. Haney, M., Ward, A.S., Gerra, G. and Foltin, R.W. Neuroendocrine Effects of d-fenfluramine and bromocriptine following Repeated Smoked Cocaine in Humans. Drug and Alcohol Dep., 64, pp. 63-73, 2001.

Repeated Maternal Separation in Neonatal Rats Alters Sensitivity to Chronic Morphine in a Sex-Dependent Manner

Research has shown that neonatal rat pups separated from their mothers for several hours each day, during the first few weeks of life, subsequently exhibit elevated stress-reactivity during adulthood. Exaggerated responsivity is evident from both behavioral and physiological indices. Moreover, animals exposed to early separation distress with this paradigm are also more sensitive to the locomotor activating effects of acute psychostimulant drugs and are more vulnerable to acquire psychostimulant self-administration. Dr. Steve Holtzman and his colleagues at Emory University School of Medicine have been examining the behavioral and physiological effects of opiates in animals exposed to the early separation procedure, and using this paradigm to uncover influences of early post-natal stress on neuroadaptations to chronic drug administration. These investigators report that 3 hours of separation from the dam, in comparison to handled and nonhandled controls, alters subsequent sensitivity to morphine's antinociceptive effects. Notably, after this extended period of early separation, male but not female offspring were less sensitive to the antinociceptive effects of morphine. Also, the development of tolerance to antinociceptive effects was enhanced in males exposed to early maternal separation, but not in females. In both male and female rats, daily 3 hour maternal separations over 12 days was also associated with an increase in the severity of withdrawal from chronic morphine, suggesting the development of a greater degree of opiate dependence in animals exposed to early maternal separation. The authors speculate that maternal separation alters morphine sensitivity via stress-induced stimulation of opioid peptides in separated pups, providing additional evidence that early deleterious environmental influences may have an impact on subsequent response to drugs of abuse. Kalinichev, M., Easterling, K.W. and Holtzman, S.G. Early Neonatal Experience of Long-Evans Rats Results in Long-Lasting Changes in Morphine Tolerance and Dependence. Psychopharmacology, 157, pp. 305-312, 2001.

Progesterone Effects in Healthy Postmenopausal Women and Normally-Cycling Women

There is accumulating evidence that the stage of the menstrual cycle influences subjective responses to abused drugs. Certain neurosteroid metabolites of progesterone, e.g. allopregnanolone, are known to bind to the GABA-A receptor and there has been some evidence that they produce sedative-like effects, suggesting that progesterone may have behavioral and subjective effects in women and could perhaps influence responses to abused drugs in women. Dr. Harriet de Wit and her colleagues at the University of Chicago examined the behavioral and subjective effects of acute injections of progesterone in two groups of women, healthy normally cycling women and postmenopausal women. Normally cycling women (n=10) who were not on hormone replacement received a single injection of progesterone (100 mg im) or placebo in two sessions conducted a month apart during the follicular phase when endogenous progesterone and estrogen are low. Postmenopausal women (n=10) received progesterone (25, 50, 100 mg im) or placebo at four one-week intervals. Extensive behavioral assessments (including measures of motor, cognitive, and memory impairment) and evaluations of subjective effects (including mood and physiological states) were conducted following each injection. The progesterone injections produced time and dose-related increases in plasma concentrations of progesterone and allopregnanolone that were similar in the two groups. Yet, the behavioral and subjective effects were only modest. In cycling women there were mild sedative effects consisting of a decrease in ratings of "vigor," "friendliness," and "arousal," and paradoxically, there was a small improvement on the motor task (digit-symbol substitution test). In post-menopausal women, only the highest dose (100 mg) slightly increased ratings of feeling "sluggish" and in "positive mood." These modest sedative-effects occurred at plasma concentrations well beyond those attained during normal menstrual cycles and suggest that brief increases (i.e., several hours) in plasma levels of allopregnanolone produce only marginal sedative-like effects. The authors suggest that the allopregnanolone may produce stronger sedative-like effects only in other phases of the menstrual cycle or when estrogen is present, or alternatively, only in certain vulnerable populations, such as women with anxiety disorders. These results indicate that allopregnanolone can affect subjective states in women, albeit weakly, and could play a role in the changes in the response to abuse drugs across the menstrual cycle. de Wit, H., Schmitt, L., Purdy, R. and Hauger, R. Effects of Acute Progesterone Administration In Healthy Postmenopausal Women and Normally-Cycling Women. Psychoneuroendocrinology, 26, pp. 697-710, 2001.

Triazolam Impairs Inhibitory Control of Behavior in Humans

Benzodiazepines (BZPs) are prescribed widely in the treatment of anxiety and insomnia, but they have high potential for abuse and dependence. In addition, they are hypothesized to produce adverse behavioral outcomes (e.g., aggressiveness) by causing a loss of control over behavior. This loss of control is manifested as an inability to inhibit responding, called disinhibition. Triazolam (TZM) is a short-acting BZP that has received considerable publicity for its association with aggressive, criminal and other socially inappropriate acts. To date, however, there have been few controlled laboratory studies of triazolam on behavioral control in humans. The present study used the stop-signal paradigm to directly measure the ability of triazolam to disinhibit responding (i.e., activate a suppressed response), without increasing behavioral arousal (i.e., non-specifically activating all responses). The stop-signal paradigm engages individuals in responding to “go” signals and occasionally requires them to inhibit the response when a “stop” signal occurs. The present study was designed to test the hypothesis that triazolam impairs the ability to inhibit responding. The effects of two doses of triazolam (0.125 mg and 0.25 mg) were tested in a double blind, placebo-controlled design. During the stop-signal task, subjects were instructed to press one of two keys on the keyboard as quickly and as accurately as possible to the presentation of the letters on a computer monitor (a “go” response), but to withhold a response when a tone sounded (a “stop” response). Subjects were tested on this task 70 min, 120 min and 180 min after drug ingestion. The results showed that compared with placebo, triazolam reduced the number of inhibitions to stop signals and increased the RT to inhibit a response on each of the three tests. The results also indicated that triazolam increased go RT after the highest dose (0.25 mg), but that this effect only emerged 3 hr after TZM administration. These findings indicate that triazolam can impair the ability to inhibit behavioral responses and the ability to execute responses. The impairing effects of triazolam on inhibitory control of behavior resemble those observed after a moderate dose of alcohol. Fillmore, M.T., Rush, C.R., Kelly, T.H., and Hays, L. Triazolam Impairs Inhibitory Control of Behavior in Humans. Experimental and Clinical Psychopharmacology, 9, pp. 363-371, 2001.

Behavioral Economics of Human Drug Self-administration: Progressive Ratio versus Random Sequences of Response Requirements

Progressive-ratio (PR) schedules have been used widely to examine the relationship between drug consumption and drug price (i.e. demand curves) in the study of the behavioral economics of drug abuse. Sequential effects produced by the increasing response requirements of progressive-ratio schedules might influence the shape of demand curves for drug reinforcers. This study compared progressive, ratio schedule and random sequences of ratio requirements, each incremented across sessions in a within-subject design, to determine if they produced similar behavioral economic and traditional measures of reinforcer efficacy. Self-administration of standardized cigarette puffs (70 cc each) was studied with eight smokers. Puffs were available at nine ratio requirements (e.g. 3, 100, 300, 600, 1500, 3000, 6000, 12,000, 24,000 responses/three puffs), presented in ascending (progressive-ratio schedule) or random sequence across daily sessions. The parameter estimates obtained on measures of reinforcing efficacy (e.g. breakpoint, peak response rates, elasticity of demand) were similar for both methods of incrementing prices. The authors found no evidence the PR and random sequences of fixed-ratio (FR) schedules, incremented across daily sessions, resulted in difference demand curves. Giordano, L.A., Bickel, W.K., Shahan, T.A., and Badger, G.J. Behavioral Economics of Human Drug Self-administration: Progressive Ratio Verses Random Sequences of Response Requirements. Behavioral Pharmacology, 12 (5), pp. 343-347, 2001.

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Director's Report to the National Advisory Council on Drug Abuse
February, 2002

Research Findings

Treatment Research and Development

Motivational Interviewing with Cocaine-Dependent Patients: A Pilot Study

Drs. Stotts, Schmitz, Rhoades, and Grabowski at the University of Texas Medical School at Houston, evaluated a brief Motivational Interviewing (MI) intervention for cocaine-dependent patients during an outpatient detoxification program prior to entry to a relapse prevention treatment study. In this study, 105 cocaine dependent patients (84 men and 21 women) were randomly assigned to the MI intervention or the detox-only conditions. Findings from this pilot study indicate that although the participants completed the detoxification program at equal rates, completers who received the MI intervention increased use of behavioral coping strategies and had fewer cocaine positive urine samples on beginning the primary treatment. MI patients with lower initial motivation were more likely to complete detoxification. These findings support the use of Motivational Interviewing with cocaine-dependent patients and provide the impetus for further MI treatment research with this population. Stotts, S.L., Schmitz, J.M., Rhoades, H.M., and Grabowski, J. Journal of Consulting and Clinical Psychology, 69(5), pp. 858-862, 2001.

Fluoxetine Treatment of Cocaine-Dependent Patients with Major Depressive Disorder

Dr. Joy Schmitz and Colleagues at the University of Texas at Houston examined the efficacy of fluoxetine treatment for cocaine dependent patients with major depressive disorder. Sixty-eight male and female patients 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 the cocaine use and the 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. These 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. Drug and Alcohol Dependence, 1: 63(3), pp. 207-214, August 2001.

Exposure Therapy in the Treatment of PTSD Among Cocaine-Dependent Individuals: Preliminary Findings

In a study conducted by Dr. Kathleen Brady and Colleagues, Medical University of South Carolina, 39 individuals participated in an outpatient, 16 session individual, manual-guided psychotherapy designed to treat concurrent Posttraumatic Stress Disorder and cocaine dependence. Therapy consisted of a combination of imaginal and in-vivo exposure therapy techniques to treat PTSD symptoms and cognitive-behavioral techniques to treat cocaine dependence. Although the dropout rate was high, treatment completers (i.e., patients who attended at least 10 sessions; n= 15) demonstrated significant reductions in all PTSD symptom clusters and cocaine use from baseline to end of treatment. Significant reductions in depressive symptomatology, as measured by the Beck Depression Inventory, and psychiatric and cocaine use severity, as measured by the Addiction Severity Index, were also observed. These improvements in PTSD symptoms and cocaine use were maintained over a 6-month follow-up period among treatment completers. The average pre- to post treatment effect size was 1.80 for PTSD symptoms and 1.26

for drug and alcohol use severity. Baseline comparisons between treatment completers and noncompleters revealed significantly higher avoidance symptoms, as measured by the Impact of Events Scale, and fewer years of education among treatment non-completers as compared to completers. This study provides preliminary evidence to suggest that exposure therapy can be used safely and may be effective in the treatment of PTSD in some individuals with cocaine dependence. However, this study is limited by the uncontrolled nature of the study design, small number of subjects, and high drop out rate. Brady, K.T., Dansky, B.D., Back, S.E., Foa, E.B., and Carroll, K.M. Journal of Substance Abuse Treatment, 21(1), pp. 47-54, 2001.

Influence of Antisocial Personality Subtypes on Drug Abuse Treatment Response

Dr. King and colleagues, Johns Hopkins University, examined the impact of antisocial personality disorder and other psychiatric comorbidity on drug use and treatment retention in 513 new admissions to methadone maintenance treatment. Patients were classified into one of four groups: antisocial personality disorder only (APD), antisocial personality disorder plus other psychiatric disorder (APD Mixed) other psychiatric disorder, and no psychiatric disorder. Patients completed research assessments and were then followed for one year of treatment. Patients with APD had longer histories of heroin and cocaine use than non-APD patients and were more likely to meet criteria for cocaine dependence. Distinct clinical profiles emerged that differentiated APD Only from APD Mixed. APD Only patients exhibited higher rates of cocaine and heroin use, whereas those with APD Mixed exhibited higher rates of benzodiazepine use. Self-report measures supported urinalysis results, but group differences did not affect treatment retention. These differences in clinical profiles should be considered when evaluating treatment performance in substance abusers with antisocial personality disorder. King, V.L., Kidorf, M.D., Stoller, K.B., Carter, J.A., and Brooner, R.K. Journal of Neurological and Mental Dis., 189(9), pp. 593-601, 2001.

Tobacco Use and Quit Attempts Among Methadone Maintenance Clients

Dr. Kimber Richter at the University of Kansas conducted a survey in a 4-county metropolitan area to establish the prevalence of cigarette smoking and interest in quitting among methadone clients. Findings show that 77% of the clients smoked cigarettes. Three quarters of the current smokers had attempted to quit at least once, with an average of 5 attempts. Most smokers (80%) were very or somewhat interested in quitting. The quit ratio among methadone maintenance treatment clients was 12 %, compared with 50% nationwide. The authors suggest that future research into smoking behaviors and viable treatment options for methadone maintained clients is important. Richter, K.P., Gibson, C.A., Ahluwalia, J.S., and Schmelzle, K.H. American Journal of Public Health, 91, pp. 296-299, 2001.

Acupuncture for the Treatment of Cocaine Addiction

A large multi-site study was conducted to investigate the effectiveness of auricular acupuncture as a treatment for cocaine addiction. Six-hundred and twenty cocaine-dependent adults, who were addicted to cocaine alone or to both cocaine and opiates and were receiving methadone maintenance, were randomized to one of three conditions: auricular acupuncture, a needle-insertion control, or a relaxation control. All patients also received drug counseling. Results showed that there was a significant overall reduction in cocaine use, but no differences by treatment condition. There were also no differences between the conditions in treatment retention. The authors conclude that this study does not support the use of acupuncture as a stand-alone treatment for cocaine addition or when patients receive only minimal concurrent psychosocial treatment. They suggest that further research is needed to examine acupuncture's contribution to addiction treatment. Margolin, A., Kleber, H.D., Avants, S.K., Konefal, J., Gawin, F., Stark, E., Sorensen, J., Midkiff, E., Wells, E., Jackson, T.R., Bullock M., Culliton, P.D., Boles, S., Vaughan, R. JAMA, 287, pp. 55-63, 2002.

Enhanced Cognitive-Behavioral HIV Prevention Intervention for Adolescents Abusing Alcohol and Other Drugs

Dr. Robert Malow and colleagues at the University of Miami have designed an intervention to reduce HIV risk behaviors among adolescents in inpatient substance abuse treatment. An initial efficacy study showed that, compared to a Health-Promotion group intervention, an enhanced cognitive-behavioral intervention produced significantly better condom use skills and more favorable attitudes toward condoms. Malow, Deviux, and Rosenberg, Addictions Newsletter, 8, pp. 2 –14, 2001.

Buprenorphine Treatment of Pregnant Opioid-dependent Women: Maternal and Neonatal Outcomes

Researchers at the Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine

reported an open-label prospective study that examined maternal and neonatal safety and efficacy outcome measures during and following prenatal buprenorphine exposure. Three opioid-dependent pregnant women received 8 or 12 mg sublingual buprenorphine tablets daily for 15-16 weeks prior to delivery. Results showed that buprenorphine in combination with comprehensive prenatal care was safe and effective in these women. Prenatal exposure to buprenorphine resulted in normal birth outcomes, a mean of 4.33 days (minimum possible=4) hospitalization, and a 'relatively mild' neonatal abstinence syndrome comprised primarily of tremors (disturbed), hyperactive moro and shortened sleep after feeding. The infants required no pharmacological treatment. Onset of neonatal abstinence signs occurred within the first 12 h after birth, peaked by 72 h and returned to below pre-12 h levels by 120 h. It is concluded that buprenorphine has potential utility for the treatment of pregnant opioid-dependent women. Johnson, R.E., Jones, H.E., Jasinski, D.R., Svikis, D.S., Haug, N.A., Jansson, L.M., Kissin, W.B., Alpan, G., Lantz, M.E., Cone, E.J., Wilkins, D.G., Golden, A.S., Huggins, G.R., and Lester, B.M. Buprenorphine Treatment of Pregnant Opioid--Dependent Women: Maternal and Neonatal Outcomes. Drug Alcohol Depend, 63(1), pp. 97-103, 2001.

Enadoline, A Selective Kappa Opioid Agonist: Comparison with Butorphanol and Hydromorphone in Humans

The availability of the highly selective and specific kappa opioid agonist enadoline provides an opportunity to explore the function of kappa receptors in humans and their potential utility as a target for substance abuse pharmacotherapy development. The purpose of this study was to characterize the pharmacodynamic effects of enadoline, a selective kappa agonist, and to compare it with butorphanol, a mixed mu/kappa agonist, and hydromorphone, a mu agonist, in humans. Pilot evaluation (n=3) served to establish intramuscular doses of enadoline (20, 40, 80, and 160 microg/70 kg), butorphanol (1.5, 3, 6, and 12 mg/70 kg), and hydromorphone (1.5, 3, and 6 mg/70 kg) of comparable activity. These acute doses were examined under double-blind, placebo-controlled and constrained randomized conditions with a minimum of 72 h between tests in volunteers with polysubstance abuse histories (n=6). Physiological and subject- and observer-rated measures were collected 30 min before and for 4 h after administration. The results showed that enadoline significantly increased measures of sedation, confusion and dizziness, produced visual distortions and feelings of depersonalization, and increased urinary output. The highest dose (160 microg/70 kg) was not tolerated and led to psychotomimetic effects. Hydromorphone produced prototypic mu opioid effects including respiratory depression, miosis, and euphoria. Butorphanol was most similar to hydromorphone and shared few effects with enadoline. These results provide information with respect to the potential use and safety of kappa agonists for clinical indications. Walsh, S.L., Strain, E.C., Abreu, M.E., and Bigelow, G.E. Enadoline, A Selective Kappa Opioid Agonist: Comparison with Butorphanol and Hydromorphone in Humans. Psychopharmacology (Berl), 157(2), pp. 151-162, 2001.

Enadoline and Butorphanol: Evaluation of Kappa-agonists on Cocaine Pharmacodynamics and Cocaine Self-administration in Humans

Preclinical studies have demonstrated that kappa-opioid agonists can attenuate the neurochemical and behavioral effects of cocaine that are related to its reinforcing efficacy, suggesting that kappa-agonists may serve as pharmacotherapies for cocaine dependence. This 8-week inpatient study examined the ability of enadoline, a selective and high-efficacy kappa-agonist, and butorphanol, a mixed agonist with intermediate efficacy at both mu- and kappa-receptors, to reduce the direct pharmacodynamic effects and self-administration of intravenous cocaine in humans (n = 8). Acute doses of intramuscular enadoline (20, 40, and 80microg/kg), butorphanol (1.5, 3, and 6 mg/70 kg) and placebo were examined separately as pretreatments during each of three test sessions with cocaine in a constrained random order. A cocaine dose-effect session (0, 20, and 40 mg cocaine i.v., 1 h apart) examined direct pharmacodynamic interactions on subjective and physiological indices; self-administration sessions examined choice behavior for cocaine (40 mg i.v. for six trials) versus money 1) in the presence of a sample cocaine dose with money choices presented in ascending value, and 2) in the absence of a sample dose with money choices presented in descending values. Enadoline (80 microg/70 kg) significantly ($p < 0.05$) reduced some of the positive subjective effects of cocaine (e.g., ratings of "high"), while butorphanol failed to modify subjective responses. Both agents were safely tolerated in combination with cocaine without adverse physiological responses. Cocaine self-administration was significantly greater across all pretreatment conditions when the sample dose was given and ascending money choices were used. Enadoline and butorphanol failed to modify cocaine self-administration. These data suggest that these kappa-agonists may be safely administered in the presence of cocaine but do not produce significant attenuation of cocaine's direct effects or self-administration under these acute dosing conditions. Walsh, S.L., Geter-Douglas, B., Strain, E.C., Bigelow, G.E. Enadoline and Butorphanol: Evaluation of Kappa-agonists on Cocaine Pharmacodynamics and Cocaine Self-administration in Humans. J Pharmacol Exp Ther., 299(1), pp. 147-158, 2001.

Human Therapeutic Cocaine Vaccine: Safety and Immunogenicity

The safety and immunogenicity of a therapeutic cocaine vaccine, TA-CD, was assessed in a randomized, double blind, phase I clinical trial conducted in 34 former cocaine abusers. The patients received a course of 3 injections of 13 ug, 82 ug, or 709 ug of vaccine over the course of 2 months. In a one-year follow-up study on 15 patients, antibody levels correlated with vaccine dose and number of injections. Antibody levels peaked at 3 months and declined to baseline by 1 year. The vaccine was well tolerated and had no serious drug-related adverse events. This group speculates that TA-CD will be most effective for relapse prevention in cocaine abusers who are motivated to maintain abstinence, as it is likely that some subjects may attempt to overcome the anti-cocaine antibody effect through use of sufficiently large amounts of cocaine. TA-CD may be most effective at reducing the priming effect of using small amounts of cocaine. Kosten, T.R., Rosen, M., Bond, J., Settles, M., St. Clair Roberts, J., Shields, J., Jack, L., and Fox, B. Human Therapeutic Cocaine Vaccine: Safety and Immunogenicity. Vaccine, 2959, pp. 1-9, 2001.

Low Level of DA D2 Receptors in Methamphetamine Abusers Associated with Metabolism in Orbitofrontal Cortex.

Drs. Nora Volkow, Linda Chang, and colleagues at the Brookhaven National Laboratory conducted a positron emission tomography (PET) study to explore the association between low levels of dopamine D2 receptors and reduced levels of metabolism in the orbitofrontal cortex of methamphetamine abusers. Twelve abstinent methamphetamine abusers were scanned and compared to normal, matched controls, and results showed that dopamine D2 receptors were significantly lower in caudate and putamen. This measure was correlated with decreased metabolism in the orbitofrontal cortex. Similar reductions in D2 receptors have also been observed in cocaine-, alcohol-, heroin-dependent individuals as well as in pathologically obese individuals. It was concluded that brain changes may contribute to compulsive drug taking and the inability to stop. Volkow, N.D., Chang, L., et al., American Journal of Psychiatry, 158, pp. 2015-2021, 2001.

Dopamine Transporter Loss in Methampetamine Abusers Recovers in Protracted Abstinence

Studies in methamphetamine abusers have revealed significant loss of dopamine transporters (DATs) in methamphetamine abusers (MAs). The question of predisposition to neurodegenerative disorders, such as Parkinson's disease, is unclear and may depend on the nature and degree of recovery. The purpose of this study by Drs. Volkow, Chang and colleagues was to determine the effects of protracted abstinence on the loss of DATs in the striatum using PET in MAs at both 6 weeks and again at 6 months, as well as on performance on a battery of neuropsychological tests. Study results showed significant recovery (16-19%) of DATs in striatum after prolonged abstinence (at least 9 months). Neuropsychological evaluation revealed slight improvement on some tests; however, these results were not significant. This lack of behavioral improvement did not parallel the neurobiologic recovery observed suggesting that the increase in DATs was not sufficient for complete recovery. Volkow, N.D., Chang, L., et al., Journal of Neuroscience, 21(23), pp. 9414-9418, 2001.

Context of Uncertainty Modulates Subcortical Response to Predictability

Dr. Berns and colleagues at Emory University School of Medicine used BOLD fMRI to investigate regional brain activity associated with both increases and decreases in predictability. Normal, healthy humans were presented with four horizontally arranged square stimuli and were told to press a key when one of the squares was illuminated in a specific color. A repetitive, i.e. predictable, spatial sequence of varying predictability was embedding in a larger random sequence. Activations in the right dorsolateral prefrontal cortex and the right caudate nucleus were positively correlated with increasing predictability, whereas the left posterior parietal cortex exhibited a negative correlation. The activation in the caudate nucleus exhibited an order effect, i.e., the caudate was activated only during transitions from high to low predictability but not from low to high predictability. Thus, activation of the caudate nucleus in response to changes in predictability is sensitive to the larger context of such changes. Bischoff-Grethe et al., J. Cognitive Neuroscience, 13(7), pp. 986-993, 2001.

Beautiful Faces Have Variable Reward Value

Dr. Breiter and colleagues at the NMR Center of Massachusetts General Hospital used BOLD fMRI to map the brain areas activated during presentation of human faces that varied in attractiveness. Subjects were healthy normal heterosexual males. One group of subjects provided a subjective rating for each face for attractiveness. A second group of subjects were presented with the same faces and were required to keep pressing a key in order to keep the face on the display. Thus, the amount of key presses provided a behavioral index of attractiveness that complemented the subjective ratings. There was a dissociation between the subjective and behavioral measures in that male and female faces were both rated as attractive, but more key presses were made to keep the female faces visible than the male faces. A third group of subjects was presented passively with the faces during the fMRI scans.

Passive viewing of beautiful female faces activated the same network of brain regions previously observed during cocaine administration and monetary rewards. Prominent among these regions is the nucleus accumbens, basal forebrain, ventral tegmental area, and orbitofrontal cortex. In addition, activation of this set of paralimbic and subcortical regions was more related to key-press behavior than the subjective ratings. These results suggest that activity in this reward network reflect factors other than the aesthetic assessments. These data provide further evidence for a generalized reward network in the human brain. Breiter et al., Neuron, 32, pp. 1-20, 2001.

Networks in Brain Responding to the Hedonic Value of Stimuli

Dr. Breiter and colleagues at the NMR Center of Massachusetts General Hospital used BOLD fMRI to map the brain areas activated during presentation of noxious thermal stimuli. Heating the skin to 46o C activated two different networks of brain regions. One network corresponds to structures comprising classical pain pathways. The second network was similar to the areas previously observed during presentation of stimuli with hedonic value including cocaine administration, monetary rewards, and attractive human faces. Prominent among these regions is the nucleus accumbens, basal forebrain, and ventral tegmental area. There was also dissociation in these two networks with respect to the time course of activation. The regions in the reward network exhibited an early peak of activation whereas the structures in the classical pain pathways exhibited a relatively delayed peak in activation. These data suggest that regions in a network in the human brain respond to the net hedonic value of a stimulus, whether rewarding or aversive. Breiter et al., Neuron, 32, pp. 927-946, 2001.

Comparison of Three Decision-Making Tasks in Cocaine Abusers

Dr. Monterosso and colleagues at the Treatment Research Center of the University of Pennsylvania tested the relationship between 3 different decision-making tasks. Cocaine-dependent subjects were tested on an outpatient basis before entry to a treatment program. Subjects were tested on a delayed discounting task where they had to choose between smaller-sooner rewards and larger-later rewards, the Bechara Gambling Task that requires choices involving small rewards associated with small punishments versus large rewards associated with large punishments, and the Rogers Decision-Making Task that requires choices based on higher or lower probability gambles. Drug abusers have previously been shown to be impaired on each of these tasks, but it is unclear whether these tasks test the same underlying cognitive process. Performance on the delayed discount task was positively correlated with Gambling Task performance, but performance on neither of the two tasks was correlated with performance on the Rogers Decision-Making Task. However, performance on these two tasks was weakly correlated with reaction times on the Roger's Decision-Making task. On the other hand, there was no relationship between performance on these tasks and a psychometric index of impulsivity (Zuckerman Sensation Seeking Scale). These data suggest that there is a partial commonality to the cognitive functions assessed by these three tasks, possibility related to processing of delayed reward or assessment of risk, but that this functionality is not related to a common personality measure of impulsivity. Monterosso et al., Addiction, 96, pp. 1825-1837, 2001.

Neuropsychological Performance in Long-Term Cannabis Users

Drs. Pope, Yurgelun-Todd, and colleagues at McLean Hospital investigated whether long-term, heavy marijuana smokers exhibited residual cognitive impairments. Three groups of subjects were given a battery of neuropsychological tests. The first group consisted of current heavy users, who had smoked cannabis and, who were smoking daily at study entry. The second group consisted of former heavy users, who had smoked fewer than 12 times in the last 3 months. The third group consisted of control subjects, who had smoked no more than 50 times in their lives. Subjects underwent 28-day washout from cannabis use. Marijuana use was observed by urine samples. On days 0, 1, 7, and 28, subjects were administered neuropsychological test battery to assess general intellectual function, abstraction ability, sustained attention, verbal fluency, and ability to learn and recall new verbal and visuospatial information. Current heavy users scored significantly below control subjects on recall of word lists early during the first week of the abstinence period (days 0, 1 and 7). This performance deficit was associated with users' urinary cannabinoid concentrations at study entry. There were virtually no significant differences among the groups on any of the test results by the end of 28-day abstinence period, however. There were also no significant associations between cumulative lifetime cannabis use and test scores. Thus, heavy marijuana use does not appear to lead to long-term residual cognitive deficits. Rather, memory impairments in heavy cannabis users appear to be reversible and related to recent cannabis exposure rather than irreversible and related to cumulative lifetime use. Pope et al., Arch Gen Psychiatry, 58, pp. 909-1015, 2001.

Positive Subjective Effects are Enhanced when Smoking Marijuana after Drinking Ethanol

Drs. Lukas and Orozco of McLean Hospital have found that individuals who smoke marijuana after ethanol had increased levels of THC in plasma compared to those who had placebo ethanol but only on the rising part of the

curve. Once THC reached peak levels, there was no difference among groups with respect to THC levels at several measured intervals. Subjective effects were also affected following ethanol, but these were dependent somewhat on the strength of the marijuana dose. For those with a heavier ethanol (0.7 g/kg), latency to marijuana effects increased significantly with the increase of THC strength, but the number of euphoric events decreased, as did the duration of the euphoria. By contrast, those with half the ethanol dose (0.35 g/kg), did not differ from those with placebo ethanol in latency to effect, but had increasing numbers and duration of euphoric events with increased THC strength. (Those with placebo ethanol also had increasing number and duration of euphoria but significantly less.) These results are opposite to a previous report where prior marijuana reduced the psychoactive effects of ethanol. Importantly and in contrast, the results indicate why the combination of these drugs is popular in natural settings. Lukas, S.E. and Orozco, S., Drug Alcohol Depend., 64, pp. 143-149, 2001.

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Director's Report to the National Advisory Council on Drug Abuse
February, 2002

Research Findings

Research on AIDS and Other Medical Consequences of Drug Abuse

Neural Correlates of Attention and Working Memory Deficits in HIV Patients

Dr. Linda Chang and colleagues evaluated the neural correlates of attention and working memory deficits in patients with HIV-1. Functional magnetic resonance imaging (fMRI) was used with the blood oxygen level dependent (BOLD) contrast to evaluate regional brain activity in HIV-positive (HIV+) and HIV-negative (HIV-) controls while performing a battery of tasks that required different levels of attention for working memory. Results revealed that those HIV+ individuals showed greater brain activation in the parietal regions when performing simple tasks compared with seronegative controls, but those HIV+ individuals also showed task difficulty-dependent increases in frontal activation. Reaction times were slower, but accuracy was similar in the HIV+ individuals compared with controls. Thus, neuronal injury caused by HIV infection may necessitate greater attentional modulation reflected by a greater use of brain reserve in general and more specifically excessive attentional modulation due to frontostriatal brain injury. Chang L., et al., Neurology, 57(6), pp. 1001-1007, 2001.

Sex-related HIV Risk Reduction Behavior Among Adolescents in DATOS-A

This study examines changes in levels of HIV-related risky sexual behaviors pre- and post- treatment in relation both to patient characteristics and treatment services, received among 796 adolescents entering drug treatment programs in four cities in the United States. More than half of the adolescents (54%) reported reductions in risky sex behavior after treatment or sustained low levels of risk. Conduct-disordered adolescents with abuse history, unmet physical and emotional needs, and low commitment to school were associated with lack of improvement. Furthermore, conduct-disordered adolescents who perceived treatment to be effective were more likely to show posttreatment improvement, with the exceptions that those who scored high on hostility or low in self-perception were not likely to improve. Among adolescents without conduct disorder, receipt of mental health services was associated with improvements in their risky sex behavior The effect of drug treatment on HIV risk reduction can be increased when attention is focused on adolescents' pretreatment risk factors, service needs, in treatment responses, and key personality characteristics. Joshi, V., Hser, Y.I., Grella, C.E., and Houlton, R. Journal of Adolescent Research, 16(6), pp. 642-660, 2001.

A Cluster Analysis of HIV Risk Among Felony Drug Offenders

HIV risk profiles were investigated using cluster analysis with 247 male felony drug offenders. Two clusters were produced, distinguishable by high frequency of sex behaviors that were largely unprotected, or high frequency drug use. Exploratory analysis examining latent HIV predictors by risk type found older age, troubled feelings over drug problems, memory and concentration difficulties, higher frequency of burglary charges, and physical abuse history were predictive of drug-related HIV risk. Family problems, spending free time with family or friends, troubled feelings over medical problems, driving under the influence of drugs, anxiety, high risk-taking, polysubstance use, and using wages for drugs were predictive of sex-related HIV risk. Findings suggest intervention efforts for felony drug offenders need to address differential risk behaviors. Lang, M.A., and Belenko, S. Criminal Justice and Behavior, 28(1), pp. 24-61, 2001.

Meta-Analysis of HIV Risk-Reduction Interventions Within Drug Abuse Treatment Programs

A meta-analysis was conducted on studies using a treatment-comparison group design to evaluate HIV/AIDS risk-reduction interventions for clients enrolled in drug abuse treatment programs. Overall, the interventions studied were found to have a reliable positive (weighted) effect size (d = 0.31), and this was unlikely to be due to publication bias. Effect sizes for specific categories of outcome variables were 0.31 for knowledge, attitudes, and beliefs; 0.26 for sexual behavior; 0.62 for risk-reduction skills; and 0.04 for injection practices. A number of potential moderators were examined. Effect sizes were negatively correlated with the presence of predominantly ethnic minority samples and positively correlated with the number of intervention techniques used, the intensity of the intervention, intervention delivery at a later stage of drug treatment or within methadone treatment, and the presence of a number of specific intervention techniques. Prendergast, M.L., Urada, D., and Podus, D. J Consult Clin Psychol., 69(3), pp. 389-405, 2001.

Association of Alcohol Consumption with HIV Sex- and Drug-Risk Behaviors Among Drug Users

The relationship between alcohol use and HIV transmission is well recognized but not fully understood. In particular, the role of alcohol abuse as a mediator of HIV risk behavior among drug users is not well documented. We hypothesized that alcohol use in drug users will result in greater HIV risk-taking behavior. Participants were 354 drug users, of whom 105 were recent injection drug users. Multiple regression models were used to characterize the association between alcohol use, sexual risk behavior and injection drug use. HIV risk behavior was related to alcohol consumption, controlling for other potentially associated factors. We found that sexual HIV risk-taking behavior is associated with increased alcohol consumption among women ($p = 0.02$), with women having more risky sexual behavior than males. However, contrary to our hypothesis, there was no significant association of alcohol consumption with risky injection drug behavior. Addressing alcohol problems among drug users, particularly women, may be an important opportunity to reduce HIV sexual risk behavior among this high-risk population. Rees, V., Saitz, R., Horton, N.J. and Samet, J. Journal of Substance Abuse Treatment, 21(3), pp. 129-134, 2001.

Specific Drug Use Patterns Associated with Different Health Outcomes, HIV

A study in Baltimore assessed types of drugs used and routes of administration among 672 street-recruited drug users, and explored correlations of drug use patterns with social affiliation, HIV status, and lifestyle stability. Participants reported 63 patterns of drug use, which were categorized into five groups, including: sniff heroin only, smoke crack and snort cocaine, sniff heroin and smoke crack, inject heroin and cocaine, and inject heroin and cocaine, smoke crack, and may snort heroin. Social network analysis revealed that heroin sniffers and crack smokers both tended to associate with those with similar drug use pattern. Non-injecting drug use, particularly heroin sniffing, appeared to have the lowest risk of HIV infection, but high symptoms of drug dependence were observed among heroin users irrespective of mode of administration. Drug injectors who smoke crack are a bridge population to crack smokers who do not inject, and crack smoking compared to non-crack smoking was associated with higher sexual risk behaviors in terms of numbers of sex partners and drug-using sex partners. Specific drug use patterns may be more likely than others to facilitate HIV transmission, suggesting that, for example, HIV prevention interventions that target subgroups of cocaine and opiate users based on drug use patterns may be more effective in controlling HIV and preventing transitions from non-injecting to injecting drug use. Differential affiliation by drug use patterns suggests caution in snowball sampling for recruiting drug users, since some studies have found that interventions that bring together high-risk individuals may lead to unanticipated negative outcomes. Mixing groups of heroin sniffers or crack users with injectors, especially if they use both heroin and cocaine, may increase the risks of HIV transmission for the non-injectors and may facilitate injection of drugs. Latkin, C.A., Knowlton, A.R., and Sherman, S. Routes of Drug Administration, Differential Affiliation, and Lifestyle Stability Among Cocaine and Opiate Users: Implications to HIV Prevention. J Subst Abuse, 13, pp. 89-102, 2001.

Relationships and Diseases Among Drug Users and Non-Users

HIV and syphilis are relationship-based diseases that are typically transmitted by the cooperative activities (sex or drug injection) of two persons. In this study, researchers sampled 215 drug users and 52 socio-demographically matched nonusers to examine the behaviors and relationships related to HIV and syphilis transmission. They found that, although drug users had more risk opportunities (more sex partners and more injection partners) than nonusers, actual sex risk behaviors (never using condoms) did not differ appreciably among drug users and nonusers or with opposite-sex partners and same-sex partners. Similarity in sexual risk was evidenced by the similar levels of syphilis between drug users and nonusers. The unique risk to drug users (i.e., higher risk of exposure to disease than nonusers) was drug injection, although drug users were found to engage in fewer risky injection behaviors (sharing of drug injection equipment) than the risky sexual behaviors in which all participants engaged. Although drug users interacted as frequently with partners as nonusers, nonuser relationships were longer lasting and emotionally closer.

Bell, D.C., Lee, D., Yang, S., and Health, V. Relationships and Diseases Among Drug Users and Nonusers. J Urban Health, 78(2), pp. 313-326, 2001.

Drug Use, Sex Partners, and Behaviors of 18-24 Year-Olds in a High Risk Neighborhood

Researchers sought to determine how stigmatized drug use is related to sexual risk behaviors and network characteristics among youth. They conducted in-person interviews with a probability household sample (n=363) and a targeted, street-recruited sample of cocaine, heroin, crack, or injecting drug users comprising 18-24 year-olds in an inner city neighborhood. Drug use in the preceding 12 months was scaled hierarchically on the basis of lowest to highest social stigma, from none, to marijuana, non-injected cocaine, non-injected heroin, crack, and injected drugs. Findings indicate that users of the more stigmatized drugs had more sex partners. They were more likely to report a history of concurrent sex partners, sex with someone who also had engaged in sex with a network member, commercial sex work, and unprotected sex. Findings also showed crack use and drug injection to be associated more strongly with increased sex risk among women than among men. Young users of the more stigmatized drugs are at much greater network and behavior risk for sexually transmitted diseases. Drug use prevention and treatment programs can help to reduce sex risk because young people who use drugs engage in more sex risk behaviors and are more likely to have concurrent or shared partners than those who do not use drugs. Risk reduction interventions that address sex risk of drug users can also help to encourage condom use and fewer sex partners, and to refer drug users to screening and treatment services for sexually transmitted infections. Flom, P., Friedman, S., Kottiri, B., Neaigus, A., Curtis, R., Des Jarlais, D., Sandoval, M., and Zenilman, J. Stigmatized Drug Use, Sexual Partner Concurrency, and Other Sex Risk Network and Behavior Characteristics of 18- to 24-Year Old Youth in a High-Risk Neighborhood. Sexually Transmitted Diseases, 28(10), pp. 598-607, 2001.

Crack Cocaine Users, Predictors of Change, and Condom Use

Researchers examined whether sexual activity and partner characteristics differentiate people in different stages of change. Behavior change, primarily the reduction of high-risk sexual activity through the promotion of condom use, is the best method of reducing the incidence of new HIV infections. Many interventions attempt to reach people who are ready to make a behavior change, and miss those who are only beginning to think about it or not thinking about it at all. In this study, factors expected to distinguish people in different stages of change were partner type, drug use during sex, and HIV status. Three discriminant functions emerged from the data: partner type was the strongest predictor that distinguished people in the pre-contemplation stage from those in the preparation, action, and maintenance stages; when controlling for partner type, HIV status was the best predictor for distinguishing between the people in the maintenance stage and those in the other stages. The overall classification results indicate that individuals using crack cocaine and engaging in high-risk sexual behaviors can be classified into the stages of change for condom use based on these variables. Timpson, S., Pollak, K., Williams, M., Ross, M., Kapadia, A., Bowen, A., McCoy, C., and McCoy, V. Predictors of Stages of Change for Condom Use in Crack Cocaine Users. AIDS and Behavior, 5(1), pp. 65-74, 2001.

Residential Status and HIV Risk Behaviors Among Puerto Rican IDUs in NY and PR

Researchers investigated the association between residential status and HIV risk behaviors among island and New York Puerto Rican (PR) IDUs. They assigned 561 participants from New York City and 312 from Puerto Rico to 5 residential status categories: living in parents' home, living in own home, living in others' home, living in temporary housing, and homeless. Dependent variables were injection- and sex-related risk behaviors (sharing syringes, sharing other injection paraphernalia, shooting gallery use, and having paid sex). Chi square, t tests, and multivariate logistic analysis tests were performed separately by site. About 25% of the participants at each site were homeless. Island PRs were more likely to live with parents (44% vs 12%, p<. 001) and more NY IDUs lived in their own home (30% vs 14%, p<. 001). In NY, gallery use and paid sex were associated with living in other's home, living in parent's home, and being homeless. Sharing paraphernalia was related to living in other's home, living in temporary housing, and being homeless. In Puerto Rico, having paid sex was associated with homelessness. High-risk behaviors were more likely among homeless IDUs in both sites. Programs to provide housing and target outreach and other prevention programs for homeless IDUs are recommended to help reduce HIV risk. Andia, J., Deren, S., Kang, S., Robles, R., Colon, H., Oliver-Velez, D., Finlinson, A., Beardsley, M., and Friedman, S. Residential Status and HIV Risk Behaviors Among Puerto Rican Drug Injectors in New York and Puerto Rico. Am J Drug Alcohol Abuse, 27(4), pp. 719-735, 2001.

Evaluation of a Brief HIV Risk Reduction Intervention in a Community Setting

Researchers evaluated a brief educational intervention strategy designed to reduce the risks of HIV infection associated with injecting drug use and risky sexual behaviors. Participants (N=7,733) were not-in-treatment drug

users at high risk for HIV infection or transmission in multiple sites in the US and Puerto Rico. Multi-item needle and sex risk measures were developed to assess the efficacy of the intervention. Behavioral change was assessed within 6 empirically derived homogenous risk groups. Drug users in all 6 groups reduced their needle use and sexual risks after participating in the brief intervention. Sexual risks were reduced to a greater extent than were risks associated with needle use, both in relative terms and when measured as a percentage of risk exhibited at intake. Brief educational interventions may be more effective in reducing sexual risk behaviors than it was previously believed. Needle risk, on the other hand, appears to be more resistant to change, especially among high frequency cocaine injectors. These findings suggest that HIV prevention strategies may be more effective and more efficient if drug users are triaged into an intervention appropriate to their level of needle risk. Williams, M., McCoy, V., Bowen, A., Saunders, L., Freeman, R., and Chen, D. An Evaluation of a Brief HIV Risk Reduction Intervention Using Empirically Derived Drug Use and Sexual Risk Indices. AIDS and Behavior, 5(1), pp. 31-43, 2001.

HIV Risk in Men who Abuse their Spouses

This study examines the relationship between perpetrating intimate partner violence and HIV risk behavior among a sample of men in methadone maintenance treatment programs (MMTPs). Data were collected on 273 sexually active men, who were recruited from four inner-city MMTP clinics. More than a third of the sample reported perpetrating intimate physical abuse and 15% reported severe physical abuse in the past 12 months. Results from multiple logistic regression analyses indicate that after adjusting for demographic, poverty, and drug-use factors, men who abused an intimate partner were almost 4 times more likely to have more than one intimate partner, almost 3 times more likely to have unprotected anal sex, and 2.6 times more likely to have sex with a drug-injecting sexual partner than their counterparts. This study showed that men who perpetrated partner violence were at higher risk for HIV transmission. HIV prevention interventions need to consider the complex relationship between partner violence and HIV risk. El-Bassel, N., Fontdevila, J., Gilbert, L., Voisin, D., Richman, B.L., and Pitchell, P. J Subst Abuse, 13(1-2), pp. 29-43, 2001.

Additional Cost of Enhanced Prevention Intervention is Small, While Benefit is Large

An important objective of the NIDA Cooperative Agreement (CA) for AIDS Community-Based Outreach/Intervention Research Program was to develop and evaluate innovative interventions to reduce drug and sexual risk-taking behaviors. Findings from the multi-site CA suggest that NIDA's brief standard intervention has a positive effect in reducing HIV risk behaviors. Researchers evaluated the costs, effectiveness, and cost-effectiveness of outreach-based HIV prevention interventions for out-of-treatment drug users at risk for HIV in North Carolina, as part of the NIDA CA. Participants in the study were given the 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 using simple means analysis and multiple regression models; the incremental effectiveness of the enhanced intervention was also estimated relative to the standard intervention; and cost-effectiveness ratios were computed for several drug use outcomes and compared to a general estimate of the benefit of reducing drug use. Findings indicate that the estimated cost of implementing the standard intervention is $187.52 per person, and the additional cost of the enhanced intervention is $124.17 per person. Cost-effectiveness ratios range from $35.68 to $139.52 per reduced day of drug use, which is 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 strategy should be considered an important additional component for out-of-treatment drug users. Zarkin, G., Lindrooth, R., 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 Services Research, 36(2), pp. 335-355, 2001.

Longitudinal Predictors of Depressive Symptoms Among Low Income IDUs

In this study, researchers assessed the effects of changes in physical health status and drug use, and prior social support on depressive symptoms in low income IDUs. Data are from 503 participants enrolled at baseline who remained at 1-year follow up (393 IDUs, or 79%); 37% were HIV+ and 36% female. Physical health was measured by HIV symptoms, AIDS, CD4 count and functional limitation. One third scored high on depressive symptoms at 1-year follow up, representing no statistically significant change from baseline (38%). In multiple logistic regression, after controlling for baseline depression scores (OR=6.11, $p<0.001$) and drug use (OR=1.20, $p=0.192$), baseline functional limitation (OR=3.28, $p<0.001$) and declining functioning (OR=3.60, $p<0.001$) were positively, and quitting drug use was negatively, associated with depressive symptoms at follow-up. Low social support at baseline (OR=0.58), $p<0.10$) was marginally predictive of depressive symptoms. Depressive symptoms did not differ by gender. For HIV-positive respondents, functional limitation was predictive of depressive symptoms, but HIV illness and drug use were not. Facilitating drug treatment and preventive medical care may aid in reducing depression in this population. For HIV-positive drug users, drug treatment prior to AIDS may help reduce depressive symptoms, with

potential implications for HIV service utilization and medical adherence. Knowlton, A., Latkin, C., Schroeder, J., Hoover, D., Ensminger, M., and Celentano, D. Longitudinal Predictors of Depressive Symptoms Among Low Income IDUs. AIDS Care, 13(5), pp. 549-559, 2001.

Study Examines Intention to Practice Safer Sex Among High-Risk Crack Smokers

Crack cocaine smokers are at particularly high risk for HIV due to heterosexual exposure with HIV-infected partners. In this study, researchers investigated predictors of intention to use condoms and related therapy processes among 586 heterosexual crack users in Washington, DC, Miami, and Collier County, Florida who reported having primary and casual sex partners. Participants responded to questionnaire items derived from the theory of reasoned action, the theory of planned behavior, and the trans-theoretical model of behavior change. Condom use beliefs and therapy processes used to initiate and maintain condom use were assessed. Outcome expectancies and normative beliefs were the strongest predictors of intention to use condoms with a primary partner. In turn, beliefs that condoms inhibit sexual romance and decrease sexual pleasure strongly predicted outcome expectancies. Therapy processes found to be associated with these constructs include: self-liberation, counter conditioning, and stimulus control/reinforcement. Results suggest that HIV risk reduction interventions using a group format and targeting condom beliefs related to sexual romance and pleasure will decrease negative outcome expectancies about condom use. Reinforcing attempts to use condoms with intimate partners should increase positive outcome expectancies and intention to initiate or maintain condoms with a primary partner. Bowen, A., Williams, M., McCoy, H., and McCoy, C. Crack Smokers' Intention to Use Condoms with Partners: Intention Development Using the Theory of Reasoned Action, Condom Beliefs, and Processes of Change. AIDS Care, 13(5), pp. 579-594, 2001.

Drug-Drug Interactions Between AZT and Opioid Dependence Pharmacotherapies

Dr. McCance-Katz and her colleagues (Albert Einstein College of Medicine, NY) had previously reported that methadone increased zidovudine (AZT) concentrations. Now they report that other opioid dependence pharmacotherapies such as LAAM, buprenorphine, or naltrexone have no significant effect on AZT levels. The investigators studied the pharmacokinetics of AZT in 69 patients (25 women, 44 men; 18-65 years of age) treated with LAAM (21 patients), buprenorphine (16 patients), naltrexone (15 patients), and controls (17 patients). They found no significant differences in AZT concentrations in patients treated with any of the medications. They conclude that, although methadone maintenance may result in AZT toxicity and possibly require dose adjustments, other opioid pharmacotherapies are not associated with AZT toxicity. McCance-Katz, E., Rainey, P.M., Friedland, G., Kosten, T.R., Jatlow, P. Effect of Opioid Dependence Pharmacotherapeutics on Zidovudine Disposition. Am. J. Addictions, 10(4), pp. 296-307, 2001.

Risk Factors for Skin and Soft Tissue Abscess Among Injection Drug Users: A Case Control Study

Murphy and his colleagues (UCSF) report that subcutaneous (sc) or intramuscular (im), instead of intravenous (iv), injection is a major risk factor for soft tissue abscess among IDUs. The investigators conducted a case control study where they enrolled 151 IDU cases with new diagnoses of abscess requiring incision and drainage, and 267 IDU controls without abscess or other bacterial infection during the previous year. They matched the controls to cases by age, sex, and race. Data were obtained from the medical record and a questionnaire, and antibodies to viruses such as HIV, HTLV-I and II subtypes were measured in blood samples. Results showed abscess diagnosis was associated with sc or im injection or "skin popping" (OR=6.13, 95% CI 3.51-10.70); use of dirty needles (OR=3.34, 95% CI 1.75-6.82); injection of "speedball" (OR=3.31, 95% CI 1.37-7.95), and drawing blood into the syringe prior to injection or "booting" in those who did not "skin pop" (OR=2.33, 95% CI 1.46-3.70). Cleaning the skin with alcohol prior to injection was protective (OR=0.48, 95% CI 0.32-0.74). Neither HIV nor HTLV-II seropositivity was significantly associated with abscess. It was concluded that sc or im injection was associated with abscess among IDUs, and that injection of "speedball" may predispose to abscess by inducing soft tissue ischemia. Murphy, E.L., Liu, H., Leung, P., Edlin, B.R., DeVita, D., Vittinghoff, E., and Ciccarone, D.H. Clinical Infectious Disease, 33(1), pp. 35-40, 2001.

How Injection Drug Users Coped with Testing HIV-Seropositive: Implications for Subsequent Health-Related Behaviors

Margolin and his colleagues (Yale) find that IVUs have coping problems after testing positive for HIV that result in poor health and risky behaviors. The team assessed a group of 94 HIV+ IDUs entering a methadone treatment program. The instrument (Coping Responses Inventory) asked them to describe their feelings and experiences when they first learned that they were positive for HIV. Results showed that avoidance of coping was highly correlated with high levels of recent HIV risk behaviors at entry into the treatment program. Other independent predictors of

continued risk behavior were poor health, lack of social support, and low levels of HIV/AIDS knowledge. The authors identify a strong need for interventions to help IDUs cope subsequent to testing HIV seropositive. Avants, S.K, Warburton, L.A., and Margolin, A. AIDS Education and Prevention, 13(3), pp, 207-218, 2001.

Opioid Modulation of HIV Infection

Kappa opioids have been observed to inhibit HIV growth in special cell cultures. The present study demonstrates that delta opioids are immunosuppressive in cultured human lymphocytes of HIV growth. Thus drugs of this type would appear to be an even more important adjunctive treatment for AIDS in humans. However, no delta ligand is presently available for studies in humans. 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 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 of the peripheral blood mononucleocytes (PBMC) population by 48 h. 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 the p24 Antigen of HIV. SNC-80 maximally suppressed both lymphocytotropic and monocytotropic strains of HIV. 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 Immunology, 167, pp. 1097-1102, 2001.

Naltrexone Potentiates anti-HIV-1 Activity of Antiretroviral Drugs in CD4(+) Lymphocyte Cultures

Another study focused on the amplification of anti-HIV drug treatment. The addition of naltrexone in vitro to lymphocytes enhanced the inhibition of HIV growth in the presence of either of the major types of anti-viral drugs now in therapy. Clinical studies are envisioned by this group to see if the in vitro effects observed here relate to treatment of this disease in humans. CD4(+) T lymphocytes are the primary cell target for human immunodeficiency virus-1 (HIV-1), and these cells are known to express opioid receptors. Due to the need for new treatment approaches to HIV-1 infection, we sought to determine whether the non-selective opioid receptor antagonist naltrexone would affect HIV-1 expression in CD4(+) lymphocyte cultures and whether naltrexone would alter the antiviral properties of zidovudine (AZT) or indinavir. Activated CD4(+) lymphocytes were infected with a monocytotropic or T-cell tropic HIV-1 isolate, and p24 antigen levels were measured in supernatants of drug-treated or untreated (control) cultures. While naltrexone alone did not affect HIV-1 expression, naltrexone increased the antiviral activity of AZT and indinavir 2-3-fold. Similar findings with a Kappa-opioid receptor (KOR) selective antagonist supported the possible involvement of KOR in naltrexone's potentiation of the antiretroviral drugs. The results of this in vitro study suggest that treatment of alcohol or opiate dependent HIV-1-infected patients with naltrexone is unlikely to interfere with the activity of antiretroviral drugs. Also, based upon naltrexone's safety profile and its synergistic activity in vitro, these findings suggest clinical trials should be considered of naltrexone as an adjunctive therapy of HIV-1 infection. Gekker, G., Lokensgard, J.R., and Peterson, P.K. Naltrexone Potentiates anti-HIV-1 Activity of Antiretroviral Drugs in CD4(+) Lymphocyte Cultures. Drug Alcohol Depend, 64, pp. 457-463, 2001.

HIV Infection Requires Integration of the Virus into the Host Genome or DNA

This integration takes place by DNA strand breaks and subsequent repair of these breaks. One enzyme activated by DNA strand breaks and involved in the repair process is Poly (ADP-ribose) polymerase-1 (PARP-1), an enzyme that is expressed mostly in the nucleus. It has been hypothesized that PARP-1 mediates the integration of HIV into the host genome. However, studies using benzamide derivatives and benzopyrone inhibitors, weak inhibitors of PARP, have not been conclusive in showing reduction of viral infection. To more definitively demonstrate the role of PARP-1 in HIV integration and infection, Dr. Snyder and his colleague at Johns Hopkins University Medical School attempted to infect mouse fibroblast derived from a genetically engineered mouse that is deficient in PARP-1. In the March 13, 2001 issue of the Proceedings of the National Academy Science, Dr. Snyder reports a profound reduction of HIV infection in mouse fibroblasts lacking PARP-1 and results from an inhibition of viral integration. These results suggest that potent and selective inhibitors of PARP-1 may prove useful in the treatment of HIV infection. In animal models, these inhibitors have already been shown to be effective in treating stroke, myocardial infarction, diabetes, sepsis, and

inflammation. Ha, H.C., Juluri, K., Zhou, Y., Leung, S., Hermankova, M. and Snyder, S.H. Poly(ADP-ribose) polymerase-1 (PARP-1) is Required for Efficient HIV-1 Integration. Proceedings of the National Academy of Sciences, 98, pp. 3364-3368, 2001.

HIV Transmission and the Cost Effectiveness of Methadone Maintenance

This project determined the cost effectiveness of expanding methadone maintenance treatment for heroin addiction, particularly its effect on the HIV epidemic. The investigators developed an epidemic model to study the effects of increased methadone maintenance capacity on health-care costs and survival, measured as quality-adjusted life years (QALYs). The investigators considered communities with HIV prevalence among injection drug users (IDUs) of 5% and 40%. Results included: additional methadone maintenance capacity costs $8,200 per QALY gained in the high-prevalence community and $10,900 per QALY gained in the low-prevalence community. Individuals who do not inject drugs gain more than half of the benefits. Even if the benefits realized by treated and untreated IDUs are ignored, methadone maintenance expansion costs between $14,100 and $15,200 per QALY gained. Additional capacity remains cost effective even if it is twice as expensive and half as effective as current methadone maintenance slots. Importantly, expansion of methadone maintenance is cost effective based on commonly accepted criteria for medical interventions. Barriers to methadone maintenance deny IDUs access to a cost-effective intervention that generates significant health benefits for the general population. Zaric, G., Barnett, P., and Brandeau, M. American Journal of Public Health, 90, pp. 1100-1111, 2000.

The Cost Effectiveness of Buprenorphine Maintenance Therapy for Opiate Addiction in the United States

The aims of this project were to determine the cost-effectiveness of buprenorphine maintenance therapy (BMT) for opiate addiction in the United States, particularly its effect on the HIV epidemic. The researchers developed a model to capture the effects of adding buprenorphine maintenance to the current opiate dependence treatment system. The evaluated incremental costs, including all health care costs, and incremental effectiveness, measured as quality-adjusted life years (QALYs) of survival. The investigators considered communities with HIV prevalence among injection drug users of 5% and 40%. Because no price has been set in the United States for a dose of buprenorphine, the investigators considered three prices per dose: $5, $15, and $30. Authors found that if buprenorphine increases the number of individuals in maintenance treatment by 10%, but does not affect the number of individuals receiving methadone maintenance, the cost-effectiveness ratios for BMT are less than $45,000 per QALY gained for all prices, in both the low-prevalence and high-prevalence communities. If the same number of individuals enter buprenorphine maintenance (10% of the number currently in methadone), but half are injection drug users newly entering maintenance, and half are individuals who switched from methadone to buprenorphine, the cost-effectiveness ratios in both communities are less than $45,000 per QALY gained for the $5 and $15 prices, and greater than $65,000 per QALY gained for the $30 price. The authors conclude that at a price of $5 or less per dose, buprenorphine maintenance is cost-effective under all scenarios considered. At $15 per dose, it is cost-effective if its adoption does not lead to a net decline in methadone use, or if a medium to high value is assigned to the years of life lived by injection drug users and those in maintenance therapy. At $30 per dose, buprenorphine will be cost-effective only under the most optimistic modeling assumptions. Barnett, P., Zaric, G., and Brandeau, M. Addiction, 96, pp. 1267-1278, 2001.

Prenatal Cocaine Exposure and Intrauterine Growth

Researchers at the University of Miami, with collaborators at Johns Hopkins University, have recently reported findings of a specific cocaine-related deficit in fetal growth and gestational age. The analyses in this report involved a high degree of covariate control (e.g., prenatal substance exposures other than cocaine, maternal age, maternal education), using structural equations and multiple regression models. The findings support previously reported research regarding influences of prenatal cocaine on fetal growth and gestational age, and call into question the notion that head circumference is disproportionately affected compared to overall somatic growth. Head circumference was affected, but not disproportionately. There was also evidence that some of the cocaine effects on fetal growth were direct and some were indirect, mediated by a cocaine influence on gestational age. The study sample was drawn from the Miami Prenatal Cocaine Study, which involved 476 full-term infants born to inner-city, African-American women. Bandstra, E.S., Morrow, C.E., Anthony, J.C., et al. Intrauterine Growth of Full-Term Infants: Impact of Prenatal Cocaine Exposure. Pediatrics, 108, pp. 1309-1319, 2001.

Neuropsychological Performance in Long-term Cannabis Users

Pope and his colleagues (Harvard/McLean Hospital) have found that in long-term heavy cannabis using adults, some cognitive deficits are detectable on days 0, 1, 7, and not on days 28, after cannabis use is discontinued. The team

recruited individuals aged 30 to 55 in 3 groups: 63 current heavy users who had smoked cannabis at least 5000 times in their lives and who were smoking daily at study entry; 45 former heavy smokers who had also smoked at least 5000 times but fewer than 12 times in the last 3 months; and 72 control subjects who had smoked no more than 50 times in their lives. Subjects underwent a 28-day washout from cannabis use, monitored by observed urine toxicology. On days 0, 1, 7, and 28, the subjects were administered a neuropsychological test battery to assess general intellectual function, abstraction ability, sustained attention, verbal fluency, and ability to learn and recall new verbal and visuospatial information. Test results were analyzed by repeated-measures regression analysis, adjusting for potentially confounding variables. Results showed that at days 0, 1, and 7, current heavy users scored significantly below control subjects on recall of word lists, and this deficit was associated with users' urinary 11-nor-9-carboxy-THC (THC metabolite) concentrations at study entry. By day 28, there were virtually no deficits that could be associated with cumulative lifetime cannabis use. The authors concluded that cognitive deficits were reversible and related to recent cannabis use rather than irreversible and related to cumulative lifetime use. Pope, H., Gruber, A.J., Hudson, J.I., Huestes, M.A., and Yurgelum-Todd, D. Arch. Gen. Psychiatry, 58, pp. 909-915, 2001.

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Director's Report to the National Advisory Council on Drug Abuse
February, 2002

Research Findings

Epidemiology, Etiology and Prevention Research

Effects of Aggregating High Risk Youth

This paper focuses on three-year outcomes associated with a preventive intervention trial in which high-risk youth were aggregated into cognitive-behavioral groups. Participants were 158 at-risk youth between the ages of 11 and 14. The participating youth and their teachers were interviewed each year over a three-year period following the intervention. Analyses of covariance and latent growth modeling revealed that the intervention contributed to three-year escalations in self-reported smoking and teacher-reported delinquency. Interactions between participants' characteristics (i.e., initial status, age, and gender) and intervention were also tested. A statistically reliable interaction was found, suggesting that those with initially low levels of delinquency were especially affected by the peer intervention group. Poulin, F., Dishion, T. J., and Burraston, B. 3-year Iatrogenic Effects Associated with Aggregating High-risk Adolescents in Preventive Interventions. Applied Developmental Science, 5(4), pp 214-224, 2001.

An Integrated Components Preventive Intervention for Aggressive Elementary School Children: The Early Risers Program

The Early Risers prevention program aims to alter the developmental trajectory of children with early onset aggressive behavior that puts them at significant risk of drug use in adolescence. The program features 4 CORE components: (a) an annual 6-week summer school program, (b) a teacher consultation and student mentoring program, (c) child social skills groups, and (d) parent education and skills-training groups, all delivered in tandem with a FLEX family support program individually tailored to address the unique needs of families. At baseline, the mean age of the sample was 6.6 years. Following 2 years of intervention, program children showed significant improvement relative to controls in academic achievement and school behaviors. Change on behavioral self-regulation was moderated by level of child aggression, with intervention effects found for only the most severely aggressive children. Parents with high program attendance rates showed improvement in discipline methods. August, G.J., Realmuto, G.M., Hektner, J.M., and Bloomquist, M.L. An Integrated Components Preventive Intervention for Aggressive Elementary School Children: The Early Risers Program. Journal of Consulting and Clinical Psychology, 69 (4), pp. 614-626, 2001.

Project Towards No Drug Abuse: Generalizability to a General High School Sample

This study examined the generalizability of a successful classroom-based prevention program developed for youth at alternative high schools (high risk) to youth at general high schools. A replication of a previously tested prevention program in a general high school population was conducted with 1-year follow-up data. Classrooms within each of three schools (n =1208) were randomly assigned to two conditions, classroom education or standard care control. Statistically significant effects on alcohol and illicit drug use were achieved in this population through a 1-year period following the program, although effects were not achieved on cigarette smoking and marijuana use. These results suggest that this program (Project Towards No Drug Abuse) has applicability to a wide range of older teens. Preventive Medicine, 32(6), pp. 514-520, 2001.

Social Skills and Problem-solving Training for Children with Early-onset Conduct Problems

Families of 99 children with early-onset conduct problems were randomly assigned to a child training treatment group utilizing the Incredible Years Dinosaur Social Skills and Problem Solving Curriculum or a waiting-list control group. Children participating in the intervention had significantly fewer externalizing problems at home, less aggression at school, more prosocial behavior with peers, and more positive conflict management strategies than control children. The intervention group children also showed clinically significant improvements on reports and independent observations of aggressive and non-compliant behavior. The differential treatment response was evaluated according to child comorbidity with attention deficit hyperactivity disorder, parenting discipline practices, and family risk factors. The only risk factor related to failure to make improvements in child conduct problems after treatment was negative parenting. Most significant post-treatment changes were maintained at the 1-year follow-up. Webster-Stratton, C., Reid, J., and Hammond, M. Social Skills and Problem-solving Training for Children with Early-onset Conduct Problems: Who Benefits? Journal of Child Psychology and Psychiatry, 42(7), pp. 943-952, 2001.

Session-specific Effects of a Universal Parent-Training Intervention

Preparing for the Drug Free years is a parent training intervention designed to prevent adolescent substance abuse and other problem behaviors. Two hundred nine rural families were randomly assigned to receive the intervention or the wait-list control condition. Analysis of covariance comparing adjusted posttest scores revealed that parents in the intervention condition reported significant improvements in parenting behaviors targeted by specific intervention sessions when compared with controls. Effects were most pronounced among mothers. No significant effects were found for nontargeted 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, D.J., Haggerty, K., 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.

Modeling Factors Influencing Enrollment in Family-Focused Prevention Intervention Research

This study tests an extension of a previously supported model of family contexts and health belief predictors of parental inclination to enroll in preventive interventions. Model testing was conducted with a sample of 635 parents of 6th graders who completed a prospective participation factors survey and were recruited for an intervention research project six months later. The model fit was strong and all but one of the primary hypothesized effects were supported. Both stated inclination to enroll in an intervention and in the research project had significant positive effects on actual project enrollment occurring 6 months later. Perceived intervention benefits and barriers had significant effects on both types of stated inclination to enroll. Examination of modification indices for the model suggested an additional path linking educational attainment with actual enrollment. Spoth, R., Redmond, C., and Shin, C. Modeling Factors Influencing Enrollment in Family-Focused Preventive Intervention Research. Prevention Science, 1(4), pp. 213-225, 2000.

Long-term follow-up of Brief Family Interventions for General Populations

This study examines the long-term substance use outcomes of two brief interventions designed for general population families of young adolescents. Thirty-three public schools were randomly assigned to three conditions: the 5-session Preparing for the Drug Free Years Program, the 7-session Iowa Strengthening Families Program, and a minimal contact control condition. Assessments included multiple measures of initiation and current use of alcohol, tobacco, and marijuana. The pretest involved 667 6th graders and their families. Follow-up data were collected in the 10th grade. Significant intervention-control differences in initiation and current use were found for both interventions. It is concluded that brief family skills-training interventions designed for general populations have the potential to reduce adolescent substance use. Spoth, R.L., Redmond, C., Shin, C. Randomized Trial of Brief Family Interventions for General Populations: Adolescent Substance Use Outcomes four Years Following Baseline. Journal of Consulting and Clinical Psychology, 69(4), pp. 627-642, 2001.

Preadolescent Predictors of Substance Initiation

This study examines potentially modifiable family and peer factors known to be predictors of early substance initiation. A theoretically derived model of substance initiation was tested using structural equation modeling. Results indicate that both family and peer factors have an impact on early substance initiation when children in this sample were 11 and 12 years old. The model explained 69% of the variance in substance initiation. Prosocial family processes (rules, monitoring, and attachment) had a significant impact on child peer association, decreasing involvement with antisocial peers. These prosocial family processes had a significant negative effect on substance

initiation even while modeling the influence of antisocial peers. Oxford, M.L., Harachi, T.W., Catalano, R.F., Abbott, R.D. Preadolescent Predictors of Substance Initiation: A Test of Both the Direct and Mediated Effects of Family Social Control Factors on Deviant Peer Associations and Substance Initiation. American Journal of Drug and Alcohol Abuse, 27(4), pp. 599-616, 2001.

Social Competence and Substance Use Among Rural Youth

Social competence is a construct that has been shown to play a key role in youth development and there has been growth in the study of skills training in social and interpersonal competence in order to prevent drug use, antisocial, and aggressive behavior. This study of 1568 rural junior high school youth was conducted to uncover the mechanisms by which social competence may be associated with substance use during early adolescence. Structural equation modeling indicated that social competence had a direct, protective association with substance use in that those youth who were more socially confident, assertive, and had better communication skills reported less smoking and drinking. Furthermore, the relationship between social competence and substance use was fully mediated by social benefit expectancies of use. Thus, poorly competent youth use cigarettes and alcohol because they perceive that there are important social benefits to these behaviors. Griffin, K.W., Epstein, J.A., Botvin, G.J., and Spoth, R.L. Social Competence and Substance Use Among Rural Youth: Mediating Role of Social Benefit Expectancies of Use. Journal of Youth and Adolescence, 30(4), pp. 485-498, 2001.

Protective Role of Personal Competence Skills in Adolescent Substance Use: Psychological Well-being as a Mediating Factor

Adolescents who use a variety of cognitive and behavioral self-management strategies have been shown to report reduced rates of early-stage substance use, but little is known about how these personal competence skills may be protective. In a series of structural equation models, this study examined the association between competence skills and substance use over a 3-year period among 849 suburban junior high school students, and whether psychological distress, well-being, or both mediated this relation. Findings indicated that well-being fully mediated the relation between early competence and later substance use, but distress did not. Youth with good competence skills reported greater subsequent well-being, which in turn predicted less later substance use. Findings suggest that competence skills protect youth by enhancing well-being and that prevention programs should aim to enhance competence in order to promote resilience. Griffin, K.W., Scheier, L.M., Botvin, G.J., and Diaz, T. Protective Role of Personal Competence Skills in Adolescent Substance Use: Psychological Well-being as a Mediating Factor. Psychology of Addictive Behaviors 15(3), pp. 194-203, 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.

Marijuana Abstinence Effects in Marijuana Smokers Maintained in their Home Environment

Budney and his colleagues assessed withdrawal effects in a group of 12 daily marijuana smokers on 16 consecutive days during which they smoked marijuana as usual (days 1-5), abstained from smoking marijuana (days 6-8), returned to smoking (days 9-13) and again abstained on days (14-16). The authors reported that the study validated several specific effects of marijuana abstinence in heavy marijuana smokers, i.e., irritability, aggression, decreased

appetite, restlessness, sleep difficulty, depression, craving for marijuana and general discomfort and showed that they were reliable across at least one abstinence period and clinically significant. These withdrawal effects appear similar in type and magnitude to those observed in studies of nicotine withdrawal. Budney, A., Hughes, J.R., Moore, B.A., and Novy, P.L. Arch. Gen. Psychiatry, 58, pp. 917-924, 2001.

Drug Use and Lifestyle Among College Undergraduates: A 30-year Longitudinal Study

In order to examine trends in the prevalence of substance use and its relationship to attributes of lifestyle among college students over a 30-year period, Pope and his colleagues distributed anonymous questionnaires to seniors at a large New England college in 1999, using methodology identical to that they had used in 1969, 1978, and 1989. In 1999, the sample size was: 424 'non-users', and 369 'users'. Most forms of drug use rose to peak in 1978, then fell over the next 21 years with the exception of MDMA. These observations were similar to those from the Monitoring the Future Study. For example, according to the MTF survey, the lifetime prevalence of marijuana fell from a peak of 65% in 1980 to 49.9% in 1998, similar to the authors' findings of 76% in 1978 to 46% in 1999. Cocaine use fell from 22% in 1978 to 8% in 1999 (MTF), similar to their findings of 29.8% to 6.9%. MDMA use (which has now become the second most frequently tried illegal drug after marijuana) rose from 3.8% in 1989, 4.6% in 1997 to 6.8% in 1998, similar to authors' numbers of 4.1% in 1989 and 10.1% in 1999. On several variables, college substance users differed more sharply from non-users in 1999 than in previous decades. In earlier decades, drug users differed from non-users only on visits to a psychiatrist and level of heterosexual activity. In 1999, the users and non-users differed in terms of homosexual activity and time spent in extracurricular activities. The authors conclude that although limited to a single institution, the findings suggest that college drug use has been declining, and that users have increasingly diverged from non-users in their values and lifestyles. Pope, H., Ionescu-Pioggia, M., and Pope, K.W. Drug Use and Lifestyle Among College Undergraduates: A 30-year Longitudinal Study, Am J. Psychiatry, 158, pp. 1519-1521, 2001.

Ethnic Labels and Ethnic Identity Predict Drug Use

This article examines the value of ethnic labels and ethnic identity in predicting self-reported drug use and exposure to drugs of an ethnically diverse group of seventh grade students from a southwestern US city. Four hundred eight Mexican American (52%), non-Hispanic white (23%), mixed ethnicity (14%), and African American (12%) students completed a questionnaire where they reported frequency of cigarette, alcohol, marijuana, and hard drug use in the past month. Students also reported on lifetime use of specific drugs and age of initial use. Ethnic minority students with stronger ethnic pride reported less frequent drug use and exposure than those with a weaker sense of ethnic pride while ethnic pride among white students is associated with increased risk. Ethnic minority students who viewed their behavior, speech, and appearance as consistent with their ethnic group reported more drug use and exposure, while their white counterparts reported less. This study demonstrates that ethnic labels are superior explanatory constructs when used in combination with ethnic identity measures. Marsiglia, F.F., Kulis, S., and Hecht, M.L. Ethnic Labels and Ethnic Identity as Predictors of Drug Use among Middle School Students in the Southwest. Journal of Research on Adolescence, 11(1), pp. 21-48, 2001.

School-Based Support Groups for Adolescents with an Addicted Parent: Using Principles of Solution Focused Therapy

In every classroom, there are approximately 5 children on average with chemically dependent parents. Few of these children receive supportive services, despite the fact that they attend school less often, are often late for school, and have a higher incidence of learning disabilities. To address this, many school districts offer school-based support groups (SBSG). Consistent with the principles of solution-focused therapy, the SBSG emphasizes the strengths and resiliency of these youth and helps them develop problem-solving strategies and find solutions. This study was a qualitative evaluation of SBSG for adolescents with an addicted parent. Gance-Cleveland, B.L., and Rothman, A. School-Based Support Groups for Adolescents with an Addicted Parent: Using Principles of Solution Focused Therapy. The Drug and Alcohol Professional, 1(1), pp. 17-29, 2001.

Self-Reported High-Risk Locations of Drug Use Among Drug Offenders

The present study used a detailed, multiple-choice, self-report questionnaire to collect and analyze data on home, work, and other public locations where drug offenders report using drugs. In addition, these settings were examined as a function of gender, ethnicity, type of drug used, and drug abuse/dependence status. The participants for the present study were 462 individuals attending drug diversion programs in southern California. The single most frequently reported location of use was the subjects' living room with a small group of friends. However, heavier users used different drugs across a greater variety of locations. Not surprisingly, drugs were used least at work (though a surprising 47% had used at work). Popular situations of drug use among drug offenders are similar to that

of high-risk youth. Sussman, S., Ames, S.L., Dent, C.W., and Stacy, A.W. Self-Reported High-Risk Locations of Drug Use Among Drug Offenders. American Journal of Drug and Alcohol Abuse, 27 (2), pp. 281-299, 2001.

Workplace Substance Abuse Prevention: Comparison of Two Approaches

Employees fail to seek help for alcohol or drug (AOD) abuse because of unhealthy work climates, stigma, and distrust in Employee Assistance Programs (EAPs). To address such problems, the authors randomly assigned groups of municipal employees (N = 260) to 2 types of training: a 4-hr informational review of EAPs and policy and an 8-hr training that embedded messages about AOD reduction in the context of team building and stress management. Pre- and post-training and 6-month follow-up surveys assessed change. Group privacy regulation, EAP trust, help seeking, and peer encouragement increased for team training. Stigma of substance users decreased for information training. EAP/policy knowledge increased for both groups. A control group showed little change. Help seeking and peer encouragement also predicted EAP utilization. Integrating both team and informational training may be the most effective for improving help seeking and EAP utilization. Bennett, J.B., and Lehman, W.E.K. Workplace Substance Abuse Prevention and Help Seeking: Comparing Team-oriented and Informational Training. Journal of Occupational Health Psychology, 6(3), pp. 243-254, 2001.

Multilevel Modeling of Individual and Group Level Mediated Effects

This article combines procedures for single-level mediational analysis with multilevel modeling techniques in order to appropriately test mediational effects in clustered data. A simulation study compared the performance of these multilevel mediational models with that of single-level mediational models in clustered data with individual- or group-level initial independent variables, individual- or group-level mediators, and individual level outcomes. The standard errors of mediated effects from the multilevel solution were generally accurate, while those from the single-level procedure were downwardly biased, often by 20% or more. The multilevel advantage was greatest in those situations involving group-level variables, larger group sizes, and higher intraclass correlations in mediator and outcome variables. Multilevel mediational modeling methods were also applied to data from a preventive intervention designed to reduce intentions to use steroids among players on high school football teams. This example illustrates differences between single-level and multilevel mediational modeling in real-world clustered data and shows how the multilevel techniques may lead to more accurate results. Krull, J.L. and MacKinnon, D.P. Multilevel Modeling of Individual and Group Level Mediated Effects. Multivariate Behavioral Research, 36(2), pp. 249-277, 2001.

A Further Look at the Prognostic Power of Young Children's Reports of Depressed Mood and Feelings

A primary objective of this study was to determine the validity of first graders' self-reports of depressed mood and feelings. To that end, the prognostic power of first grade self-reports of depressed mood and feelings was examined with respect to later psychopathology and adaptive functioning in a population of urban school children (N=496). First grade self-reports of depressed mood predicted later child academic functioning, the need for and use of mental health services, suicidal ideation, and a diagnosis of major depressive disorder by age 14. The prognostic power of these early self-reports suggests that children as young as 5 or 6 years of age are capable of providing valid reports of depressed mood and feelings. Ialongo, N.S., Edelsohn, G., and Kellam, S.G. A Further Look at the Prognostic Power of Young Children's Reports of Depressed Mood and Feelings. Child Development, 72(3), pp. 736-747, 2001.

Reported Motivations for Drug and Alcohol Use

Norm Focus theory distinguishes between injunctive, norms (what people ought to do), descriptive norms (what people actually do) and personal norms (internalized values & expectations for one's own behavior). Based on Norm Focus Theory, this study describes alcohol and other drug use norms of adolescents and their perceived motivation for their behavioral norms. Structured interviews were conducted with sixty-seven African American and European American adolescents from an urban area (mean age 13). Drugs were viewed as available and commonly used. European Americans only, and mostly males, used justifications for their alcohol and marijuana use. Motivations to use drugs included social needs and enjoyment, however European American adolescents only mentioned using drugs for curiosity, boredom, problem solving, and protecting or furthering one's image. Reasons to avoid drugs offered by European American adolescents included motivations related to self-concept while African American adolescents described physical and psychosocial threats. Barnett, J.M. and Miller, M. Adolescents' Reported Motivations to Use or Not to Use Alcohol or Other Drugs. The Social Studies, 92, pp. 209-212, 2001.

Children of Substance Abusers are at Risk for Psychiatric Disorders

Investigators compared psychiatric disorders and problem behavior scores in pre-adolescent children of fathers with

alcohol or other drug dependence and ASP (SD+/ASP+), children whose fathers had substance dependence without ASP (SD+/ASP-), and children whose fathers were without either disorder (SD-/ASP-). SD+/ASP+ children showed elevated rates of major depression, conduct disorder, attention deficit hyperactivity disorder, oppositional defiant disorder, and separation anxiety disorder when compared to SD+/ASP- and SD-/ASP- children. SD+/ASP+ children had higher internalizing and externalizing problem behavior scores than the other two groups of children. The results suggest that SD+/ASP+ children are at significant risk for internalizing and externalizing psychopathology. Moss, H.B., Baron, D.A., Hardie, T.L., and Vanyukov, M.M. Am J Addict, 10(3), pp. 269-78, 2001.

Child Psychopathology Predicts Heavier Drug Use in Adolescence

The authors examined early psychopathology as a predictor of trajectories of drug use from ages 13-18 years. Six years of annual data were analyzed for 506 boys using a mixed effects polynomial growth curve model. They tested whether distinct measures of psychopathology and behavioral problems (i.e., attention-deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder, depression, and violence) assessed in early adolescence could prospectively predict level and change in alcohol and marijuana use. Higher levels of all of the types of psychopathology predicted higher levels of alcohol use, and higher levels of attention-deficit/hyperactivity disorder, conduct disorder, and violence predicted higher levels of marijuana use. Only conduct disorder predicted linear growth in alcohol use, and none of the measures predicted growth in marijuana use. The results suggest that drug use prevention programs should target youths with early symptoms of psychopathology. White, H.R., Xie, M., Thompson, W., Loeber, R., Stouthamer-Loeber, M. Psychology of Addictive Behaviors, 15(3), pp. 210-218, 2001.

The Adult Antisocial Syndrome with and without Antecedent Conduct Disorder: Comparisons from an Adoption Study

DSM antisocial personality disorder (ASPD) requires a retrospective diagnosis of conduct disorder-historical behavior not present in everyone with adult ASPD criteria. Using adoption study data, we examined the impact of this requirement on biological and environmental risk associations. We defined three subgroups: DSM-III ASPD (n = 30), adult antisocials without conduct disorder (n = 25), and controls (n = 142). Having an antisocial biological parent was a specific risk factor for ASPD. In contrast, fetal alcohol exposure, male gender, and adverse environment were associated with the adult antisocial syndrome, regardless of conduct disorder history. The two antisocial groups were similar with respect to sociopathy scales, co-occurring diagnoses, and the incidence of most individual symptoms. However, the phenotypic expression of the biological-possibly genetic-risk for ASPD appears to be manifest before adulthood. Despite this, we could not detect clinically important differences between the two sociopathic groups. The conduct disorder requirement therefore may be more relevant to etiological than clinical understanding of adult antisocial behavior. Langbehn, D.R., and Cadoret, R.J. Comprehensive Psychiatry, 42(4), pp. 272-282, 2001.

Drug use in Vietnam Associated with Premature Death

Large numbers of young men were exposed to high-quality opiates for a relatively short time period during military service in Vietnam. This study examined the relationships of opiate and other drug abuse before, during, and shortly after their time of service in Vietnam with the subsequent 25-year mortality among the cohort of 1227 US Army enlisted returnees and their matched civilians previously studied in 1972 and 1974. Results of path analytic models applied to selected significant measures showed that both in-Vietnam and post-Vietnam drug use factors were large and significant predictors of mortality, controlling for pre-service drug use, continuity to later drug use, and demographic and other behavioral measures. The magnitude of the direct effect of drug use on mortality was larger than those of the covariates that were entered in the path analyses, except age. Notwithstanding the high remission rate from opiate addiction, drug use in Vietnam had considerable predictive utility for premature death in this cohort. In light of the re-emergence of increased heroin use since the mid-1990s, the findings point to the importance of early intervention of drug use and comorbid problems for today's youth now initiating heroin use. Price, R.K., Risk, N.K., Murray, K.S., Virgo, K.S., and Spitznagel, E.L. Drug Alcohol Depend, 64(3), pp. 309-318, 2001.

Temperament Related to Early-onset Substance Use

We tested a theoretical model of early-onset substance (tobacco, alcohol, and marijuana) use. A sample of 1,810 public school students was surveyed in sixth grade (M age 11.5 years) and seventh grade. Temperament dimensions were related to substance use, and structural modeling analyses showed indirect effects through self-control constructs. Good self-control had a path to higher academic competence and had direct effects to less peer use and less adolescent substance use; poor self-control had a path to more adolescent life events and more deviant peer affiliations. Academic competence and life events had indirect effects to adolescent substance use, through peer affiliations. Findings from self-report data were corroborated by independent teacher ratings. Effects were also noted for family variables and demographic characteristics. Implications of epigenetic theory for prevention research are

discussed. Wills, T.A., Cleary, S., Filer, M., Shinar, O., Mariani, J., and Spera, K. Prev Sci, 2(3), pp. 145-163, 2001.

Patterns of Remission and Treatment Use among Vietnam Veterans

Using an epidemiologically obtained sample, investigators examined patterns of illicit drug use, abuse, and remission over a 25-year period and recent treatment use. The surviving members of the cohort (n = 841), previously surveyed in 1972 and 1974, comprised 3 subsamples of Vietnam War enlisted men and civilian controls. Retrospectively obtained year-to-year measures from the 1996-1997 survey included use and remission of sedatives, stimulants, marijuana, cocaine, and opiates, as well as substance abuse and psychiatric treatment use. Relatively stable patterns of frequent use in adulthood were found, with the mean duration from initiation to the last remission ranging from 9 to 14 years. A majority attempted to quit; however, most did not use traditional drug treatment in their last attempts. Fewer than 9% of the then-current drug users were treated in inpatient or outpatient settings at the time of data collection. Most drug abusers who had started using drugs by their early 20s appeared to gradually achieve remission. Spontaneous remission was the rule rather than the exception. Nonetheless, considerable unmet needs existed for those who had continued use into middle age. Price, R.K., Risk, N.K., and Spitznagel E.L. Am J Public Health, 91(7), pp. 1107-1113, 2001.

Peer Isolation and Drug Use among White non-Hispanic and Mexican American Adolescents

The social-emotional characteristics and drug-use patterns of adolescents who reported having no friends (i.e., isolates) were compared to those of adolescents in drug-using and non-drug-using peer groups. Adolescents who did not have drug-using peers reported the lowest drug use and those with drug-using peers had the highest drug use, with adolescents who were isolated falling in between. Isolated youth reported more shyness, greater feelings of alienation, and lower social acceptance than did those in the other groups. Isolated youth also reported more anger and depression than did youth with non-drug-using peers, but less anger and equivalent depression when compared to adolescents with drug-using peers. Results are discussed in terms of social-emotional characteristics of isolated youth and risk/protective factors. Tani, C.R., Chavez, E.L., and Deffenbacher, J.L. Adolescence, 36(141), pp. 127-139, 2001.

Gender Differences in the Relationship of Homelessness to Symptom Severity, Substance Abuse, and Neuroleptic Noncompliance in Schizophrenia

This study examined gender differences in the relationship of homelessness in schizophrenia to symptom severity, risk behaviors, and prognostic features. Four hundred subjects with schizophrenia were studied: 100 homeless men, 100 homeless women, 100 never homeless men, and 100 never homeless women. Assessments included derivation of five symptom factors by using the Positive and Negative Syndrome Scale (PANSS). Homelessness for the entire sample was associated with greater severity of positive, activation, and autistic preoccupation symptoms, younger age at first hospitalization, and substance abuse (SA). For men only, homelessness was associated with neuroleptic noncompliance (NN). When NN and SA were statistically controlled, symptom severity was not different between the homeless and never homeless. Women, independent of residential status, had more severe negative, activation, and autistic preoccupation symptoms that were not associated with prognostic features or risk behaviors. For both men and women, SA was associated with homelessness, but independent of residence, SA was less severe in women. Additionally, SA was less severe in homeless women than never homeless men. Thus, symptom severity in homeless individuals with schizophrenia appears as an interaction of symptom profiles and risk behaviors that are gender specific. Although cross-sectional analyses cannot distinguish cause from effect, these findings suggest gender-specific routes to homelessness among indigent urban adults with schizophrenia. Opler, L.A., White, L., Caton, C.L., Dominguez, B., Hirshfield, S., and Shrout, P.E., J Nerv Ment Dis, 189(7), pp. 449-456, 2001.

The Effects of a High-risk Environment on the Sexual Victimization of Homeless and Runaway Youth

Based on the structural-choice theory of victimization, the current study examines the effects of a high-risk environment on the sexual victimization of 311 homeless and runaway youth. Results from logistic regression revealed that survival sex, gender, and physical appearance were significantly associated with sexual victimization. Results from a series of interactions also revealed that the effects of deviant behaviors on sexual victimization varied by gender and age. Although males and females engaged in similar activities, young women were more likely to be victims of sexual assault. These findings suggest that engaging in high-risk behaviors predispose some people to greater risks but it is the combination of these behaviors with gender and/or age that determines who will become victimized. Tyler, K.A., Hoyt, D.R., Whitbeck, L.B., Cauce, A.M., Violence Vict.,16(4), pp. 441-455, 2001.

Social Learning Processes and Smoking Cessation

Maturing out and social learning are the two predominant hypotheses to explain cessation from various psychoactive drugs. This study examined the predictors of smoking cessation in a nonclinical 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. Addict Behav, 26(4), pp. 517-529, 2001.

Risk Factors for Adolescent Marijuana Use across Cultures and across Time

This integrated analysis of data from 3 different longitudinal studies was conducted to examine the early psychosocial predictors of later marijuana use among adolescents. The data used in the analysis were derived from (a) a sample of 739 predominantly White adolescents representative of the northeastern United States, (b) a sample of 1,190 minority adolescents from the East Harlem section of New York City, and (c) a sample of 1,374 Colombian adolescents from two cities in Colombia, South America. In 2 of the samples, participants were interviewed in their homes, and in the 3rd study, participants were assessed in school. The predictors included a number of variables from (a) the personality domain, reflecting the adolescents' conventionality and intrapsychic functioning; (b) the family domain, representing the parent-child mutual attachment relationship and parental substance use; (c) the peer domain, reflecting the peer group's delinquency and substance use; and (d) the adolescents' own use of legal drugs. The dependent variable was adolescent marijuana use. The results of the analysis demonstrated remarkable consistency in the risk and protective factors for later marijuana use across the 3 samples, attesting to the robust nature of these predictors and their generalizability across gender, time, location, and ethnic/cultural background. These findings have important implications for designing intervention programs. Programs aimed at preventing adolescent marijuana use can be designed to incorporate universal features and still incorporate specific components that address the unique needs of adolescents from different groups. Brook, J.S., Brook, D.W., Arencibia-reles, O., Richter, L., and Whiteman, M. J Genet Psychol, 162(3), pp. 357-374, 2001.

Dramatic-erratic Personality Disorder Symptoms: I. Continuity from Early Adolescence into Adulthood

This longitudinal study examined dramatic-erratic personality disorder symptoms (histrionic, borderline, and narcissistic symptoms) in a community sample of 407 adolescents to assess whether this diagnostic construct is meaningful in young people. Based on latent variable models and dimensional symptom scales, these so-called Cluster B symptoms were highly stable across an eight-year interval from early adolescence to early adulthood. Furthermore, when compared with internalizing and externalizing symptoms, dramatic-erratic symptoms were more stable over time than these well-established Axis I symptom clusters. Based on high correlations with co-occurring internalizing and externalizing symptoms, Cluster B symptoms clearly reflect emotional distress during adolescence. These analyses reinforce recent efforts to establish personality disorders as a clinically significant and valid diagnostic construct in young people. Crawford, T.N., Cohen, P., and Brook, J.S. J Personal Disord, 15(4), pp. 319-35, 2001.

Dramatic-erratic Personality Disorder Symptoms: II. Developmental Pathways from Early Adolescence to Adulthood

This study examined the relationship over time between Cluster B personality disorder symptoms (borderline, histrionic, and narcissistic symptoms) and comorbid internalizing and externalizing symptoms in a community sample of 407 adolescents. Cross-lagged longitudinal models tested (a) the hypothesis that Cluster B symptoms reflect primary disturbances that give rise to co-occurring internalizing and externalizing symptoms; and (b) the alternative hypothesis that these Axis I symptom clusters reflect primary problems that interfere with normal personality development. Internalizing and externalizing symptoms each predicted subsequent Cluster B symptoms in girls, although these effects occurred only at specific developmental stages. Cluster B symptoms in boys and girls at ages 10 to 14 years predicted externalizing symptoms two years later. Instead of clearly supporting one hypothesis over the other, longitudinal models suggested gender-specific developmental effects that were partially consistent with both hypotheses. Crawford, T.N., Cohen, P., and Brook, J.S. J Personal Disord, 15(4), pp. 36-50, 2001.

Monitoring the Future (MTF) Study

Results from the MTF study were released on December 19, 2001. The findings summarized below focus on statistically significant changes from 2000 to 2001. This year's sample consisted of a total of 44,346 8th, 10th, and 12th grade students in 424 schools. For more information, go to http://www.nida.nih.gov and to http://monitoringthefuture.org, the MTF website at the University of Michigan.

Major Findings

The major findings of the 2001 MTF study were (1) a decrease in cigarette use by 8th and 10th graders from 2000 to 2001; (2) a slowing of the rise in MDMA (ecstasy) use; and (3) a decline in heroin use among 10th and 12th graders. With a few isolated exceptions, use of most other drugs and alcohol remained stable, as did most beliefs and attitudes regarding drug use.

The decline in cigarette use in the 2001 survey continued a general pattern of declining rates seen between 1996 and 2000. Decreases were observed in the lifetime, past month, and daily smoking measures for 8th and 10th graders. Past month cigarette use declined from 14.6 percent to 12.2 percent among 8th graders, and from 23.9 percent to 21.3 percent among 10th graders. 12th graders' rates of smoking declined significantly from 1999 to 2000 and continued to decline, although not statistically significantly from 2000 to 2001. The increase in students' MDMA use reported in the last two MTF surveys slowed in 2001. While increases were observed in all three grades, they were generally not as steep as in the past two years and were not statistically significant. In addition, the perceived risk of harm from trying MDMA once or twice increased among seniors from 37.9 percent to 45.7 percent. Increases in perceived risk are often harbingers of future reductions in rates of use.

Lifetime and past year use of heroin decreased from 2000 to 2001 among 10th and 12th graders, and past month use decreased among 12th graders. For 10th graders, past year use decreased from 1.4 percent to 0.9 percent, and for 12th graders it was down from 1.5 percent to 0.9 percent. This decrease resulted largely from a decline in use of the drug without a needle (i.e., snorting or smoking it). For 12th graders, this year's decrease in heroin use reverses an increase between 1999 and 2000 that brought it to the highest level seen in the history of the survey; the rate for 2001, 0.9 percent for past year use, is the lowest since 1994.

Use of most other illicit drugs remained stable from 2000 to 2001. Illicit drug use rates are below their recent peaks in 1996 for 8th graders, but for 10th and 12th graders, they remain largely unchanged from recent peak levels seen in 1997. However, 27-year trend data for 12th graders indicate current levels of illicit drug use are well below their peaks in the late 1970s and early 1980s.

Other Findings

Illicit Drugs

- Marijuana use in the lifetime, past year, and past month remained statistically unchanged from 2000 to 2001 in each grade. Among 8th graders, marijuana use is below its recent peak in 1996. Rates of use among 10th and 12th graders have been stable since their recent high points in 1997. In 2001, past year rates of marijuana use were 15.4 percent of 8th graders, 32.7 percent for 10th graders, and 37.0 percent for 12th graders.
- Use of cocaine, including both powder and crack, decreased from 2000 to 2001 among 10th graders. Lifetime use of cocaine in any form among students in this grade declined from 6.9 percent to 5.7 percent; lifetime use of crack decreased from 3.7 percent to 3.1 percent; and past year use of cocaine powder declined from 3.8 percent to 3.0 percent.
- Inhalant use continued the gradual declining trend seen in recent years, though the decrease from 2000 to 2001 was statistically significant only in past year use among 12th graders, which went from 5.9 percent to 4.5 percent. In 2001, 9.1 percent of 8th graders, 6.6 percent of 10th graders, and 4.5 percent of 12th graders reported using inhalants in the past year.
- Hallucinogen use overall remained stable from 2000 to 2001 among 8th, 10th and 12th grade students. This stability follows declines between 1999 and 2000 in past month use of these drugs among 10th and 12th graders and in past year use among 12th graders.
- LSD, in an exception to the overall pattern of stability for hallucinogens, showed mixed changes from 2000 to 2001. Past month LSD use among 12th graders increased from 1.6 percent to 2.3 percent, but among 10th graders past year use declined from 5.1 percent to 4.1 percent.
- Steroid use in the lifetime, past year, and past month increased among seniors from 2000 to 2001. Past year use, for example, increased from 1.7 percent to 2.4 percent. Past year steroid use in 2001 stood at 1.6 percent for 8th graders and 2.1 percent for 10th graders.

Alcohol

- Between 2000 and 2001, alcohol use indicators remained mostly stable. Two comparisons were statistically significant: having been drunk in the past year decreased from 18.5 percent to 16.6 percent among 8th graders, and daily alcohol use in the past month increased from 2.9 percent to 3.6 percent among 12th graders.

Tobacco Products Other Than Cigarettes

- Use of bidis decreased among 8th and 10th graders. Past year use of these small, flavored cigarettes went from 3.9 percent to 2.7 percent among 8th graders and from 6.4 percent to 4.9 percent among 10th graders.
- Rates of smokeless tobacco use remained statistically unchanged between 2000 and 2001. In 2001, 4.0 percent of 8th graders, 6.9 percent of 10th graders, and 7.8 percent of 12th graders reported using smokeless tobacco in the past month.

Perceived Harm, Disapproval, and Perceived Availability

- Perceived harmfulness of trying inhalants increased from 41.2 percent to 45.6 percent among 8th and from 46.6 percent to 49.9 percent 10th graders.
- Perceived harmfulness of regularly smoking marijuana decreased from 74.8 percent to 72.2 percent among 8th graders.
- Perceived harmfulness of regularly taking LSD declined from 57.5 percent to 52.9 percent among 8th graders and from 72.0 percent to 68.8 percent among 10th graders.
- As noted above, perceived harmfulness of trying MDMA once or twice increased among seniors, the only grade asked this question.
- Seniors' disapproval of using heroin once or twice without a needle declined from 94.0 percent in 2000 to 91.7 percent in 2001, a change that is somewhat unexpected in view of the decrease in rates of use noninjection use of heroin among these students.
- Disapproval of steroid use decreased among seniors.
- Perceived availability of MDMA (ecstasy) increased sharply among seniors, from 51.4 percent to 61.5 percent.
- Perceived availability of crack and cocaine powder declined among 10th graders. The percent that thought cocaine powder would be "very" or "fairly easy" to get went from 34.5 percent to 31.0 percent.

The Decline of Substance Use in Young Adulthood: Changes in Social Activities, Roles, and Beliefs

The Monitoring the Future team at the University of Michigan published a new book based on their longitudinal panel data. This volume examines how changes in social and religious experiences and changes in attitudes towards substance use among young adults are related to changes in substance use, family transitions, living arrangements, education, and employment. The analysis included over 38,000 young people followed from the initial survey, when they were high school seniors (age 18), into adulthood (up to age 32) and covers the last 25 years, a period when drug use and views about drugs underwent important changes. An earlier book by the MTF investigators showed that the new freedoms of young adulthood are associated with increases in substance use, while the responsibilities of adulthood--marriage, pregnancy, parenthood--contribute to later declines in substance use. The new findings clarify some of the mediators involved in these changes, such as religiosity and perceived risk and disapproval of substance use, factors whose importance is borne out even when controlling for a number of possible confounders. The initial freedoms of young adulthood often lead to frequent evenings out, parties and visits to bars, patterns that may be associated with increases in substance use, but later these behaviors are often crowded out by adult responsibilities to spouse and children. In addition to removing individuals from these higher-risk venues, engagement, marriage, pregnancy, and parenthood tend to heighten both disapproval and perceptions of risk of substance use. The study suggests that while these attitudinal variables are fairly stable, it is important to intervene early to strengthen them if substance use is to be reduced. The authors also discuss the need to intervene with younger adults prior to assumption of full adult roles to involve them in prosocial activities that will compete with substance use. Bachman, J.G., O'Malley, P.M., Schulenberg, J.E., Johnston, L.D. Bryant, A.L., and Merline, A.C. The Decline of Substance Use in Young Adulthood: Changes in Social Activities, Roles, and Beliefs. Mahwah, NJ, US: Lawrence Erlbaum Associates, Inc., Publishers, 2002.

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Director's Report to the National Advisory Council on Drug Abuse
February, 2002

Research Findings

Services Research

Correlates and 6-month Outcomes for Co-occurring Cannabis Use in Rural and Urban At-risk Drinkers

Little is known about the functional correlates of recent cannabis use when such use is additional to an "alcohol disorder" in non-treatment populations. Researchers report on data from a prospective study of a large probability community survey of 733 at-risk drinkers in six Southern U.S. states (Alabama, Arkansas, Georgia, Louisiana, Mississippi, and Tennessee) conducted from 1995 to 1996. Twenty-one percent reported cannabis use during the past six months at the baseline interview. These cannabis users were significantly less likely to be married, employed, or a high school graduate ($p < .05$). They were also more likely to have a diagnosis of "antisocial personality disorder" or "panic disorder. Recent cannabis users also reported more negative consequences of their alcohol use, including more frequent recent diagnoses of an "alcohol disorder," legal difficulties associated with their drinking, and more social consequences attributed to drinking. At the six-month follow-up interview, negative alcohol outcomes were associated with concurrent cannabis use, including higher frequency and quantity of alcohol consumption, greater frequency of recent "alcohol abuse" and "dependence," and greater social consequences of drinking. These results all point to substantially poorer functioning and experiences of individuals with concurrent at-risk alcohol and cannabis use. Authors suggest that cannabis use may be a marker for greater impairment associated with at-risk drinking. Booth, B.M., Kirchner, J.A.E. Substance Use & Misuse, 36(6-7), pp. 717-733, 2001.

Engagement Models for Adolescents in DATOS-A

Considerable research conducted with adults in drug treatment has demonstrated that engaging patients is essential for maximizing treatment retention, completion, and posttreatment outcome. This study applies a model of treatment engagement previously developed and tested with adults. Based on the importance of during-treatment activities for improving outcomes, relationships between patient background, treatment readiness, and therapeutic engagement were examined in a national sample of adolescents admitted to 20 treatment programs representing three modalities. Adolescent patients with higher readiness for treatment at intake subsequently became more therapeutically involved, replicating previous findings on relationships between motivation and engagement in adult samples. One of the most influential background factors associated with higher treatment readiness was patient relationships with family and friends. Interventions that focus on treatment readiness appear to be appropriate strategies for improving treatment engagement. Broome, K.M., Joe, G.W., Simpson, D.D. Journal of Adolescent Research, 16(6), pp. 608-623, 2001.

Treatment Service Patterns and Organizational Structures: An Analysis of Programs in DATOS-A

Findings from earlier studies have suggested that like adults, adolescent patient profiles differ by modality. As a first step in examining drug abuse treatment typologies for adolescents, the researchers investigated the relationship between patient needs and program characteristics. They hypothesized that there may be systematic differences in the types of services provided that are a function of program characteristics as well as the needs of patients entering treatment. The availability of a variety of treatment services was examined within a national sample of programs treating adolescent drug abuse patients. Treatment service delivery profiles were created and examined in the

context of organizational variables such as program modality program directors' academic credentials, program capacity staff composition, accreditation, and patient problems. Results suggested that distinct profiles of services existed within residential and outpatient modalities and that these service profiles were related both to organizational factors and to patient problem profiles. Delany, P.J., Broome, K.M., Flynn, P.M., and Fletcher, B.W. Journal of Adolescent Research, 16(6), pp. 590-607, 2001.

Attrition Prevention with Individuals Awaiting Publicly Funded Drug Treatment

The aim of this study was to evaluate the effectiveness of a motivational intervention to reduce attrition from a waiting list for substance abusers seeking publicly funded treatment. Randomized clinical trial compared an “attrition prevention" condition to standard care while awaiting treatment admission. The study was conducted at a centralized substance abuse assessment and referral center in Seattle, Washington. Study participants comprised substance abusers (n = 654) eligible for publicly funded drug abuse treatment. Measurements collected were: alcohol and drug use, substance-related negative consequences, areas in need of help, perceived need for help, emotional status, readiness to change, reasons for seeking and perceived barriers to entering treatment. Overall, approximately 70% of clients entered treatment, and of these approximately 70% completed their assigned treatment. Those who entered treatment showed significant reductions in substance use and improved psychosocial function at a short-term 3-month follow-up. However, the attrition prevention intervention had no differential effect on treatment entry, completion, or outcome compared to the standard waiting list. Further, there were no differences across therapists on these outcome measures. Authors concluded that a motivational attrition prevention intervention did not enhance treatment entry, completion, or outcome among treatment-seeking substance abusers and suggested that alternative strategies, such as contingency management and case management, may help facilitate treatment entry for individuals seeking publicly funded treatment. Donovan, D.M., Rosengren, D.B., Downey, L., Cox, G.B., and Sloan, K.L. Addiction, 96(8), pp. 1149-1160, 2001.

Drug Abuse Treatment and Comprehensive Services for Adolescents

Data from two national studies of treatment spanning two decades-Treatment Outcome Prospective Study (TOPS), 1979 to 1981, and Drug Abuse Treatment Outcome Studies for Adolescents (DATOS-A), 1993 to 1995-provided a comparison of treatment and services provided to 261 TOPS and 1.519 DATOS-A in treatment adolescent patients in a cross-modality sample of 24 TOPS and 31 DATOS-A programs. The authors used patient self-reports of treatment needs and services received to compare unmet needs for six services. Findings showed a general decline over treatment eras in services received that was only partially offset by significant decreases in some self-reported service needs in DATOS-A. Unmet needs increased significantly over treatment eras for specific services, including psychological, family, employment, and financial services. The highest need in both studies was for family services. The DATOS-A appeared to be addressing family needs better than the TOPS program much of which was more adult focused. Across all DATOS modalities, from 40% to 50% patients reported unmet need for psychological services, considerably higher than the 7% to 10% of TOPS patients. Potential explanations for the increases in unmet needs include changes in treatment access and decreases in program resources for services. Etheridge, R.M., Smith, J.C., Rounds-Bryant, J.L., and Hubbard, R.L. Journal of Adolescent Research, 16(6), pp. 563-589, 2001.

The Effect of Drug Treatment on Criminal Behavior among Adolescents in DATOS-A

This study examined the effects on criminal behavior among 1,167 adolescents who participated in a community-based substance abuse treatment study (Drug Abuse Treatment Outcome Studies for Adolescents) (DATOS-A). The primary goals of this study were to assess the effect of substance abuse treatment on adolescent crime and to identify the patient characteristics that were most closely associated with reductions in crime during the posttreatment period. Results confirmed that among adolescents who had engaged in criminal activity during the 12 months prior to entering DATOS-A treatment, reductions in alcohol or marijuana use were independently associated with significant reductions in the likelihood of committing crimes during the 12-month follow-up period. The present study also provides further support for emphasizing dynamic rather than static patient characteristics to predict the likelihood of continued drug-related offending among substance-abusing adolescents. Farabee, D., Shen, H.K., Hser, Y.I., Grella, C.E., and Anglin, M.D. Journal of Adolescent Research, 16(6), pp. 679-696, 2001.

Using the Drug Abuse Screening Test (DAST-10) to Analyze Health Services Utilization and Cost for Substance Users in a Community-based Setting.

The dual purpose of this study was to: (1) determine whether problematic drug users, defined through the Drug Abuse Screening Test (DAST-10), exhibited differences in health services utilization and cost relative to a combined group of non-problematic drug users and non-drug users; and (2) assess whether the findings were similar to those for chronic drug users (CDUs) and injecting drug users (IDUs). Results showed that health services utilization and

total cost were very similar for problematic drug users defined through quantity-frequency (i.e., CDU, IDU) and diagnostic (i.e., DAST-10) criteria. Findings suggest that quantity/frequency criteria, for problematic drug use were reasonable approximations for diagnostic-based measures. French, M.T., Roebuck, M.C., McGeary, K.A., Chitwood, D.D., and McCoy, C.B. Substance Use & Misuse, 36(6-7), pp. 927-946, 2001.

Transportation and Retention in Outpatient Drug Abuse Treatment Programs

To determine whether certain types of transportation assistance improve outpatient treatment retention beyond thresholds shown to have therapeutic benefits, we analyzed data from 1,144 clients in 22 outpatient methadone maintenance (OMM) programs and 2,031 clients in 22 outpatient drug-free (ODF) programs in the Drug Abuse Treatment Outcomes Study (DATOS), a national, 12-month, longitudinal study of drug abuse treatment programs. Directors' surveys provided information about provision of car, van, or contracted transportation services or individual vouchers/payment for public transportation. Chart-abstracted treatment retention was dichotomized at 365 days for OMM and 90 days for ODF. Separate multivariate hierarchical linear models revealed that provision of car, van, or contracted transportation services improved treatment retention beyond these thresholds for both OMM and ODF, but individual vouchers or payment for public transportation did not. Future research should validate whether car, van, or contracted transportation services improve retention and other treatment outcomes in outpatient drug abuse treatment. Friedmann, P.D., Lemon, S.C., and Stein, M.D. Journal of Substance Abuse Treatment, 21(2), pp. 97-103, 2001.

Prospective Risk Factors and Treatment Outcomes Among Adolescents in DATOS-A

The researchers applied a problem behavior approach to examining the relationship between pretreatment risk factors and posttreatment outcomes among 292 admissions to nine outpatient drug-free (ODF) and 418 admissions to eight residential (RES) adolescent programs. Assessments were administered at intake into treatment and 12 months following discharge. Using a structural modeling approach, the researchers found stability over time for alcohol use, criminal involvement, and psychological maladjustment. For adolescents treated in outpatient programs, (a) severity of drug use predicted lower rates of treatment retention, and (b) family drug involvement was related to higher posttreatment rates of alcohol use. Among those treated in residential programs, (a) family drug involvement and criminal involvement predicted lower rates of treatment retention, and (b) conduct disorders were related to more marijuana use at follow-up. The findings underscore the need for intervention strategies that address the intrapsychic and interpersonal functioning of drug-abusing adolescents to improve their behavioral outcomes. Galaif, E.R., Hser, Y.I., Grella, C.E., and Joshi, V. Journal of Adolescent Research, 16(6), pp. 661-678, 2001.

Risk Transfer and Accountability in Managed Care Organizations' Carve-Out Contracts

This study examined characteristics of contracts between managed care organizations (MCOs) and managed behavioral health organizations (MBHOs) in terms of delegation of functions, financial arrangements between the MCO and the MBHO, and the use of performance standards. Nationally representative administrative and clinical information about the three largest types of commercial products offered by 434 MCOs in 60 market areas was gathered by telephone survey. These products comprised services provided by health maintenance organizations, preferred provider organizations, and point-of-service plans. Chi square tests were performed between pairings of all three types of products to ascertain differences in the degree to which claims processing, maintenance of provider networks, utilization management, case management, and quality improvement were delegated to MBHOs through specialty contracts among the various types of products. Contractual specifications about capitation arrangements, risk sharing, the use of performance standards, and final utilization review decisions were also compared. For all types of products, almost all the major functions were contracted by the MCO to the MBHO. Although most contracts assigned some risk for the costs of services to the MBHO, the degree of this risk varied by product type. Except in the case of preferred-provider organizations, a large number of performance standards were identified in MCOs' contracts with MBHOs, although financial incentives were rarely tied to such standards. Findings led the authors to conclude that MCOs that contract with MBHOs place major responsibility, both financial and administrative, on the vendors. Garnick, D.W., Horgan, C.M., Hodgkin, D. Merrick, E.L., Goldin, D., Ritter, G. and Skwara, K.C. Psychiatr Serv, 52, pp. 1502-1509, 2001.

12-step Program Participation and Effectiveness: Do Gender and Ethnic Differences Exist?

Although 12-Step is increasingly utilized as a recovery resource and is viewed by many addiction specialists as an integral component of treatment and long-term recovery, questions regarding participation and effectiveness of 12-Step programs for women and ethnic minorities have been raised. Utilizing data from the Los Angeles Target Cites Evaluation Project (n = 356), participants in adult outpatient alcohol and drug treatment were followed for 24 months and rates of 12-Step participation and effectiveness were assessed for all gender and ethnic groups. Contrary to

reports that 12-Step is more appropriate for European-American males, statistical analyses reveals that women and ethnic minorities are equally likely to attend 12-Step programs, and to recover in conjunction with such participation as European-American males. Although 12-Step may not appeal to all seeking to cease alcohol and drug use, the clinical implications for treatment providers and other addiction specialists points to the benefits of integrating 12-Step components into traditional treatment programs and recommending 12-Step participation for clients of all gender and ethnic groups. Hillhouse, M.P., and Fiorentine, R. J Drug Issues, 31(3), pp. 767-780, 2001.

Effects of Program and Patient Characteristics on Retention of Drug Treatment Patients

The objective of this study was to examine effects of program and patient characteristics on patient retention in residential drug treatment programs, outpatient drug-free programs (ODF), and methadone maintenance (NIM) programs. Patient data were based on admission and discharge records for individuals entering treatment programs in Los Angeles County during 1992 and 1993. Program data were collected from program directors via a mail survey. The study sample included 26,047 patients in 87 programs. The dependent variable was patient completion of a critical threshold of treatment (360 days for MM and 180 days for the other two modalities). Authors applied logistic regression hierarchical linear modeling analysis for each modality. Principal findings showed that threshold retention rates were generally low in all three modalities (18.1% for residential programs, 22.9% for ODF, and 13.6% for MM). An articulated programmatic focus and low caseload increased patient retention in residential programs. A lower level of group therapy focus increased patient retention in ODF programs. A low programmatic focus and a low percentage of recovering staff were associated with high retention rates among MM patients. For ODF programs, none of the slopes showed random effects, while for residential and MM programs, some program factors contributed to the explanation of the random effects in several slopes (e.g., drug use severity). Authors concluded that program practice and service provision played important roles in determining patient retention in treatment. Service providers and planners should consider these key factors to improve retention of patients, which is likely to increase overall treatment effectiveness and efficiency. Hser, Y.I., Joshi, V., Maglione, M., Chou, C.P., and Anglin, M.D. Evaluation and Program Planning, 24(4), pp. 331-341, 2001.

Relationships Between Counseling Rapport and Drug Abuse Treatment Outcomes

This study examined the association between counseling rapport and drug abuse treatment outcomes. Two cohorts of outpatients who were being treated with methadone in four cities were studied. Cohort 1 comprised 354 patients in community-based nonprofit programs, and cohort 2 comprised 223 patients from a private for-profit program. Logistic regression analyses were used to assess the importance of counseling rapport as a predictor of drug use and criminality relative to treatment retention in the index treatment, satisfaction with treatment, and whether additional treatment was received after the index treatment. In both cohorts, ratings made by counselors, during treatment, of therapeutic involvement and relationships with patients provided a useful measure of counseling rapport. A lower level of rapport during treatment predicted worse post-index treatment outcomes, including more cocaine use and criminality, both by itself and after adjustment for treatment retention, satisfaction with treatment, and post-index treatment status. Counseling strategies were associated with the development of counseling rapport. Findings led authors to conclude that counseling rapport is a vital part of the therapeutic process and helps explain why and when treatment is effective. It contributes explicitly to the prediction of outcomes, apart from treatment retention, and accounts in part for the usual association between treatment retention and outcomes. Joe, G.W., Simpson, D.D., Dansereau, D.F., Rowan-Szal, G.A. Psychiatr Serv, 52(9), pp. 1223-1229, 2001.

A Self-administered Instrument for Assessing Therapeutic Approaches of Drug-user Treatment Counselors

In this article authors describe the development and psychometric properties of a self-administered instrument for assessing drug-user treatment counselors' therapeutic approaches such as psychodynamic or interpersonal, cognitive-behavioral, family systems or dynamics, 12-step, and case management. Authors generated an initial pool of items corresponding to these five approaches and modified them based on expert ratings. Three sets of items were developed. The first concerned the beliefs underlying each therapeutic approach. The second and third concerned the practices of each applicable approach within individual and group counseling, respectively. With the exception of case management, an approach that originated within social work and which is only applicable to individual counseling, the other four approaches are applicable, at least theoretically, to both individual and group counseling. Additionally, authors included items that describe techniques used exclusively with groups (i.e.. group techniques). Finally, they included some items that are not associated with any of the traditional approaches but which reflect the practical approach that drug-user treatment programs often take to both individual and group counseling (i.e., practical counseling). The initial instrument consisted of 17 subscales with a total of 76 items. This instrument was administered to 226 counselors from 45 drug-user treatment programs in Los Angeles County. Based on this data, the researchers further refined these scales using confirmatory factor analysis to ensure both construct validity and

discriminant validity. The final instrument consisted of 14 subscales with a total of 48 items. Kasarabada, N.D., Hser, Y.I., Parker, L., Hall, E., Anglin, M.D., and Chang, E. Substance Use & Misuse, 36(3), pp. 273-299, 2001.

Organizational and Financial Issues in the Delivery of Substance Abuse Treatment Services

Examination of organizational and financial characteristics of the specialty substance abuse treatment system allows an understanding of how to meet the needs of clients in the system. Further, this assessment may afford insights into how the specialty sector may adapt in the changing environment of managed care. Data from Phase I of the Alcohol and Drug Services Study (ADSS) describe the specialty substance abuse treatment system in terms of type of care, setting, level of affiliation, licensure/accreditation, ownership, revenue sources, client referral sources, client's primary substance of abuse, and managed care. Although the system is largely outpatient and remains substantially two tiered in terms of public/private funding mix, it varies along a number of organizational and financial dimensions which have implications for system structure and facility viability in the changing environment of substance abuse treatment service delivery. Horgan, C.M., Reif, S., Ritter, G.A., and Lee, M.T., Recent Dev Alcohol, 15, pp. 9-26, 2001.

Financing of Substance Abuse Treatment Services

The financing of treatment for substance abuse problems has differed from the rest of financing of health care in part because of the dominant role of the public sector as the payer of services. Nonetheless, the rise of managed care has affected substance abuse treatment services as well as the rest of the health care system. Alternative payment mechanisms are one important component of some managed care approaches. Behavioral health carve-outs are another managed care development that has affected substance abuse services. In this chapter, salient features of financing for substance abuse treatment are reviewed within the conceptual framework of payers (purchasers and intermediaries), providers, and consumers. Existing literature on substance abuse treatment financing is summarized, while recognizing that much remains to be researched. Horgan, C.M., and Merrick, E.L. Recent Dev Alcohol,15, pp. 229-252, 2001.

A Client-Treatment Matching Protocol For Therapeutic Communities: First Report

The present study is the first report on a client-treatment matching protocol (CMP) to guide admissions to residential and outpatient substance abuse treatment settings. Two cohorts, a field test sample (n = 318) and cross-validation (n = 407) sample were drawn from consecutive admissions to nine geographically distributed multisetting therapeutic communities (TCs). A passive matching design was employed. Clients received the CMP on admission, but agencies were "blind" to the CMP treatment recommendation (i.e., match) and assigned clients to treatment by the usual intake procedures. Bivariate and logistical regression analyses show that positive treatment dispositions (treatment completion or longer retention in treatment)) were significantly higher among the CMP-matched clients. The present findings provide the empirical basis for studies assessing the validity and utility of the CMP with controlled designs. Though limited to TC-oriented agencies, the present research supports the use of objective matching criteria to improve treatment. Melnick, G., De Leon, G., Thomas, G. and Kressel, D., Journal of Substance Abuse Treatment, 21(3), pp. 119-128, 2001.

Differences among Out-of-treatment Drug Injectors who Use Stimulants Only, Opiates Only or Both: Implications for Treatment Entry

The goal of this study was to compare drug and alcohol use, psychological symptoms and substance abuse treatment entry among 583 street-recruited, out-of-treatment injection drug users (IDUs) who used stimulants only, opiates only or both stimulant and opiate. Data analyzed from structured interviews indicated that stimulant-only users had the most severe alcohol problems and the highest psychological symptom scores for hostility, paranoia and psychoticism. In the 2 months following their interview only 3% of the stimulant-only users entered substance abuse treatment, as compared to nearly half of the participants in the other two groups. Even after controlling for variables that differed among the groups by logistic regression analysis, stimulant only users were still 24-25 times less likely than opiate only or both stimulant and opiate users to enter treatment. Researchers and clinicians are challenged to better understand and address the unique needs of stimulant users, including potential psychological problems and alcohol abuse, in order to attract them to treatment and serve them through a comprehensive treatment approach. John, D., Kwiatkowski, C.F., and Booth, R.E. Drug Alcohol Depend, 64(2), pp 165-172, 2001.

Selective Contracting in Managed Care: The Case of Substance Abuse Treatment

The authors address two critical questions concerning managed care and outpatient substance abuse treatment organizations. Specifically, they consider (1) to what extent selective contracting occurs between managed care firms

and treatment providers and (2) what attributes of treatment providers and their operating environments are associated with selective contracting. Using data from a nationally representative sample of outpatient treatment organizations, the authors find evidence of systematic selection. Several indicators of providers' quality and costs, including accreditation status, private ownership, size, and prior experience with managed care, are positively associated with managed care contracting. By contrast, units providing methadone treatment are less likely to be involved in managed care. To a lesser extent, characteristics of treatment providers' operating environment, including extent of competition based on costs and attributes of the Medicaid managed care program, are also positively associated with managed care contracting. Lemak, C.H., Alexander, J.A., and D'Aunno, T.A. Medical Care Research and Review, 58(4), pp. 455-481, 2001.

A Comparison of Psychosocial Barriers Among Welfare Recipients: Implications For Drug Treatment

Implementation of Temporary Assistance for Needy Families (TANF) presents welfare recipients with time-limited benefits and work requirements. However, it is estimated that over 140,000 welfare recipients meet the DSM-IV criteria for "drug dependence." In this study, samples of chronic drug using and non-drug using female TANF recipients were compared with regard to: current employment, psychological functioning, self-perceived employment skills, barriers to employment, and need for help in seeking employment. It was found that non-drug using study participants were significantly more likely to be employed and reported significantly higher self-perceived work skills than users. Chronic users reported significantly greater barriers to seeking employment. Montoya, I.D., Atkinson, J.S., and Struse, H.M. Substance Use & Misuse, 36(6-7), pp. 771-788, 2001.
Examining the Substance Use Patterns and Treatment Needs of Incarcerated Sex Offenders Using data from a Bureau of Justice Statistics' national prison inmate survey, this paper analyzes alcohol and drug use and abuse patterns among men incarcerated in state prison for sex crimes. Of the 13,986 inmates in the sample, 11.5% were incarcerated for a sex offense. Two thirds were substance-involved, meaning that they were under the influence of alcohol or drugs at the time of their crime, had committed a crime to get money for drugs, had histories of regular illegal drug use, had received treatment for alcoholism, or shared some combination of these characteristics. The level and type of substance-involvement was related to age and race, to history of victimization, and to victim characteristics. We discuss the implications of these findings for correctional program interventions, including assessing drug and alcohol problems, availability of substance abuse treatment for sex offenders, and the conjunction of such treatment with other programs. Peugh, J., and Belenko, S. Sex Abuse. 13(3), pp. 179-195, 2001.

Patient Characteristics and Treatment Outcomes for African American, Hispanic, and White Adolescents in DATOS-A

This study attempts to extend what is known about adolescent substance abusers in adolescent-oriented substance abuse treatment by describing and comparing background and pretreatment characteristics and posttreatment outcomes of African American (n = 213), Hispanic (n = 108), and White adolescent (n = 773) substance abusers who participated in the Drug Abuse Treatment Outcome Studies for Adolescents (DATOS-A). The pretreatment data indicated that patients in each group were similar only with respect to basic demographics (gender, age and primary drug use) but differed in terms of referral source, involvement with the criminal justice system and prevalence of mental disorders. Posttreatment comparisons revealed significant racial/ethnic differences in serious posttreatment criminal behavior, only. Logistic regression results indicated that African American adolescents had a lower likelihood of engaging in serious illegal activity as compared to White adolescents during the posttreatment period. The results of this study provide at mechanism for more comprehensive understanding of adolescent substance abusers, their treatment needs, and their treatment outcomes. Rounds-Bryant, J.L., and Staab, J. Journal of Adolescent Research, 16(6), pp. 624-641, 2001.

Using Cost and Financing Instruments for Economic Evaluation of Substance Abuse Treatment Services

Standardized economic evaluation instruments are an important tool in the analysis of change and performance of addiction treatment. Nevertheless, compared to other health care sectors, economic evaluation of addiction treatment is still rare. The present paper proposes two comprehensive economic evaluation instruments that are methodologically sound and that meet the objectives of comprehensiveness, standardization, and comparability. The Drug Abuse Treatment Cost Analysis Program (DATCAP) can be used to estimate the economic cost of treatment services; the Drug Abuse Treatment Financing Analysis Program (DATFAP) is a companion instrument and analyzes the complexity and change of treatment financing. This paper outlines the contents of each instrument and, for illustrative purposes, presents results from several case studies. Suggestions for updates and enhancements for each instrument are also discussed. Salome, H.J., and French, M.T. Recent Dev Alcohol.,15, pp. 253-269, 2001.

The Organization of Substance Abuse Managed Care

Managed care came to dominate the delivery of substance abuse services during the 1990s. This paper uses literature and new data to describe and analyze the set of arrangements it implies. The description suggests that substance abuse managed care typically is "carved out" of the general health care plan and treatment is coordinated by a behavioral health managed care company that manages treatment access, length, type, and intensity. This administrative agent is provided financial incentives to keep costs low and otherwise faces such mandates as to ensure timely access to treatment and to deliver reports. A typical agent has some interest in improving the quality of decision-making, but has few incentives for controlling the treatment technology. In contrast, agents tend to control treatment providers through relatively rigid rules that substitute outpatient for inpatient care, regulate the length and intensity of services, provide limited social services, mandate accreditation, allow limited clinician discretion, administer an entire "network" of providers as an only slightly differentiated mass, and rarely shape the details of the treatment process. These patterns are analyzed in terms of transaction cost economics and institutional and resource dependency theories. In general, it is argued that managed care reflects an interest in controlling costs but also in ensuring access within an environment where there is uncertainty accompanying competing demands, varying conceptions of the client, and controversies over the efficacy of specific treatment technologies. Sosin, M.R., and D'Aunno, T. Recent Dev Alcohol, 15, pp. 27-49, 2001.

Effects of Managed Care on Programs and Practices for the Treatment of Alcohol and Drug Dependence

Managed care is affecting the organization and financing of treatment services for alcohol and drug dependence. This paper examines the effects of managed care on program operations including the use of clinical protocols, the administrative burden, information systems, staffing, and program consolidation. It also reviews the effects of managed care on system performance related to employer-sponsored health plans, state employee health plans, and Medicaid and other public plans. This review of managed care's influences on the alcohol and drug abuse treatment system finds evidence of systemic reductions in access to inpatient care and increased reliance on outpatient services. Moreover, although analyses of behavioral health carve-outs often suggest increases in the use of outpatient care, evaluations of substance abuse claims report reductions in ambulatory utilization for the treatment of alcohol and drug dependence. Recent Dev. Alcohol, 15, pp. 51-71, 2001.

Social Support Systems of Women Offenders who Use Drugs: A Focus on the Mother-daughter Relationship

Conceptually, social support among very heavily drug-involved women is complex and multidimensional. This article examines the structure and function of the social support systems of women offenders (N = 100) who used drugs during the last 6 months before entering court-mandated drug-free treatment programs. These systems typically contain about nine supporters, almost equally divided between men and women, and about half of the women's supporters are family members. The women identify parents and partners as their major providers of practical help and advice. They look most to their partners for a sympathetic ear, and to their parents for affirmation of their self-worth. Overall, two-thirds of the women identify their mothers as among their supporters. These mothers are often anxious to do whatever they can to help their daughters stop using drugs. Paradoxically, the assistance many mothers give their daughters in providing money or basic life necessities often enables the daughter's drug use. Although many daughters appreciate their mother's help, there is an element of distrust and control in many of the mother-daughter relationships, and some daughters receive unwanted help from their mothers. Drug treatment providers can benefit from understanding their clients' social support systems, especially the dynamics of important relationships with main pretreatment supporters, such as parents. By gaining this understanding and helping their clients to effectively accept and use social support, Strauss, S.M., and Falkin, G.P. American Journal of Drug and Alcohol Abuse, 27(1), pp. 65-89, 2001.

Crack Cocaine, Alcohol, and Other Drug Use Patterns among Homeless Persons with Other Mental Disorders

This study examined the co-occurrence of cocaine, alcohol, marijuana, and other drug use among treatment seeking homeless persons to determine whether alcohol use predicted cocaine use differently than marijuana and other drugs predicted cocaine use. Participants were 141 homeless persons with substance use and other nonpsychotic mental disorders seeking drug treatment at a metropolitan health care agency for homeless persons. They were 72.3% male, 27.7% female, 82.7% African American, 17.3% Caucasian, with an average age of 37.7 (SD 7.1) years and had 13.1 (SD 2.4) average years of education. Results supported the assertion that cocaine use was strongly associated with extent of alcohol use and that the association between cocaine and alcohol was stronger than the association

between cocaine and other drug use, including marijuana. Participants with cocaine plus alcohol disorders were retained longer in treatment than disorders of cocaine only with no differences in abstinence outcome. The findings should drive further research into the use of alcohol as a trigger or predictor of cocaine use, the deleterious effects of the combined use of cocaine and alcohol, and specialized treatments for polysubstance users. Usdan, S.L., Schumacher, J.E., Milby, J.B, Wallace, D., McNamara, C., and Michael, M. Am J Drug Alcohol Abuse, 27(1), pp. 107-120, 2001.

Rural-Urban Differences In Substance Use And Treatment Utilization Among Prisoners

Surveys of incarcerated offenders and arrestees consistently report high rates of both alcohol and drug use 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. The American Journal of Drug and Alcohol Abuse, 27(2), pp. 265-280, 2001.

Social Support and Abstinence from Opiates and Cocaine during Opioid Maintenance Treatment

Social support may play an important role in helping drug users achieve abstinence; however these benefits may depend on the type of support experienced. In this prospective observational study, we examined the extent to which general and abstinence-specific support, both structural and functional, predicted opiate and cocaine abstinence in 128 opioid maintenance patients receiving either methadone or LAAM. A new multidimensional self-report instrument assessing abstinence-specific functional support was developed for the study. Previously validated measures were used to assess the remaining types of support. With baseline abstinence and other statistically important covariates adjusted, hierarchical logistic regression analyses demonstrated that the associations between social support at study baseline and biochemically confirmed abstinence 3 months later varied by type of support and by drug. Greater abstinence-specific structural support (operationalized as fewer drug users in the social network) and decreases in three types of negative abstinence-specific functional support (Complaints about Drug Use, Drug Exposure, and Demoralization) predicted cocaine, but not opiate abstinence. There were no effects for general support, whether structural or functional, on abstinence from either drug. Interventions that focus on modifying patients' abstinence-specific support may be helpful in reducing the high rates of cocaine use disorders in this population. Wasserman, D.A., Stewart, A.L., and Delucchi, K.L. Drug and Alcohol Dependence, 65(1), pp. 75-85, 2001.

Integrating Primary Medical Care With Addiction Treatment: A Randomized Controlled Trial

The prevalence of medical disorders is high among substance abuse patients, yet medical services are seldom provided in coordination with substance abuse treatment. The objective of this study was to examine differences in treatment outcomes and costs between integrated and independent models of medical and substance abuse care as well as the effect of integrated care in a subgroup of patients with substance abuse-related medical conditions (SAMCs). A randomized controlled trial was conducted between April 1997 and December 1998. Subjects comprised adult men and women (n = 592) who were admitted to a large health maintenance organization chemical dependency program in Sacramento, CA. Patients were randomly assigned to receive treatment through an integrated model, in which primary health care was included within the addiction treatment program (n = 285), or an independent treatment-as-usual model, in which primary care and substance abuse treatment were provided separately (n = 307). Both programs were group based and lasted 8 weeks, with 10 months of aftercare available. Main outcome measures included: abstinence outcomes, treatment utilization, and costs 6 months after randomization. Both groups showed improvement on all drug and alcohol measures. Overall, there were no

differences in total abstinence rates between the integrated care and independent care groups (68% vs. 63%, P = .18). For patients without SAMCs, there were also no differences in abstinence rates (integrated care, 66% vs. independent care, 73%; P = .23) and there was a slight but nonsignificant trend of higher costs for the integrated care group ($367.96 vs. $324.09, P = .19). However, patients with SAMCs (n = 341) were more likely to be abstinent in the integrated care group than the independent care group (69% vs. 55%, P =.006; odds ratio [OR], 1.90; 95% confidence interval [CI], 1.22-2.97). This was true for both those with medical (OR, 3.38; 95% CI, 1.68-6.80) and psychiatric (OR, 2.10; 95% CI, 1.04-4.25) SAMCs. Patients with SAMCs had a slight but nonsignificant trend of higher costs in the integrated care group ($470.81 vs. $427.95, P =.14). The incremental cost-effectiveness ratio per additional abstinent patient with an SAMC in the integrated care group was $1581. Authors concluded that individuals with SAMCs benefit from integrated medical and substance abuse treatment, and such an approach can be cost-effective. These findings are relevant given the high prevalence and cost of medical conditions among substance abuse patients, new developments in medications for addiction, and recent legislation on parity of substance abuse with other medical benefits. Weisner, C., Mertens, J., Parthasarathy, S., Moore, C., and Lu, Y. JAMA. 286(14), pp. 1715-1723, 2001.

Drug Courts - A Bridge Between Criminal Justice and Health Services

There is striking overlap between the public health threats of drug abuse and crime. Crimes are often drug related, and drug abusers frequently encounter the criminal justice system. However, with few exceptions (e.g., Treatment Alternatives to Street Crime, TASC), the intersection of drug abusers with the courts has rarely addressed the defendants' drug problems. Drug courts represent an innovative approach to addressing both crime and drug abuse. Especially promising, and of great importance given that drug abuse is associated with a host of other health and social service needs, is the link that drug courts represent between the criminal justice and health services systems. Connections to health services are considered vital to drug courts but are poorly understood. The need for a bridge between criminal justice and health services is discussed, and a conceptual framework for its investigation is presented. Using data collected from site visits of 14 drug courts across the United States and Puerto Rico, the services available to drug court clients are described and linkages between drug courts and health services (including drug treatment providers) are explained. Wenzel, S.L., Longshore, D., Turner, S., and Ridgely, M.S. Journal of Criminal Justice, 29(3), pp. 241-253, 2001.

Risk Adjustment Alternatives in Paying for Behavioral Health Care under Medicaid

The aim of this study was to compare the performance of various risk adjustment models in behavioral health applications such as setting mental health and substance abuse (MH/SA) capitation payments or overall capitation payments for populations including MH/SA users. The 1991-93 administrative data from the Michigan Medicaid program were used. Authors compared mean absolute prediction error for several risk adjustment models and simulated the profits and losses that behavioral health care carve outs and integrated health plans would experience under risk adjustment if they enrolled beneficiaries with a history of MH/SA problems. Models included basic demographic adjustment, Adjusted Diagnostic Groups, Hierarchical Condition Categories, and specifications designed for behavioral health. Differences in predictive ability among risk adjustment models were small and generally insignificant. Specifications based on relatively few MH/SA diagnostic categories did as well as or better than models controlling for additional variables such as medical diagnoses at predicting MH/SA expenditures among adults. Simulation analyses revealed that among both adults and minors considerable scope remained for behavioral health care carve outs to make profits or losses after risk adjustment based on differential enrollment of severely ill patients. Similarly, integrated health plans have strong financial incentives to avoid MH/SA users even after adjustment. Authors concluded that current risk adjustment methodologies do not eliminate the financial incentives for integrated health plans and behavioral health care carve-out plans to avoid high-utilizing patients with psychiatric disorders. Ettner, S.L., Frank, R.G., McGuire, T.G., and Hermann, R.C. Health Serv Res, 36(4), pp. 793-811, 2001.

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Director's Report to the National Advisory Council on Drug Abuse
February, 2002

Research Findings

Intramural Research

Treatment Section, Clinical Pharmacology & Therapeutics Research Branch

Shaping Cocaine Abstinence by Successive Approximation

Contingency management, a behavioral therapy in which positive behavior changes are reinforced with incentives, is one of the most effective treatments for cocaine dependence. Most commonly, patients receive an incentive each time their urine tests negative for cocaine. Though effective in many patients, this procedure sometimes fails because some patients can cut down their cocaine use, but are not immediately able to abstain long enough for their urine to test negative and earn an incentive. Investigators in the Treatment Section tested a treatment variation that reinforced patients' decreases in cocaine use prior to requiring them to be totally abstinent. Cocaine-using methadone-maintenance patients were randomized to standard contingency management (Abstinence group, n=49) or a contingency designed to increase contact with reinforcers (Shaping group, n=46). For 8 weeks, both groups earned escalating-value vouchers based on thrice-weekly urinalyses: the Abstinence group earned vouchers for cocaine-negative urine specimens only; the Shaping group earned vouchers for each urine specimen with a &Mac179;25% decrease in cocaine metabolite (first 3 weeks) and then for negative specimens only (last 5 weeks). Cocaine use was lower in the Shaping group but only in the last 5 weeks when the response requirements were identical. Thus, the shaping contingency appeared to better prepare patients for abstinence. Preston, K.L., Umbricht, A., Wong, C.J., and Epstein, D.H. Journal of Consulting and Clinical Psychology, 69, pp. 643-654, 2001.

Clinical Pharmacology Section, Clinical Pharmacology & Therapeutics Research Branch

Weight Gain and Liver Tests in Drug-Dependent Adults

This study evaluated liver function and prevalence of underweight and overweight among 264 consecutive medically screened, physically healthy drug-dependent adults admitted to the research unit of the National Institute on Drug Abuse Intramural Research Program. Liver function was assessed in terms of serum liver transaminase (ALT, AST) concentrations at admission, mid-stay, and discharge. The average length of stay on the unit was 3 weeks. At admission, the prevalence of underweight (body mass index [BMI] < 19) was 6% and of overweight [BMI > 25] 27%. Among the 204 subjects who remained on the unit at least one week, the mean weight gain was 0.14 kg/day; 69% of subjects gained weight. Heroin users had the most average weight gain; cocaine users the least. Among the 71 subjects who provided 3 blood samples, mean serum transaminase concentrations increased significantly (50-100%) from admission to mid-stay, then declined significantly (20-25%) by discharge. No adverse events were associated with the increased transaminase concentrations. There was a significant positive correlation between weight gain on the unit and increase in liver transaminase concentrations, i.e., the greater the weight gain, the greater the increase in transaminases. These findings suggest that weight gain due to refeeding can be a benign cause of abnormal liver tests in otherwise healthy drug-dependent adults. Fontaine K.R., Cheskin L.J., Carriero N.J., Jefferson L., Finley C.J., and Gorelick D.A. Journal of the American Dietetic Association, 101, pp. 1467-1469, 2001.

Brain Imaging Section, Neuroimaging Research Branch

Smoking History and Nicotine Effects on Cognitive Performance

Effects of abstinence from smoking, smoking history, and nicotine administration on visual attention (Two-Letter Search Task), verbal information processing (Logical Reasoning Task), and working memory (N-Back Tasks) were studied in 14 smokers, 15 ex-smokers, and 9 never-smokers. Subjects participated in two test sessions and received either 4 mg nicotine gum or placebo, respectively. Smokers were 12-h abstinent when they received gum. Nicotine produced significant increases in diastolic pressure and heart rate in all three groups. With respect to cognitive effects, an effect of acute nicotine administration (independent of smoking history) was observed only on the Two-Letter Search Task as reaction time was shorter after nicotine gum than after placebo in all three groups, suggesting withdrawal from or tolerance to nicotine were not significant factors. Working memory performance was related to smoking history as smokers performed most poorly and never-smokers performed best. The Logical Reasoning Task showed no effects of either acute or chronic nicotine exposure. Our determination that nicotine improves reaction time rather than accuracy of task performance, while task specific, is consistent with previous reports. Our findings further indicate that nicotine may influence focusing of attention in smokers as well as nonsmokers, and that trait-like differences in some cognitive domains, such as working memory, may be either long-term effects or etiological factors related to smoking. Ernst, M., Heishman, S.J., Spurgeon, L, and London, E.D. Neuropsychopharmacology, 25, pp. 313-319, 2001.

5-Iodo-6-[18F]fluoro-3-(2(S)-azetidinylmethoxy)pyridine, a Novel PET Radioligand for Nicotinic Acetylcholine Receptors: Synthesis and Initial Evaluation

Nicotinic acetylcholine receptors (nAChRs) are of growing interest due to their involvement in a variety of brain functions, including cognitive processes, and disorders (e.g., tobacco dependence and neurodegenerative disorders, such as Alzheimer's disease). Accordingly, there has been an increasing interest in non-invasive imaging of using positron emission tomography (PET) and single photon emission computed tomography (SPECT). Radiohalogenated analogs of 3-(2(S)-azetidinylmethoxy) pyridine (A-85380) have been recognized as promising probes for in vivo imaging of brain nAChRs with PET and SPECT. To develop an 18F-labeled PET radioligand for nAChRs that retains high affinity for central alpha4beta2 nAChRs, while being superior to similar ligands with respect to safety, we synthesized 5-iodo-6-fluoro-3-(2(S)-azetidinylmethoxy) pyridine (5I-6F-A-85380) and its radiolabelled variety ([18F]). Synthesis of 5I-6F-A-85380 and its [18F]-labelled version required the synthesis of novel compounds to complete the syntheses of both compounds. In vitro characterization determined that both 5I-6F-A-85380 and 5I-6[18F]F-A-85380 had high affinities for alpha4beta2 nAChRs, Ki=15± 2 pM and Kd=17±3 pM, respectively, and in vivo studies in mice demonstrated reduced toxicity relative to closely related analogues (6F-A-85380). PET studies in Rhesus monkeys demonstrated specific accumulation of 5I-6[18F]F-A-85380 in the brain with a regional distribution consistent with alpha4beta2 nAChRs, with the highest density in the thalamus. We conclude that 5I-6[18F]F-A-85380 is a promising PET radioligand for in vivo imaging as it represents an improvement in terms of nAChR affinity, nAChR subtype selectivity and safety. Koren, A.O., Chefer, S.I., Mukhin, A.G., Pavlova, O.A., Horti, A.G., Vaupel, D.B., London, E.D. and Kimes, A.S. Journal of Labeled Compounds and Radiopharmaceuticals, 44 (S1), pp. S257-259, 2001.

Imaging studies in Humans Demonstrate that [123I]5-I-A-85380 is a Promising Single-Photon Emission Tomography (SPET) Ligand for the Study of alpha4beta2 Nicotinic Receptors in Brain Disorders

The biodistribution of radioactivity after the administration of a new tracer for alpha4beta2 nicotinic acetylcholine receptors (nAChRs), [123I]5-iodo-3-[2(S)-2-azetidinylmethoxy]pyridine (5-I-A-85380), was studied in ten healthy human subjects. Following administration of 98±6 MBq [123I]5-I-A-85380, serial whole-body images were acquired over 24 h and corrected for attenuation. One to four brain single-photon emission tomography (SPET) images were also acquired between 2.5 and 24 h. Estimates of radiation absorbed dose were calculated using MIRDOSE 3.1 with a dynamic bladder model and a dynamic gastrointestinal tract model. The estimates of the highest absorbed dose (µGy/MBq) were for the urinary bladder wall (71 and 140), lower large intestine wall (70 and 72), and upper large intestine wall (63 and 64), with 2.4-h and 4.8-h urine voiding intervals, respectively. The whole brain activity at the time of the initial whole-body imaging at 14 min was 5.0% of the injected dose. Consistent with the known distribution of alpha4beta2 nAChRs, SPET images showed the highest activity in the thalamus. These results suggest that [123I]5-I-A-85380 is a promising SPET agent to image 42 nAChRs in humans, with acceptable dosimetry and high brain uptake. Whole-body Biodistribution, Radiation Absorbed Dose, and Brain SPET Imaging with [123I]5-I-A-85380 in Healthy Human Subjects. Fujita, M., Seibyl, J.P., Vaupel, D.B., Tamagnan, G., Early, M., Zoghbi, S.S., Baldwin, R.M., Horti, A.G., Koren, A.O., Mukhin, A.G., Khan, S., Bozkurt, A., Kimes, A.S., London, E.D., and Innis, R.B. European Journal of Nuclear Medicine, published online 4 Dec. 2001. http:/link.springer-ny.com/link/service…/00695/paper/s00259-001-0695-zch110.html

Development and Plasticity Section, Cellular Neurobiology Research Branch

A Murine Dopamine Neuron-Specific cDNA Library and Microarray: Increased COXI Expression during Methamphetamine Neurotoxicity

Due to brain tissue heterogeneity, the molecular genetic profile of any neurotransmitter-specific neuronal subtype is unknown. The purpose of this study was to purify a population of dopamine neurons, construct a cDNA library, and generate an initial gene expression profile and a microarray representative of dopamine neuron transcripts. Ventral mesencephalic dopamine neurons were purified by fluorescent-activated cell sorting from embryonic day 13.5 transgenic mice harboring a 4.5-kb rat tyrosine hydroxylase promoter-lacZ fusion. Nine-hundred sixty dopamine neuron cDNA clones were sequenced and arrayed for use in studies of gene expression changes during methamphetamine neurotoxicity. A neurotoxic dose of methamphetamine produced a greater than twofold up-regulation of the mitochondrial cytochrome c oxidase polypeptide I transcript from adult mouse substantia nigra at 12 h posttreatment. This is the first work to describe a gene expression profile for a neuronal subtype and to identify gene expression changes during methamphetamine neurotoxicity. Barrett T., Xie, T., Piao, Y., Dillon-Carter, O., Kargul, G.J., Lim, M.K., Chrest, F.J., Wersto, R., Rowley, D.L., Juhaszova, M., Zhou, L., Vawter, M.P., Becker, K.G., Cheadle, C., Wood, W.H. III, McCann, U.D., Freed, W.J., Ko, M.S., Ricaurte, G.A., and Donovan, D.M. Neurobiology of Diseases, 8(5), pp. 822-833, 2001.

Application of cDNA Microarrays to Examine Gene Expression Differences in Schizophrenia

Using cDNA microarrays IRP scientists have investigated gene expression patterns in brain regions of patients with schizophrenia. A cDNA neuroarray, comprised of genes related to brain function, was used to screen pools of samples from the cerebellum and prefrontal cortex from a matched set of subjects, and middle temporal gyrus, from a separate subject cohort. Samples of cerebellum and prefrontal cortex from neuroleptic naive patients were also included. Genes that passed a 3% reproducibility criterion for differential expression in independent experiments included 21 genes for drug-treated patients and 5 genes for drug-naive patients. Of these 26 genes, 10 genes were increased and 16 were decreased. Many of the differentially expressed genes were related to synaptic signaling and proteolytic functions. A smaller number of these genes were also differentially expressed in the middle temporal gyrus. The five genes that were differentially expressed in two brain regions from separate cohorts are: tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide; sialyltransferase; proteasome subunit, alpha type 1; ubiquitin carboxyl-terminal esterase L1; and solute carrier family 10, member 1. Identification of patterns of changes in gene expression may lead to a better understanding of the pathophysiology of schizophrenia disorders. Vawter, M.P., Barrett, T., Cheadle, C., Sokolov, B.P., Wood, W.H. III, Donovan, D.M., Webster, M., Freed, W.J., and Becker, K.G. Brain Research Bulletin 55(5), pp. 641-650, 2001.

Involvement of GDNF in Neuronal Protection against 6-OHDA-Induced Parkinsonism Following Intracerebral Transplantation of Fetal Kidney Tissues in Adult Rats

Exogenous application of transforming growth factors-beta (TGFbeta) family proteins, including glial cell line-derived neurotrophic factor (GDNF), neurturin, activin, and bone morphogenetic proteins, has been shown to protect neurons in many models of neurological disorders. Finding a tissue source containing a variety of these proteins may promote optimal beneficial effects for treatment of neurodegenerative diseases. Because fetal kidneys express many TGFbeta trophic factors, we transplanted these tissues directly into the substantia nigra after a unilateral 6-hydroxydopamine lesion. We found that animals that received fetal kidney tissue grafts exhibited (1) significantly reduced hemiparkinsonian asymmetrical behaviors, (2) a near normal tyrosine hydroxylase immunoreactivity in the lesioned nigra and striatum, (3) a preservation of K(+)-induced dopamine release in the lesioned striatum, and (4) high levels of GDNF protein within the grafts. In contrast, lesioned animals that received grafts of adult kidney tissues displayed significant behavioral deficits, dopaminergic depletion, reduced K(+)-mediated striatal dopamine release, and low levels of GDNF protein within the grafts. The present study suggests that fetal kidney tissue grafts can protect the nigrostriatal dopaminergic system against a neurotoxin-induced parkinsonism, possibly through the synergistic release of GDNF and several other neurotrophic factors. Borlongan, C.V., Zhou, F.C., Hayashi, T., Su, T.P., Hoffer, B.J., and Wang, Y. Neurobiology of Diseases, 8(4), pp. 636-646, 2001.

Region-specific Transcriptional Response to Chronic Nicotine in Rat Brain

Even though nicotine has been shown to modulate mRNA expression of a variety of genes, a comprehensive high-throughput study of the effects of nicotine on the tissue-specific gene expression profiles has been lacking in the literature. In this study, cDNA microarrays containing 1117 genes and ESTs were used to assess the transcriptional response to chronic nicotine treatment in rat, based on four brain regions, i.e. prefrontal cortex (PFC), nucleus accumbens (NAs), ventral tegmental area (VTA), and amygdala (AMYG). On the basis of a non-parametric resampling method, an index (called jackknifed reliability index, JRI) was proposed, and employed to determine the inherent

measurement error across multiple arrays used in this study. Upon removal of the outliers, the mean correlation coefficient between duplicate measurements increased to 0.978+/-0.0035 from 0.941+/-0.045. Results from principal component analysis and pairwise correlations suggested that brain regions studied were highly similar in terms of their absolute expression levels, but exhibited divergent transcriptional responses to chronic nicotine administration. For example, PFC and NAs were significantly more similar to each other (r=0.7; P<10(-14)) than to either VTA or AMYG. Furthermore, we confirmed our microarray results for two representative genes, i.e. the weak inward rectifier K(+) channel (TWIK-1), and phosphate and tensin homolog (PTEN) by using real-time quantitative RT-PCR technique. Finally, a number of genes, involved in MAPK, phosphatidylinositol, and EGFR signaling pathways, were identified and proposed as possible targets in response to nicotine administration. Konu, O., Kane, J.K., Barrett, T., Vawter, M.P., Chang, R., Ma, J.Z., Donovan, D.M., Sharp, B., Becker, K.G., and Li, M.D. Brain Research, 909, pp. 194-203, 2001.

Electrophysiological Evidence for Vasopressin v(1) Receptors on Neonatal Motoneurons, Premotor and other Ventral Horn Neurons

Prominent arginine-vasopressin (AVP) binding and AVP V(1) type receptors are expressed early in the developing rat spinal cord. IRP scientists sought to characterize their influence on neural excitability by using patch-clamp techniques to record AVP-induced responses from a population of motoneurons and interneurons in neonatal (5-18 days) rat spinal cord slices. Data were obtained from 58 thoracolumbar (T(7)-L(5)) motoneurons and 166 local interneurons. A majority (>90%) of neurons responded to bath applied AVP (10 nM to 3 &mgr;M) and (Phe(2), Orn(8))-vasotocin, a V(1) receptor agonist, but not V(2) or oxytocin receptor agonists. In voltage-clamp, postsynaptic responses in motoneurons were characterized by slowly rising, prolonged (7-10 min) and tetrodotoxin-resistant inward currents associated with a 25% reduction in a membrane potassium conductance that reversed near -100 mV. In interneurons, net AVP-induced inward currents displayed three patterns: decreasing membrane conductance with reversal near -100 mV, i.e., similar to that in motoneurons (24 cells); increasing conductance with reversal near -40 mV (21 cells); small reduction in conductance with no reversal within the current range tested (41 cells). A presynaptic component recorded in most neurons was evident as an increase in the frequency but not amplitude (in motoneurons) of inhibitory and excitatory postsynaptic currents (IPSCs and EPSCs), in large part due to AVP-induced firing in inhibitory (mainly glycinergic) and excitatory (glutamatergic) neurons synapsing on the recorded cells. An increase in frequency but not amplitude of miniature IPSCs and EPSCs also indicated an AVP enhancement of neurotransmitter release from axon terminals of inhibitory and excitatory interneurons. These observations provide support for a broad presynaptic and postsynaptic distribution of AVP V(1) type receptors and indicate that their activation can enhance the excitability of a majority of neurons in neonatal ventral spinal cord. Oz, M., Kolaj, M., and Renaud, L.P., Journal of Neurophysiology, 86(3), pp. 1202-1210, 2001.

Characterization of Human Cleaved N-CAM and Association with Schizophrenia

The neural cell adhesion molecule (N-CAM) is a cell recognition molecule involved in cellular migration, synaptic plasticity, and CNS development. A 105- to 115-kDa isoform of N-CAM (cleaved N-CAM or cN-CAM) is increased in schizophrenia in hippocampus, prefrontal cortex, and CSF. We purified and partially characterized cN-CAM, a putative novel isoform, and confirmed that the first 9 amino acids were identical to exon 1 of N-CAM, without the signal sequence. Analysis of trypsin-digested cN-CAM fragments by matrix-assisted laser desorption ionization on a time-of-flight mass spectrometer yielded peptides that could be identified as being derived from the first 548 amino acid residues of the expected N-CAM amino acid sequence. Immunological identification with four specific N-CAM antisera directed toward cytoplasmic, secreted, variable alternative spliced exon, or GPI epitopes failed to indicate other known splice variants. Neuraminidase treatment of cN-CAM produced a minor alteration resulting in a faster migrating immunoreactive band, indicating partial glycosylation of cN-CAM. Membranous particles from cytosolic brain extract containing cN-CAM were obtained by ultracentrifugation; however, CSF contained few such particles. cN-CAM and synaptophysin were colocalized on these particles. Both cN-CAM and N-CAM 180 were present in synaptosomal preparations of human brain. Following incubation of synaptosomes or brain tissue without protease inhibitors, N-CAM 180 was degraded and cN-CAM was increased. A cN-CAM-like band was present in human fetal neuronal cultures, but not in fetal astrocyte cultures. Thus, cN-CAM represents a protease- and neuraminidase-susceptible fragment possibly derived by proteolytic cleavage of N-CAM 180. An enlargement in ventricular volume in a group of adult patients with schizophrenia over a 2-year interval was found to be correlated with CSF cN-CAM levels as measured at the time of the initial MRI scan (r = 0.53, P = 0.01). cN-CAM is associated with ventricular enlargement; thus, the release of N-CAM fragments may be part of the pathogenic mechanism of schizophrenia in vulnerable brain regions such as the hippocampus and prefrontal cortex. Alternatively, the increases in cN-CAM in schizophrenia may be a reflection of a more general abnormality in the regulation of proteolysis or of extracellular matrix stability. Vawter, M.P., Usen, N., Thatcher, L., Ladenheim, B., Zhang, P., VanderPutten, D.M., Conant, K., Herman, M.M., van Kammen, D.P., Sedvall, G., Garver, D.L., and Freed, W.J., Experimental Neurology, 172, pp. 29-

46, 2001.

Cellular Neurophysiology Section, Cellular Neurobiology Research Branch

5-HT3-Receptor Subunits A and B are Co-expressed in Neurons of the Dorsal Root Ganglion

The type 3 serotonin (5-HT3) receptor is the only ligand-gated ion channel receptor for serotonin (5-HT). Many pharmacological, behavioral and electrophysiological studies indicate heterogeneous properties for this receptor. Although the basis for this heterogeneity is unknown, one possible explanation for these findings resides in the subunit composition of the receptor. Two 5-HT3-receptor subunits have been cloned: the 5-HT3-receptor subunit A (5-HT3A) and the 5-HT3-receptor subunit B (5-HT3B). Recombinant co-expression of 5-HT3A and 5-HT3B subunits produces a functional heteromeric 5-HT3A/3B receptor with pharmacological and electrophysiological properties different that those displayed by the 5-HT3A homomeric receptor. In the present report, IRP investigators used in situ hybridization histochemistry to demonstrate that the 5-HT3B subunit is expressed in rat dorsal root ganglion (DRG) neurons. Authors determined with cellular resolution that 5-HT3B subunit mRNA was expressed in 43.2%±2.8 of the total population of DRG neurons. By comparison, the 5-HT3A subunit was more widely expressed, with 70.0%±2.8 of the total population of DRG neurons expressing this subunit. Further analyses showed that most of the neurons containing mRNA for the 5-HT3B subunit (91.5%±3.4) also expressed the 5-HT3A subunit. In contrast, nearly half of the population of neurons expressing 5-HT3A subunit lacked (52.8±5.9) transcripts for the 5-HT3B subunit. These results provide the first evidence indicating that the 5-HT3B subunit of the 5-HT3 receptor is expressed in DRG, and suggest that sensory neurons have the capacity to synthesize at least two structurally different 5-HT3 receptors: a heteromeric 5-HT3A/3B receptor and a homomeric 5-HT3A receptor. Consequently, 5-HT3 receptors with different properties might be present in peripheral and central axons of the DRG. These findings open the possibility that distinct types of 5-HT3 receptors may be involved in perception and/or processing of sensory information. Furthermore, understanding the distribution, electrophysiological and pharmacological characteristics, as well as, possible participation of the different 5HT3 receptors in nociceptive perception and processing may be useful for the development of alternative drugs to opioid analgesics. Morales, M. McCollum, N., and Kirkness, E.F. 5-HT3-receptor Subunits A and B are Co-expressed in Neurons of the Dorsal Root Ganglion. Journal of Comparative Neurology, 438, pp. 163-172, 2001.

GFRa-1 mRNA in Dopaminergic and Non-dopaminergic Neurons in the Substantia Nigra and Ventral Tegmental Area

Glial cell line derived neurotrophic factor (GDNF) is a potent survival factor for several types of neurons, including dopaminergic (DAergic) neurons. GDNF binds with high affinity to the GDNF-family receptor a-1 (GFRa-1) that is highly expressed in the midbrain. Using anatomical and lesion techniques, IRP scientists demonstrated that GFRa-1 was expressed in DAergic and non-DAergic neurons in the rat midbrain. Immunohistochemical characterization of GFRa-1 expressing neurons indicated that 87%-92% of all neurons immunopositive for the DAergic marker tyrosine hydroxylase (TH) expressed GFRa-1 in the substantia nigra pars compacta (SNC). In contrast, nearly half (44%-66%) of TH containing neurons expressed GFRa-1 in the substantia nigra pars reticulata (SNR). Likewise, 50%-74% of TH-immunoreactive neurons expressed GFRa-1 in the ventral tegmental area (VTA). Depletion of GFRa-1/TH neurons was observed in the SNC following treatment with the neurotoxin 6-hydroxydopamine (6-OHDA); however, GFRa-1 expression remained in some neurons located in the SNR. The GABAergic nature of GFRa-1 expressing neurons located in the SNR which were resistant to 6-OHDA, was established by their expression of glutamic acid decarboxylase (GAD, the synthesizing enzyme for GABA). Semiquantitative analysis demonstrated rostrocaudal variability in the co-expression of GFRa-1 and GAD. Of all GAD expressing neurons, 5%-48% co-expressed GFRa-1 and GAD mRNAs in the SNR. Similar results were found in the substantia nigra pars lateralis (SNL) and VTA, where co-expression of GFRa-1 and GAD was present in 34%-52% of all GAD neurons in the SNL and 24%-45% of all GAD neurons in the VTA. Midbrain DAergic and GABAergic neurons have been previously classified according to their Ca2+ binding protein (CaBP) contents; thus, the authors also sought to investigate the proportion of midbrain GFRa-1 expressing neurons containing parvalbumin (PV), calbindin (CB) and calretinin (CR) in the midbrain. While GFRa-1 expression was found mainly in CB- and CR-immunoreactive neurons, it was rarely observed in PV immunolabeled neurons. Analysis of the proportion of GFRa-1 expressing neurons for each CaBP subpopulation indicated co-existence of GFRa-1 with CR in the VTA and all subdivisions of the SN, double labeled GFRa-1/CR neurons were distributed in the SNC (41%-67%), SNR (29%-50%), SNL (61%-90%) and VTA (40%- 62%). GFRa-1/CB neurons were also detected in the SNC (29%-42%), SNL (63%-84%) and VTA (31%-54%). This contrasts with the low proportion of GFRa-1/PV neurons (3%-16%), which were confined to the SNR. Expression of GFRa-1 in DAergic and non-DAergic neurons in the rat SN and VTA suggest that GDNF, via GFRa-1, might modulate DAergic and GABAergic functions in the nigrostriatal, mesolimbic and nigrothalamic circuits in the adult rat. Sarabi A., Hoffer, B.J., Olson, L. and Morales, M. GFRa-1 mRNA in Dopaminergic and Non-dopaminergic Neurons in the Substantia Nigra and Ventral Tegmental

Area. Journal of Comparative Neurology, 441 pp. 106-117, 2001.

Molecular Neuropsychiatry Section, Cellular Neurobiology Research Branch

Amphetamine-induced Toxicity in Dopamine Terminals in CD-1 and C57BL/6J Mice: Complex Roles for Oxygen-based Species and Temperature Regulation

In order to examine differential strain susceptibility to neurotoxic effects of amphetamine and to assess the potential role of superoxide radicals in amphetamine-induced dopaminergic damage, the drug was injected into mice with different levels of copper/zinc superoxide dismutase (Cu/Zn SOD) enzyme. Administration of amphetamine (10 mg/kg, i.p., given every 2 h, a total of four times) to wild-type CD-1 and C57BL/6J mice caused significant decreases in dopamine and 3,4-dihydroxyphenylacetic acid levels, in [(125)I]RTI-121-labeled dopamine transporters as well as a significant depletion in the concentration of dopamine transporter and vesicular monoamine transporter 2 proteins. The amphetamine-induced toxic effects were less prominent in CD-1 mice, which have much higher levels of Cu/Zn SOD activity (0.69 units/mg of protein) in their striata than C57BL/6J animals (0.007 units/mg of protein). Transgenic mice on CD-1 and C57BL/6J background, which had striatal levels of Cu/Zn SOD 2.57 and 1.67 units/mg of protein, respectively, showed significant protection against all the toxic effects of amphetamine. The attenuation of toxicity observed in transgenic mice was not caused by differences in amphetamine accumulation in wild-type and mutant animals. However, CD-1-SOD transgenic mice showed marked hypothermia to amphetamine whereas C57-SOD transgenic mice did not show a consistent thermic response to the drug. The data obtained demonstrate distinctions in the neurotoxic profile of amphetamine in CD-1 and C57BL/6J mice, which show some differences in Cu/Zn SOD activity and in their thermic responses to amphetamine administration. Thus, these observations provide evidence for possible complex interactions between thermoregulation and free radical load in the long-term neurotoxic effects of this illicit drug of abuse. Krasnova, I.N., Ladenheim, B., Jayanthi, S., Oyler, J., Moran, T.H., Huestis, M.A., and Cadet J.L. Neuroscience, 107(2), pp. 265-74, 2001.

Molecular Neurotoxicological Models of Parkinsonism: Focus on Genetic Manipulation of Mice

Parkinson's disease is a neurodegenerative disorder that affects mainly the nigrostriatal dopaminergic system in humans. Several propositions have been put forward to explain the cellular and molecular pathobiology of this syndrome. Initial attempts were made through the use of various agents to manipulate the deleterious effects of toxins that destroy dopaminergic cells both in vitro and in vivo. These studies led to the idea that oxidative stress is an important factor in killing these cells. More recent attempts have made use of genetically modified mice to eliminate or over-express genes of interest. These experiments have suggested that the destruction of dopaminergic cells might be the result of the convergence of dependent and independent molecular pathways and that trigger cellular events might lead to the demise of these dopaminergic cells. Cadet, J.L. Parkinsonism Related Disorders, 8(2), pp. 85-90, 2001.

Behavioral Neuroscience Section, Behavioral Neuroscience Research Laboratory

D1 Receptors and Cocaine Reinforcement

Robert Ranaldi at the University of Mississippi and Roy Wise in the IRP have found that blockade of D1-type dopamine receptors in the ventral tegmental area attenuates the rewarding effects of intravenous cocaine. D1-type and D2-type dopamine receptors are clearly localized to different cellular elements in this region; the D-1 type receptors are localized to GABA- and glutamate-containing nerve terminals. Dopamine is thought to reach these receptors as a result of release from dopaminergic dendrites, and the effects of blockade of these receptors is among the first to suggest functional importance for dendritic dopamine release other than autoregulation of dopaminergic cell firing via the D2-type autoreceptors that are localized on dopaminergic cell bodies. Among the interesting possibilities is that modulation of GABAergic output of the ventral tegmental area--output that is "downstream" from the rewarding effect of dopamine released in nucleus accumbens--may be part of the brain circuitry of cocaine reward. Ranaldi, R., Wise, R.A. Journal of Neuroscience, 21, pp. 5841-5846, 2001.

Incubation of Cocaine Craving

Performance of a response that has been repeatedly reinforced by intravenous cocaine is the most objective and reliable indication of cocaine craving in animal models. Responding in the absence of reinforcement at various intervals after the last cocaine reinforcement gives evidence of the time-course of changes in cocaine craving following periods of cocaine intoxication. Such time-course can then be correlated with the time-course of decay of

the various neuroadaptations that are caused by cocaine intoxication and that might be thought to contribute to states of cocaine craving. Jeffrey Grimm and colleagues have found evidence from this approach suggesting the cocaine craving, like learning and memory, increases as a function of the length of periods of "incubation" between the last intoxication and the first opportunity to respond again. Cocaine craving appears to continue to incubate for periods of two or more months after the last cocaine intoxication in laboratory rats. Grimm, J.W., Hope, B.T., Wise, R.A., and Shaham, Y., Nature, 412, pp. 141-142, 2001.

Addiction-prone and Addiction-resistant Rats; No Difference in Sensitivity to Cocaine Reward

Roy Wise and collaborators at Concordia University and the University of Nijmegen have found that Fischer and Lewis rats and high-responder and low-responder rats, known to be dramatically different in their likelihood to learn to self-administer intravenous cocaine, are very similar in their responsiveness to the rewarding actions of cocaine. The differences in acquisition of cocaine self-administration habits appear to result from differences in the animals' emotional responses to the testing environment rather than to any significant differences in sensitivity to the drug itself. Ranaldi, R., Bauco, P., McCormick, S., Cools, A.R., Wise, R.A. Behavioural Pharmacology, 12, pp. 527-534, 2001.

Psychobiology Section, Medications Discovery Research Branch

Comparison of Interactions of D1-like Agonists, SKF 81297, SKF 82958 and A-77636, with Cocaine: Locomotor Activity and Drug Discrimination Studies in Rodents

Recent data suggest that dopamine (DA) D1-like receptor full agonists may be potential pharmacotherapeutic agents for treating cocaine abuse. The structurally novel isochroman D1-like agonist, A-77636, has not been well characterized and may prove to be useful as such an agent. The interactions of cocaine and A-77636 were compared to those obtained with the better investigated benzazepine D1-like dopamine agonists, SKF 82958 and SKF 81297. The alterations in the locomotor stimulant and discriminative-stimulus effects of cocaine by the full D1-like dopamine receptor agonists were investigated across a full range of doses in order to characterize their interactions. In Experiment 1 mice were pretreated with SKF 81297, SKF 82958 or A-77636 (1-10 mg/kg) and cocaine (5-56 mg/kg) prior to a 30-min period in which locomotor activity was assessed. Cocaine maximally stimulated activity at 20-40 mg/kg with higher and lower doses stimulating activity less. Each D1-like agonist produced a dose-related decrease in cocaine-induced locomotor activity and lowered its maximal rate. In Experiment 2, rats were trained to discriminate saline from cocaine (10 mg/kg) injections. Each of the D1-like agonists partially substituted for cocaine. In combination with cocaine, SKF 82958 and SKF 81297 shifted the cocaine dose-effect curve to the left – effects of cocaine were enhanced. In contrast, A-77636 either did not affect the cocaine dose-effect curve or shifted it to the right. In conclusion, all three D1-like agonists produced similar effects on cocaine-induced locomotor activity, however the discriminative-stimulus effects of cocaine were attenuated by A-77636. These results suggest fundamental differences in the actions of these D1 agonists. Because A-77636 consistently attenuated the present effects of cocaine, it may prove more useful than the others as a pharmacotherapy to treat cocaine abuse. Chausmer, A.L. and Katz, J.L. Psychopharmacology, 155, pp. 69-77, 2001.

Cocaine-Induced Locomotor Activity And Cocaine Discrimination in Dopamine D2 Receptor Mutant Mice

Previous studies have found that dopamine D2-like antagonists block several effects of cocaine, including its stimulation of locomotor activity and interoceptive discriminative-stimulus effects. However, given the lack of selectivity of most of these compounds among D2, D3 and D4 dopamine receptors, the specific roles of these dopamine receptors remains unclear. The role of D2 dopamine receptors in the discriminative stimulus and locomotor stimulant effects of cocaine was investigated using dopamine D2 receptor knockout (DA D2R KO), heterozygous (DA D2R HET) and wild-type (WT) mice. In addition, the role of D2 receptors was further examined in studies of the antagonism of the discriminative-stimulus effects in these mice using the relatively selective DA D2-like antagonist, raclopride. Mice were treated with cocaine (5-56 mg/kg) or vehicle and their horizontal locomotor activity was assessed for a 30-min period. The same mice were trained (FR 20) to discriminate IP injections of saline from cocaine (10 mg/kg) using a 2 response-key food-reinforcement procedure. A range of doses of cocaine (1.0 - 17 mg/kg), either alone or in combination with raclopride (0.1-1.0 mg/kg) were administered prior to a 15 min test session. Both DA D2R KO and HET mice showed reduced levels of control horizontal locomotor activity compared to WT mice. Cocaine dose-dependently stimulated locomotor activity in the WT mice, and at the highest dose studied in the DA D2R KO and HET mice, though the stimulation produced in these subjects was not to the same level as even the control level in WT mice. All three genotypes acquired the discrimination of 10 mg/kg cocaine. Once trained there was

a dose-dependent generalization in each group, with doses of 1.0 to 10.0 mg/kg producing dose-related increases in the number of responses on the cocaine-appropriate key. In contrast, the D2 antagonist raclopride did not produce a proportion of cocaine-appropriate responding greater than 85% (full substitution). The doses of raclopride examined ranged from those having no effect to those decreasing response rates in WT mice. Raclopride dose dependently shifted the cocaine dose-effect curve to the right in DA D2R HET and WT mice, however in DA D2R KO mice raclopride was inactive as an antagonist. The present data indicate an involvement of D2 dopamine receptors in the locomotor-stimulating effects and the interoceptive discriminative-stimulus effects of cocaine in WT subjects. However, the D2 receptor is not necessary for the effects, suggesting redundant dopaminergic mechanisms in subjects with an intact DA D2R system for the discriminative-stimulus interoceptive effects of cocaine. Chausmer, A.L. and Katz, J.L. Psychopharmacology, Published online: 22 September 2001.

Medicinal Chemistry and Psychobiology Sections, Medications Discovery Research Branch

[3H]MFZ 2-12: A Novel Radioligand for the Dopamine Transporter

In an effort to develop a tritiated dopamine transporter radioligand with higher affinity than the widely used [3H]WIN 35,428, we have synthesized [3H]2b-carbomethoxy-3b-[3'4'-dichlorophenyl)tropane ([3H]MFZ 2-12). Unlabeled MFZ 2-12 and the N-demethylated intermediate (MFZ 2-13) inhibited dopamine uptake by the human dopamine transporter with IC50s of 1.1 and 1.4 nM, respectively. The N-nor-intermediate (MFZ 2-13) was treated with CT-3I resulting in [3H]MFZ 2-12, S.A.= 80 Ci/mmol. [3H]MFZ 2-12 reversibly bound with a KD of 2.8 nM to human dopamine transporter expressed heterologously in EM4 cells, which is ~20-fold higher affinity than [3H]WIN 35,428. Thus at a ligand concentration of 2.5 nM, ~50% occupancy is achieved with [3H]MFZ 2-12 in contrast to ~6% by [3H]WIN35,428. Since the nonspecific binding of these two ligands is a similar fraction of the total added counts and since they are of similar specific activity, at 2.5 nM the signal and the signal to noise ratio achieved with [3H]MFZ 2-12 are approximately ten times that observed with [3H]WIN 35,428. For these reasons, [3H]MFZ 2-12 is better suited for saturation analysis, filtration assays, and use with adherent cells expressing hDAT. Newman, A. H., Zou, M-F., Ferrer, J.V. and Javitch, J.A. Bioorganic Medicinal Chemistry Letters, 11, pp. 1659-1661, 2001.

Novel Tropane-based Irreversible Ligands for the Dopamine Transporter

Novel irreversible ligands for the dopamine transporter were prepared in order to provide the required molecular tools to further characterize the binding domains at which structurally divergent dopamine transporter inhibitors bind. We previously prepared a benztropine-based photoaffinity label, [125I]GA 2-34, that covalently attached to the 1-2 transmembrane spanning region of the dopamine transporter (DAT). This was in contrast to the 4-7 transmembrane spanning region labeled by a cocaine-based photoaffinity label, [125I] RTI 82. The syntheses of the target compounds were achieved using a modification of the strategy previously developed. Evaluation of these compounds for displacing [3H]WIN 35,428 binding at DAT in rat caudate-putamen revealed that the 4'-azido-3'-iodophenyl-butyl substituent provided optimal binding affinity and was chosen to replace the N-CH3 group on RTI 82. Both the 4'-azido-3'-iodophenyl- and the 4'-isothiocyanatophenylbutyl analogs were synthesized. Both products bound to DAT with comparable potency (IC50=30 nM) to RTI 82. In addition, the isothiocyanate demonstrated wash resistant displacement of [3H]WIN 35,428 in HEK 293 cells stably transfected with hDAT. Our lead compound, MFZ 2-24, was recently radioiodinated and preliminary studies show that it binds with high affinity and in a proteolytic-resistant manner to an 80 kDa protein from rat striatum, previously identified as the DAT. Future immunological and proteolytic studies with this compound, in comparison with other irreversible ligands previously prepared in this lab and others, will allow further characterization of the binding domains on the dopamine transporter. Zou, M., Kopajtic, T., Katz, J.L., Wirtz, S., Justice, Jr., J.J. and Newman, A.H. Journal of Medicinal Chemistry, 44, pp. 4453-4461, 2001.

Design and Synthesis of Novel Ligands Selective for the Dopamine D3 Receptor Subtype

The dopamine D3 receptor subtype has been recently targeted as a potential neurochemical modulator of the behavioral actions of psychomotor stimulants, such as cocaine. However, definitive behavioral investigations have been hampered by the lack of highly selective D3 agonists and antagonists. In an attempt to design a novel class of D3 ligands with which to study this receptor system, a series of chemically divergent compounds that possessed various structural features that exist within several classes of reputed D3 agents was screened and compared to the recently reported NGB 2904. Based on these results, a novel series of compounds was designed that included functional moieties that were required for high affinity and selective binding to D3 receptors. All the compounds in this series included an aryl-substituted piperazine ring, varying alkyl chain linker (C3-C5) and a terminal aryl amide. The compounds were synthesized and evaluated in vitro for binding in CHO cells transfected with human D2, D3, or D4 receptor cDNAs. D3 binding affinities ranged from Ki=1.4-1460 nM. The most potent analog in this series demonstrated a D3/D2 selectivity of 64 and a D3/D4 selectivity of 1300. Structure-activity relationships for this class of ligands at D3 receptors will provide new leads toward the development of highly selective and potent molecular

probes that will prove useful in the elucidation of the role D3 receptors play in the psychomotor stimulant and reinforcing properties of cocaine. Robarge, M.J., Husbands, S.M., Kieltyka, A., Brodbeck, R., Thurkauf, A. and Newman, A.H. Journal of Medicinal Chemistry, 44, pp. 3175-3186, 2001.

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Director's Report to the National Advisory Council on Drug Abuse
February, 2002

Program Activities

New NIDA PAs and RFAs

On October 19, 2001, NIDA released a Program Announcement entitled **Role of Limbic System and Brain Ontogeny in Drug Abuse (PA-02-015).** This initiative is designed to support basic research into the fundamental mechanisms of development of the midbrain and basal forebrain structures that mediate the euphoric properties of drugs as well as understanding how drugs of abuse affect the cellular and molecular mechanisms underlying nervous system development. This PA replaces in its entirety PA-98-032, published in the NIH Guide February 25, 1998.

On October 22, 2001, NIDA issued a Program Announcement entitled **Minority Institutions' Drug Abuse Research Development Program (MIDARP) (PAR-02-016).** The purpose of this PA is to increase the capacity of minority institutions with limited sponsored reseach experience in the biomedical, social and behavioral sciences to conduct research in drug abuse and addiction. Grants will be provided to develop the capacity of minority institutions and their minority faculty, staff and students, in particular, to conduct rigorous drug abuse research in all areas of research supported by NIDA including neuroscience, epidemiology, behavioral, clinical, social science, public health, biological, HIV/AIDS, health disparities and health services areas.

On November 20, 2001, NIDA issued a new RFA entitled **Expansion of the National Drug Abuse Treatment Clinical Trials Network (DA-02-003).** Through this RFA, NIDA invites cooperative agreement applications from established clinical investigators to participate in the National Drug Abuse Treatment Clinical Trials Network (CTN). Applications from geographic areas not currently well represented in the CTN are particularly encouraged. This RFA is the third solicitation for participation in the CTN. Letter of Intent Receipt Date for this RFA is January 22, 2002; Receipt date for applications is February 22, 2002.

On November 26, 2001, NIDA issued a new RFA entitled **Inhalant Abuse: Supporting Broad-Based Research Approaches (DA-02-002).** Through this RFA, NIDA requests applications to broaden the understanding of the epidemiology, social, behavioral, cognitive, and neurobiological consequences, treatment and prevention of inhalant abuse. Letter of Intent Receipt Date for this RFA is March 12, 2002; Application Receipt Date is April 10, 2002.

NIDA released a new RFA on December 6, 2002 entitled **Modifying and Testing Efficacious Behavioral Therapies to Make Them More Community Friendly (DA-02-006).** The purpose of this initiative is to support studies that will adapt existing, efficacious behavioral therapies for community treatment settings, or prepare for such adaptation by identifying key components of efficacious therapies to be retained in adapted therapies. Letter of Intent Receipt Date for this RFA is March 11, 2002; Application Receipt Date is April 11, 2002.

On December 31, 2001, NIDA issued an RFA entitled **New Approaches to Prevent HIV/Other Infections in Drug Users (DA-02-009).** The purpose of this RFA is to stimulate research on the development of new, improved, and innovative intervention approaches to prevent HIV and other blood-borne and sexually transmitted infections in drug users and their sexual partners. Letter of Intent Receipt Date for this RFA is March 18, 2002; Application Receipt Date is April 16, 2002.

In December 2001, NIDA released three RFAs in support of its new National Prevention Research Initiative (NPRI), comprised of three components: 1) **Using Basic Science to Develop New Directions in Drug Abuse Prevention Research (DA-02-010), 2) Transdisciplinary Prevention Research Centers (TPRCs) (DA-02-005), and 3)**

Community Multi-Site Prevention Trials (CMPT) (DA-02-004). The purpose is to accelerate the development and testing of new prevention interventions through translational research that spans a continuum from basic science through laboratory efficacy testing to small- and large-scale field effectiveness studies.

On January 23, 2002, NIDA issued an RFA entitled **Hepatitis C Diagnosis, Treatment and Interaction with HIV/AIDS (DA-02-008).** The primary intent of this RFA is to support studies that relate directly to the development and testing of protocols for hepatitis C diagnosis and treatment in drug abusing populations, so as to provide data essential to the formulation of clinical guidelines in these areas. Letter of Intent Receipt Date for this RFA is March18, 2002; Application Receipt Date is April 16, 2002.

On February 4, 2002, NIDA released an RFA entitled **National Criminal Justice Drug Abuse Treatment Research System (DA-02-011).** Through this RFA, NIDA invites cooperative agreement applications to participate in the National Criminal Justice Drug Abuse Treatment Research System (CJ-DATS). Awardees will conduct and participate in coordinated multi-site studies to conduct rigorous scientific research with offender populations across multiple settings including jails, prisons, and in the community. The goal of this cooperative research program is to establish a research infrastructure to develop and test research-based systems-level models that integrate public health and public safety approaches for criminal justice-involved individuals with addictive disorders. Letter of Intent Receipt Date for this RFA is April 12, 2002; Application Receipt Date is May 13, 2002.

Recent PAs/RFAs Issued In Collaboration with Other NIH Components

Research on HIV/STD Prevention Messages (PA-01-139)

Neurotechnology Research, Development and Enhancement (PA-02-003)

Bioenginnering Research Partnerships (PAR-02-010)

Bioenginnering Research Grants (PA-02-011)

Jointly Sponsored NIH Predoctoral Training Program in the Neurosciences (PAR-02-017)

Planning Grants to Organize Programs for International Clinical, Operational, and Health Services Research Training for AIDS and Tuberculosis (PA-02-022)

Development of PET and SPECT Ligands for Brain Imaging (SBIR Award) (PA-02-028)

Social and Cultural Dimensions of Health (PA-02-043)

Identifying Functional Links Between the Immune System and Brain Function Including Behavior (PA-02-045)

Dissertation Research Grants for Underrepresented Minorities in the Ethical, Legal and Social Implications (ELSI) of Genetics Research (PA-02-048)

Interrelationship Between Sleep and Heart, Lung and Blood Diseases (RFA-HL-01-009)

Development of PET and SPECT Ligands for Brain Imaging (Phased Innovation Award) (RFA-MH-02-003)

Neuroimaging Technology Development to Assess Brain and Behavior in Pediatric Populations (RFA-DA-02-001)

Elucidation of the Underlying Mechanisms of Placebo Effect (RFA-AT-02-002)

Studies of the Ethical, Legal and Social Implications (ELSI) of Human Genetic Variation Research for Individuals and Diverse Racial and Ethnic Groups (RFA-HG-02-003)

International Collaborative Genetics Research Training Program (RFA-TW-02-001)

Specialized Centers of Research on Sex and Gender Factors Affecting Women's Health (RFA-OD-02-002)

Other Program Activities

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 their clinical participation on January 6, 2002 and their 30-day follow-up on February 6, 2002. There have been 38 physicians' offices and 33 pharmacies that participated in this study. 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. The breakdown of patients, by race, was 78.4% white, 8.1% black, 1.9% Asian/Pacific Islander, 1.0% Native American, and 10.5% other. Additionally, 17% of the patients identified themselves as Hispanic. As of October 16, 2001, 114 patients had completed, and 126 were still following the protocol. The main reasons for dropout were failure to return to clinic (67%) followed by the patient's request to discontinue (7.3%).

CTN Protocol Update

CTN 0001 (Buprenorphine/Naloxone for Detoxification in Inpatient Settings)--six sites across five nodes have begun enrollment. Total enrollment has reached about one-third of the total target enrollment.

CTN 0002 (Buprenorphine/Naloxone for Detoxification in Outpatient Settings)--all six sites across five nodes are enrolling patients. Total enrollment has reached over two-thirds of the total target enrollment.

CTN 0003 (Buprenorphine/Naloxone: Comparison of Three Taper Schedules for Opiate Detoxification)--thirteen sites across eight nodes are set to begin enrollment in January 2002.

CTN 0004 (Motivational Enhancement Therapy)--four sites have begun enrolling, two additional sites will be launched soon.

CTN 0005 (Motivational Interviewing)--all five sites are currently enrolling patients. Total enrollment has reached nearly half of the total target enrollment.

Spanish versions of protocol CTN 0004 and CTN 0005 are being developed for new Spanish-speaking enrollees.

CTN 0006 (Motivational Incentives in Drug Free Clinics)--four sites are currently enrolling patients, another four sites will begin enrollment in the next month. Total enrollment has reached about one-fifth of the target enrollment.

CTN 0007 (Motivational Incentives in Methadone Clinics)--six sites across four nodes are enrolling patients. Total enrollment has reached about one-third of the target enrollment.
Five new protocols are in the final stages of approval before being launched in the CTN. It is expected that all five will be enrolling by this summer. Seven new research concepts were reviewed and approved for further development into protocols. These will be launched in the fall or winter. By the end of 2002, it is projected that nineteen protocols will be actively enrolling patients throughout the CTN.

CTN Support Contracts Awarded

Three new contracts were awarded in September 2001 to support CTN activities. These are: NO1DA-1-2200, entitled Clinical Trials Network Pharmacy Support; NO1DA-1-2201, entitled Clinical Trials Network Administrative Support Center; and NO1DA-1-2204, entitled Clinical Laboratory Services.

NIDA Evaluation of the ONDCP Media Campaign

NIDA and ONDCP released the third report of findings from the Evaluation of the National Youth Anti-Drug Media Campaign, conducted under contract to NIDA by Westat, Inc., and the Annenberg School for Communications, University of Pennsylvania, in November. This report, entitled Evaluation of the National Youth Anti-Drug Media Campaign: Third Semi-Annual Report of Findings, October 2001, reported on the attitudes, beliefs and behaviors of parents and youth during the third wave of data collection, covering the period from January-June 2001. Trend data reflects comparisons between Wave 3 and Wave 1, covering November 1999-May 2001, the baseline for comparison. NIDA and Westat briefed ONDCP senior staff and the campaign team in late November.

The following are some of the highlights:

- There are substantial levels of recalled exposure to Campaign anti-drug messages among parents and youth. Among parents, approximately 70% recalled seeing general anti-drug ads at least once a week across all media; about 20% recalled seeing specific Campaign TV ads. Among youth, close to 80% recalled seeing general anti-

drug ads at least once a week; close to 50% recalled seeing specific Campaign TV ads. Youth recall of specific TV ads significantly increased from 35% in Wave 1 to 48% in Wave 3.

- The branding innovation of the Campaign—i.e., "The Anti-Drug"—was recalled by 60% of 12-to-18-year-olds and 46% of parents.
- There is evidence consistent with a Campaign effect on parents. There are positive changes in four out of five outcomes including talking about drugs with, and monitoring of, children. Also, parents who report more exposure to Campaign messages report better scores on those outcomes—talking and monitoring attitudes and behaviors. There is also an indication that these outcomes are associated with youth anti-drug intentions and behaviors.
  - Fathers appeared to be changing more in their attitudes and behaviors and these changes are associated with general and specific ad exposure —e.g., they have increased in their positive beliefs about the value of monitoring from 65% in Wave 1 to 86% in Wave 3. They also increased in actual monitoring behaviors.
- Thus far there is little evidence of direct Campaign effects on youth. There is no statistically significant change in marijuana use or in beliefs and attitudes about marijuana use, and no tendency for those reporting more exposure to Campaign messages to hold more desirable beliefs.
- Future semiannual reports will include follow-ups of those parents and children interviewed at Waves 1-3. This will provide data on how youth drug-related attitudes and behaviors change as they age into the more at-risk teenage years and how exposing to Campaign messages is affecting those attitudes and behaviors. There will be more examination of over-time effects; examination of some indirect effects—e.g., the effects of parents' attitudes and behaviors on youth marijuana use; and more capability of analyzing whether the Campaign is producing the preventive effects on drug use.

PET Imaging of Brain Nicotinic Acetylcholine Receptors with 2-[18F]F-A-85380 Injection

NIDA's Brain Imaging Center has received approval for a Phase I Investigator-Sponsored IND (Investigation New Drug) application from the Food and Drug Administration entitled, "PET Imaging of Brain Nicotinic Acetylcholine Receptors with 2-[18F]F-A-85380 Injection." The IND allows the Brain Imaging Center to initiate the first human studies in the United States using this new radiotracer, which was specifically developed to image alpha4beta2 nicotinic receptors in the brain using positron emission tomography (PET). The compound [18F]2-F-A-85380 has both high affinity and selectivity for the alpha4beta2 subtype of nicotinic receptor and has a wide margin of safety. This subtype of the nicotinic receptor comprises the primary form found within the brain and is thought be associated with receptors linked to nicotine dependence and the loss of nicotinic receptors observed in neurodegenerative diseases. [18F]2-F-A-85380 was developed by a team of radiochemists and neuroscientists at the Brain Imaging Center and represents the first new radioligand to be both produced for and evaluated in humans within the laboratory. The team of investigators includes Alane S. Kimes, PhD., Carlo Contoreggi, M.D., Andrew G. Horti, Ph.D., Svetlana I. Chefer, Ph.D., Andrei O. Koren, Ph.D., Edythe D. London, Ph.D., Alexey G. Mukhin, M.D., Ph.D., Olga Pavlova, M.D., Ph.D., Monique Ernst, M.D., Ph.D., John A. Matochik, Ph.D., and Varughese Kurian, M.S., M.H.S.

SIP and MRTP Programs

The NIH Summer Internship Program (SIP) and the Minority Recruitment & Training Program (MRTP) are now accepting applications for the Summer 2002. Both programs provide training opportunities for students who are interested in the scientific basis of drug abuse. In this program, students gain basic science and/or clinical laboratory experience, attend student seminars, and participate in a summer poster presentation. The goal of this program is to expose students to the realities of research, from experimental design to data analysis, interpretation and presentation. For information and an application for the SIP, go to www.training.nih.gov or contact Dr. Stephen Heishman (sheish@intra.nida.nih.gov). For an application or to receive information about the MRTP, contact Christie Brannock (cbrann@intra.nida.nih.gov)

NIDA's New and Competing Grants Awarded Since September 2001

Adler, Martin -- Temple University
Opioids, Cannabinoids, Chemokines--Neuroimmune Interaction

Akil, Huda -- University of Michigan at Ann Arbor
Stress/Vulnerability To Drug Abuse: Neural Correlates

Alger, Bradley E. -- University of Maryland Baltimore Prof School

Endocannabinoids and GABAergic Control of Plasticity

Anderson, Richard G. -- University of Texas SW Medical Center/Dallas
Identification of Marker Proteins for Neuronal Caveolae

Anthony, James C. -- Johns Hopkins University
Clusters of Drug Involvement In Chile

Atkinson, Nigel S. -- University of Texas Austin
Abused Inhalants and Drosphila K+ Channel Transcription

Bajjalieh, Sandra M. -- University of Washington
The Role of Ceramide Kinase in Neurosecretion

Baker, Lisa E. --Western Michigan University
GHB: Discrimination and Effects on Learning

Ball, Samuel A. -- APT Foundation, Inc.
Psychotherapy Enhancement for TC Retention

Beals, Janette L. -- University of Colorado Health Sciences Center
Drug Use and Health Disparities In 2 Indian Populations

Bergmeier, Stephen C. -- Ohio University Athens
Analogues of Methyllycaconitine

Berns, Gregory S. --Emory University
Hyperscan: Simultaneous FMRI Across the Internet

Bidlack, Jean M. -- University of Rochester
Opioid Binding to U51: A Human Herpes Virus Protein

Bidlack, Jean M. -- University of Rochester
Opioid Modulation of Immunocompetence

Blakely, Randy D. -- Vanderbilt University
A Neurogenomic Model for Dopamine Transporter Regulation

Bockting, Walter -- University of Minnesota Twin Cities
Gender Identity and HIV Risk

Booth, Brenda M. -- University of Arkansas Medical Sciences Little Rock
Cocaine and Chest Pain: ER Patient Care and Outcomes

Borkowski, John G. -- University of Notre Dame
Predicting and Preventing Neglect In Teen Mothers

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

Boyer, Edward W. -- Children's Hospital (Boston, MA)
Relationship Between the Internet and Illicit Drug Use

Breiter, Hans C. -- Massachusetts General Hospital
Cocaine Addiction--Alterations In Reward Circuitry

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

Brown, Richard A. -- Butler Hospital (Providence, RI)

Applying Exercise Intervention To Drug Treatment

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

Bucholz, Kathleen K. -- Washington University
Gene-Enviroment In Outcomes of PSUD Twins' Offspring

Bucholz, Kathleen K. -- Washington University
Symptom Based Transitions In Addiction In Male Twins

Buckley, Todd C. -- Boston University
Nicotine, Attention, and Conditioned Arousal In PTSD

Budney, Susan E. -- Weill Medical College of Cornell University
Trauma and Addicted Female Offenders Treatment Outcome

Busto, Usoa E. -- Center for Addiction and Mental Health
Brain Reward System, Depression and Nicotine Dependence

Buydens-Branchey, Laure B. -- Narrows Institute for Biomedical Research, Inc.
Effects of Buspirone In Withdrawal From Opiates

Byrnes, Elizabeth M. -- Tufts University Boston
Reproductive Consequences of Pubertal Morphine Abuse

Campbell, James S. -- Biographics, Inc.
System to Test Medications Developed to Treat Drug Abuse

Carelli, Regina M. -- University of North Carolina Chapel Hill
Combined Voltammetry/Electrophysiology In Behaving Rats

Carey, Robert J. -- Central New York Research Corporation
A Study of Stimulant Induced Conditioned Drug Effects

Carlezon, William A. -- McLean Hospital (Belmont, MA)
A Simple Behavioral Model of Cocaine Withdrawal In Rats

Carroll, Marilyn E. -- University of Minnesota Twin Cities
Vulnerability To Drug Abuse--Experimental Interventions

Carvajal, Scott C. -- University of Arizona
Determinants of Latino/European American Youths' Substance Use

Celentano, David D. -- Johns Hopkins University
Reducing Youth Drug Related HIV/STD Risk In Thailand

Clark, D. J. -- Videodiscovery
Neuroscience Digital Library

Clark, Duncan B. -- University of Pittsburgh at Pittsburgh
Drug Addiction Transitions from Adolesence to Adulthood

Clark, Vincent P. -- University of Connecticut School of Medicine and Dentistry
Neural Function In Cocaine Dependence and Relapse

Clayton, Richard R. -- University of Kentucky
Drug Abuse Prevention - A Lifecourse Perspective

Cobb, Melanie H. -- University of Texas SW Medical Center/Dallas

Protein Kinase Substrates for Assays In Single Neurons

Colder, Craig R. -- State University of New York at Buffalo
Disinhibition and Risk For Early Substance Use

Costello, Elizabeth J. -- Duke University
Prepubertal Comordity: Gender & Developmental Heterotypy

Cottler, Linda B. -- Washington University
Tricity Study of Club Drug Use, Abuse and Dependence

Crunelli, Vincenzo -- University of Wales
Electrophysiological Action of GHB In Brain Reward Areas

Dannals, Robert F. -- Johns Hopkins University
Design/Charcterization of Alpha-7 Nicotinic Radioprobes

Davis, Michael S. -- Inflexxion, Inc.
Multimedia Divorce Education

Davis, Michael S. -- Innovative Training Systems
Multimedia Divorce Adjustment For Young Children

De La Garza Ii, Richard -- Yeshiva University
Depression Enhances Vulnerability To Cocaine Relapse

Dehaven, Robert N. -- Adolor Corporation
Discovery of K Opioid Analgesics Using Chimeric Receptor

Dehaven, Robert N. -- Adolor Corporation
Novel Cannabinoid Receptor Agonists As Analgesics

Detrick, Pamela L. -- Westcare California, Inc.
Treatment of PTSD In Women In A Therapeutic Community

Difranza, Joseph R. -- University of Massachusetts Medical School
Transition of Nicotine Dependence

Dugovic, Christine -- Northwestern University
Importance of Sleep & Genotype In Drug Abuse Studies

Durell, Jack – Deltametrics
Substance Abuse Treatment Planning & Placement Systems

Dusenbury, Linda A. -- Tanglewood Research, Inc.
All Stars Plus: Enhanced Competency and Skills Training

Easa, David -- University of Hawaii at Manoa
Planning Grant For Clinical Research Training

Ellen, Jonathan M. -- Johns Hopkins University
Drug Use and HIV Infected Female Adolescents' Care Use

Elman, Igor -- Massachusetts General Hospital
Neuroimaging of Drug Craving In Cocaine Dependence

Ensminger, Margaret E. -- Johns Hopkins University
A High Risk Prospective Study of Drug Use and Crime

Estape, Estela S. -- University of Puerto Rico Medical Sciences

Postdoctoral Master In Clinical Research

Evans, Thomas G. -- University of California Davis
North-Central California-Center For AIDS Research

Farrens, David L. -- Oregon Health & Science University
Purification & Structural Analysis/Cannabinoid Receptor

Feldman, Michael J. -- New York State Psychiatric Institute
Adolescent Substance Use, Suicide and Sexual Orientation

Feldman, Steven R. -- Wake Forest University
Reinforcing Properties of UV Light In Tanning Bed Users

Ferris, Craig F. -- University of Massachusetts Medical School
MRI of Brain Function and Receptors In Cocaine Addiction

Festinger, David S. -- Treatment Research Institute, Inc. (TRI)
Ethics of Participant Payment In Drug Abuse Research

Fishbein, Diana H. -- Research Triangle Institute
Neurocognitive Prerequisites For Preventing Drug Abuse

Flay, Brian R. -- University of Illinois at Chicago
The Positive Action Program: Outcomes and Mediators

Fleming, Michael F. -- University of Wisconsin Madison
Opioid Addiction In Primary Care Chronic Pain Patients

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

France, Charles P. -- University of Texas Health Sciences Center San Antonio
GHB Abuse--Chemistry and Neurobiology

Fricker, Lloyd D. -- Yeshiva University
Prosaas, A Novel Peptide Substrate of Carboxypeptidase E

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

Fung, Ho-Leung -- State University of New York at Buffalo
Toxicokinetics and Toxicodynamics of GHB and Precursors

Galli, Aurelio A. -- University of Texas Health Sciences Center San Antonio
Molecular Mechanisms of Stimulant Abuse

Gant, Larry M. -- University of Michigan at Ann Arbor
HIV Risk Reduction For Drug Dependent Black Men

Garavan, Hugh P. -- Medical College of Wisconsin
The Role of Executive Functions In Cocaine Abuse

Gelberg, Lillian -- University of California Los Angeles
Homeless Women--Drugs, Race/Ethicity, and Health Care

George, Tony P. -- Yale University
Optimizing Treatment For Schizophrenic Smokers

Gerber-Allred, Carol M. -- Positive Action, Inc.

A Web Site and CD-Rom For 6th Graders on Drug Prevention

Gerber-Allred, Carol M. -- Positive Action, Inc.
Interactive CD-Rom & Website For Monitoring & Training

Gerhardt, Greg A. -- University of Kentucky
Neurochem Chip: Study of Neurotransmitter Release

Gevins, Alan S. -- Sam Technology, Inc.
nNice (Neurocognitive Index Of Cannabis Effects) System

Gibb, James W. -- University of Utah
Differential Effects of Methamphetamine and Cocaine

Giles, Steven M. -- Tanglewood Research, Inc.
Building Teacher Mastery Via An Internet Training System

Goda, Yukiko -- University of California San Diego
Synapse Remodeling on Photoconductive Silicon Interface

Gogineni, Aruna -- Brown University
Drug Reduction Intervention For Needle Exchange Clients

Grabowski, John G. -- University of Texas Health Sciences Center Houston
Opioid Maintenance: Optimal Stabilization & Withdrawal

Greenbaum, Paul E. -- University of South Florida
Mapping Substance Abuse Service Use

Greenblatt, David J. -- Tufts University Boston
Haart Regimens In Substance Abusers

Griffin, Kenneth W. -- Weill Medical College of Cornell University
Ethnic Differences In Competence and Adolescent Drug Use

Groopman, Jerome E. -- Beth Israel Deaconess Medical Center
Pathogenesis of Hepatic Injury With HCV/HIV Coinfection

Hagan, Holly C. -- Seattle-King County Public Health Department
Etiology and Prevention of Blood Borne Viruses In IDUs

Hall, Sharon M. -- University of California San Francisco
Maintaining Nonsmoking: Treatment of Older Smokers

Hallfors, Denise D. -- University of North Carolina Chapel Hill
Research To Practice: An Indicated Prevention Program

Hammett, Theodore -- ABT Associates, Inc.
Cross Border HIV Prevention Project--China and Vietnam

Hansen, William B. -- Tanglewood Research, Inc.
Drug Prevention In High Schools: All Stars, Sr.

Hatsukami, Dorothy K. -- University of Minnesota Twin Cities
Interventions For Tobacco Dependent Adolescents

He, Zhigang -- Children's Hospital (Boston, MA)
Signaling Mechanisms Mediating Effects of Semaphorin3a

Heberlein, Ulrike A. -- University of California San Francisco

Molecular Genetics / Nicotine-Induced Behaviors / Drosophila

Heimer, Robert -- Yale University
HIV Transmission In Russia Through Liquid Drug Injection

Hemby, Scott E. -- Emory University
Molecular Fingerprint of Cocaine Abuse Analysis

Hemby, Scott E. -- Emory University
Accumbens-Pallidal GABA and Morphine Reinforcement

Herting, Jerald R. -- University of Washington
Differential Effectiveness In Drug Prevention Programs

Hochhaus, Guenther -- Nanocoat Technologies
Slow Release Coatings For Inhaled Dynorphins

Hoebel, Bartley G. -- Princeton University
Accumbens Acetylcholine In A Neural Circuit For Aversion

Hogue, Aaron T. -- Fordham University
Adherence and Competence In Adolescent Drug Use Therapy

Holtz, Kristen D. -- Danya International, Inc.
Research Club For Elementary School-Aged Students

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

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

Hutchison, Kent E. -- University of Colorado at Boulder
Progression of Craving and Addiction: Genetic Factors

Iguchi, Martin Y. -- RAND Corporation
Partner-Oriented Drug Treatment and HIV Risk Reduction

Irvine, A. B. -- Oregon Center For Applied Science
Interactive Training For Parents of At-Risk Adolescents

Izenwasser, Sari -- University of Miami
Behavioral Consequences of Drug Exposure In Adolescents

Jacobs, Russell E. -- California Institute of Technology
In Vivo Imaging of Neuronal Activity - After the Fact

Jacobsen, Leslie K. -- Yale University
Smoking, Brain Function and Outcome In Adolescents

Janda, Kim D. -- Scripps Research Institute
Immunopharmacotherapy for the Treatment of Cocaine Abuse

Jarbe, Torbjorn U. -- Temple University
Exogenous / Endogenous Cannabinoids--A Comparison

Javitch, Jonathan A. -- Columbia University Health Sciences
Archaeal & Bacterial Homologs of Dopamine Transporter

Jerome, Albert -- Behavioral Research Associates, Inc.

Netschedules: Internet-Based Gradual Smoking Cessation

Johnson, James R. -- James R. Johnson and Associates, LLC
Long Acting Naltrexone Biodegradable Injectable Gel

Kandel, Denise B. -- Columbia University Health Sciences
Epidemiological/Familial Aspects of Drug Use

Kandel, Denise B. -- Columbia University Health Sciences
Transition To Nicotine Dependence In Adolescence

Kelsoe, John R. -- University of California San Diego
Microarray Studies of Amphetamine Models of Psychosis

Khroyan, Taline V. -- SRI International
Nicotine Self Administration In Mice

Kinlock, Timothy W. -- Friends Research Institute, Inc.
Motivational Enhancement For Drug Court Probationers

Kirstein, Cheryl L. -- University of South Florida
Effects of Cocaine on the Developing Nucleus Accumbens

Klein, Laura -- Pennsylvania State University
Oral Nicotine Consumption In Periadolescent Mice

Klepinger, Daniel H. -- Battelle Centers/Public Health Research & Evaluation
Family, Drug Use, and Disparities In Adverse Outcomes

Knight, Danica K. -- Texas Christian University
Social Stress Among Mothers In Treatment

Krebs, Christopher P. -- Research Triangle Institute
Trends In Club Drug Use

Kumar, Anil -- University of Kansas Medical Center
Efffects of Opiate Virus/Host Response In SHIV

Lesage, Mark G. -- Minneapolis Medical Research Foundation, Inc.
Modeling Behavioral Treatments For Nicotine Dependence

Lester, Barry M. -- Emma Pendleton Bradley Hospital
Prenatal Methamphetamine Exposure and Child Development

Li, Jianghong -- Hispanic Health Council
Sociocultural Factors on Syringe Sharing and HIV Risks

Liang, Yiqing -- Clever Systems, Inc.
High Throughput Phenotyping: Drug Effects on Homecage Mouse Behavior

Liu, Ming -- Novascreen Biosciences Corporation
Identification of Novel D1 Selective Agonists

London, Edythe D. -- University of California Los Angeles
Nicotine Withdrawal, Smoking & Cognition: An FMRI Study

Lord, Sarah E. -- Inflexxion, Inc.
Next Edition: Multimedia Adolescent Drug Prevention

Lukas, Scott E. -- McLean Hospital (Belmont, MA)

Polydrug Abuse Imaging and Behavior

Macalino, Grace E. -- Brown University
IDU Access To HIV/HCV Prevention

Malow, Robert M. -- University of Miami
HIV Prevention For Adolescents: Research To Practice

Manev, Hari -- University of Illinois at Chicago
GHB and GABA-B Receptor In Drosophila

Marcelin, Louis H. -- University of Miami
Haitian Youth: Risk of Drug Use and HIV Infection

Mark, Gregory P. -- Oregon Health & Science University
Central Cholinergic Involvement In Cocaine Addiction

Marlowe, Douglas B. -- Treatment Research Institute, Inc. (TRI)
Services Research on Sanctions/Rewards In Drug Court

Marrocco, Richard T. -- University of Oregon
The Neurochemistry of Visuospatial Attention

Marsch, Lisa A. -- Healthsim, Inc.
Applying Web Technology To Buprenorphine Treatment

Marsch, Lisa A. -- University of Vermont
Chemotherapy for Opioid-Dependent Adolescents

Marsiglia, Flavio -- Arizona State University
Drug Resistance Strategies: The Next Generation

Martinez, Charles R. -- Oregon Social Learning Center, Inc.
A Parent Intervention To Prevent Latino Youth Drug Use

Martinez-Maldonado, Manuel -- Ponce School of Medicine
Master Degree In Public Health at Ponce School of Medicine

Mash, Deborah C. -- University of Miami
Rapid Screening Method: Gamma-Hydroxybutyrate Detection

Matsumoto, Rae R. -- University of Oklahoma Health Sciences Center
Synthesis & Evaluation of Cocaine Antagonists

McCoy, Clyde B. -- University of Miami
Drug Abuse and AIDS Research Center at University of Miami

McCoy, Clyde B. -- University of Miami
Alternative Strategies In the Prevention of HIV/STDs

Mcgaugh, James L. -- University of California Irvine
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Meaney, Michael J. -- McGill University
Individual Differences In Mesolimbic Dopamine Systems

Mello, Nancy K.-- McLean Hospital (Belmont, MA)
Cocaine Abuse and the Role of Gonadal Steroid Hormones

Meucci, Olimpia -- MCP Hahnemann University

Role of Chemokine Receptors In Neuronal Survival

Mezzich, Ada C. -- University of Pittsburgh at Pittsburgh
Female Adolescent Drug Abuse: Biobehavioral Development

Michael, Adrian C. -- University of Pittsburgh at Pittsburgh
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Michels, Peter C. -- Albany Molecular Research, Inc.
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Milby, Jesse B. -- University of Alabama at Birmingham
Abuse Therapies for the Homeless

Mintzer, Miriam Z. -- Johns Hopkins University
Neuroimaging of Benzodiazepine-Induced Amnesia

Mody, Istvan -- University of California Los Angeles
Mechanisms/GHB/Models/Acute/Chronic GBH Intoxication.

Mogil, Jeffrey S. -- McGill University
QTL Mapping of Multiple Analgesic Modalities

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

Murguia, Edward E. -- Texas A&M University System
Youth, Technology, and the Proliferation of Drug Use

Naar-King, Sylvie -- Wayne State University
Motivational Therapy/Reduce Risk Behaviors/HIV/Youth

Nader, Michael A. -- Wake Forest University
Transition To Cocaine Abuse In Monkey: Role of Dopamine

Nagarkatti, Mitzi -- Virginia Commonwealth University
Cannabinoid-Induced Apoptosis of Immune Cells

Nagy, Andras -- Samuel Lunenfeld Research Institute
New Directions In Mutagenized Es Cell Libraries

Neaigus, Alan -- National Development & Research Institutes
Network Risks Among Injecting Drug Users

Neff, James A. -- University of Texas Austin
Research Program on Drug Abuse Interventions

Nemes, Susanna -- Danya International, Inc.
Smoking Cessation Intervention For Youth

Neumeyer, John L. -- McLean Hospital (Belmont, MA)
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Norris, Keith C. -- Charles R. Drew University of Medicine & Science
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Electrophysiology of Behavioral Sensitization

O'Dowd, Diane K. -- University of California Irvine
Role of Nicotine In Regulation of naChRs In Drosophila

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

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Planning Grant For Clinical Research Training

Ondersma, Steven J. -- Wayne State University
Interactive Motivational Media For Perinatal Drug Abuse

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Clinical Research To Improve Drug Abuse Treatment Entry

Owens, Samuel M. -- University of Arkansas Medical Sciences Little Rock
Preclinical Testing of Antibody Therapy for Meth Abuse

Paul, Robert H. -- Miriam Hospital
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Anatomical Basis For Nicotine Addiction In Mice

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

Pilowsky, Daniel J. -- Columbia University Health Sciences
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Piomelli, Daniele -- University of California Irvine
Endocannabinoid Release and Inactivation

Pitt, Jane R. -- Columbia University Health Sciences
Women and Infants Transmission Study (WITS IV)

Poland, Russell E -- Cedars-Sinai Medical Center
Developmental Exposure To Nicotine

Polich, John M. -- Scripps Research Institute
Neuroelectric Assessment of MDMA (Ecstasy) Use In Adults

Price, Rumi K. -- Washington University
Follow-Up of Vietnam Veterans at Risk For Suicide

Pruitt, Steven C. -- Roswell Park Cancer Institute Corp.
Development of A High Throughput Gene Trap Vector

Rao, Uma -- University of California Los Angeles
Markers of Risk For Nicotine Dependence In Youngsters

Regan, Jeffrey F. -- Dermal Systems International, Inc.
A Novel Drugs-of-Abuse Longitudinal Abstinence Monitor

Reich, Theodore -- Washington University
The Collaborative Genetic Study of Nicotine Dependence

Renshaw, Perry F. -- McLean Hospital (Belmont, MA)

High Field MR Research In Drug Abuse

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

Riley, William T. -- Personal Improvement Computer Systems
Community Based Automated Smoking Assessment

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

Robbins, Michael S. -- University of Miami
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Roman, Paul M. -- University of Georgia
CTN Membership and Adoption of Innovative Tx Practices

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Therapeutic Communities--Management and Performance

Rush, Craig R. -- University of Kentucky
GABA Agonists As Pharmacotherapies For Cocaine Abuse

Sacks, Joann Y. -- National Development & Research Institutes
Women's Prison TC--Outcomes, Process & Economic Analysis

Sanders-Phillips, Kathy -- Howard University
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Scheier, Lawrence M. -- University of Nevada Las Vegas
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Schottenfeld, Richard S. -- Yale University
HIV Risk Reduction And Drug Abuse Treatment In Malaysia

Schwartz, Robert P. -- Friends Research Institute, Inc.
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Seeman, Philip -- University of Toronto
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Semba, Richard D. -- Johns Hopkins University

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Siegel, Shepard -- McMaster University
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Sindelar, Jody L. -- Yale University
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Slesnick, Natasha -- University of New Mexico Albuquerque
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Slotkin, Theodore A. -- Duke University
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Sorensen, James -- University of California San Francisco
Therapeutic Community and Opioid Replacement Therapy

Sorg, Barbara A. -- Washington State University
Cocaine and Brain Extracellular Matrix

Spence, Richard T. -- University of Texas Austin
A Study of Heroin Inhalers

Spence, Richard T. -- University of Texas Austin
Drug Attitudes and Behavior on the US/Mexico Border

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

Steketee, Jeffery D. -- University of Tennessee Health Sciences Center
Medial Prefrontal Cortex and Cocaine Sensitization

Sterk, Claire E. -- Emory University
Club Drugs: Ecstasy Use Patterns and HIV Risk

Sterns, Ronni S. -- Creative Action, Inc.
PIRL: Prison Information Resource Library

Strathdee, Steffanie A. -- Johns Hopkins University
Reduce Transmission Risks & Improve HCV Treatment Access

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

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

Stroud, Laura R. -- Miriam Hospital
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Sweat, Michael D. -- Johns Hopkins University
Evaluation of A 3-Component IDU Intervention

Sweedler, Jonathan V. -- University of Illinois Urbana-Champaign

Neuropeptides In The CNS With Imaging Mass Spectrometry

Tancer, Manuel E. -- Wayne State University
Effects of the Ecstasy Drug In Humans

Tangney, June P. -- George Mason University
Recidivism, Drug Abuse, and HIV Risk Behaviors

Tao, Rui -- Rutgers University
Opioids & Plasticity In Regulation of Serotonin Release

Tarazi, Frank I. -- Biostream Therapeutics, Inc.
Neuroadaptive Effects After Chronic CTDP 31446 Treatment

Tidey, Jennifer W. -- Brown University
Transdermal Nicotine and Bupropion-SR In Schizophrenics

Tsibulsky, Vladimir -- University of Cincinnati
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Tulsky, Jacqueline P. -- University of California San Francisco
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Tunnicliff, Godfrey -- Indiana University-Purdue University at Indianapolis
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Tuomalo, Ruth E. -- Brigham and Women's Hospital
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Hispanic Heroin Users, Transitions To Injecting and HIV

Vander Stoep, Ann -- University of Washington
Emergence: Co-Occurring Depression/Externalizing Problems

Volsky, David J. -- St. Luke's-Roosevelt Institute for Health Sciences
Toward A Mouse Model of HIV Infection & Drug Addiction

Waldron, Holly B. -- University of New Mexico Albuquerque
Resistant Adolescent Substance Abusers In Treatment

Walsh, J. M. -- Walsh Group, PA
Web-Based Drug-Free Workplace Development

Waltz, Jennifer A. -- Behavioral Technology Transfer Group
Skills Training Video For Dialectical Behavior Therapy

Waters, Andrew J. -- Georgetown University
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Wecker, Lynn -- University of South Florida
Regulation of Neuronal Nicotinic Receptors

Weerts, Elise M. -- Johns Hopkins University
Studies on the Role of GABA In Cocaine Addiction

Weerts, Elise M. -- Johns Hopkins University
Dependence Potential of GHB, GBL and 1,4-Bd

Wells, Jennifer J. -- Oregon Center for Applied Science

Preventing Substance Abuse In Special Education Students

Wenzel, Suzanne L. -- RAND Corporation
Quality of Care In the Therapeutic Community

Wetter, David W. -- University of Texas MD Anderson Cancer Center
Race/Ethnicity and the Process of Smoking Cessation

Whitbeck, Leslie B. -- University of Nebraska Lincoln
Partnerships For Culturally Specific Drug Prevention

Wilson, Darcy B. -- Mixture Sciences, Inc.
Mimic Peptides of HIV1 Epitopes As Vaccines

Winter, Jerrold C. -- State University of New York at Buffalo
Behavioral & Pharmacological Analysis of Drugs of Abuse

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

Woods, Kristy F. -- Meharry Medical College
Planning Grant for Clinical Research Training

Woolverton, William L. -- University of Mississippi Medical Center
Dopaminergic Mechanisms In Stimulant Self Administration

Wu, Z. H. -- University of Texas Medical Br Galveston
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Xu, Ming -- University of Cincinnati
Molecular Determinants of Compulsive Cocaine-Taking

Young, Paul A. -- Nova Research Company
Adolescent HIV/STD Risk of Exposure Screen Development

Young, Rebecca M. -- National Development & Research Institutes
Measuring Sexual Minority Status Among Women Drug Users

Zaveri, Nurulain T. -- SRI International
Design of Small-Molecule Nociceptin Receptor Ligands

Zeltser, Gregory -- Physical Optics Corporation
Immunofluorometric Drug Detection System

Zlotnick, Caron -- Butler Hospital (Providence, RI)
Treatment for PTSD and Substance Abuse In Prisoners

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Director's Report to the National Advisory Council on Drug Abuse
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Extramural Policy and Review Activities

Reviews

For this Council cycle, the Office of Extramural Affairs arranged and managed fifteen review meetings for applications in its standing committees, applications in conflict- of-interest with standing committees, and submissions to special initiatives. One contract proposal review meeting was held and sixteen concept reviews were completed.

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. Six Special Emphasis panels were constituted for reviews of specific mechanisms: centers, program projects, conferences, and Minority Institutions Drug Abuse Research Development Program applications. In addition, OEA staff managed the reviews for B/START and Cutting Edge Basic Research Award (CEBRA) mechanisms.

The Contracts Review Branch managed the following reviews of proposals:

Proposal Review	
NO1DA-2-1108	**Research Dissemination to the Entertainment Industry**
SBIR Concept Reviews	
N43DA-2-7727	**Analytical Techniques Program**
N43DA-2-5518	**Prevention Training**
N43DA-2-1109	**Development of Science Education Materials**
N43DA-2-8819	**Medicinal Chemistry-Design Synthesis of Treatment Agents for Drug Abuse**
N43DA-2-8820	**Dosage Form Development**
N43DA-2-5517	**Developing New Technologies for Drug Abuse Prevention Delivery: Translation of Empirically Validated Prevention Strategies and Programs into New Technology**
N43DA-2-7731	**Novel Drug Delivery System for the Mouse**
N43DA-2-7726	**Functional Imaging Agent**
N43DA-2-7714	**Technologies for Localizing Gene Expression**
N43DA-2-7715	**Activity-based Protein Profiling**
N43DA-2-7730	**High-Throughput Screening of Functional Activity of Proteins Using Bio-**

	sensor-based Technology
N43DA-2-5506	**Developing Methodologies for Cost Analysis of Substance Abuse Prevention Programs**
N43DA-2-5506	**Developing Prevention Services Analytic Tools for Improved Substance Abuse Prevention Delivery**
N43DA-2-5513	**Develop and Maintain Substance Abuse Prevention Methodological Software**
N43DA-2-7709	**Virtual Reality for Treatment of Pain**
N43DA-2-7710	**Virtual Reality for Treatment of Drug Abuse**

Staff Training and Policy Development

The OEA Symposium Series continued its monthly meetings for staff development, under the direction of Dr. Mark Swieter, SRA, Basic Sciences Review Branch. A variety of case studies and updates on NIH extramural policies were presented and discussed.

Dr. Teresa Levitin, Director, OEA, has represented NIDA on an NIH-wide committee to address continuing education requirements.

Mr. Eric Zatman, Contracts Review Branch, is representing NIDA on a trans-NIH committee that is examining and updating the NIH policies and procedures for review of contracts, as contained in the NIH Manual section entitled, “Initiation, Review, Evaluation, and Award of Research & Development (R&D) Contract Projects.”

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Congressional Affairs

FY 2002 APPROPRIATIONS

The House and Senate cleared the $123.8 billion FY 2002 Labor/HHS/Education spending bill before the end of the first session of the 107th Congress. The House voted 393-30 to adopt the conference report on the bill (HR 3061) on December 19; the following day, the Senate voted 90-7 to adopt the report. The President signed the bill into law on January 10, 2002 [P.L. 107-116]. The bill authorizes $54.2 billion for the Department of Health and Human Services (DHHS), a $5 billion increase over FY 2001. The bill also authorizes $12 billion for the Labor Department and $48.9 billion for the Education Department.

NIH received the largest portion of the DHHS increase, with $23.285 billion, nearly $3 billion more than the FY 2001 NIH funding level. The NIH total actually comes to $22.888 billion after funding for other programs such as Global AIDS and evaluation taps are subtracted. The conference agreement provides a 14.7% increase for the NIH overall. Most institutes received increases between 12% and 14%. NIDA received $888.1 million, a 13.7% increase over FY 2001.

Conferees split the difference on funding the NIH. The Senate bill would have appropriated about $23.7 billion while the House bill would have appropriated about $22.9 billion. The conference committee blocked an attempt by Senate conferees to attach a provision that would expand insurance coverage for mental illness.

FY 2002 funding for programs of the Substance Abuse and Mental Health Services Administration (SAMHSA) in the Labor/HHS/Education bill included the Substance Abuse Block Grant at $1.725 billion, an increase of $60 billion over FY 2001; for the Center for Substance Abuse Prevention (CSAP) of $198 million, an increase of $23 million; and for the Center for Substance Abuse Treatment (CSAT) of $291.5 million, an increase of $35.5 million.

The Treasury Postal Appropriations Act included FY 2002 funding for the National Anti-Drug Media Campaign at $180 million, a reduction of $5 million from FY 2001; and funding for the Drug Free Communities Act (DCFA) of $50.6 million, an increase of $10.6 million over last year.

HEARINGS

Senate Caucus on International Narcotics Control Hearing – “Looking the Other Way: Rave Promoters and Club Drugs” – December 4, 2001

On December 4, the Senate Caucus on International Narcotics Control (Senators Joseph Biden [D-DE] and Charles Grassley [R-IA], Co-Chairs) held a hearing to examine the use of club and rave drugs. In his opening statement, Senator Biden explained that over the past two years the drug Caucus has held several hearings on the trafficking and use of the drug ecstasy. He said the December 4th hearing was held to take an in-depth look at the phenomenon of the all-night dance parties called “raves” and discuss events at the federal, state and local level to crack down on rave promoters.

Dr. Glen Hanson, Acting Director, NIDA, joined Asa Hutchinson, Administrator, Drug Enforcement Agency, on the first panel. Dr. Hanson presented some of the latest scientific information about a diverse group of compounds commonly referred to as club drugs. Drugs such as MDMA, methamphetamine, Ketamine, Rohypnol, and GHB are reportedly

being used at alarming rates among adolescents and young adults in a wide variety of social settings including raves. Dr. Hanson testified that substantial scientific evidence demonstrates that these drugs are not benign and harmless, as they are often perceived by some users or sometimes portrayed in the popular media. In fact, the scientific evidence is clear. These drugs can have short and long-term detrimental health consequences to both the user and to society in general. Dr. Hanson stated that NIDA would continue to support and disseminate the results of research to prevent and treat drug abuse and addiction, and to help everyone make more informed decisions about these and other substances of abuse. The text of Dr. Hanson's formal statement can be found on the NIDA website at www.drugabuse.gov.

OxyContin Hearing Before Senate HELP Committee

Prescription drug abuse and misuse is an important emerging public health problem, and one of particular concern to Members of Congress. NIDA was invited to testify at a hearing in September 2001 before the Senate HELP (Health, Education, Labor and Pensions) Committee on "Abuse of OxyContin," an opioid analgesic prescribed for pain. The hearing, twice postponed, was rescheduled for February 12, 2002. The new focus of the hearing is to address treatment options in rural areas as well as allegations that there has been inappropriate promotion of the drug by the manufacturer. NIDA was asked to submit testimony for the record.

BILLS OF INTEREST

(To view the actual text of any bill, go to http://thomas.loc.gov and enter the bill number in the bill search.)

President Signs Drug Free Communities Act Reauthorization Bill

On December 14, the President signed into law the Drug Free Communities Support Act Reauthorization Bill (HR 2291), which became Public Law, P.L. 107-82. The law reauthorizes for five years the Drug Free Communities Support Program, and authorizes a total of $345 million over that period. Enacted in 1997, the Drug Free Communities Act (P.L. 105-20) established a program of direct grants to community organizations that demonstrate a comprehensive, long-term commitment to reduce drug use among youngsters. The measure also authorizes grants that may be provided to community anti-drug coalitions beyond the terms of their initial grants, and "mentoring" grants that may be used by coalitions to support the development of other anti-drug groups. The law also establishes a National Community Anti-drug Coalition Institute that will provide education and training for community coalition leaders; develop standards and mechanisms to evaluate the success of coalitions receiving funding; and translate research findings into information that coalitions can use.

HR 1 "No Child Left Behind" - Education Bill Becomes Law

After many months of conference between the House and the Senate, the Education Bill (HR 1) passed both Houses of Congress and was cleared for the President on December 18, 2001 (Congressional Record p. S13422). The final language does not require "prior written consent" as a standard for school-based research, as provided for by the "Tiahrt amendment" in the House version of the bill. However, Local Education Agencies (LEAs) can do so if they choose, which may impact multi-site school-based research studies.

Among other provisions, the bill preserves the Safe and Drug Free Schools and Communities (SDFSC) program as a separate authority. The final bill specifies that any program or activity funded through the SDFSC program must meet the following "Principles of Effectiveness," which were codified in the bill: (1) be based upon an assessment of objective data about community needs for the activities; (2) be based upon performance measures established by the LEA; (3) be based upon "scientifically based research" that provides evidence that the program or activity will be effective (there is a waiver for innovative programs with a likelihood of success); (4) be periodically evaluated with the results used to improve the program or activity; (5) be based upon an analysis of risk factors and protective factors; and (6) include consultation with parents.

A SDFSC Advisory Committee is established to consult with the Secretary of Education. The Committee shall be composed of representatives from the Department of Education; the Centers for Disease Control and Prevention; the National Institute on Drug Abuse; the National Institute on Alcoholism and Alcohol Abuse; the Center for Substance Abuse Prevention; the Center for Mental Health Services; the Office of Juvenile Justice and Delinquency Prevention; the Office of National Drug Control Policy; State and local governments, including education agencies; and researchers and expert practitioners.

S. 304 - the Drug Abuse Education, Prevention, and Treatment Act of 2001

On November 29, the Senate Committee on the Judiciary [Senator Patrick Leahy (D-VT) Chairman] ordered reported S. 304, the Drug Abuse Education, Prevention, and Treatment Act of 2001, with an amendment in the nature of a substitute. The amended legislation is aimed at reducing illegal drug use and trafficking and helping to provide appropriate drug education, prevention, and treatment programs. S. 304 as amended contains a provision requiring the HHS Secretary to enter into a contract with the Institute of Medicine of the National Academy of Sciences to conduct a study to determine if combining NIDA and NIAAA into a "National Institute on Addiction" would 1) strengthen the scientific research efforts on substance abuse at the NIH and 2) be more economically efficient. The bill also calls for the expansion of drug abuse prevention and treatment research at NIDA. In addition, S. 304 contains provisions requiring that the Directors of NIAAA and NIDA, in conjunction with the Administrator of SAMHSA, 1) ensure results of all current substance abuse research that is set aside for services (and other appropriate research with practical consequences) is widely disseminated to treatment, prevention, and general practitioners in an easily understandable format, 2) ensure the implementation of best practices based on the research, and 3) make technical assistance available to CSAT and CSAP to assist alcohol and drug treatment and prevention practitioners, including general practitioners, to make permanent changes in treatment and prevention activities through the use of successful models. The bill, as amended, omits authorization levels. At the end of the session, the text of S 304 was swept into the Department of Justice Reauthorization bill (HR2215). That measure, as amended, passed in the Senate by unanimous consent on December 20, 2001 (Congressional Record p. S14075).

SENATE CONFIRMED DRUG CZAR NOMINEE

On December 5th the Senate confirmed by voice vote John P. Walters as the Director of the Office of National Drug Control Policy. The Senate Judiciary Committee had approved Walters' nomination on November 8th on a vote of 14-5.

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International Activities

Continuing efforts that began in 1999 with an Exchange of Letters between the two countries, 29 scientists participated in the **U.S. - Netherlands Workshop on Bi-National Research Collaboration on Drug Abuse and Drug Addiction**, convened September 6 and 7, 2001, in Cumberland, Maryland. The symposia and workshop sessions focused on MDMA (Ecstasy) epidemiology, pharmacology, psychology, and neurotoxicity; treatment models; the impact of stress and anxiety on addiction; public health issues; and collaborative research proposals. Presenters included then NIDA Director, Dr. Alan I. Leshner; Dr. Glen Hanson, DNBR; Mr. Richard A. Millstein, Deputy Director, NIDA and Acting Director, DESPR; Dr. Steven Gust, OSPC; Dr. Frank Vocci, DTR&D; and Dr. Betty Tai, CCTN. NIDA and the Netherlands Research and Development Program on Substance Use and Addiction will initially support three collaborative research projects: 1) Dr. Alfons Crijnen, Erasmus Medical Center of Rotterdam, and Dr. Nicholas Ialongo, Johns Hopkins, will conduct comparative studies on prevention of initial drug use in early adolescence in Baltimore and four Dutch cities; 2) Dr. Dirk Korf, University of Amsterdam, and Dr. Lana Harrison, University of Delaware, will compare potential influences on drug-related violence among youth; and 3) Dr. Dorret I. Boomsma, Free University of Amsterdam, and Dr. Michael Neale, Virginia Commonwealth University will conduct molecular genetic studies to identify genes implicated in nicotine addiction.

NIDA and the Mexican National Council of Science and Technology (CONADIC) cosponsored a pre-conference research symposium at the **4th U.S. - Mexico Binational Conference on Demand Reduction** in Mexico City. Participants evaluated binational collaborative research, training, and professional development, and discussed priorities for future binational research in drug abuse prevention, treatment, and epidemiology. Participants included Ms. Ana Anders, OD, and former INVEST Research Fellows, Dr. Guilherme Borges and Dr. Silvia Cruz.

NIDA welcomed the 2001-2002 **Hubert H. Humphrey Drug Abuse Research Fellows** with an orientation program December 7, 2001. NIDA staff members who briefed the Fellows about Institute activities included: Dr. Timothy P. Condon, Associate Director, NIDA; Dr. Steven W. Gust, Acting Director, International Program; Dr. Frank Vocci, DTR&D; Dr. David Shurtleff, DNBR; Ms. Helen Cesari, CAMCODA; Dr. Peter Delany, DESPR; and Dr. Betty Tai, CCTN. Four Fellows are supported by NIDA: Dr. Monica Beg, Bangladesh; Dr. Petra Exnerova, Czech Republic; Ms. Olga Toussova, Russia; and Dr. Svitlana Pkhidenko, Ukraine.

The 2000-2002 **INVEST Research Fellows** have begun their postdoctoral research and training with NIDA grantees. Dr. Zhao Min, China, is working with Dr. Howard Liddle, University of Miami, focusing on multidimensional family therapy and research on the relationship of parental psychopathology and treatment outcomes. Dr. Tatiana Tsarouk, Russia, 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. Dr. Debasish Basu, India will work with Dr. Joel Gelernter, Yale University, to study genetic susceptibility to opioid or cocaine dependence.

NIDA supported the participation of Dr. Ken Winters, University of Minnesota, at the Center for Youth Integration 4th International Symposium on Drug Abuse in Mexico City, December 6 and 7, 2001.

Drs. Jag H. Khalsa and Henry (Skip) Francis of the Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA) initiated, planned, organized, and conducted a conference on "**Blood-borne and Sexually Transmitted Infections Among IVDUs and their Partners in the United States, Latin America, and the Caribbean: Experiences and Lessons Learned**" in Buenos Aires, Argentina, December 17-19, 2001. Dr. Jerry Flanzer, DESPR

also presented at the conference. This was NIDA's first collaboration with the Pan American Health Organization (PAHO)/World Health Organization (WHO). Collaborators from PAHO included Drs. Rafael Mazin, Armando Peruga, and Fernando Zacarias. The objectives of the conference were: (a) to facilitate the exchange of experiences, lessons learned and "best practices" between experts in the Western Hemisphere; (b) to discuss medical, behavioral and other relevant public health consequences of infections and injecting drug use, as well as the current situation and trends in these regions; and (c) to review successful behavioral, medical and public health interventions implemented both in the U.S.A. and in Latin America and the Caribbean that may be adopted/adapted by each other. A group of 32 clinicians, scientists, and other health care providers, including Dr. Mercedes Weissenbacher (University of Argentina, Buenos Aires), from these regions reviewed and/or discussed the current information on the topic and made recommendations for further research and collaborations among the investigators. A brief summary in English, Spanish and Portuguese will appear on the Homepage soon. A publication of the proceedings in a professional journal is also planned. In addition, PAHO will issue a bulletin in Spanish.

Drs. Eve Reider and Jerry Flanzer presented to a delegation of seven visitors from Central Asia that was held at the Fogarty International Center on August 28, 2001. The visitors were from the Freedom Support Grant Project for Central Asia. Their focus was on HIV/AIDS Awareness and their visit was conducted by the U.S. Department of State International Visitor Program for Central Asia. They included clinicians, agency administrators, NGO directors, epidemiologists and educators specializing in HIV/AIDS and drug abuse prevention from five countries of Central Asia.

Dr. Timothy P. Condon, Associate Director, NIDA, presented "Improving Addiction Treatment: Blending Research and Practice" at the 44th International ICAA Conference on the Prevention and Treatment of Dependencies in Heidelberg, Germany on September 4, 2001.

Drs. Steven Gust, Acting Director, NIDA International Program, Jack Stein, Deputy Director, OSPC, Catherine Sasek, OSPC, and Elizabeth Robertson, DESPR met with Mr. Colin Bramfitt, Executive Director, Foundation for Alcohol and Drug Education, Auckland, New Zealand on September 5, 2001. Discussions included NIDA school and workplace prevention efforts and science education programming.

Dr. Elizabeth Robertson, DESPR met with a delegation of 17 participants from Latin America as part of the **Western Hemispheric Regional Project: U.S. Drug Demand Reduction Efforts**. The group met on September 13, 2001 to discuss NIDA programs on drug abuse prevention research.

Moira O'Brien and Dr. Elizabeth Robertson, DESPR, briefed Mr. Gert Bogers, Policy Advisor for the Ministry of Health, Welfare and Sport in the Netherlands on October 23, 2001, on substance abuse trends and prevention in the United States.

Drs. Eve Reider and Jerry Flanzer presented on drug abuse prevention and services research to a delegation of visitors from the Ternopil (Ukraine) Public Health group that was held at the Fogarty International Center on October 30, 2001. The group included physicians and researchers who were visiting the United States through the U.S. Department of State Bureau of Educational and Cultural Affairs and Legacy International.

Dale Weiss, NIDA International Program, OSPC, provided an overview of NIDA at a briefing for a group of WHO/PAHO International Health Fellows from the Americas on November 8, 2001.

Dr. Steven Gust, Acting Director, International Program, OSPC, led a NIDA briefing for a delegation from Norway on November 20, 2001. NIDA staff, including Drs. Eve Reider and Moira O'Brien, DESPR made presentations concerning prevention and epidemiology. The visiting delegation included Knut Brofoss and Astrid Keretting, National Institute for Alcohol and Drug Research (SIRUS), Martha Rubiano Skretteberg, Pål Winnæs and Jon Nysted, Norwegian Directorate for the Prevention of Alcohol and Drug Problems, Bernt Bull, Norwegian Temperance Alliance, Trude Sletteberg, Juvente, and Trine Stensen Lunde, AlkoKutt.

Drs. Glen Hanson and David Shurtleff, DNBR, met with Mr. Christian Cabal, depute de l'Assemblee Nationale Francaise (Senator), representing the Region of Saint-Etienne, France, his staffer, Mr. Daniel Constant, and Mr. Wahid Bakouche, Scientific Attache at the French Embassy on November 26, 2001. They discussed areas of interest to Mr. Cabal, such as the molecular mechanisms involved in drug use and dependence, the molecular mechanisms involved in the brain when drugs are used, what kind of receptors and what kind of mediators are involved. Also, discussed were the long-term effects of drug use at the cellular levels, on memory, and on brain abilities.

Dr. Timothy Condon, Associate Director, NIDA and Dr. Steven Gust, Acting Director, International Program, OSPC, hosted a meeting with Greek and Turkish Cypriots on December 5, 2001. Also speaking to the group were Dr.

Elizabeth Robertson, Prevention Research Branch, DESPR and Dr. Ivan Montoya, CCTN. The Greek Cypriots included Bishop Chrysostomos Macheriotis, Dr. Kyriacos Veresies, and Mr. Nicos G. Mousoulides. The Turkish Cypriots included Dr. Mehmet Cakici, Dr. Inci Tasyurek and Ece Yoldas. The visitors discussed their long-term goal of working towards a bi-communal program to promote advancement of common issues experienced by both sides of the divided island of Cyprus. The NIDA participants offered advice and guidance concerning drug abuse prevention and treatment efforts and avenues for possible collaborations.

Drs. Peter Delany, Bennett Fletcher, and Jacques Normand, and Nicholas Kozel and Susan David, DESPR, briefed representatives of the French government, on December 7, 2001, on epidemiology, prevention, and services research. There was a particular interest in the use of epidemiology and survey data to assess the impact of national programs.

Dr. Elizabeth Robertson and Susan David, Prevention Research Branch, DESPR, met with two Humphrey Fellows on December 17, 2001, who were interested in developing and evaluating national drug abuse prevention media campaigns in their home countries of the Czech Republic and Romania.

Dr. Eve Reider, Prevention Research Branch, DESPR, and Dr. Peter Hartsock, CAMCODA, participated in a meeting hosted by NIAID on December 19, 2001, for a group of visiting Russian Clinicians and Prevention Researchers from Khabarovsk Krai and the Jewish Autonomous Region (both in Eastern Siberia near Vladivostok and Manchuria) and the Republic of Tartastan (Kazan). They were accompanied by Harvey Sloan, M.D., Eurasian Medical Education Program, Washington D.C. The Institute for Health Policy Analysis in partnership with the American College of Physicians directs this program of continuing medical education for Russian physicians.

Drs. Frank Vocci and Ahmed Elkashef, DTR&D, represented NIDA at the 2001 International Society of Addiction Medicine (ISAM) conference: Sharing International Responsibilities in a Changing World in Trieste, Italy from September 12-14, 2001. Dr. Vocci chaired a session on Treatment of Addictions and presented a talk entitled, “Medications for the Treatment of Opiate Dependence: Current Therapies and New Developments”. Dr. Elkashef presented a talk entitled,” Medications Development for the Treatment of Cocaine Dependence at NIDA”.

Dr. Frank Vocci presented a plenary lecture entitled, ”Current Efforts and New Directions in Addictions Pharmacotherapy: Research and Treatment” at an ISAM satellite symposium in Ljubljana, Slovenia on September 15, 2001.

Dr. Peter Hartsock, CAMCODA, participated in the International AIDS Vaccine 2001 Conference that took place from September 5-8, 2001 in Philadelphia, PA. Dr. Hartsock presented on NIDA’s AIDS epidemiology prevention and epidemiology research with applications to vaccine development and vaccine distribution to high risk groups such as drug users. Dr. Hartsock also met with NIH Office of AIDS Research staff, NIH/NIAID staff, and visiting Russian colleagues to develop U.S.-Russian coordination in AIDS vaccine development and vaccine availability to high risk groups.

Through arrangements made with the Fogarty International Center of the National Institutes of Health, the Japan Society for the Promotion of Science awarded Dr. Cesario V. Borlongan a short-term fellowship to pursue collaborative research in Japan, November 22 through December 8, 2001. These fellowships are intended to enhance American-Japanese collaboration in biomedical and behavioral research by providing flexible opportunities for capable American scientists to work with colleagues in leading Japanese laboratories on substantive projects of mutual interest. Dr. Borlongan conducted research collaboration on “Transplantation of melatonin-secreting pineal gland in stroke animals” with Dr. Hitoo Nishino (Japanese collaborator), Department of Physiology, Nagoya City University Medical School.

Dr. Cesario Borlongan, IRP, give a talk entitled “Immunosuppressants as Neuroprotective Agents for Neurological Disorders” at the symposium entitled “New Strategy for Neural Transplantation”, November 25-27, 2001, Nagoya, Japan.

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Director's Report to the National Advisory Council on Drug Abuse
February, 2002

Meetings/Conferences

On September 10-11, 2001, Ms. Beverly Jackson, Chief, Public Information and Liaison Branch, OSPC, and other members of the Branch held a **meeting of the Public Information Officers of the Clinical Trials Network (CTN)** in Arlington, Virginia. Approximately 20 grantee institutions from the CTN were represented. This conference included briefings by NIDA officials regarding the CTN concept, progress reports on the CTN, discussions about outreach projects for the media in all regions of the country, and how to stimulate effective communication between NIDA and others in the network.

NIDA hosted its **7th Constituent Conference, Blending Research and Practice**, at the Westfields Marriott in Chantilly, Virginia, December 3-4, 2001. The Constituent 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. Dr. Glen R. Hanson, NIDA Acting Director, opened the conference with an update to constituent representatives on NIDA's research, new initiatives, achievements, and future directions since NIDA's last constituent conference in December 1999. A number of NIDA Division and Office Directors also presented on their specific research portfolios, followed by a facilitated discussion. In addition, several of NIDA's constituent representatives presented on activities their organizations are involved in and gave examples regarding actions they have taken to blend research and practice. Also, for the first time, NIDA used an automated response system to gain instant feedback from constituents on a number of areas concerning NIDA research and dissemination activities.

The Special Populations Office organized NIDA's first health disparities conference to address drug abuse research in ethnic minority populations. The conference, **Bridging Science and Culture to Improve Drug Abuse Research in Minority Communities**, was held September 24-26, 2001, in Philadelphia, Pennsylvania. The conference provided a forum for over 450 researchers, practitioners, community providers, and others to share research needs, concerns, and opportunities. Plenary sessions and workshops covered such topics as treatment, epidemiology, interaction of culture, race, ethnicity and science, pharmacological and behavioral treatments with minority clients, prevention and treatment in correctional settings, challenges of minority and majority researchers and grants development. Additionally, 25 NIDA staff conducted roundtables on various NIDA programs, research opportunities and areas of drug abuse research. NIDA staff and extramural researchers from work groups were instrumental in the overall planning of the conference.

On November 10, 2001, at the Annual Society for Neurosciences meeting held in San Diego, CA, NIDA (along with NINDS) sponsored a satellite meeting titled, **Translation of Genetic Research to Pain Treatment**. This symposium highlighted the development of molecular biology-based treatments for pain. Four speakers, all NIDA grantees, presented their latest findings on the use of genetic research in the development of new pain treatments. Drs. David Yeoman (Stanford), Li-Yen Huang (University of Texas) and Andrew Mannes (University of Pennsylvania) discussed their findings concerning how gene therapy may be useful in the treatment of various types of pain. Dr. Jeffery Mogil (University of Illinois) discussed how genetic techniques might be used to identity new targets for pharmaceutical and gene therapy. Overall, this symposium showed how findings from molecular biology might be translated into treatments for pain. The co-chairs of this session were Dr. Dave Thomas, DNBR, NIDA and Dr. Robert Caudle, University of Florida.

Drs. David Shurtleff, OD, DNBR, Steve Grant, CNB, DTR&D, Minda Lynch, BCSRB, DNBR and Jerry Frankenheim, PICNRB, DNBR chaired a symposium entitled **Neuroscience Perspectives on the Effects of Ecstasy (MDMA)** at this year's Society for Neuroscience annual meeting in November. The evening session overviewed findings on MDMA-

induced neurotoxicity from preclinical and clinical investigations, and compared cellular mechanisms of action to the effects of other psychostimulants. New data on the persistence of psychological and cognitive consequences seen with repeated abuse were also discussed. Presentations were delivered by Dr. Glen Hanson of NIDA, Dr. Brian Yamamoto from Case Western University, Dr. Annette Fleckenstein from the University of Utah, Dr. Linda Chang from Brookhaven National Laboratory, and Dr. Michael Morgan from the University of Sussex in the U.K.

Drs. Karen Skinner, and Jonathan D. Pollock, DNBR, organized a satellelite symposium at the 2001 Annual Meeting of the Society for Neuroscience, entitled, **Microarray Research - Evolving Standards** that was held on November 9, 2001 at the San Diego Convention Center. Microarray technology allows you to profile the expression of genes in any tissue. This satellite symposium addressed the issue of developing standards for microarray research so that results can be compared among laboratories. The second part of the meeting was a mini-symposium on the technical challenges of microarray analysis of human post-mortem brain tissue that included Drs. Francine Benes, James Eberwine, Deborah Mash, Christine Konradi, and Giulio Pasinetti.

Drs. David Shurtleff, Steve Grant and Herb Weingartner, DNBR, chaired a NIDA-sponsored symposium at the annual meeting of the Society for Neuroscience entitled **The Role of Frontal Cortex in Drug Addiction: Current Knowledge and Future Directions**. Invited speakers included: Marina E. Wolf, Ph.D., Anthony A. Grace, Ph.D., Linda Porrinio , Ph.D., Deborah A. Yurgelun-Todd, Ph.D., Hugh Garavan, Ph.D., Antoine Bechara, Ph.D., Mark D'Esposito, Ph.D., and Trevor Robbins, Ph.D.

NIDA's Women and Gender Research Group presented a poster, **Gender Matters in Neuroscience Investigations of Drug Abuse** at the annual meeting of the Society for Neuroscience, San Diego, CA, November 10-15, 2001.

Dr. Jonathan D. Pollock, DNBR and Dr. Eric Nestler, UT Southwestern organized a workshop at the 2001 American College of Neuropharmacology, entitled, **Dendritic Morphology and Neuropsychopharmacology: Overview of Molecular Mechanisms**, held at the Hilton Waikoloa Village on the Big Island of Hawaii, December 11, 2001. The purpose of this workshop was to discuss possible mechanisms underlying the increases in dendritic spine density, specifically in nucleus accumbens medium spiny neurons and prefrontal cortical pyramidal neurons after long-term exposure to the psychostimulants cocaine and amphetamine that have been suggested to mediate sensitized responses to these drugs even after prolonged periods of withdrawal. The workshop participants included Drs. Paul Worley, Betty A. Eipper, Liquin Luo, and Rafael Yuste.

Drs. Thomas Aigner and Roger Brown, DNBR, co-chaired a session at the 40th Annual Meeting of the American College of Neuropsychopharmacology in Waikoloa, HI, December 9-13, 2001. The session was entitled **Functional Brain Imaging in Animals: Implications for Drug Abuse**.

Dr. Nancy Pilotte, DNBR, organized **Intracellular Protein Trafficking and Drugs of Abuse** at the NIH, January 7-8, 2002. Speakers included: J. Benovic, R. Edwards, R. Elde, A. Fleckenstein, A. Galli, S. George, G. Hanson, L-Y Liu-Chen, R. Mains, H. Melikian, M. Robinson, A. Sorkin, T. Sudhof and M. von Zastrow.

Jag H. Khalsa, Ph.D., Paul Coulis, Ph.D., Sander Genser, M.D., M.P.H., and Henry Francis, M.D. of CAMCODA planned, organized and presented an outstanding workshop on: **Interventions for Metabolic and Endocrine Complications of HIV/AIDS and Drug Abuse** November 26-27, 2001 at Natcher Building, NIH Campus, Bethesda. A group of nationally and internationally known clinicians and scientists presented current research and made recommendations for future research on the subject. A brief summary is in preparation for the NIDA website. The proceedings will be published in Clinical Infectious Diseases.

A National CTN Steering Committee Meeting was held January 28-30, 2002, in Charleston, South Carolina.

The 51st biannual meeting of the **Community Epidemiology Work Group (CEWG)**, chaired by Nicholas J. Kozel, DESPR, was held in San Diego, California on December 11-14, 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, and negative health and social consequences related to drug abuse. 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 - Although still at high levels, cocaine/crack indicators decreased in 10 CEWG areas, remained stable or mixed in 9, and increased in only 2 (Atlanta and Seattle). As crack use has decreased, powder cocaine has become more available in some CEWG areas including Denver, Miami/South Florida, Phoenix, and Washington, D.C.

Heroin - Heroin use indicators increased in 15 CEWG areas, remained stable in 2, and decreased in 4. Decreases were reported in Honolulu, Los Angeles, San Francisco, and Seattle, areas in which Mexican black tar is the primary type of heroin available. Areas located on the east coast, including Boston, New York, Newark, and Philadelphia, report that heroin is relatively cheap, widely available, and of high purity.

Other Opiates - Indicators of the illicit use of prescription semi-synthetic narcotic drugs, such as oxycodone and hydrocodone, increased in the 14 CEWG areas that reported on these drugs. Oxycodone emergency department (ED) mentions were highest in Philadelphia (195), Boston (122), and Seattle (94). The Massachusetts Department of Public Health drug lab reported 374 oxycodone samples in 2000 (145 in the Boston area). It was also reported that oxycodone could be purchased near methodone clinics in Washington, D.C. In 2000, there were 52 deaths involving hydrocodone and 8 involving oxycodone in Texas.

Marijuana - Marijuana use indicators increased in 12 CEWG areas, remained stable or mixed in 8, and decreased in 1 (Atlanta). Although marijuana ED mentions, arrests, and treatment admissions have been increasing, there is reportedly less stigma associated with the use of this drug than in prior years, and it is widely available in all CEWG and surrounding areas. In 2000, high proportions of clients entering drug treatment programs in Denver (42.4 percent), New Orleans (29.2 percent), St. Louis (27.5 percent), New York (25.4 percent), and Atlanta (21.1 percent) reported marijuana as their primary drug of abuse. In 2001 Minneapolis/St. Paul reported that 22.9 percent of treatment admissions were for primary marijuana abuse.

Methamphetamine - Methamphetamine use indicators increased in 6 (Denver, Honolulu, Los Angeles, Phoenix, San Diego, and Seattle) of the 7 CEWG areas that have relatively high rates of ED methamphetamine mentions and/or high percentages of methamphetamine (primary drug of abuse) treatment admissions. The 7th, San Francisco, was the only one reporting a decrease in methamphetamine indicators in 2000–2001. Increases in methamphetamine indicators were also reported in Atlanta, Minnesota/St. Paul, St. Louis, and cities in Texas. Other CEWG areas such as Chicago, Detroit, New York, Philadelphia, and Washington, D.C. reported increases in methamphetamine availability and use but still at low levels.

Club Drugs - MDMA (ecstasy) indicators increased in 18 CEWG areas and remained stable (at low levels) in 3—Baltimore, New Orleans, and Newark. Although the numbers of MDMA ED mentions are still small compared with those for other drugs, they have been increasing dramatically in most CEWG areas. The Benelux countries of Belgium, the Netherlands, and Luxembourg have been the main sources of MDMA in this country. There have been reports of attempts to establish clandestine labs capable of producing MDMA in CEWG sites, including Minneapolis, San Diego and in areas in Michigan and South Florida. The drugs produced in these labs are adulterated with many different substances. Pills sold as ecstasy were found to contain mixtures of a variety of chemicals/substances, making them more dangerous to use; some do not contain any of the precursors needed to produce MDMA.

PCP - PCP indicators were reported in 14 CEWG areas. In 2000, PCP ED mentions were especially high in Chicago (n = 1,003) and relatively high in Washington, D.C. (317), Dallas (120), and St. Louis (98). Los Angeles reported 51 PCP-involved deaths in 2000. Only a small number of ADAM arrestees tested positive for PCP

Impact of September 11, 2001 Events

Washington, D.C	Immediately following the terrorist attacks on September 11th, heroin, cocaine, marijuana, and MDMA became less available in areas of the District. While drug trafficking was disrupted, drug market activity increased when police were diverted to other areas of the city.
New York City	Since the World Trade Center attacks, areas of New York City have reported a shortage of heroin and other drugs. Bags of heroin are reported to contain less of the drug.

A CTN Annual Meeting was held September 10-13, 2001, in Arlington, Virginia. This was an opportunity to bring together researchers and practitioners that participate in the CTN to meet each other, network and interchange ideas and experiences. Multiple break out meetings were held for professional development and training. The meetings were cut short by the September 11th disasters.

On October 22-24, 2001, the CTN Steering Committee met in Bethesda, MD. The members discussed future funding plans for new nodes, agreed on a common assessment battery instrument for all future CTN trials, approved new protocol teams, and met with managed health care providers.

The CTN held its quarterly meeting of the Data & Safety Monitoring Board on Oct. 29, 2001 (postponed from Sept 17). The Board reviewed 6 current trials for safety and scientific integrity. Reports were presented on all Serious Adverse Events, and on the 6 trials' progress. No protocol changes were recommended. Discussion will continue on procedures for reviewing new protocols.

During the months of August – December, over 160 conference calls were held in the CCTN. These conference calls were held by national committees, subcommittees, and work groups within the network.

Mr. Richard A. Millstein, NIDA Deputy Director, met with Drs. Joseph Autry, Acting Administrator, SAMHSA, and Ruth Sanchez-Way, Director of CSAP, on collaborations on prevention research and practice, October 10, 2001, Rockville, MD. A followup meeting of Mr. Millstein, Drs. Elizabeth Robertson and Jackie Kaftarian of DESPR, and Dr. Sanchez-Way and staff was held on February 11, 2002.

Mr. Millstein gave two talks at the annual meeting of the American Public Health Association on "Drug Abuse Research: The Foundation for Policy" and "Bringing Research Knowledge to Community Practice," October 22-24, 2001, Atlanta, GA.

Mr. Millstein presented to the National Hispanic Science Network on "PAs, RFAs, and Strategies for Successful Grant Writing," November 8, 2001, Washington, D.C.

Mr. Millstein presented on DESPR programs and priorities at NIDA's 7th Constituent Conference, December 3, 2001, Chantilly, VA.

Mr. Millstein spoke to Leadership Montgomery on "What Science Tells Us About Drug Abuse", December 5, 2001, Gaithersburg, MD.

Dr. Timothy P. Condon, Associate Director, NIDA, presented and was a discussant at the Club Drug Use and Gay Men's Health Colloquium of the American Psychological Association Convention in San Francisco, CA on August 24, 2001.

Dr. Timothy P. Condon presented "Addiction as a Brain Disease: New Implications for Research and Practice" for the Connecticut Statewide Addiction Medicine/Psychiatry Grand Rounds interactive web broadcast on September 20, 2001.
Dr. Timothy P. Condon presented "Blending Research and Practice: What Research Can Tell Us" at the Demand Treatment! Leadership Institute II in Denver, Colorado on September 24, 2001.

Dr. Timothy P. Condon briefed two American Managed Behavioral Healthcare Organization member groups on the effectiveness of drug addiction treatment and on NIDA's Clinical Trials Network on October 17, 2001 in Washington, D.C.

Dr. Timothy P. Condon presented and led discussions on club drugs, the science of addiction, and drug abuse prevention and treatment strategies during a half day symposium entitled "Science Advances in the Emerging Drug Problem: Blending Research and Practice" at the Alcohol and Drug Abuse Division of the State of Hawaii Department of Health Conference in Honolulu, HI on October 23, 2001.

Dr. Timothy P. Condon presented "Developmental Consequences of Prenatal Exposure to Drugs of Abuse" at the Intrauterine Effects of Substances of Abuse Institute of the 48th Annual Meeting of the American Academy of Child & Adolescent Psychiatry on October 24, 2001 in Honolulu, HI.

Dr. Timothy P. Condon presented "Advances in Drug Abuse and Addiction Research: Implications for Criminal Justice Populations" at the Eighth National TASC Conference on Drugs and Crime on October 30, 2001 in Orlando, FL.

Drs. Timothy P. Condon, OSPC, and Jerry Flanzer, DESPR, participated in Proposition 36: A Working Meeting on Research on November 9, 2001 in San Francisco, CA.

Dr. Timothy P. Condon participated in the Robert Wood Johnson Foundation Substance Abuse Policy Research Program Annual Grantee Meeting on November 14, 2001 in St. Augustine, FL.

Dr. Timothy P. Condon participated in the 2001 National Conference on Tobacco OR Health on November 27, 2001 in New Orleans, LA.

Dr. Timothy P. Condon presented an "Update on Research Dissemination" at NIDA's Seventh Constituent Conference in Chantilly, VA on December 4, 2001.

Dr. Timothy P. Condon presented “Drug Abuse & Addiction: What’s New on the Research Scene” at the CADCA National Leadership Forum XII on December 13, 2001 in Washington, D.C.

Dr. Jack Stein, Deputy Director, OSPC, participated in a plenary session “Practice Improvement: Bridging the Gap Between Practice and Research” at the Alcohol & Substance Abuse Providers of New York State 5th Annual Treatment Prevention Conference in Saratoga Springs, New York on October 23, 2001.

Dr. Jack Stein conducted a half-day workshop on club drugs at the Annual Department of Education’s Alcohol and Drug Abuse Forum in Crystal City, Virginia on November 8, 2001.

Dr. Jack Stein and Dr. Jerry Frankenheim, DNRB, conducted a workshop entitled “MDMA (Ecstasy) What Research is Telling Us” at the CADCA National Leadership Forum in Washington, DC on December 14, 2001.

Dr. Cindy Miner, Chief, Science Policy Branch, OSPC, organized and presented “NIDA/NIMH Grantwriting Workshop and Mock IRG Panel” along with Dr. Cheryl Boyce, NIMH, at the American Academy of Child and Adolescent Psychiatry meeting, Friday, October 26, 2001 in Honolulu, Hawaii. This workshop was designed to familiarize child and adolescent psychiatrists with the NIH grants and review process.

Dr. Cindy Miner gave a presentation on club drugs for the Gerber Adult Seminars, Science and Technology series on November 19, 2001 at the Jewish Community Center, Rockville, Maryland.

Dr. Cindy Miner organized and presented along with Dr. Howard Kurtzman, NIMH, a grantwriting workshop at the annual meeting of the Gay and Lesbian Medical Association in New Orleans, LA, September 29, 2001.

Dr. Cindy Miner presented “Prescription Drug Misuse, Abuse and Addiction” at the CADCA National Leadership Forum, December 13, 2001, Washington, D.C.

Dr. Lula Beatty, Chief, Special Populations Office, presented a seminar on research opportunities at NIDA at George Washington University for students and faculty on November 2, 2001.

Dr. Lula Beatty presented a session on research funding opportunities at NIDA as part of the colloquia series at the School of Social Work, Howard University, on Nov. 19, 2001.

Dr. Lula Beatty presented a session on "Steps to NIH Support" at a meeting sponsored by the NIH Office on AIDS entitled "HIV/AIDS Prevention, Care and Research: Gathering for the Circle of Life" in Albuquerque on January 10, 2002.

In December 2001, Dr. Lula Beatty reviewed convention proposal submissions for Divisions 35 (Society for the Psychology of Women) and 45 (Society for the Psychological Study of Ethnic Minority Issues) of the American Psychological Association.

In September 2001, Dr. Lula Beatty reviewed conference proposal submissions for the Sixth National Head Start Research Conference.

Ana Anders, Senior Advisor on Special Populations, worked with ONDCP, other Federal Agencies (SAMHSA, Dept. of Education, Justice Dept., Dept. of Transportation, etc.) and representatives of the Mexican government on the planning of the U.S./Mexico Binational Drug Demand Reduction annual conference held in Mexico City, Mexico in November 2001. She was responsible for planning and co-chairing the pre-conference Research Symposium. Additionally, she planned and developed research workshops for the Conference Research Track.

Ana Anders participated in planning the 2001 national observance of World Health Day with the American Association for World Health, the Pan American Health Organization and other Federal agencies.
Ana Anders co-chaired the planning meeting for the Latino Behavioral Health Institute annual conference held in Los Angeles, California in September 2001.

Ana Anders, as the NIDA Project Officer of a contractual agreement with the University of Miami, participated in the planning and development of the first national conference of the National Science Network on Drug Abuse held in Washington, D.C., November 2001

Ana Anders, as President of the NIH Hispanic Employee Organization, planned and hosted the Hispanic Heritage Month Observance for the NIH in September 2001.

Flair Lindsey, Program Analyst, Special Populations Office, coordinated the fifth annual Summer Research with NIDA program. The program allowed high school and undergraduate students to engage in drug abuse research with NIDA grantees for 8-10 weeks during the summer. In 2001, 40 students and 17 grantees participated in the program.

On September 24-26, 2002, Mary Ann Stephens, Ph.D., CCTN, attended and hosted sessions at the Health Disparities Conference in Philadelphia, PA.

Dr. Jack Blaine, CCTN, gave a presentation on the CTN at the American Methadone Treatment Association Conference, October 7, 2001, in St. Louis, MO. At that same meeting, several CTN community treatment providers discussed the clinical treatment provider perspective on participating in research and CTN principal investigators discussed overcoming barriers to blending clinical practice and research.

Dr. Betty Tai, CCTN, presented on CTN efforts in outreach to Hispanic patient populations and future collaborations with the National Hispanic Science Network on Drug Abuse, November 8-10, 2001, in Washington, D.C., co-sponsored by the Puerto Rico/Virgin Island ATTC.

Dr. Mark Swieter, OEA, presented a talk in November at American University in Washington, DC. This talk, addressed to graduate students and faculty in a variety of scientific areas, covered NRSA fellowships, the grants process, and the “do’s and don’ts” of putting together an application.

Dr. Rita Liu, Associate Director for Receipt and Referral, OEA, and co-chair of the NIDA Neuroscience Consortium Workgroup, assisted in the organization of a poster session on NIDA program priorities and review issues at the November meeting of the Society for Neuroscience in San Diego. The Office of Extramural Affairs was represented by Drs. Teresa Levitin, Director, OEA; Khursheed Asghar, Chief, Basic Sciences Review Branch; and Rita Liu.

Mr. Richard Harrison, Chief, Contracts Review Branch, OEA, provided information and recruitment activities with a NIDA Exhibit Booth for American Indian students at the November meeting of the American Indian Science and Engineering Society held in Albuquerque, NM.

Dr. William C. Grace served as a reviewer for HIV research proposals for the National Institute of Allergy and Infectious Diseases Prevention Science Review Committee in November.

Drs. William C. Grace, Deputy Director, OEA, Teresa Levitin, Director, OEA, and Susan Coyle, (formerly of OEA) presented “Characteristics of Successfully Recruited Grant Application Peer Reviewers” at the Fourth International Congress on Peer Review in Biomedical Publication held in Barcelona, Spain, September 14-16, 2002. Since air travel disruption precluded the authors’ attendance at this meeting, a poster session displaying their data was presented on their behalf.

Dr. Marina Volkov, SRA, Clinical, Epidemiological, and Applied Sciences Review Branch, OEA, presented a talk at City College of the City University of New York. Her talk was titled "Navigating the Bureaucratic Haze: How to Get Funding from NIH," and it was presented on December 10, 2001.

Dr. Minda Lynch, BCSRB, DNBR presented on “Club Drugs” to the Montgomery County Alcohol and Other Drug Abuse Advisory Council in January 2001.

Dr. Cora Lee Wetherington, DNBR and NIDA’s Women & Gender Research Coordinator, gave the keynote talk, “Developmental Vulnerabilities for Women and Substance Abuse,” in the workshop, “ Women and Substance Abuse” at the California Society of Addiction Medicine: State of the Art in Addiction Medicine meeting in Marina Del Rey, CA, October 19, 2001.

Dr. Cora Lee Wetherington served as co-host of the Women and Drug Abuse Special Interest Luncheon Table at the National Hispanic Science Network on Drug Abuse first national conference, Hispanic Drug Abuse Research: Advancing the Field, November 8-10, 2001, Washington, DC.

A NIDA sponsored Workshop; “Using Buprenorphine in Office-Based Practice” was held on Monday October 8, 2001 at the American Methadone Treatment Association Meeting in St. Louis, Missouri. This session was organized by Drs. Dorynne Czechowicz, Robert Walsh and Frank Vocci, all of NIDA’s Division of Treatment Research and Development.

NIDA sponsored a symposium on the prevention and treatment of adolescent drug abuse at the ASAM state-of –the art conference in November 2001, Washington, D.C. This session was organized by Dorynnne Czechowicz, M.D., DTR&D, in collaboration with the NIDA Child and Adolescent Research Workgroup.

On November 16, 2001, at the Association for Advancement of Behavior Therapy meeting in Philadelphia, Dr. Lisa Onken, DTR&D, discussed “Writing Behavioral Treatment Research Grants for NIDA“ at a symposium organized by Steven Beach, Ph.D. on “Writing Grants for NIDA, NIMH, and the CDC.”

On November 17, 2001, at the Association for Advancement of Behavior Therapy meeting in Philadelphia, Dr. Lisa Onken, DTR&D, participated in a symposium organized by Linda Dimeff, Ph.D. entitled, “Getting It Out There In A Big Way: Three National Models of Dissemination.” Her presentation was on “Behavioral Treatment Research at NIDA.”

Debbie Grossman and Dr. Ivan Montoya, both of DTR&D, represented NIDA at the Youth Tobacco Cessation Collaborative Meeting (YTCC) in Washington, D.C., on December 11, 2001. The YTCC is a collaborative group composed of representatives of major organizations that fund research, program, and policy initiatives related to controlling youth tobacco use.

Robert Walsh, DTR&D, presented “Studying Buprenorphine in Office-Based Settings NIDA/VACSP Study #1018”at the NIDA sponsored workshop entitled “Using Buprenorphine in Office-Based Practice” on October 8, 2001, at the American Methadone Treatment Association Meeting in St. Louis, Missouri. Dr. Dorynne Czechowicz, Mr. Robert Walsh and Dr. Frank Vocci, DTR&D organized this session.

Dr. Steven Grant, DTR&D, co-chaired a satellite symposium with Drs. David Shurtleff and Herb Weingartner entitled “Neuroscience Perspectives on the Effects of Ecstasy (MDMA)” at the 31st annual meeting of the Society for Neuroscience, San Diego, California November 14, 2001. Speakers at the symposium were Brian Yamamoto, Cleveland VA Medical Center, Annette Fleckenstein, University of Utah, Linda Chang, Brookhaven National Laboratory, Michael Morgan, University of Wales and Glen Hanson, NIDA.

Drs. Steven Grant, Harold Gordon, and Joseph Frascella represented the Clinical Neurobiology Branch, DTR&D at the NIDA booth during the Society for Neuroscience Meeting in San Diego, CA, November 12-15, 2001.

Drs. Joseph Frascella and Frank Vocci, DTR&D, conducted a session entitled “Strategies for Successful Grant Writing” at the First National Conference Hispanic Drug Abuse Research: Advancing the Field held in Washington, DC, November 8, 2001.

Dr. Joseph Frascella, DTR&D, presented a poster on the Institute’s Clinical Neurobiology program at a symposium of the 31st annual meeting of the Society for Neuroscience entitled “Transition from Drug Use to Addiction: Neuroscience Advances and Opportunities”, November 13, 2001 in San Diego, CA.

Dr. Steven Grant, DTR&D, co-chaired a symposium with Charles O’Brien, M.D., Ph.D. (University of Pennsylvania) entitled “Transition to Addiction: Does Pushing the Lever Pull the Switch” at the 40th annual meeting of the American College for Neuropsychopharmacology in Waikolola, Hawaii December 8-13, 2001. Speakers at the symposium were James Anthony, Johns Hopkins University, Elliot Stein, Medical College of Wisconsin, Linda Porrino, Wake Forrest University, and Barry Everitt, Cambridge University.

In November 2001, Dorynne Czechowicz, M.D., DTR&D, represented the National Institute on Drug Abuse, at a DHHS meeting on International Drug Scheduling. The purpose of this meeting was to discuss the coordination of international scheduling activities among the various Federal agencies.

On November 9, 2001, Dr. Lisa Onken, DTR&D, gave a presentation entitled, “Behavioral Treatment Research at NIDA: Opportunities for Hispanic Researchers & Research,” at the meeting of the National Hispanic Science Network on Drug Abuse in Washington, D.C.

Dr. Eve Reider, Prevention Research Branch, DESPR, represented NIDA at the Center for Mental Health Services (CMHS)’, Substance Abuse and Mental Health Services Administration, Roundtable on Shared and Unique Perspectives of Evidence-Based Prevention Practices, on October 5, 2001 in Washington, D.C.

Dr. Reider represented NIDA at The National Prevention Coalition meeting held on October 9, 2001 held at the National Mental Health Association in Alexandria, Virginia.

Dr. Reider represented NIDA at the National Summit, When Terror Strikes: Addressing the Nation’s Mental Health and Substance Abuse Needs- Strengthening the Homeland through Recovery, Resilience and Readiness, sponsored by the U.S. Department of Health and Human Services (DHHS) and Substance Abuse and Mental Health Services Administration (SAMHSA). The summit was held November 14-16, 2001 in New York City. Dr. Reider was the reporter for a roundtable discussion entitled Research, Evaluation, and Best Practices.

Dr. Reider represented NIDA at an Interagency Juvenile Justice meeting held November 27, 2001 at Office of National Drug Control Policy (ONDCP) in Washington, D.C.

Drs. Liz Robertson, DESPR, and Suman Rao, OSPC, presented a seminar titled Principles of Prevention Research: An Update at the Community Anti-Drug Coalitions of American National Leadership Forum XII, on December 14, 2001, in Washington, D.C.

Arnold Mills, DESPR, attended the 53rd Annual Meeting of the American Society of Criminology held in Atlanta, Georgia November 7-10, 2001. He served as the discussant for one of the sessions entitled Drugs and Crime: A National Research Agenda.

Moira O'Brien, DESPR, gave a presentation on Brains, Behavior and Culture: Integrating Perspectives on Drug Abuse and Addiction in a National Research Program, and participated in a cross-NIH session on extramural research opportunities during the annual meeting of the American Anthropological Association in Washington, D.C. on December 1, 2001.

Dr. Kevin Conway, DESPR, attended the 53rd Annual Meeting of the American Society of Criminology held in Atlanta, Georgia November 7-10, 2001. He presented a paper entitled Substance Use Disorders, Psychopathology, and Reported Violence.

Dr. Conway organized a bioethics panel for the NIDA Genetics Consortium Meeting, December 4, 2001. The expert panelists discussed the ethics considerations surrounding issues third parties involved in human genetics research.

Dr. Jerry Flanzer, DESPR, gave two lectures, one on the state of health services research regarding adolescent drug abuse treatment and service delivery in 2001, the other on the directions for drug abuse health services research for the next decade at the Health Services Disparities Conference, Galveston, Texas, October 31-November 2, 2001.

Dr. Flanzer and Dr. Thomas Hilton, DESPR, represented NIDA at the International Oxford House Conference, Washington, DC, November 30, 2001.

Drs. Peter Delany and James Colliver of DESPR conducted briefings on the findings of the 2001 Monitoring the Future Study for the Department of Health and Human Services and the Office of National Drug Control Policy.

Dr. Colliver represented NIDA at the annual meeting of the Healthy People 2010 Consortium in Atlanta on October 19, 2001 and gave a presentation on progress toward substance abuse objectives.

Dr. Dionne J. Jones, CAMCODA, moderated a workshop entitled "Special Issues to Consider with Substance Abusers" and served as Discussant on a second workshop entitled, "Interventions for At Risk Minority Substance Abusing Women" at the American Public Health Association Annual Meeting in Atlanta, GA, October 22-25, 2001.

Dr. Jones chaired a NIDA-sponsored symposium entitled "Drug Abuse, HIV Risk, and HIV Disease in the Brain" at the Annual Meeting of the Society for Neuroscience in San Diego, CA, November 12-15, 2001.

Dr. Toni Shippenberg, IRP, was co-chair and presenter of a panel symposia entitled "Opioid-Induced Plasticity From Neuron To The Addict; New Perspectives for the Treatment of Drug Addiction" at the 2001 American College of Neuropharmacology Meeting, December 9-13, 2001, Waikoloa, Hawaii.

Dr. Amy Newman, IRP, presented two invited lectures entitled " A Medicinal Chemistry Strategy in Drug-Abuse Research" and "Novel Probes for the Dopamine Transporter: In Search of a Cocaine-Abuse Therapeutic" at the Department of Chemistry, Northern Arizona University, Flagstaff, AZ, in November 2001.

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Media and Education Activities

Press Releases

July 24, 2001 - **NIDA News*Scan***

- Propranolol Useful in Treating Cocaine Addicts with Severe Withdrawal Symptoms
- Researchers Use PET Scans to Understand Effects of Nicotine on Brain Function During Performance of a Working Memory Task
- Researchers Investigate Potential New Treatment for Drug Abuse Relapse Related to Environmental Cues

As a result of NewsScan promotion, coverage appeared in Substance Abuse Letter.

August 1, 2001—**Therapy To Help Women Reduce Their Concerns About Gaining Weight Found To Be Effective in Helping Them to Stop Smoking.**
Researchers at the University of Pittsburgh School of Medicine found that a treatment program that focuses on reducing women's concerns about weight is the first treatment to significantly improve smoking cessation in weight-concerned women. The research was published in the August 2001 issue of Journal of Consulting and Clinical Psychology. Coverage of this paper appeared in Substance Abuse Letter and Social Work Today.

August 9, 2001—**NIDA Initiative Provides Increased Funding For Science-Based Drug Abuse Prevention Research**.
NIDA announced at the 2nd National Conference on Drug Abuse Prevention Research that it would commit $30 million over the next two years to stimulate research that will fill critical gaps in the knowledge and use of science-based drug abuse prevention programs.

August 29, 2001—**NIDA NewScan**

- Studies Show Effects of Cocaine Use During Pregnancy on Infants' Brains
- Rhesus Monkeys as a Model for Cocaine Abuse in Pregnant Humans
- Prenatal Cocaine Exposure Interferes With New Cell Formation and Increases the Incidence of Cell Death in the Developing Cerebral Cortex
- Chronic Prenatal Cocaine Exposure Leads to Long-term Changes in the Primate Brain

September 21, 2001—**National Conference Focuses on Drug Abuse and Addiction in Minority Communities**.
In September 2001, NIDA hosted "Bridging Science and Culture to Improve Drug Abuse Research in Minority Communities". This conference brought together researchers, students, academicians, health care providers, and community leaders interested in improving drug abuse research and expanding opportunities for minorities in this field.

September 28, 2001—**Scientists Find New Approach to Developing Medications To Prevent Relapse to Cocaine Use**.
Research teams from the Drug Abuse Program of the VU Medical Center in the Netherlands and the intramural laboratories of the National Institute on Drug Abuse (NIDA) identified a process in the brain that may lead to a new generation of medications to prevent relapse to cocaine use. The findings of this study were published in the October

1 issue of Nature-Medicine. Coverage of this publication appeared in Social Work Today, Substance Abuse Letter, Web MD, Alcoholism and Drug Abuse Weekly and Reuters Health Information.

October 16, 2001—**NIDA NewScan**

- Scientists Show Marijuana Use Affects Learning, Other Memory Skills
- Early Age at First Drink May Reflect Genetic Risk For Later Substance Abuse
- Adult Male Mice Exposed to Methamphetamine In Utero Have Increased Neurotoxicity Risk
- EEG Shown to Reliably Predict Drug and Alcohol Relapse Potential
- Study Finds Combination Therapy May Help Those With a History of Recurrent Depression to Quit Smoking

As a result of NewsScan promotion, coverage appeared in Alcoholism and Drug Abuse Weekly, Reuters Health Information, Substance Abuse Letter and Join Together Online.

November 27, 2001—**NIDA NewsScan**

- Brief Family Interventions in 6th Grade Cut Substance Abuse in 10th Grade
- Integrating Medical Care and Treatment for Substance Abuse Provides Better Outcomes

As a result of NewsScan promotion, coverage appeared in Substance Abuse Letter and, Ascribe Newswire.

November 30, 2001—**Dr. Glen Hanson Named Acting Director NIDA.**
Glen Hanson, Ph.D., D.D.S., was named the Acting Director of the National Institute on Drug Abuse by Ruth Kirschstein, M.D., Acting Director of the National Institutes of Health. His appointment followed the resignation of Dr. Alan I. Leshner, who served as NIDA's Director since 1994 and left to become the Chief Executive Officer of the American Association for the Advancement of Science. Coverage of this announcement appeared in The Salt Lake Tribune, Open Minds Online, Substance Abuse Letter and Alcoholism and Drug Abuse Weekly.

December 1, 2001—**Imaging Studies Expand Understanding of How Methamphetamine Affects the Human Brain.**
It is well known that methamphetamine abuse damages the nerve endings of human brain cells containing dopamine, a chemical messenger that plays a role in memory, mood, and motor coordination. The damage affects dopamine nerve endings located in a part of the brain known as the striatum. Two recently published studies about methamphetamine offer additional insights about the actions of this drug. The findings are reported in the December 2001 issues of the American Journal of Psychiatry and the Journal of Neuroscience. Coverage from these papers appeared in United Press International, Alcoholism and Drug Abuse Weekly and Medscape Health Online.

December 19, 2001—**2001 Monitoring the Future Survey Released.**
Use of cigarettes by American teenagers decreased from 2000 to 2001 according to the annual Monitoring the Future Survey released by the Department of Health and Human Services. This decline, observed for 8th and 10th graders, continues a decreasing trend begun around 1996. Decreases have also been found for seniors in recent years. These reductions in teenage smoking come on the heels of increases from the early to mid-1990s and are excellent news in the nation's battle to reduce the toll exacted by this leading cause of preventable death and disease. Coverage of this release appeared in CNN, MSNBC, The New York Times, USA Today, Washington Post, Washington Times, Wall Street Journal, Chicago Tribune, Reuters Health Online, AP Online, The San Francisco Chronicle, Join Together Online and the Kansas City Star

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Articles of Interest

July 28, 2001, The Economist— "The Case for Legalizing Drugs"

August 18, 2001, National Journal— Interview with Alan I. Leshner, Ph. D. — "Special Report, Prevention Takes a Different Track"

September 25, 2001, The New York Times— Interview with Alan I. Leshner, Ph.D.—"For Partygoers Who Can't Say No, Experts Try to Reduce the Risks"

October 26, 2001, Washington City Paper— Interview with Alan I. Leshner, Ph.D., and Frank Vocci, Ph.D.— "Magic Pill"

October 26, 2001, Reuters Health—Interview with Frank Vocci, Ph. D. —“Heroin Prescription May Help Addicts: Study”

November 6, 2001, The Wall Street Journal— Interview with Alan I. Leshner, Ph.D.—“FDA Permits Test Of Ecstasy as Aid In Stress Disorder”

December 3, 2001, The Washington Times— Letter from Alan I. Leshner, Ph.D. —“Dear Abby”

December 3, 2001, Reuters Health—Interview with Nancy Pilotte, Ph.D. — “ADHD Drugs May Lower Odds of Cocaine Abuse”

December 15, 2001, The New York Times—“After Two-Decade Halt, Marijuana Research is Set”

December 19, 2001, Associated Press—Interview with Glen Hanson, Ph.D., D.D.S., and Lloyd D. Johnston, Ph. D. “Study Shows U.S. Teens Smoking Less”

Dr. Frank Vocci, Director, DTR&D, was interviewed on September 15, 2001, by Ms. Simona Gorse of Slovenian television on medications development. He also was interviewed by Ms. Helena Kocmur of Slovenian print media on treatments for heroin addiction and the neurobiology of addiction.

Dr. Frank Vocci was interviewed on September 28, 2001, by Mr. Clark Collis regarding substance abuse in the professional music community.

Dr. Frank Vocci was interviewed on October 5, 2001, by Ms. Garance Franke-Ruta of The City Paper (Washington D.C.) regarding behavioral and pharmacological approaches to addictions treatment.

Dr. Frank Vocci was interviewed by Ms. Amy Norton on October 26, 2001, regarding a Lancet publication on treating heroin addicts with small doses of heroin.

Dr. Frank Vocci was interviewed on November 5, 2001, by Ms. Mary Duenwald, NY Times Science section writer, regarding ultra rapid opiate detoxification, and treatment of opiate addiction with buprenorphine and buprenorphine/naloxone.

Dr. Frank Vocci was interviewed on November 26, 2001, by Ms. Anna Synnevag, Norwegian Public Radio, on the NIDA funded medications and behavioral treatments development efforts for opiate and stimulant addictions.

Dr. Frank Vocci was interviewed on December 10, 2001, by Ms. Arline Kaplan of Psychiatric Times for an upcoming article on behavioral and pharmacological treatments for addictive disorders.

Dr. Frank Vocci was interviewed on December 17, 2001, by Seth Manoukan of Salon.com concerning information on rapid opiate detoxification. Dr. Vocci noted that Dr. Herb Kleber of Columbia University was conducting studies of this technique and that Dr. Thomas Kosten of Yale University had written a review article on the subject.

Dr. Frank Vocci was interviewed on December 18, 2001, by James Bartiromo of Popular Science magazine. Dr. Vocci discussed clinical neurobiology, behavioral, immunological and pharmacological treatments for addiction for an article being written for Popular Science.

Dr. Steven Grant, DTR&D, was interviewed for the article “Behavioral Addictions: Do They Exist” that appeared in Science (294: 980-982, 2001).

Training

A two day protocol training session for the “Buprenorphine/Naloxone: Comparison of Three Taper Schedules for Opiate Detoxification” protocol was held December 10-11, 2001, in Durham, North Carolina. CTN providers and staff from across the nation attended this meeting.

A 3-day protocol training session took place for the "Telephone Enhancement of Long-term Engagement" protocol on December 3-5, 2001, in Rancho Mirage, CA. Staff from the North Carolina, South Carolina, and Michigan sites attended the training.

NIDA Exhibits Program

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

October 3-7, 2001	American Academy of Family Physicians Annual Scientific Assembly Meeting
October 6-10, 2001	American Methadone Treatment Association Conference
October 21-25, 2001	American Public Health Association
October 21-24, 2001	Alcoholism and Substance Abuse Providers of New York State
October 23-28, 2001	American Academy of Child and Adolescent Psychiatry
October 27-30, 2001	15th Annual Conference on Hispanic Association of Colleges and Universities
October 31 – November 3, 2001	Annual Biomedical Research Conference for Minority Students
November 8-10, 2001	Association for Medical Education and Research In Substance Abuse
November 10-15, 2001	31st Society for Neuroscience Conference
November 13-18, 2001	American Indian Science and Engineering Society
December 3, 2001	NIDA Constituent Meeting
December 11-14, 2001	Community Anti-Drug Coalitions of America
December 13-16, 2001	American Academy of Addiction Psychiatry

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Planned Meetings

NIDA will host **Blending Clinical Practice & Research** at the Grand Hyatt, New York, March 14-15, 2002. This conference will provide an opportunity for clinicians and researchers to examine the latest findings about drug abuse and addiction and their application to clinical practice. Conference participants will also have the opportunity to help determine additional areas related to drug addiction treatment.

Planned Meetings Related to the CTN:

- National CTN Steering Committee Meetings are planned for the follow dates and locations: March 13, 2002, in New York City; July 15-17, 2002, in Seattle, Washington; and October 21-24, 2002, in Bethesda, Maryland.
- The Data and Safety Monitoring Board will meet February 13-14, April 15-16, July 22-23, and October 10-11, 2002, in Bethesda, Maryland.
- The Protocol Review Board will meet February 12, May 14, August 20, and November 5, 2002 in Bethesda, Maryland.
- The CTN Criminal Justice System Interest Group is planning a meeting on February 27-28, 2002, in Bethesda, MD. The meeting will focus on: reviewing current treatment research status, exploring opportunities/needs for court involved patients, identifying possible research concepts, and detecting protocol implementation barriers and solutions.

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Publications

Epidemiologic Trends in Drug Abuse – Community Epidemiology Work Group, Volume I – June 2001
NIH Pub. No. 01-4916A

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.

Epidemiologic Trends in Drug Abuse – Community Epidemiology Work Group, Volume II – June 2001
NIH Pub. No. 01-4917A

This report provides an in-depth analysis of the epidemiologic trends and special reports for a limited audience made up primarily of drug abuse researchers who utilize this volume to identify potential areas for further research.

NIDA Community Drug Alert Bulletin – Stress & Substance Abuse
NIH Pub. No. 02-5087

Given the heightened reports of increase in substance abuse in times of stress and the well-documented data that establish the connection between increased drug abuse during times of stress, NIDA has developed a new publication on Stress and Drug Abuse as part of its Community Drug Alert Bulletin series. The Alert is part of NIDA's efforts to ensure that clinicians, researchers, and members of the public have the most reliable and timely information available on this topic.

Principles of Drug Addiction Treatment: A Research-Based Guide (Spanish) (2001)
NCADI # BKD347S

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

Inhalant Abuse - Research Report Series (Spanish) (2001)
NCADI # PHD675S

Based on research on the use and prevalence of inhalants, this report presents information on the types of inhalants, the consequences of their use, who is abusing inhalants, and how to recognize inhalant abuse.

Prescription Drug Abuse - Research Report Series (Spanish) (2001)
NCADI # PHD866S

This report describes the dangers of prescription drug abuse and reviews recent research in this area. It offers approaches for patients and providers to help them avoid the misuse of prescription drugs. The report reviews most commonly abused prescription drugs.

Native American/Alaska Natives Calendar 2002
NIH Pub. No. 01-4996

This is an intergenerational calendar for Native Americans/Alaska Natives. Through photography, text, and quotations that reinforce Indian identity and pride, the calendar is designed to increase the audience's knowledge and awareness of the signs, symptoms, and physiological effects of various drugs.

NIDA NOTES

NIDA NOTES, Volume 16, Issue No. 4
NIH Pub. No. 02-3478

This issue contains a special message from the NIDA director about coping with the stress associated with the terrorist attacks of September 11, 2001. Dr. Leshner points out that stress is one of the most powerful triggers for drug craving and relapse to drug abuse and that NIDA is placing a high priority on research on the relationship between stress and drug abuse.

In the Director's Column, Dr. Leshner describes how NIDA provides appropriate information about drug abuse and addiction to its many audiences.

The cover story reports on the results of a 33-year study of the patterns and consequences of heroin addiction in almost 600 heroin-addicted criminal offenders. The researchers found that the participants' lives were characterized by increased risk of crime, health problems, and death. Those able to achieve 5 years of abstinence realized major quality-of-life gains. Another story describes a study demonstrating that buprenorphine, a medication developed through NIDA research to treat heroin addiction, is equally effective when taken three times a week as when taken daily. Other stories report on a biochemical abnormality found in the brains of children prenatally exposed to cocaine; similar brain characteristics of drug addicts and individuals with pathological obesity; and how TV public service announcements aimed at sensation-seeking adolescents achieved a reduction in marijuana use in the targeted group. Also included is a report on the 25th anniversary meeting of NIDA's Community Epidemiology Work Group, accompanied by information about current drug abuse trends across the country. The Tearoff reports on NIDA's science education products, including "Brain Power!" a program for second-and third-grade students and their teachers.

Other Publications

5th Annual NIDA International Forum
Building International Research on Drug Abuse: Drug Abuse Treatment in the New Millennium

This volume provides summaries of oral presentations, workshops, and discussion sessions; abstracts of oral and poster presentations; the agenda; and a participant list from the June 2000 meeting held in San Juan, Puerto Rico immediately before the Annual Scientific Meeting of the College on Problems of Drug Dependence.

Pacific Regional Research Conference on Methamphetamine and Other Amphetamine-Type Stimulants

This volume summarizes the oral presentations and includes the agenda and participant list from this November 2000 meeting cosponsored by NIDA and the Thai Ministry of Public Health to discuss scientific data about the physiological and behavioral effects of these drugs, epidemiological trends, and strategies for prevention and treatment.

NIDA's International Collaboration and Fellowship Programs

Advises NIDA grantees of opportunities to mentor Fellows or collaborate with scientists from other countries through programs administered by the International Program: INVEST Research Fellowships for postdoctoral drug abuse researchers; NIDA Hubert H. Humphrey Drug Abuse Research Fellowships for international researchers, treatment providers, prevention specialists, program planners, or government officials; and the Distinguished International Scientist Collaboration Program Award for senior drug abuse researchers from other countries.

NIDA INVEST Letter, Fall 2001

The lead story in this issue reported on the Sixth NIDA International Forum, Building International Research on Drug Abuse: Children and Youth at Risk, and announced the abstract deadline for the 2002 Forum, which will focus on drug abuse treatment innovations June 6 through 8 in Quebec City, Canada. International researchers were invited to apply for the 2002 WHO/NIDA/CPDD International Traveling Fellowships, offered in conjunction with the Forum. The 2001-2002 INVEST Research Fellows were announced.

Drs. Harold Gordon, DTR&D, Maria D. Majewska, DTR&D and Pushpa Thadani, DNBR, were guest editors for a double issue of Psychoneuroendocrinology 27(1-2), January, 2002, entitled "Stress and Drug Abuse" including invited papers from presenters at three NIDA-sponsored workshops on this topic. Harold Gordon was the author of a paper in that issue entitled "Early Environmental Stress and Biological Vulnerability to Drug Abuse,"; the other guest editors also wrote articles.

Dr. Peter Hartsock and NIDA grantees at the University of New Mexico and University of Alaska produced the lead paper, titled “Stigma, Ethics, and the Frontier” in a special (Spring/Summer) issue of the National Science Foundation (NSF) journal, Arctic Research of the United States. The NIDA-funded five-year project reported on ethically important aspects of rural health care for stigmatizing illnesses (e.g., substance abuse, HIV/AIDS, and sexually transmitted diseases).

Thirteen 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.

The Fall/Winter 2001 edition of the CTN Report, a quarterly newsletter on the CTN, was distributed in late January, 2002.

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Director's Report to the National Advisory Council on Drug Abuse
February, 2002

Staff Highlights

Staff Honors and Awards

Dr. Frank Vocci, Director, DTR&D, was awarded a 2001 Presidential Rank Award (Meritorious Executive) for his leadership activities in the Division of Treatment Research and Development. President George W. Bush spoke to the Awardees on October 15, 2001 at a ceremony titled: “Dedicated to Serving America” at Constitution Hall.

Dr. Lula Beatty, Chief, Special Populations Office, was appointed by the governor of Maryland to the state's Women's Health Promotion Council in September 2001.

Dr. Toni Shippenberg, IRP, was awarded the “Grass Lectureship in Neuroscience” by the American Society of Neuroscience.

Dr. Cesario V. Borlongan, IRP, received the NIH 2002 Fellows Award for Research Excellence (FARE) in recognition of his outstanding scientific research in general neuroscience.

Staff Changes

Wilson Compton, M.D., M.P.E., has been appointed Director of NIDA’s Division of Epidemiology, Services and Prevention Research. He will join NIDA full-time in March 2002. Dr. Compton is currently Director of Barnes-Jewish Hospital Chemical Dependency Services, Director of the Master of Psychiatric Epidemiology Program at Washington University School of Medicine, and Associate Professor, Department of Psychiatry, Washington University School of Medicine. Dr. Comptom obtained his Doctorate of Medicine from Washington University in 1986 and a subsequent M.P.E. in Psychiatric Epidemiology. After completing an internship and chief residency in psychiatry at Barnes and Allied Hospitals, he joined Washington University School of Medicine faculty in 1990, where he has been active in the academic, training, research and clinical programs.

David Shurtleff, Ph.D., Deputy Director for Program, Division of Neuroscience and Behavioral Research (DNBR), was named the Division’s Acting Director in December 2001. Before becoming Deputy Director, Dr. Shurtleff served as a Health Scientist Administrator in the Behavioral Sciences Research Branch within DNBR where he supported extramural research in the basic behavioral sciences, including research in the cognitive sciences, behavioral economics, decision theory and human and animal models of impulsivity, risk taking and other aspects of drug addiction. Before coming to NIDA, Dr. Shurtleff was a Research Psychologist at the Naval Medical Research Institute in Bethesda, MD. While with the Navy he conducted basic behavioral, electrophysiological, cognitive and field research on a variety of issues related to cognitive performance, environmental stress, and peripheral neuropathy.

Jonathan D. Pollock, Ph.D. has been appointed as the Chief of the Genetics and Molecular Neurobiology Branch of the Division of Neuroscience and Behavioral Research (DNBR). Dr. Pollock joined NIDA in 1996 as a program director in the Basic Neurobiology and Biological Sciences Research Branch. In December 2000, he became the Acting Chief for DNBR’s Genetics and Molecular Neurobiology Branch.

Mary E. Abreu, Ph.D. was recruited to the Center for Clinical Trials Network in October 2001. Dr. Abreu received her Ph.D. in pharmacology from the University of Texas Medical Branch in Galveston. After completing postdoctoral training in neuroscience at Johns Hopkins University School of Medicine, she joined a pharmaceutical company where

she led a discovery research program focused on identifying novel pharmacotherapies for psychiatric and neurologic diseases. Subsequently, Mary was with the Medications Development Division of NIDA where she served for 2 years as a health scientist administrator in the Pharmacology & Toxicology Branch. In 1997, Mary left NIDA for a large pharmaceutical company to gain expertise in the conduct and management of all aspects of pharmocotherapy clinical trials.

Ling Chin, M.D., M.P.H. joined the CCTN in November 2001. Dr. Chin received her medical degree from the George Washington University Medical Center in 1986. She was trained in Primary Care Internal Medicine at Francis Scott Key Medical Center in Baltimore, MD, and completed her residency in Preventive Medicine at Johns Hopkins. She is board certified in Preventive Medicine, and is a Fellow of the American College of Preventive Medicine. She was at NIDA from 1990 to 1994, in the Division of Epidemiology and Prevention Research. She was at FDA, in the Center for Drug Evaluation and Research (CDER), from 1994 till November, 2001, involved with switching drugs from prescription to over the counter status, including the development of label comprehension and actual use trial design and methodology.

Ms. Jessica Clements recently joined the Division of Treatment Research and Development. She will work with the Medications Discovery and Toxicology and Chemistry and Pharmaceutics Branches.

Christine Colvis, Ph.D. recently joined NIDA as a program director in the Genetics and Molecular Neurobiology Branch of the Division of Neuroscience and Behavioral Research. Dr. Colvis did her graduate work in the laboratory of Dr. Ted Acott at the Casey Eye Institute, Oregon Health Sciences University in Portland, Oregon. Her research there focused on the kinetics and thermodynamics of matrix metalloproteinase-3 and its role in an aqueous humor outflow model system. As a research fellow under Dr. Donita Garland at the National Eye Institute, Christine studied proteomics of human lens and cataract. Christine is interested in proteins and proteomics of neurons and neural tissue as it relates to drug abuse and addiction. She is a member of the newly formed Proteomics Interest Group (ProtIG) at the NIH and also sits on the steering committee for that group.

Aria Davis Crump, Sc.D., joined NIDA's Division of Epidemiology, Services and Prevention Research on September 10, 2001. She received a Doctor of Science from the Johns Hopkins University Bloomberg School of Public Health in Behavioral Sciences and Health Education. Prior to coming to NIDA, Dr. Crump completed a postdoctoral fellowship in the Prevention Research Branch at NICHD and served as an Assistant Professor in the Department of Public and Community Health, University of Maryland at College Park. Her program areas at NIDA include family-based prevention research, substance use prevention in ethnic minority communities, persuasive communications research, and drug abuse training programs.

Ms. Indira Hills joined the Regulatory Affairs Branch of the Division of Treatment Research and Development in November 2001. Ms. Hills was formerly with the Center for Drug Evaluation and Research, Food and Drug Administration.

Shakeh Jackie Kaftarian, Ph.D., joined NIDA's Division of Epidemiology, Services and Prevention Research in September 2001. Formerly with SAMHSA, Dr. Kaftarian is a health psychologist and an adjunct Research Professor at the Uniformed Services University of the Health Sciences, Department of Psychiatry. At NIDA she has responsibility for the development of the prevention research services area of DESPR, the management of the school and community-based prevention research grants, and has an interest in the expansion of the international substance abuse prevention activities of DESPR.

Janet Levy, Ph.D., joined the CCTN as a statistician in November 2001. She received her doctorate in educational psychology and research from the University of Kansas, with an emphasis in psychometrics and statistics. She was the data analyst and statistician for the Ralph L. Smith Research Center at the University of Kansas Medical Center, supporting basic research in human development. For the last six years, Dr. Levy has been managing and developing mathematical models to predict a variety of consumer behaviors for large banks and telecommunication companies

Yu "Woody" Lin, Ph.D., joined the Division of Neuroscience and Behavioral Research at NIDA as a Health Science Administrator in October 2001. His research experience includes neuropharmacological studies with central dopaminergic, muscarinic, glutamatergic, purinergic and opioid systems and their relationship to drug abuse, neurotoxicity and cell injury. He has broad training in using in vivo, ex vivo and in vitro disease models and behavioral tests for pain and neurological deficits. Dr. Lin's recent research included the functional fluorescence "real-time imaging" assessment of ionic dynamics and the electrophysiological analysis of neuronal activities. Before coming to NIDA, Dr. Lin worked in the New York State Health Department as a Research Affiliate scientist and in the Walter Reed Army Institute of Research as a Research Associate scientist. Dr. Lin has also been trained in mainland

China as a physician. His research in China concerned mechanisms of endogenous opioid systems and their translation into acupuncture therapy.

Brian Marquis joined OSPC in January 2002 as the Information Center Manager for the Public Information and Liaison Branch. Prior to joining OSPC, Mr. Marquis worked at the AHRQ Publications Clearinghouse and as a contractor at NHLBI. He has a B.S. in Family Studies from University of Maryland and he is currently working on completing his M.B.A.

Sara Rosario joined OSPC in September 2001 as Writer-Editor for the Public Information and Liaison Branch. Prior to September, Ms. Rosario spent a year as a communications intern at NIDA, through the H.A.C.U. program, while completing a Bachelor of Arts degree in Public Communication at the University of Puerto Rico.

Paul Wakim, Ph.D., joined the CCTN as a mathematical statistician in December 2001. He received an M.A. in Statistics in 1980, an M.S. in Industrial Engineering and Operations Research in 1982 and a Ph.D. in Statistics in 1983 from the University of California at Berkeley. He has 19 years of technical consulting experience providing a wide range of statistical services to both internal and external clients. From 1984 to 1993, he taught evening courses in mathematics and statistics at the University of Maryland University College at College Park.

Dale Weiss joined OSPC in October 2001 as a Program Analyst for NIDA's International Program. Prior to joining OSPC, Ms. Weiss worked in NIDA's Contract Management Branch as a Contracting Officer for 13 years. Prior to joining NIDA, Ms. Weiss worked at the Department of Commerce, and the U.S. Coast Guard.

Cecelia McNamara, Ph.D. joined the Behavioral Treatment Development Branch, DTR&D in October 2001 as a Health Scientist Administrator. She manages a portfolio of grants that includes behavioral therapy and psychotherapy studies of adult drug abusers, dual diagnosis, and criminal justice populations and will be developing a research portfolio concerned with studying behavioral therapy training and supervision, and ways to use information technology to deliver and improve behavioral treatments. She previously worked in NIDA's Clinical Trials Network.

Ivan D. Montoya, M.D., M.P.H., Medical Officer, transferred from the Clinical Trials Network to the DTR&D's Medications Research Grants Branch in October 2001. Dr. Montoya's previous experience includes seven years as clinical investigator in the Intramural Research Program of NIDA, and four years in academia.

Catherine Law has left NIDA to accept a writer-editor position in the Office of Communications at the National Center for Complementary and Alternative Medicine. She had been with NIDA since July 2000 as a writer-editor in OSPC's Science Policy Branch.

Susan L. David, M.P.H. retired from NIDA after 34 years of federal service. At NIDA she served as Chief of the Public Information Branch in the Office of Science Policy and Communication and, most recently, as the Deputy Branch Chief in the Prevention Research Branch in the Division of Epidemiology, Services and Prevention Research. In the latter capacity she managed the evaluation contract for the White House Office of National Drug Control Policy's National Youth Anti-Drug Media Campaign and developed and managed a portfolio on persuasive communications.

Ms. Celeste Proctor of the Division of Treatment Research and Development retired on September 30, 2001 after 30 years in Federal Service.

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

Dr. Linda Caldwell, Penn State University, received the 2001 National Therapeutic Recreation Society Professional Research Award for “significant contributions to the profession of therapeutic recreation.”

Dr. F. Ivy Carroll, Vice President for Chemistry and Life Sciences at the Research Triangle Institute in North Carolina has been awarded the 2002 Medicinal Chemistry Award of the American Chemical Society (ACS) Division of Medicinal Chemistry. This is the ACS’s top honor in medicinal chemistry. This award cited Dr. Carroll’s international recognition in a variety of research areas, and particularly highlighted the development of the 3-phenyl-tropane class of compounds as potential treatment agents for cocaine abuse, and his work on kappa selective antagonists and nicotinic receptor antagonists.

Dr. Linda Cottler, Washington University School of Medicine in St. Louis, was chosen to receive the Boston University School of Public Health Alumni Award.

Dr. Thomas Dishion, University of Oregon, was selected as a fellow in the American Psychological Society.

Dr. Lewis Donohew, University of Kentucky, was honored as the National and International Communication Associations' Health Communication Scholar of the Year for 2001-2002 for his landmark work in translating basic research on risk-taking and sensation-seeking personality into the study and development of research-based prevention media campaigns.

Dr. Michael Hecht, Penn State University, is the recipient of the National Communication Association's 2001 Gerald R. Phillips Award for Distinguished Scholarship in Applied Communication Research.

Dr. Steve Maier of the University of Colorado, Department of Neuroscience (Denver) was named a Distinguished University Professor in December 2001. He is only the 19th person to receive this honor. Dr. Maier receives NIDA support to look at the activity in the serotonin system under conditions of controllable and uncontrollable stress.

Eileen Pencer, President of a CTN Community Treatment Provider in the New York Node was elected as President of the Association of Alcoholism and Substance Abuse Providers of New York State, in November 2001.

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