National Institute on Drug Abuse

Director's Report

to the

National Advisory Council on Drug Abuse

September, 1997

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National Institute on Drug Abuse

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Research Findings

Basic Research

Neurochemical Basis of Marijuana Withdrawal

George Koob and co-workers at Scripps Research Institute in La Jolla, California recently report a link between withdrawal from marijuana, behavior that appears to be like an anxiety state, and a peptide called corticotrophin-releasing factor (CRF). When the researchers measured CRF levels in the amygdala of THC-withdrawn rats, there was a doubling to tripling of the peptide which paralleled the anxiety and stress levels of the rats. Science 276, pp. 2050-2054, 1997.

Methamphetamine and Neurotoxicity

Dr. Charles Vorhees and his co-workers recently reported that in adult rats, exposure to methamphetamine (MA) produces localized depletion of glutamate-positive neurons and astrogliosis in somatosensory cortex. In developing animals, MA had no effect on glutamate-positive neurons suggesting that the mechanism underlying glutamatergic neurotoxicity is not acquired before postnatal age of 40 days. Other studies by these investigators show that administration of alpha-phenyl-N-*tert*-butylnitrone, a free radical spin trapping compound, attenuated MA-induced dopamine depletion in the adult rat caudate-putamen without altering MA-induced hyperthermia. These results support a role for free radicals in the generation of MA-induced dopaminergic neurotoxicity. Pu, C., Broening, H.W., and Vorhees, C. Synapse. 23, pp. 328-334, 1996; Cappon, G.D., Broening, H.W., Pu, C., Morford, L. and Vorhees, C. Synapse, 24, pp. 173-181, 1996.

Methylenedioxyamphetamines (MDA) and Neurotoxicity

Recent research reports that a putative metabolite of MDA, 2,5-bis-(glutathiol-S-yl)-alpha-methyldopamine, reproduced the neurobehavioral effects of the parent amphetamine. In addition, it produced changes in serotonergic system which appeared to be selective for nerve terminal fields as the levels of 5-HT were unaffected in the regions of the cell bodies. Since this metabolite caused long-term depletion in 5-HT without adversely affecting the dopaminergic system, it mimics the selectivity of MDA/MDMA. In contrast, administration of other metabolites of MDA produced only behavioral changes in animals that were similar to MDA. Thus, these results suggest a possible role of quinone-thioethers in the neurobehavioral and neurotoxicological effects of MDA/MDMA. Miller, R.T., Lau, S.S., and Monks, T.J., European J. Pharmacology, 323, pp. 173-180, 1997.

Orphanin FQ(OFQ)/Nociceptin(N), Antinociceptive Mechanisms and Receptor Subtypes

Orphanin FQ/Nociceptin, is a heptadecapeptide and a closely related to the cloned opioid receptor family . Orphanin produces hyperalgesia in mice when administered intra-ventricularly. Dr. Gavril W. Pasternak and colleagues of Sloan Kettering Institute for Cancer Research have been characterizing the pharmacology of OFQ. They found, in addition to hyperalgesia, which is observed soon after administration of OFQ, OFQ also produces a delayed analgesia response. Unlike OFQ-induced hyperalgesia, OFQ-induced analgesia is readily reversed by the opioid antagonist naloxone, implying an opioid mechanism of action. In view of the very poor affinity of OFQ for all the known traditional opioid receptors and the low affinity of opioids for the ^{125}I[Tyr^{14}]OFQ binding site, OFQ-induced analgesia is probably mediated through a novel OFQ receptor subtype. In contrast to supraspinal administration, spinal administration of OFQ elicits a rapidly appearing, naltrexone-reversible, dose-dependent analgesia in the tailflick assay without any indication of hyperalgesia. Two OFQ/N (1-7) and OFQ/N (1-11), are active, but far weaker. Blockade of sigma receptors with haloperidol enhances the analgesic potency of spinal OFQ/N, OFQ (1-7) and OFQ (1-11), but not as dramatically as supraspinal OFQ. Antisense probes targeting the second and third coding exons, but not the first exon, of the cloned mouse OFQ/N receptor (KOR-3) partially block OFQ/N analgesia. It appears that while spinal analgesia is mediated through an OFQ/N receptor, it is not clear that this is the same receptor which has been cloned. Future work is needed to define the receptor mechanisms mediating these analgesia actions. King, M.A., Rossi, G.C., Chang, A.H., Williams, L. and Pasternak, G.W. Spinal Analgesic Activity of Orphanin FQ/Nociceptin and its Fragments. Neurosci. Lett., 223, pp. 113 116, 1997; Rossi, G.C., Leventhal, L. and Pasternak, G.W., Naloxone-Sensitive Orphanin FQ/Nociceptin Analgesia in Mice. Eur. J. Pharmacol. 311, pp. R7-R8, 1996.

The PCP-Induced "Olney Lesion" Is Reproduced by Carbachol + Kainic Acid

Antagonists of the NMDA glutamate receptor, such as phencyclidine (PCP), ketamine, and dizocilpine, injure (produce vacuoles in) pyramidal neurons of the posterior cingulate/ retrosplenial (PC/RS) cortex when administered systemically to adult rats. This is sometimes termed the "Olney lesion," after the NIDA grantee, John W. Olney, M.D., its discoverer. He and other investigators hypothesize that this action may underlie the psychotomimetic effect of this class of drugs. This neurotoxic action of NMDA antagonists is hypothesized by Dr. Olney to be mediated by a complex disinhibition mechanism in which NMDA antagonists abolish GABAergic inhibition, resulting in excessive release of acetylcholine at muscarinic receptors on PC/RS cortex neurons. However, microinjection of carbachol (muscarinic agonist) into PC/RS cortex did not reproduce the Olney lesion. Because other evidence suggests that the NMDA antagonist disinhibition mechanism also releases excessive glutamate at non-NMDA receptors on PC/RS neurons, they microinjected a combination of carbachol and kainic acid (non-NMDA glutamate agonist) in very low doses into the PC/RS cortex. The combination reproduced the Olney lesion. Kainic acid alone did not reproduce the lesion. Thus, simultaneous hyperactivation of both muscarinic and non-NMDA glutamate receptors on PC/RS neurons is required for this lesion. Farber, et al., Society for Neuroscience Abstract, 1997.

Inhibition of Glutamate Transport in Synaptosomes by Dopamine Oxidation and Reactive Oxygen Species (ROS)

Dopamine can form reactive oxygen species (ROS) and other reactive metabolites that can modify proteins and other cellular constituents. Dr. Teresa G. Hastings of the University of Pittsburgh and her research team tested the effect of dopamine oxidation products, other generators of ROS, and a sulfhydryl modifier on the function of glutamate transporter proteins. They also compared any effects with those on the dopamine transporter, a protein whose function has previously been shown to be inhibited by dopamine oxidation. Preincubation with the generators of ROS, ascorbate or xanthine plus xanthine oxidase inhibited the uptake of [^{3}H]glutamate into rat striatal synaptosomes (-54 and -74%, respectively). The sulfhydryl-modifying agent N-ethylmaleimide also led to a dose-dependent inhibition of [^{3}H]glutamate uptake. Preincubation with dopamine (100 M) under oxidizing conditions inhibited [^{3}H]glutamate uptake by 25%. Exposure of synaptosomes to increasing amount of dopamine quinone by enzymatically oxidizing dopamine with tyrosinase further inhibited [^{3}H]glutamate uptake, an effect prevented by the addition of gultathione. The effects of free radical generators and dopamine oxidation on [3H]glutamate uptake were similar to the effects on [^{3}H]dopamine uptake. These findings suggest that ROS and dopamine oxidation products can modify glutamate transport function, which may have implications for neurodegenerative processes such as ischemia, methamphetamine-induced toxicity, and Parkinson's disease. Berman, S.B. and Hastings, T.G. Inhibition of Glutamate Transport in Synaptosomes by Dopamine Oxidation and Reactive Oxygen Species. J. Neurochem. 69 (3), pp. 1185-1195, 1997.

Moving from the Orphanin FQ Receptor to an Opioid Receptor Using Four Point Mutations

In spite of the high homology at both ligand and receptor level there is little direct cross-talk between the Orphanin FQ system and the endogenous opioid system. The opioid peptides show either relatively low affinity or no affinity towards the Orphanin FQ receptor. Conversely, Orphanin FQ has no affinity towards any of the opioid receptors. To investigate the molecular basis of such discrimination Dr. Huda Akil and her coworkers discovered that by mutating as few as four amino acids, they can produce a receptor which recognizes prodynorphin products with very high affinity and yet still binds Orphanin FQ as well as the wild type receptor. This suggests that the Orphanin FQ receptor has developed features which specifically exclude the opioids, and that these features are distinct from those required for the high affinity binding of its own endogenous ligand.

In a follow-up study, Dr. Akil and her coworkers aimed at shifting the binding profile of the Orphanin FQ receptor towards the opioid receptors, as a means of better understanding the critical characteristics of the opiate binding pocket. After two rounds of mutagenesis, several Orphanin FQ receptor mutants could be labeled with [^{3}H]naltrindole and showed greatly increased affinities toward the opiate antagonists naltrexone, nBNI and (-)bremazocine. Furthermore, these Orphanin FQ receptor mutants exhibited stereospecificity similar to that of opioid receptors. In addition, the binding of several opioid alkaloids to an Orphanin FQ mutant and to the delta receptor showed similar affinity-shift profiles in the presence and the absence of GTP and high salt concentration, suggesting that their agonist/antagonist nature was preserved. These results indicate that several residues in the Orphanin FQ receptor are critical to its selectivity against the opiate alkaloids, particularly antagonists in the benzomorphan family. It is reasonable to hypothesize that the corresponding residues in the opioid receptors may form a common binding pocket for opiate alkaloids. These findings may also be helpful to medicinal chemists in designing ligands for the Orphanin FQ receptor based on the structure of the opiate alkaloids. J. Biol. Chem., 271, 32016, December, 1996.

Carboxypeptidase E Activity Is Deficient in Mice with the Fat Mutation

Carboxypeptidase E (CPE) is involved in the biosynthesis of many peptide hormones and neurotransmitters. In collaboration with Dr. Leiter of the Jackson Laboratory, Dr. Lloyd D. Fricker of Albert Einstein College of Medicine was fortunate to find a mouse that has a normally occurring point mutation within CPE. This mutation (Cpe^{fat}/Cpe^{fat}), which completely eliminates CPE activity, causes the mice to be sterile and obese. Male mice, but not female mice, show markedly elevated serum glucose levels. These defects are due to the absence of CPE activity, presumably to a folding defect that causes the mutant CPE to be degraded in the endoplasmic reticulum. Peptide processing is abnormal in these mice, but not completely eliminated. This raised the possibility that a second carboxypeptidase is involved in peptide processing, and that this second enzyme can partially compensate for the defective CPE in the Cpe^{fat}/Cpe^{fat} mice. Dr. Fricker and his coworkers recently found a novel enzyme, carboxypeptidase D (CPD), that has CPE-like enzymatic properties. Recently they have discovered that in bovine and rat tissues CPD has a broad distribution. This is consistent with a role for this enzyme in the processing of numerous peptides, which would explain the ability of the Cpe^{fat}/Cpe^{fat} mice to produce small amounts of peptides.

Dr. Fricker and his coworkers also found that the opiate peptide precursor, prodynorphin, is not correctly processed in the Cpe^{fat}/Cpe^{fat} mouse brain. The processing of prodynorphin by the endopeptidases (the step that precedes CPE) is decreased in the Cpe^{fat}/Cpe^{fat} mice, suggesting that the CPE defect somehow feeds back on the previous step. CPE could play a role in the sorting of peptide precursors into the regulated secretory pathway, and the absence of CPE in the Cpe^{fat}/Cpe^{fat} mice causes missorting which then alters the processing. J. Biol. Chem., 271, 30619, November, 1996.

Placenta and Neurotransporter

Dr. Ganapathy and his research team has recently published reports that demonstrate that tyrosine phosphorylation is an essential component in the signaling pathways participating in the regulation of the human serotonin transporter gene expression. Regulation of the transporter gene expression also appeared to be modulated by a neuro-protective agent, aurin tricarboxylic acid (ATA) and epidermal growth factor (EGF) as both agents increased the transporter activity in JAR human placental choriocarcinoma cells. However, ATA appeared to elicit this, at least in part, by activating the EFG receptor through tyrosine phosphorylation. Other findings demonstrated that interleukin-1b turned on the human serotonin transporter gene expression by activating the transcription factor NF-kB via the mitogen-activated protein kinase signaling pathways. Although the physiologic role of the serotonin transporter in normal

human placenta remains to be established, these data suggest a possibility that the placental serotonin transporter may be involved in the maintenance of serotonin levels in the intervillous space and thereby optimize utero placental blood flow. A defective clearance of serotonin from the maternal circulation due to dysfunctional serotonin expression in the placenta may play a role in the pathogenesis of intra-uterine growth retardation. Prasad, P.D. et al., European J Pharmacology, 325, pp. 85-92, 1997; Kekuda, R. et al., J Neurochemistry, 68, pp. 1443-1450, 1997.

Morphine and Melanocortin-4 Expression

Opiate dependence and tolerance is antagonized by melanocortin peptide but the receptors activated by these peptides has not been fully characterized. Duman and his colleagues at Yale University report the cloning and characterization of the full length rat melanocortin-4 receptor (MC4-R). This 332 amino acid long receptor shares a 95% amino acid sequence identity to the human MCR-4 receptor. The MCR-4 transcripts are most abundant in the septum and nucleus while only being moderately expressed in the periaquaductal gray, hypothalamus, neostriatum, ventral tegmentum, and olfactory bulb. Little expression is found in the cerebellum, substantia nigra, frontal cortex, and hippocampus. Chronic administration of morphine for five days was associated with a time-dependent down regulation of the MC4-R mRNA expression in the striatum and periaqueductal grey. Morphine treatment also resulted in time-dependent reduction in expression of the MC4R in the nucleus accumbens and the olfactory tubercle that was faster, occurring over 1 to 3 days. Other areas expressing the MC4-R were not affected by chronic morphine. Based on previous studies showing that melanocortins block tolerance and dependence as well as the results of the current study, Duman suggests that the down regulation of MC4-R by morphine may play a significant role in neuroadaptations to opiates and other drugs of abuse. Alvaro, J.D., Tatro, J.B., Quillan, J.M., Fogliano, M., Eisenhard, M., Lerner, M.R., Nestler, E.J., and Duman, R.S. Morphine Down-regulates Melanocortin-4 Receptor Expression in Brain Regions that Mediate Opiate Addiction. Molecular Pharmacology, 50, pp. 583-591, 1996.

Ligand Recognition by Monoamine Transporters

Transfection of cells with cDNA libraries and selection for survival in the presence of MPP+, a neurotoxin that destroys dopaminergic and other aminergic cells led to the discovery of two vesicular monoamine transporters, VMAT 1 and VMAT2. Cells overexpressing either VMAT survive because these transporters sequester the neurotoxin MPP+ in vesicles and prevent MPP+ uptake into mitochondria where MPP+ would be converted into cytotoxic compounds. VMAT1 expression is restricted to adrenal chromaffin cells while VMAT2 is expressed monoaminergic neurons in the CNS, neurons in sympathetic ganglia, mast cells, and histamine containing cells of the gut. VMAT2 has a higher affinity for serotonin, histamine and tetrabenazine than VMAT1. The differences in affinity between the two transporters appears to be conferred by differences in the transmembrane domains 5-8 (TMD 5-8) and transmembrane 9-12 (TMD 9-12). In this study Finn and Edwards determined how specific mutations in TMD 9-12 converted the activity of VMAT2 to VMAT1. Substitution of tyrosine at amino acid position 434 with phenylalanine and the substitution of asparagine for aspartate at amino acid position 461 reduced the affinity for tetrabenazine, histamine, and serotonin without affecting the recognition of dopamine. The replacement of lysine at amino acid 446 with glutamine reduced the affinity of VMAT2 for tetrabenzanine and serotonin and not histamine whereas substitution of tyrosine for phenylalanine at amino acid 464 reduced serotonin affinity but not tetrabenazine, providing evidence of specificity. These observations suggest that tyrosine-434, Lysine-446, and Aspartate-461 account for the preferential recognition of serotonin over dopamine in VMAT2. Finn III, J.P., and Edwards, R.H. Individual Residues Contribute to Multiple Differences in Ligand Recognition between Vesicular Monoamine Transporters 1 and 2. Journal of Biological Chemistry, 272, pp. 16301-16307, 1997.

Dopaminergic Mechanisms in Mediating Euphoria

The feeling of well being produced by natural rewarding stimuli and drugs of abuse appears to be mediated by a common mechanism. Opiates, cocaine, amphetamine, marijuana, caffeine, nicotine, and alcohol as well as food and sex all stimulate the release of dopamine from mesolimbic dopamine neurons. These mesolimbic dopamine neurons originate in the midbrain's ventral tegmental region and extend processes called axons to a region in the basal forebrain known as the nucleus accumbens. It is here in the nucleus accumbens that dopamine is released into the synapse. The release of dopamine in the nucleus accumbens inhibits both inhibitory and excitatory synaptic transmission by activating presynaptic D1 receptors. In this study Nicola and Malenka report that inhibition of excitatory and inhibitory synaptic transmission by dopamine and amphetamine occurs by two distinct mechanisms. Nicola and Malenka suggest that dopamine depresses the release of GABA, an inhibitory neurotransmitter by reducing calcium influx into the presynaptic terminal while excitatory synaptic transmission is reduced by a mechanism that is

independent of calcium influx. Elucidation of the mechanisms by which dopamine inhibits both excitatory and inhibitory synaptic transmission in the nucleus accumbens may lead to better pharmacological interventions and manipulations of the reward mechanism involved in addiction. Nicola, S.M. and Malenka, R.C. Dopamine Depresses Excitatory and Inhibitory Synaptic Transmission by Distinct Mechanisms in the Nucleus Accumbens. Journal of Neuroscience. 17, pp. 5697-5710, 1997.

SPECT Imaging of Dopamine Transporter

A recent report has described the preparation and in-vivo binding of a ^{99m}Tc-labeled tropane which crosses the blood-brain barrier in monkeys, and selectively labels the dopamine transporter, as visualized by SPECT imaging. The compound represents one of a series of materials containing a tropane skeleton linked by a carbon chain to a lipophilic chelator which will chelate rhenium; the latter can be displaced by technetium for imaging studies. Meltzer, P.C., Madras, B. et al, J. Medicinal Chemistry, 40, pp. 1835-1844, 1997.

Pharmacokinetic Model for Nicotine Tolerance

The parameters of a pharmacokinetic model for nicotine tolerance in humans have been recently published. The study was based on a computer-controlled infusion of nicotine to reach blood levels of 25 ng/mL, with determination of blood pressure, epinephrine level, heart rate, energy expenditure (metabolic rate) and free fatty acids. The "half-life" of tolerance reported for the first three measurements was approximately 70 minutes, with a value of 15 minutes for tolerance shown by increase in metabolic rate, and no tolerance shown for the release of fatty acids. It was suggested that there may be differences in the mechanisms of tolerance, i.e., sympathetic neural response in the case of the first three parameters, and receptor subtype desensitization in the case of metabolic rate. Benowitz, N., Verotta, D., and Fattinger, K. J. Pharmacology and Experimental Therapeutics, 281, pp. 1238-1246, 1997.

Signal Effects of a Novel Environment in the Forebrain

Novelty seeking is a trait which has been associated with drug taking behavior. In order to further explore the role of catecholamine containing neurons in the rewarding properties of novel stimuli, voltammetric recordings with electrochemically modified carbon-fiber electrodes were obtained from specific regions of the forebrain in rats given free choice access to a novel environment. Entry into novelty increased the catechol signal in the medial prefrontal cortex and shell of nucleus accumbens by more than 100% but had no consistent effect in either neostriatum or accumbal core. In both medial prefrontal cortex and accumbal shell, the novelty-induced increase in catecholaminergic activity was detectable only during initial entry into the novel compartment and did not reappear when animals returned to the familiar environment. These results support increasing evidence for a functional distinction between accumbal core and shell with the latter having been linked to brain reward mechanisms. The results also indicate that novelty activates, albeit very transiently, some of the same neurochemical systems believed to play a critical role in the reinforcing effects of certain drugs of abuse. Rebec, G.V., Grabner, C.P., Johnson, M., Pierce, R.C., and Bardo, M.T. Transient Increases in Catecholamine Activity in Medial Prefrontal Cortex and Nucleus Accumbens Shell During Novelty. Neuroscience, In press.

Review of Mesolimbic Dopamine System in Drug Reward

This paper summarizes recent work that examines the neuropharmacologic mechanisms by which drugs impinge on the mesolimbic dopamine system. Whereas dopamine plays a critical role in this circuit, other neurotransmitters (e.g., serotonin, acetylcholine, glutamate, GABA) are involved. In addition, other structures (e.g., ventral pallidus, amygdala, hippocampus and pedunculopontine) interact with the mesolimbic system to play a role in drug reward. Finally, the activation of this reward circuitry is achieved differently for different drugs of abuse. Multiple lines of research are summarized in this review article. Bardo, M.T. Neuropharmacological Mechanisms of Drug Reward: Beyond Dopamine in the Nucleus Accumbens. Neurobiology, In press.

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Research Findings

Behavioral Research

Delay Discounting Differs in Opioid-Dependent Persons

Choosing a smaller, immediately available reward could be described as an impulsive behavior if it is chosen over a larger delayed reward. Researchers at the University of Vermont examined opioid-dependent and non-drug dependent volunteers' choices between hypothetical immediate and delayed monetary rewards. The researchers found that opioid-dependent volunteers, in comparison to the controls, chose the smaller more immediate monetary reward more frequently. These results indicate that opioid-dependent subjects were more impulsive than control subjects and were more likely to consider delayed monetary gains to be less valuable ("delay discounting"). Further research is needed to determine whether delay discounting and impulsive behavior precedes or follows drug dependence. Madden, G.J., Petry, N.M., Badger, G.J, and Bickel, W.K. Experimental and Clinical Psychopharmacology, 5(3), pp. 1-7, 1997.

Potential Abuse Liability of Zipeprol

Zipeprol is marketed as a non-opioid antitussive in Europe and Asia, but may have abuse potential and also acute toxicity when taken orally. Laboratory studies indicate that Zipeprol is not discriminable from amphetamine or pentobarbital in a drug discrimination test. Zipeprol has, moreover, suppressed morphine withdrawal in non human primates, and it does substitute for the opioid alfentanil in a drug self-administration procedure. Based on these and other reported observations, the researchers conclude that Zipeprol has significant abuse liability that had not been detected previously. Acteo, M.D., et al., Drug and Alcohol Dependence, 42, pp. 93-104, 1996.

Trazodone May Be a Viable Alternative to Benzodiazepine Hypnotics

Dr. Craig Rush and colleagues at the University of Mississippi compared the acute subject-rated and performance-impairing effects of trazodone and triazolam in research volunteers. Trazodone (50, 100 and 200 mg), triazolam (0.125, 0.25, 0.50 mg) and placebo were administered orally in a double-blind, crossover design. Drug effects were measured before and after dosing for up to 6 hr. Trazodone and triazolam produced dose-related increases in subject- ratings of drug effect and sedation. The absolute magnitude of trazodone's and triazolam's effects was comparable across these measures, which suggests the doses tested were equivalent on some behavioral dimension. By contrast, triazolam, but not trazodone, increased subject ratings of "dizzy", "excited", "nervous", "restless", "stomach turning" and "itchy skin". Triazolam, but not trazodone, significantly impaired learning, recall and performance. Future studies might seek to replicate these results in a clinically relevant population such as individuals with histories of drug abuse. Rush, C.R. et al., Trazodone and Triazolam - Acute Subject Rated and Performance-Impairing Effects in Healthy Volunteers. Psychopharmacology, 131, pp. 9-18, 1997.

Evidence for a Sex-Specific Residual Effect of Cannabis on Visuospatial Memory

Dr. Harrison Pope and his colleagues at Harvard Medical School used a novel computerized battery of neuropsychological tests of attention to assess residual cognitive impairment in 25 college students who were heavy smokers of marijuana (having smoked a median of 29 days in the last 30 days). These were compared with 30 light smokers (having smoked marijuana for one day in the last 30 days). They were assessed after they had abstained from marijuana use for at least 19 hours (monitored by urine toxicology). In the visuospatial tests, the subjects were required to examine a 6x6 'checkerboard' of squares in which certain squares are shaded. The shaded squares were then erased and the subject was required to indicate with the mouse which squares had formerly been shaded. Increasing numbers of shaded squares were presented at each trial. The heavy smoking women performed poorly on the visuospatial memory tasks. They remembered significantly fewer squares and made significantly more errors than the light-smoking women. Authors concluded that it may be important to study the residual effects of marijuana on men and women separately-particularly since women have been greatly underrepresented in previous studies in this area. Pope, H.G., Jacobs, A., Mialet, J.-P. and Gruber, S. Psychother Psychosom, In press.

Effects of Stress Versus Reward on Drug Discrimination

This study was conducted in an attempt to further identify variables that predict individual differences in drug abuse liability. Rats were pretested in several different screens - novelty induced activity, novelty-induced place preference, novel-object interaction, and amphetamine-induced activity. Rats that were more sensitive to the locomotor effects of amphetamine were more active in an escapable novel environment and displayed a greater preference for a novel environment. All animals were trained to discriminate amphetamine (1 mg/kg) from saline in a two-bar discrimination procedure using food maintained responding. Following acquisition of the discrimination, two amphetamine generalization tests (0.0625, 0.125, 0.25, 0.5, 1.0 and 2.0 mg/kg) were conducted. In the second generalization test rats that were more sensitive to the activating effect of amphetamine were also more sensitive to the discriminative stimulus effects of amphetamine. Moreover, high responders in the novelty-induced activity and novelty-induced place preference screens were more sensitive than low responders to the bar-press suppressant effects of amphetamine in the first generalization test. The relations are discussed in terms of identifying processes common to the screens (e.g. stress and reward). Bevins, R.A., Klebaur, J.E. and Bardo, M.T. Individual Differences in Response to Novelty, Amphetamine-Induced Activity and Drug Discrimination in Rats. Behavioral Pharmacology, In press.

Environmental Manipulation Alters Drug Efficacy

To further test the impact of different rearing environments on subsequent behavioral and neurologic response to morphine, rats were raised from weaning to young adulthood in either an enriched-EC (group housed with various novel visual objects) or impoverished-IC (housed individually with no objects). As adults, locomotor activity and reward produced by morphine was assessed using the conditioned place preference paradigm (CPP). On Day 1, rats in both groups showed an inverted U-shaped dose effect curve for locomotor activity though the effect was greater for IC than the EC group. Across days, both groups showed locomotor sensitization; although again, the effect was greatest in the IC group. In contrast, morphine-induced CPP (the measure of 'reward') was attenuated in the IC group when compared to the EC group indicating that the locomotor versus rewarding effects were dependent on different neural substrates. To test this, measurement of mu opioid receptor density and rates of dopaminergic synthesis in the mesolimbic and nigrostriatal systems of rats from each group showed no difference between IC or EC groups. Therefore, it was concluded that while these receptors do modulate mesolimbic dopamine neurotransmission this does not account for the differential behavioral effects seen in the IC group relative to the EC group. Bardo, M.T., Robiner, P.M., and Hammer, R.F. Effect of Differential Rearing Environments on Morphine Induced Behaviors, Opioid Receptors and Dopamine Synthesis. Neuropharmacology, 36, pp. 251-259, 1997.

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Research Findings

Clinical and Services Research

Buprenorphine, Morphine, and Naloxone Effects Attenuated During Ascending Morphine Maintenance in Humans

In an inpatient study six opioid dependent volunteers were chronically maintained on ascending morphine doses of 15, 30, 60, and 120 mg/kg/day. Each morphine dose level was maintained for two weeks; acute doses of test drugs (morphine 30 mg i.m., buprenorphine 6 mg i.m., and naloxone 0.3 mg) were administered during the second week of maintenance. The acute doses of both morphine and buprenorphine constricted pupils and produced reports of opiate-like subjective effects. The magnitude of these effects was inversely related to the maintenance dose of morphine, with no effects detected at higher maintenance levels. This attenuation of effects indicates development of tolerance and cross tolerance during ascending dose morphine maintenance. At high maintenance doses of morphine, naloxone but not buprenorphine precipitated withdrawal. That buprenorphine did not act as an antagonist under these dosing conditions further supports the clinical observation that there are conditions under which patients dependent upon short-acting opiates can be comfortably transferred directly onto buprenorphine maintenance doses. On the other hand, these results suggest that individuals with relatively low levels of dependence will experience opioid-like subjective effects from buprenorphine, which may support abuse liability in this population. Schuh, K.J., Walsh, S.L., Bigelow, G.E., Preston, K.L., & Stitzer, M.L. Journal of Pharmacology and Experimental Therapeutics, 278, pp. 836-846, 1996.

Less-Than-Daily Buprenorphine May Be Clinically Feasible

The clinical utility of administering buprenorphine on a less-than-daily basis was assessed in 8 outpatients maintained on 8 mg buprenorphine in a placebo-controlled study. Pupil diameter and subjective measure of opioid withdrawal were collected at pre-test and at 0.5, 1, 2, 3, 25, 49, and 71.5 hr after test dose administration. The lack of subjective withdrawal during 71.5 hrs of dose omission suggest that less-than-daily dosing may be clinically feasible. Eissenberg T. et al., Drug and Alcohol Dependence, 45, pp. 81-91, 1997.

Effectiveness of Over-the-Counter Transdermal Nicotine for Smoking Cessation

Dr. Scott Leischow at the University of Arizona conducted a study to compare the effectiveness of the nicotine patch in smoking cessation when used in an over-the-counter (OTC) setting with no adjunct behavioral support versus a physician-based minimal behavioral intervention setting (MI)-- both reflecting "real life" situations. The OTC group received only a patch package insert. The MI group received in addition to the package insert, minimal behavioral

support and patch use guidelines from a physician at the screening and week 2 visit. No significant differences in abstinence rates were found. Abstinence rates for both groups were quite low: 7.4%, 5.4%, 5.4% and 4.7% and 6.6%, 9.3%, 5.3%, and 4.0% at weeks 2, 6, 26, and 52 for the OTC and MI groups, respectively. The use of OTC transdermal nicotine in smoking cessation is just as efficacious as its use in a physician-based minimal intervention setting with neither of the two treatment strategies being very effective. One implication of this study is that valid behavioral support programs in addition to nicotine replacement need be encouraged.

Dose-Related Efficacy of Levo-Alpha Actylmethadol (LAAM) for Treatment of Opioid Dependence

Dr. George Bigelow and colleagues at Johns Hopkins University School of Medicine conducted a 17-week randomized, double-blind, parallel group clinical trial to compare the clinical efficacy of different oral doses of LAAM. Male and female opioid-dependent patients (N=180) were assigned to one of three thrice-weekly LAAM dose conditions: low (25/25/35 mg), medium (50/50/70 mg.) or high (100/100/140 mg). Primary outcome measures were retention-in-treatment, self-reported heroin use and opioid-positive urine specimens. Although study results indicated that treatment retention was independent of dosage level, heroin use was not. For both men and women, self-report and urinalysis data showed that heroin use decreased in a dose-related manner. Thirty-four percent of the patients in the high dose condition remained opioid-abstinent for 4 consecutive weeks, as compared to 14% in the medium dose and 11% in the low dose condition (ps<.01). Eissenberg, T., Bigelow, G.E., Strain, E.C., Walsh, S.L., Brooner, R.K., Stitzer, M.L., Johnson, R.E. Dose-Related Efficacy of Levomethadyl Acetate for Treatment of Opioid Dependence: A Randomized Clinical Trial. Journal of the American Medical Association, 277(24), pp. 1945-1951, 1997.

Reliability and Validity of the Addiction Severity Index Among Seriously Mentally Ill Outpatients

Dr. Kate Carey, and her colleagues at Syracuse University collected data for the Addiction Severity Index (ASI) when administered to persons with serious and persistent mental disorders. Participants were 97 outpatients (71 men, 26 women, between the ages of 22 and 62) at a public psychiatric facility. The serious mental disorders were: schizophrenia (53%), schizoaffective disorder (13%), bipolar disorder (23%) and other (11%). A majority of the patients met the DSM-IIIR diagnosis of substance abuse or dependence. The psychometric evaluations shows that the internal consistency of the composite scores was lower in this psychiatric sample than in previous nonpsychiatric samples. Interrater reliability was acceptable for most composite scores, but low for many severity ratings. Several scores showed low temporal stability. Validity evidence was weak for the Employment and Family/Social scales, acceptable for Drug and Alcohol scales, and mixed for Psychiatric, Medical, and Legal scales. Due to mixed reliability and validity evidence, the authors concluded that caution should be exercised when using the ASI with seriously mentally ill patients. Carey, K., Cocco, K.M., and Correia, C.J., Psychological Assessment, In press.

Marijuana Use and Cancer Incidence

Sidney and his colleagues at Kaiser Permanente (Oakland, California) reviewed medical charts of approximately 65,000 patients, ages 15-49 years, who self-administered questionnaires about smoking habits, including marijuana use. The patients were enrolled in the HMO between 1979-1985. Follow-up for cancer incidence was conducted through 1993 (mean length 8.6 years). Among nonsmokers of tobacco cigarettes, ever marijuana use was associated with increased risk of prostate cancer (RR 3.1 [95% CI 1.0, 9.5] and nearly significantly increased risk of cervical cancer (RR 1.4 [95% CI 1.0, 2.1]. The investigators concluded that, in this relatively young study cohort, marijuana use and cancer were unassociated in overall analyses, but that associations in nonsmokers of tobacco cigarettes suggested that marijuana use might affect certain site-specific cancer risks Sidney, S., Charles P. Quesenberry, Gary D. Friedman, and Irene S. Takawa. Cancer Causes and Control, In press.

Effects of Intranasal Cocaine on Sympathetic Nerve Discharge in Humans

Cocaine-induced cardiovascular emergencies are thought to be mediated by excessive adrenergic stimulation. Animal studies suggest that cocaine not only blocks norepinephrine reuptake peripherally but also inhibits the baroreceptors, thereby reflexively increasing sympathetic nerve discharge. However, the effect of cocaine on sympathetic nerve discharge in humans is unknown. In 12 healthy volunteers, Victor and his colleagues (University of Texas Southwestern Medical Center) recorded blood pressure and sympathetic nerve discharge to the skeletal muscle vasculature using intraneural microelectrodes (peroneal nerve) during intranasal cocaine (2 mg/kg, n = 8) or lidocaine (2%, n = 4), an internal local anesthetic control, or intravenous phenylephrine (0.5-2.0 microg/kg, n = 4),

an internal sympathomimetic control. Experiments were repeated while minimizing the cocaine-induced rise in blood pressure with intravenous nitroprusside to negate sinoaortic baroreceptor stimulation. The investigators found that in conscious humans the primary effect of intranasal cocaine is to increase sympathetic nerve discharge to the skeletal muscle bed. The sinoaortic baroreflexes play a pivotal role in modulating the cocaine-induced sympathetic excitation and that the interplay between these excitatory and inhibitory neural influences determines the net effect of cocaine on sympathetic discharge targeted to the human skeletal muscle circulation. Jacobsen, T.N., Victor, R.G., Hillis, L.D., Lange, R.A., Landau, C., Chavoshan, B., Hansen, J., Snyder II, R.W., and Grayburn, P.A. J Clin Invest, 99(4), pp. 628-634, February 15, 1997.

Prenatal Cocaine Exposure: Dose-Response Relationships with Newborn Neurobehavior

In a study of clinically healthy full-term infants, researchers in Boston have demonstrated dose-response relationships between cocaine exposure and 3-week neurobehavioral performance, with heavily-exposed infants showing poorer state regulation and greater excitability. These associations were not observed during the first few days after birth. Three prenatal exposure groups were involved: heavily-exposed (>75th percentile self-reported days of use during pregnancy and/or >75th percentile of meconium benzoylecognine concentration, n=44), lightly exposed (<75th percentile on both indicators, n=79), and unexposed (no positive self-report or biological marker, n=101). Factors controlled in the analyses included birthweight, gestational age, motherÕs age, perinatal risk, obstetric medication, and alcohol, marijuana, and cigarette use. The investigators point out the importance of determining how this behavior progresses developmentally, because regulation of arousal and attention is critical to learning. Tronick, E., Frank, D.A., Cabral, H., et al. Pediatrics, 98, pp. 76-83, 1996.

Prenatal Cocaine Exposure: Development of Children at School Age

Gale Richardson and colleagues at the University of Pittsburgh recently reported on the development, at 6 years of age, of children who have been studied since the prenatal period. Twenty-eight children whose mothers were considered light to moderate cocaine users during pregnancy (i.e., reported an average of 3.3 g per month during the first trimester, 0.1 g per month during the second trimester, and 0.2 g per month during the third trimester) were compared with 523 children whose mothers reported no cocaine use during pregnancy, and none for the year before pregnancy. The women were interviewed about cocaine, alcohol, marijuana, tobacco, and other drug use during the 4th and 7th months of pregnancy, at delivery, and at several times postpartum. At 6 years of age, the children were assessed regarding cognitive development, academic achievement, and behavior, and underwent a physical examination. There were no significant differences between the groups on growth, intellectual ability, academic achievement, or teacher-related classroom behavior. However, children prenatally-exposed to cocaine did show deficits in their ability to sustain attention on a computerized vigilance task. Richardson, G.A., Conroy, M.L., and Day, N.L. Neurotoxicology and Teratology, 18, pp. 627-634, 1996.

Characteristics and Pretreatment Behaviors of Clients Entering Drug Abuse Treatment: 1969 to 1992

This study summarizes historical changes in admission characteristics and pretreatment behaviors with particular attention to changes in the last decade. Data are drawn from three major studies of drug abuse treatment outcomes: The Drug Abuse Reporting Program (DARP), 1969-1972; the Treatment Outcome Prospective Study (TOPS), 1979-1981; and the Drug Abuse Treatment Outcome Study (DATOS), 1991-1993. According to the authors, declines in multiple drug use and the dramatic increase in admissions reporting cocaine use are the most notable changes. Other characteristics of the changing treatment population are the decreases in patients working full-time, in reports of suicidal thoughts and/or and attempts, and in predatory crime. However, there were some notable similarities across decades among treatment modalities. The authors suggest that those commonalities indicate the distinctiveness of client characteristics and there by reinforcing the importance of studying differences among clients in different modalities when interpreting treatment outcomes. Craddock, S.G., Rounds-Bryant, J.L., Flynn, P.M., and Hubbard, R.L. Characteristics and Pretreatment Behaviors of Clients Entering Drug Abuse Treatment: 1969 to 1993. American Journal of Drug and Alcohol Abuse, 23(1), pp. 43-59, 1997.

Relationship of Personality Characteristics to Drug Treatment Effectiveness

In a study of the relationship of personality characteristics to drug treatment effectiveness, Grossweiler and Martin

analyzed data from a sample of 723 drug involved prison releasees who left prison between 1990 and 1994. Prison subjects in this study were released to one of three assigned interventions: (1) Assertive Community Treatment (ACT) which combined outpatient treatment and case management; (2) Therapeutic Community Work Release (TC) where releasees lived in a drug treatment facility, but could attend school or work in the community; or (3) a comparison group who were released to traditional parole or work release settings. As predicted, increased age, interpersonal sensitivity, and days in treatment were associated with decreased risk of relapse to drug use among those who were in the TC group. However, greater interpersonal sensitivity and attending an outpatient treatment group were associated with an increase in the likelihood of relapse to drug use and rearrest. The researchers suggest that future research should focus on common underlying traits that identify more global pathologies or personality types that severely limit treatment success. Grossweiler, R.S., and Martin, S.S. The Role of Personality in Treatment Outcome for Drug-Involved Offenders, International Journal of Sociology and Social Policy, 16(5/6), pp. 31-155, 1996.

Effect of Work Release TC and Aftercare on Drug Relapse and Criminal Recidivism

In a study of 448 patients involved in a corrections-based Therapeutic Community (TC) treatment, Dr. James Inciardi and his colleagues examined data from an 18-month follow-up for releasees who received (1) no treatment, but traditional parole or work-release settings; (2) treatment in a prison-based TC; (3) treatment in a work-release TC followed by aftercare (the 2 stage model); and (4) treatment in a prison-based TC followed by work-release TC and aftercare (the 3-stage model). According to the authors, a significantly greater percentage of respondents who received treatment in the 2-stage model (31%) and the 3-stage model (47%) were drug free (via self-report and urinalysis) at the 18-month post-release interview than respondents in the no treatment comparison group (16%, $p<.01$). Similarly, significantly greater percentages of respondents in the 2-stage model (57%) and the 3 stage model (77%) had no new arrests during the 18-month post-release period as compared to respondents in the comparison group (46%, $p<.01$). There were no significant differences in abstinence or rearrest rates between the no treatment comparison group and the prison TC-only group. These findings were supported even when adjusted for other risk factors (demographic, criminal and drug history). Inciardi, J.A., Martin, S.S., Butzin, C.A., Hooper, R.A., and Harrison, L.D. An Effective Model of Prison Based Treatment for Drug-Involved Offenders. Journal of Drug Issues, Spring 1997.

Relationship between Self-Efficacy Perceptions and In-treatment Drug Use among Regular Cocaine Users

This study, part of a national outcome study, investigates the relationship between self-efficacy and drug use in a subsample of 294 regular cocaine users who completed at least three months of community-based outpatient treatment programs. The results supported previous findings that increased self-efficacy in resisting drug use was associated with lower rates of drug use during treatment, and that self-efficacy enhancement may be an important intervention in the treatment of cocaine abuse. Although the results of this study compare favorably with results in other studies, the authors call for controlled studies of the effects of self efficacy on abstinence from drug use in outpatient settings. Rounds-Bryant, J.L., Flynn, P.M., and Craighead, L.W. Relationship between Self-Efficacy Perceptions and In-Treatment Drug Use among Regular Cocaine Users. American Journal of Drug and Alcohol Abuse, 23(3), pp. 383 395, 1997.

The Effect of an Enhanced Case Managed Intervention on Employment

Siegal and his colleagues examined the effectiveness of a strengths-based case management model for improving employment related outcomes in a sample of 632 veterans seeking treatment for substance abuse problems. They found that the patients who completed primary treatment showed significant gains in vocational functioning and that this improvement was generally correlated with improvement in each of the other areas measured by the Addiction Severity Index (ASI). These gains were reflected in three specific outcomes: average income earned, number of days worked, and the number of work-specific problems in the 30 days preceding the follow-up interview. Siegal and his colleagues also found that patients in the case managed group (CM) did significantly better than non-case managed group (NCM) in terms of average number of days employed in the last 30 days (15.6 vs. 12.1, $p<.016$). Further, CM patients reported fewer days of employment problems (7.95 vs. 12.27, $p<.019$), felt less troubled by employment problems (1.02 vs. 1.63, $p<.008$), and saw less need for employment counseling (.95 vs. 1.48, $p<.023$). Siegal, H.A., Fisher, J.H., Rapp, R.C., Kelliher, C.A., Wagner, J.H., O'brien, W.F., Cole, P.A. Enhancing Substance Abuse Treatment with Case Management: Its Impact on Employment. Journal of Substance Abuse Treatment, 13(2), pp.

93-98, 1996.

Functional MRI of Human Brain Activation during Cue-Induced Craving

Perry F. Renshaw, M.D., Ph.D. and colleagues at Harvard Medical School/McLean Hospital have used fMRI to demonstrate brain activation in areas associated with cocaine cue-induced craving. Six male subjects with a history of crack cocaine use and six control subjects were presented with audiovisual stimuli containing intervals of drug-related and neutral scenes, while brain activation was measured with fMRI. Significant activation was detected in the anterior cingulate and left dorsolateral prefrontal cortex in the cocaine-abusing group. In addition, self-reports of craving and activation also correlated in the same regions. Despite some procedural differences, the fMRI findings that presentation of cocaine cues activates the anterior cingulate and dorsolateral prefrontal cortex are consistent with previous PET studies conducted at NIDA's Intramural Research Program and at the University of Pennsylvania. The results suggest that fMRI may be an additional valuable tool to assist in the identification of the neurobiological basis of craving and may provide a means for the evaluation of new agents to modify or reduce craving. The consistent findings across different groups of researchers and different neuroimaging methods suggest that these findings are reliable and may be most helpful in further elucidating the neurobiological basis of drug addiction. Maas, L.C., Lukas, S.E., Kaufman, M.J., Weiss, R.D., Daniels, S.L., Rogers, V.W., Kukes, T.J., Renshaw, P.F. Functional MRI of Human Brain Activation during Cue-Induced Cocaine Craving. American Journal of Psychiatry, In press.

Novel Approaches to Mapping the Brain

Fred L. Bookstein, M.D. at the University of Michigan has been involved in the application of statistics to neuroimaging and mapping of human brain structures. The major areas of work have been in terms of mapping discrete points (landmarks) in the normal human brain. Also, he has been exploring solutions to the problem of analysis of brain images where many of the landmarks are ambiguous or absent. Presently, the use of sophisticated multivariate statistical procedures in data sets with missing landmarks is being investigated. Preliminary results have shown reasonable estimates even when the extent of missing data is as high as 65%. Combining medical imaging analysis and statistics will allow investigators to study patterns of relationships between brain images and behavior. In the past, normal variation of brain shape has served as a serious confound that significantly hinders neuroanatomical data analysis. This project is assembling a tool kit of methods to address the shape variability issue. New methods of shape description can prove useful in identifying regions of interest in the human brain that are important for explaining the onset, course, treatment response and severity of brain diseases, such as drug abuse. Bookstein, F.L. Landmark Methods for Forms without Landmarks: Morphometrics of Group Differences in Outline Shape. Medical Image Analysis, 1, pp. 225-243, 1996/7; Bookstein, F.L. Shape and the Information in Medical Images: A Decade of the Morphometric Synthesis. Computer Vision and Image Understanding, 66, pp. 97-118, 1997.

Heritability of the Neurophysiological Drug-Taking Risk Factor, P300

In a study of monozygotic and dizygotic twins, critical amplitudes of visual evoked potential wave forms, including P300, N1, P2 and N2 were heritable. This finding is important because P300 has been found by several laboratories to be a physiological marker of risk in children of substance abusing persons. Thus, these data demonstrate a potential genetic component for such a physiological marker of drug abuse. Katsanis, J., Iacono, W.G., McGue, M.K., and Carlson, S.R. P300 Event-Related Potential Heritability in Monozygotic and Dizygotic Twins. Psychophysiology, 34, pp. 47-58, 1997.

Neurophysiological Changes after Smoking Marijuana

In a difficult auditory oddball task, N100 amplitudes were reduced and P300 latencies were shortened in cortical potentials evoked after smoking marijuana cigarettes. These changes were observed two hours after smoking, when subjective effects were not reported. As reported previously in studies on tobacco smoking acute marijuana administration may alter cognitive processing as assessed by electrophysiological measures. Orozco, S., and Lukas, S.E. Heart-Rate, Plasma, Subjective and Cognitive Changes after Marihuana Smoking. Presented at CPDD, 1997.

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National Institute on Drug Abuse

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

September, 1997

Research Findings

AIDS Research

Increased Vertical Transmission of HIV from Hepatitis C Co-infected Mothers

A recent study from the Women & Infant Transmission Study (WITS), an NIH supported HIV cohort study co-funded by NIDA, demonstrated that maternal infection with hepatitis C virus is associated with increased HIV maternal-infant transmission. Among 487 women infected with HIV either heterosexually or through injection drug use, 33% were found to be HCV infected. HIV vertical transmission occurred in 26% of HIV/HCV infected mothers vs. 16% of HCV uninfected mothers (OR, 1.82, p=0.01). Drug use during pregnancy was highly correlated with HCV infection (53% vs. 16% in non-drug users, p=0.001) and with HIV perinatal transmission (24% vs. 16% in non-drug users, OR, 1.66, p=0.03). These data suggest that maternal HCV infection either enhances perinatal HIV transmission directly or is a marker for another co-factor such as maternal drug use. Further study is needed to confirm the findings of this study and to determine whether the association represents a biologic effect of HCV infection or is due to a confounding interaction with drug use or other factors. Hershow R.C., Riester, K.A., Lew, J et al. J of Infectious Diseases, 176, pp. 414-419, 1997.

Association Between Serum Vitamin A and E Levels and HIV-1 Disease Progression

Tang and her colleagues at Johns Hopkins Medical School conducted a non concurrent prospective study to examine the associations between serum vitamin A and E levels and risk of progression to three key outcomes in HIV-1 infection: first AIDS diagnosis, CD4+ cell decline to < 200 cells x 10(6)/l, and mortality. Serum levels of vitamins A and E were measured at the enrollment visit of 311 HIV-seroprevalent homo-/bisexual men participating in the Baltimore/ Washington DC site of the Multicenter AIDS Cohort Study. Cox proportional hazards models were used to estimate the relative hazard of progression to each outcome over the subsequent 9 years, adjusting for several independent covariates. The investigators found that men in the highest quartile of serum vitamin E levels (> or = 23.5 mumol/l) showed a 34% decrease in risk of progression to AIDS compared with those in the lowest quartile [relative hazard (RH), 0.66; 95% confidence interval (CI), 0.41-1.06)]. This effect was statistically significant when comparing the highest quartile of serum vitamin E to the remainder of the cohort (RH, 0.67; 95% CI, 0.45-0.98). Associations between serum vitamin A levels and risk of progression to AIDS were less clear, but vitamin A levels were uniformly in the normal to high range (median = 2.44 mumol/l). Similar trends were observed for each vitamin with mortality as the outcome, but neither vitamin was associated with CD4+ cell decline to < 200 cells x 10(6)/l. Men who reported current use of multivitamin or single vitamin E supplements had significantly higher serum tocopherol levels than those who were not taking supplements (P = 0.0001). Serum retinol levels were unrelated to intake of multivitamin or single vitamin A supplements. These data suggest that high serum levels of vitamin E may be associated with slower HIV-1 disease progression, but no relationship was observed between retinol levels and disease progression in this vitamin A-replete population Tang, A.M., Saah, A.J., Semba, R.D., Graham, N.M. AIDS.

11(5), pp. 613-620, April 1997.

Low Serum Vitamin B-12 Concentrations are Associated with Faster Human Immunodeficiency Virus Type 1 (HIV-1) Disease Progression

In another study, Tang et al. examined associations between serum concentrations of vitamin B-6, vitamin B-12 and folate and the risk of progression to first acquired immunodeficiency syndrome (AIDS) diagnosis and CD4+ cell decline to < 2 x 10(8) cells/L. The study population was drawn from a cohort of homosexual and bisexual men in the Baltimore-Washington, D.C., area. Eligible subjects were human immunodeficiency virus type 1 (HIV-1)-seropositive at study entry and had serum available in the serum repository from their 1984 baseline study visit. Serum micronutrient levels were assessed in 310 subjects. The follow-up period (April 1984 through December 1993) was approximately 9 years. In Kaplan-Meier analyses, participants with low serum vitamin B-12 concentrations (< 120 pmol/L) had significantly shorter AIDS-free time than those with adequate vitamin B-12 concentrations (median AIDS-free time = 4 vs. 8 years, respectively, P = 0.004). This effect persisted in Cox proportional hazards models after adjusting for HIV-1-related symptoms, CD4+ cell count, age, serum albumin, use of antiretroviral therapy before AIDS, frequency of alcohol consumption and serum folate concentration [relative hazard (RH)= 1.89, 95% confidence interval (CI) = 1.15-3.10). To further explore the temporal relation between low serum vitamin B-12 concentrations and disease progression, additional analyses were performed excluding subjects with more advanced disease at baseline. In these analyses, the increase in risk of progression to AIDS for those with low serum vitamin B-12 concentrations remained significant (RH = 2.21, 95% CI = 1.13-4.34), providing further evidence that low vitamin B-12 concentrations preceded disease progression. In contrast, low serum concentrations of vitamin B-6 and folate were not associated with either progression to AIDS or decline in CD4+ lymphocyte count. Intervention studies are needed to determine whether correction of low serum vitamin B-12 concentrations in early HIV-1 infection will influence the natural history of disease progression Tang, A.M., Saah, A.J., Chandra, R.K., and Graham, N.M. J Nutr, 127(2), pp. 345-351, February 1997.

Injection Drug Use as an Ecologic Niche for Emerging and Re-emerging Infectious Diseases

Researchers from Seattle, New York City, London, Bangkok, and Rio de Janeiro collaborated in a review of current information on the possible roles of injection drug use in the emergence and re-emergence of infectious diseases. The rapid growth in the use of illicit drugs is discussed in the context of four important factors: (1) there has been a substantial international growth in the use of illicit psychoactive drugs, (2) injecting produces a strong drug effect due to the rapid increase of drug concentration in the brain, (3) the profit margins in the sale of illicit drugs have become so large that even persons who are relatively impoverished are seen as potential customers by drug dealers, and (4) many drug injectors travel internationally (e.g., the phenomenon of "international drug tourism"), and are increasingly being incarcerated together, representing a potential contribution to the spread of blood-borne viruses among IDUs. Illicit drug injection has now been reported in 118 different countries, and is becoming an increasingly more important ecologic niche for the transmission other diseases, such as tuberculosis, that have significant interactions with HIV-related immunosuppression. Public health officials need to plan for the continued international diffusion of injecting drug use and the potential transmission of infectious agents among IDUs, their sexual partners, and their community contacts. For many emerging and re-emerging infectious diseases, protecting the health of the community as a whole will depend on protecting the health of IDUs. Des Jarlais, D.C., Stimson, G.V., Hagan, H., Perlman, D., Choopanya, K., Bastos, F. I., and Friedman, S.R. Emerging Infectious Diseases and the Injection of Illicit Psychoactive Drugs. Current Issues in Public Health, 2, pp. 130-137, 1996.

Risk Behaviors of Young Adults Residing in High Risk Neighborhoods

Researchers in New York City investigated the extent to which young adults who reside in neighborhoods with large numbers of drug injectors are infected with agents transmitted primarily by drug injection or by sexual contact, and to estimate the extent to which such young adults engage in high risk behaviors. A multistage probability household sample survey was conducted with 111 young adults ages 18 to 21 years old, in Brooklyn, from 1994 to 1995. Sexual risk behaviors are prevalent among this population (89% said they had sex in the past year, 45% with 2 or more partners; only 19% said they always used condoms). One respondent indicated a history of crack use and injection drug use, 3% reported ever using heroin, 9% reported ever using cocaine, and 48% reported use of marijuana in the past year. None of 103 subjects tested positive for HIV, HTLV-II, or syphilis, but 2% were positive for HTLV-I, 3% for HCV, 3% for HBV, 12% for chlamydia, and 50% for HSV-2. These findings indicate that heroin and cocaine use, injection drug use, and parenterally-transmitted infections are less prevalent in this population compared to sexual

risk behaviors and sexually transmitted infections. STD screening and outreach strategies are needed to prevent STD sequelae, including potential increased susceptibility to HIV infection, and to prevent transmission of infections to sexual partners. Friedman, S.R., Curtis, R., Jose, B., Neaigus, A., et al. Parenterally-and Sexually-Transmitted Diseases in a High Risk Neighborhood. Sexually Transmitted Diseases, 24, pp. 322-326, July 1997.

Multisite Study Identifies Predictors of HIV Serostatus in Out-of-Treatment Male Drug Users

The risk groups of men who have sex with men (MSMs) and injection drug users (IDUs) together account for 90% of all male AIDS cases. The extent to which each risk behavior contributes to seroprevalence among IDUs has not been determined and is critical for intervention development. Analysis of data on sexual orientation, injection drug use, and HIV serostatus was undertaken in a multisite study of 3002 male drug injectors and crack smokers recruited for HIV prevention projects. Overall HIV seroprevalence was 8.4%; 57.1% for gay men, 25.4% for bisexual men, and 7.4% for heterosexuals ($p<.001$). Logistic regression analyses indicated being gay and coming from an area where seroprevalence is high among IDUs were the best predictors of serostatus. Ever having injected was significant only in interaction with moderate or high IDU seroprevalence areas. Among this multisite sample of drug users, being a gay drug user is the strongest predictor of serostatus. Drug injection is significant only in areas of moderate or high seroprevalence among injectors. This indicates the importance of targeted outreach and intervention efforts. Deren, S., Estrada, A., Stark, M., et al. A Multisite Study of Sexual Orientation and Injection Drug Use as Predictors of HIV Serostatus in Out-of-Treatment Male Drug Users. Journal of AIDS and Human Retrovirology, 15(4), pp. 289-295, 1997.

The Number and Activities of Syringe Exchange Programs Continue to Expand in the U.S.

In 1996, researchers surveyed Syringe Exchange Programs (SEPs) in the U.S. regarding their activities during 1995 and 1996. They compared the survey findings with findings from earlier surveys in 1994 and early 1995. Eighty-seven (86%) of the 101 SEPs in the North American Syringe Exchange Network (NASEN) in 1996 participated in the survey. Findings indicate that there has been an expansion in the number of SEPs and in the scope of activities since 1994. From 1994 to 1996, there were increases in the number of SEPs participating in the surveys and in the numbers of cities and states with SEPs. The number of syringes exchanged increased by 75% (from 8 million to 14 million) from 1994 to 1996 overall. The 10 most active SEPs exchanged >500,000 syringes each and approximately 9.4 million (69%) of all syringes exchanged. The SEP in San Francisco reported exchanging the largest number of syringes in 1996 (1,461,096). Fifty SEPs reported exchanging 55,000 syringes each, and of these, 23 exchanged a mean of 2815 syringes. All SEPs provided IDUs with information about safer injection techniques and/or use of bleach to disinfect injection equipment. Other services included referral of clients to substance abuse treatment programs (97% of the programs), instruction in the use of condoms and dental dams to prevent sexual transmission of HIV and other sexually transmitted diseases (97%), and STD-prevention education (81%). Health services offered on-site included HIV counseling and testing (40%), primary health care (17%), TB skin testing (26%), and STD screening (20%). Paone, D., Des Jarlais, D. Clark, J., et al. Update: Syringe-Exchange Programs --United States, 1996. Morbidity and Mortality Weekly Report, 46(24), pp. 565-568, 1997.

Evaluation of Needle and Syringe Combinations

HIV transmission among IDUs is commonly attributed to the practice of sharing contaminated needles and syringes. The minimal infectious dose of HIV is unknown, but the volume of inoculum and quantity of virus in an exposure are believed to influence the risk of transmission. Both factors may be affected by the type of syringe used by an IDU. For example, a change was observed in syringes used by IDUs in Texas during the HIV epidemic. Syringes in current use have permanently attached needles and retain visibly less fluid and blood than syringes with detachable needles used previously. Earlier research has quantified the amount of blood in needle and syringe sharing simulations, but the type of needle and detachable or integral cannula (permanently attached) were not specified, and only one simulation incorporated the common practice among IDUs of rinsing with water between uses. Therefore, researchers undertook a series of experiments to measure differences in fluid and blood retained in four needle and syringe combinations. They found that, with the plunger fully depressed, syringes with detachable needles retained over 40 times as much fluid as integral cannula syringes. In simulations using whole blood and two rinses, syringes with detachable needles retained a minimum of 300 times as much blood as integral cannula syringes. The authors conclude that, if the volume of inoculum and the quantity of virus in an exposure affect the probability of infection, then integral cannula syringes are a less efficient means of transmission and thus a safer instrument for drug injection. Needle exchanges should be encouraged to distribute integral cannula syringes only and IDUs using

syringes with detachable needles should be warned of the higher risks. Zule, W., Ticknor-Stellato, K., Desmond, D. Et al. Evaluation of Needle and Syringe Combinations. Journal of AIDS and Human Retrovirology, 14, pp. 294-297, 1997 (letter).

Risk for HIV in IDUs Who Use Crack Cocaine and the Role of Nonbehavioral Factors

Researchers analyzed self-reported data and blood tests for HIV antibodies from a study of 4705 out-of-treatment IDUs recruited for interviews in Newark and Jersey City, New Jersey, who did or did not also use crack cocaine. The HIV seroprevalence rate in this sample was 40.5% overall. IDUs who used crack cocaine were found to have a significantly lower HIV infection rate (30.8% HIV+) compared to IDUs who did not use crack (45.0% HIV+). They were significantly more likely to be younger in age, female, Black, and frequent users of alcohol and marijuana. IDUs who used crack were also significantly different from IDUs who did not use crack in terms of: having had more multiple sex partners, having traded sex for drugs, lacking permanent housing, having a shorter history of drug injection, being less likely to inject on a daily basis, having a history of syphilis and gonorrhea, and having a sex partner who injects drugs. Possible geographic asymmetries in the distribution of HIV were examined to determine whether local neighborhood levels of HIV seroprevalence could have mediated the relationship, but the results were nonsignificant. Although the crack-using IDUs engaged in sexual and needle use risk behaviors at higher rates than IDUs who did not use crack, they were much younger, had shorter histories of drug injection, and injected drugs less frequently. In addition, the structure of social networks among the IDUs who did or did not use crack may have influenced the distribution of contagion in subgroups of IDUs who use crack. The authors cite four factors (initial rates of infection in the subgroup, rates of risk behaviors among subgroup members, likelihood of transmission from a given contact, and rate of mixing between subgroups) in describing how, if subgroups have insularity from one another --that is, if inter-group mixing patterns are relatively infrequent--there will be fewer opportunities for HIV to be introduced into the network. They caution, however, that the IDUs who used crack in this study also engaged in very high risk behaviors. Therefore, the chances are poor that the disparities in HIV infection rates between risk networks will be maintained over time. Iguchi, M. and Bux, D. Reduced Probability of HIV Infection among Crack Cocaine-Using Injection Drug Users. American Journal of Public Health, 87(6), pp. 1008-1012, 1997.

HIV Risk Behaviors Vary In Large Part by How IDUs Group into Social Networks

Researchers examined data from a study of the social networks of IDUs in Chicago and Washington, D.C. to determine how individual behavior and social network characteristics change over time. The results indicated few changes in standard network measures, such as density of ties or network size, over time. However, specific network change measures, that is, indicators of movement of network members into and out of networks (turnover-in, turnover-out) were significantly associated with more risky injection behaviors over a 3-month period. Ethnographic work showed that members of networks with few resources had to move around much more in order to secure drug supplies, syringes, and places to inject. Thus, it is not surprising that they were also forced to take substantial risks, such as sharing needles and other paraphernalia. The researchers conclude that the significant relationship between movement of members into a network and a higher likelihood of risky injection drug use over time is indicative of a lack of a stable resource base among IDU networks. Hoffman, J.P., Su, S.S., and Pach, A. Changes in Network Characteristics and HIV Risk Behavior Among Injection Drug Users. Alcohol and Drug Dependence, 46, pp. 41-51, 1997.

Runaway and Homeless Youth at Risk for HIV from Drug Use and Unsafe Sex

A study was conducted with data from 775 runaway and homeless youth under age 19 who were recruited from street settings and youth agencies in three U.S. cities. Nearly all respondents (98%) reported having engaged in sexual intercourse, and 49% had first intercourse by age 13. Fewer than half reported consistent condom use for vaginal intercourse in the last 3 months. Nearly a quarter of the males (23%) and 14% of the females reported having exchanged sex for money. Most (97%) had used alcohol or drugs, and 21% had injected drugs. Overall, 75% of the youth reported having had sex while under the influence of alcohol or drugs. The findings show that runaway and homeless youth are at very high risk for HIV from both use of drugs and unsafe sexual activity. Kral, A.H., Molnar, B.E., Booth, R.E., and Watters, J.K. Prevalence of Sexual Risk Behavior and Substance Use Among Runaway and Homeless Adolescents in San Francisco, Denver, and New York City. International Journal of STDs and AIDS, 8, pp. 109-117, 1997.

Innovative Risk Prevention Efforts are Needed for Substance Abusers Who Engage in High Risk Sex

In this critical review of the literature, researchers focus on subgroups of gay and bisexual men who, in spite of near-universal knowledge about HIV infection and sexual safety and widespread intentions to be safe, continue to use drugs, engage in unprotected sex, and experience high rates of HIV seroconversion. Explanatory models that link risk taking and prevention to rational processes such as those involved in knowledge processing, social norms, behavioral intentions, or perceived vulnerability to infection cannot fully account for this continued risk behavior. Innovative conceptions of risk prevention are needed that emphasize nonrational, affective processes in risk taking and decision making. The authors examine psychosocial models of HIV risk behavior, outline a cognitive escape model with particular emphasis on substance abuse as a behavioral risk factor, and discuss implications of an escape model for behavioral interventions aimed at gay and bisexual men who combine substance use with risky sexual behaviors. They argue that, for many people, sexual risk does not stem from a lack of community norms or personal standards, but from a desire to escape cognitive awareness of very rigorous norms and standards. They propose that both substance use and the approach of high-stimulation or other sexual settings facilitate this cognitive disengagement, wherein people enact automatic sexual scripts and/or become more responsive to external pressures toward risk. Ostrow D. And McKirnan, D. Prevention of Substance-Related High-Risk Sexual Behavior Among Gay Men: Critical Review of the Literature and Proposed Harm Reduction Approach. Journal of the Gay and Lesbian Medical Association, 1(2), pp. 97-110, 1997.

HIV Seropositivity is Associated with Travel to AIDS Epicenters by IDUs

Injection drug users continue to be at risk for HIV despite having high levels of knowledge about the risk factors for HIV transmission. Yet, the chances of becoming HIV seropositive vary substantially among not-in-treatment IDUs. In this study, researchers examined the factors which may facilitate the introduction of HIV into networks of IDUs in low seroprevalence cities. Specifically, they analyzed data from a large (n=9,492), multisite sample of IDUs recruited in 11 low seroprevalence cities between June 1988 and June 1991 as part of NIDA's National AIDS Demonstration Research (NADR) project. Univariate and multivariate associations between drug injection, sexual behaviors, and travel to an AIDS epicenter suggest that, next to male-to-male sexual contact, having sex at least twice in an AIDS epicenter was the strongest predictor of HIV infection. Racial/ethnic characteristics, daily drug injection, and injecting drugs in an AIDS epicenter were also associated with an increased likelihood of being HIV seropositive. The authors discuss the role of travel to and from AIDS epicenters in facilitating the spread of HIV into areas of low HIV seroprevalence. Specifically, when traveling to a high seroprevalence area, IDUs residing in a low seroprevalence area can become infected with HIV as a result of multi-person use of syringes and other injection equipment as well as high risk sexual behaviors. When returning home, these same persons may introduce the virus into a local network of drug injectors who, in spite of their injection behaviors, have remained free of HIV because of their relative isolation in a low seroprevalence area. The findings suggest that an extremely important consideration in preventing the spread of HIV/AIDS is the continuation of prevention efforts in areas where HIV infection among injectors are low. Williams, M., Zhao, Z., Bowen, A., et al. Introduction of HIV into Drug Injector Networks Outside AIDS Epicenters. International Journal of STDs and AIDS, In press.

Sociometric Risk Networks Are Pathways for HIV among IDU Peer Groups

A cross-sectional serosurvey was conducted of 767 street-recruited injection drug users to measure larger scale (i.e., "sociometric") risk networks. Linkages were analyzed using graph-theoretical algebraic techniques to detect 92 separate connected components (i.e., drug injectors who are linked to each other directly or through others) and a 105-member 2-core within a large connected component of 230 members. IDUs in the 2-core of the large component were found to be more likely to be infected with HIV. Seronegative 2-core members engage in a wide range of high risk behaviors, including engaging in risk behaviors with infected drug injectors. The findings suggest that sociometric risk networks seem to be pathways through which HIV travels among drug injecting peer groups. The cores of large components can be centers of high risk behaviors and can become a pocket of HIV infection. Preventing HIV from reaching the cores of large components may thus be crucial in preventing widespread HIV epidemics. Network-based prevention programming may help reduce HIV transmission in high prevalence localities and prevent new epidemic breakouts. Friedman, S. R., Neaigus, A., Jose, B., et al. Sociometric Risk Networks and HIV Risk. American Journal of Public Health, August 1997.

Drug Treatment Experiences of Rural and Urban Drug Users

A study was conducted to investigate the treatment seeking behaviors of drug users in urban and rural populations. Data were drawn from the Miami and Immokalee sites of NIDA's Cooperative Agreement for AIDS Outreach/Intervention Research Program. As expected, drug users in Miami were more likely to have been in drug treatment compared to their rural counterparts (2.57 times more likely), likely because of rural/urban differences in the availability, accessibility, and acceptability of drug treatment and health care services. Metsch, L.R. and McCoy, C.B. Drug Treatment Experiences: Rural and Urban Comparisons. Substance Use and Misuse, In press.

Predictors of Behaviors and Beliefs of Female Drug Users in Two Cities

This study was conducted to examine predictors of behaviors and beliefs about the use of condoms among women who use drugs and who report having recent vaginal sex with main and/or paying partner s. A total of 338 drug-using women were recruited for the study, all of whom reported vaginal sex during the past 30 days. Forty percent of the women resided in East Harlem, N.Y., a high HIV seroprevalence area, and 60% of the women resided in Long Beach, California, a low HIV seroprevalence area. Recruitment site was identified as a significant predictor for a number of variables for both main and paying partners: Women recruited in East Harlem were more likely than those recruited in Long Beach to believe that use of condoms for sex with a main partner would harm the relationship, for example. They were also more likely to have used condoms with a main partner in the past 30 days, and to believe that condoms provided protection from disease. Race/ethnicity was a significant predictor for main sex partners, with African American women significantly more likely to have positive cognitions about use of condoms and to report greater self-efficacy for, and greater intention of, using condoms with main partners. The researchers discuss the implications of their findings in terms of intervention development to prevent HIV and other diseases. Specifically, because factors which predict condom beliefs, intention to use, and behaviors are different for main and paying partners, interventions which are designed to increase condom use should recognize that cognitive factors associated with condom use may vary by partner type, race/ethnicity, and recruitment site, particularly when contextual variables, such as local seroprevalence levels, vary. Wood, M. Tortu, S., Rhodes, F., and Deren, S. Differences in Condom Behaviors and Beliefs among Female Drug Users Recruited from Two Cities. Women and Health, In press.

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National Institute on Drug Abuse

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

September, 1997

Research Findings

Epidemiology, Etiology and Prevention Research

Antisocial Behavior and Affiliation with Adult Boyfriends Predicts Female Adolescents' Substance Use and Risky Sexual Behavior

In a study of pathways to substance use and risky sexual behavior, investigators at the Center for Education and Drug Abuse Research (CEDAR) at the University of Pittsburgh used behavioral, psychiatric interview, and self-report measures to index behavioral dysregulation, negative affectivity, childhood victimization, internalizing symptomatology, antisocial behavior, affiliation with adult boyfriends, and outcome variables in 125 substance abusing female adolescents and 78 controls 14-18 years old. Results of structural equation modeling indicated that behavioral dysregulation, negative affectivity, and childhood victimization were related to substance use and risky sexual behavior. Age of menarche was correlated with affiliation with an older boyfriend and risky sexual behavior. Antisocial behavior mediated the associations of behavioral dysregulation, negative affectivity and childhood victimization with substance use and risky sexual behavior. Affiliation with an adult boyfriend was directly associated with substance use and accounted for the relationship between chronological age and risky sexual behavior. From a prevention and treatment standpoint, these results suggest that reducing dysregulation through behavior modification procedures developed for conduct-disordered children might provide a mechanism for interrupting the development of substance use and risky sexual behavior in young females. Mezzich A.C., Tarter, R.E., Giancola, P.R., Lu, S., Kirisci, L., and Parks, S. Substance Use and Risky Sexual Behavior in Female Adolescents. Drug and Alcohol Dependence, 14; 44 (2-3), pp. 157-166, 1997.

Predictors of Substance Use in Children of Substance Abusers

The social development model (Catalano and Hawkins 1996) hypothesizes that strong bonds to prosocial others and institutions contribute to prosocial behavior, while strong bonds to antisocial others and institutions contribute to antisocial behavior. Consistent with this perspective, previous research indicates that bonding to parents and child substance use are negatively associated for children of substance abusers. This paper examines the interactive relationship between parent drug use, bonding to parents and child substance use in a longitudinal study of families headed by substance abusers in methadone treatment for opiate addiction. Bonding to parents and child substance use are moderately negatively correlated in children whose parents ceased using drugs but are weakly positively correlated in children whose parents continued using drugs. These results support the social development model and suggest that family interventions for preventing substance use in children of substance abusers should focus on reducing parent drug use and promote bonding to parents who are abstinent. Fleming, C.B., Brewer, D.D., Gainey, R.R., Haggerty, K.P., and Catalano, R.F. Parent Drug Use and Bonding to Parents as Predictors of Substance Use in Children of Substance Abusers. Journal of Child and Adolescent Substance Abuse, In press.

Inclusion of Drug Use Data From School Dropouts

This study examined, across three racial/ethnic groups, how the inclusion of data on drug use of dropouts can alter estimates of adolescent drug use rates. Self-report rates of lifetime prevalence and use in the previous 30 days were obtained from Mexican American, White non-Hispanic, and Native American students (n=738) and dropouts (n=774). Rates for the age cohort (students and dropouts) were estimated with a weighted correction formula. Rates of use reported by dropouts were 1.2 to 6.4 times higher than those reported by students. Corrected rates resulted in changes in relative rates of use by different ethnic groups. When only in-school data are available, errors in estimating drug use among groups with high rates of school dropout can be substantial. Correction of student-based data to include drug use of dropouts leads to important changes in estimated levels of drug use and alters estimates of the relative rates of use for racial/ethnic minority groups with high dropout rates. Swaim, R.C., Beauvais, F., Chavez, E.L., and Oetting, E.R. The Effect of School Dropout Rates on Estimates of Adolescent Substance Use Among Three Racial/Ethnic Groups. American Journal of Public Health, 87, pp. 51-55, 1997.

Psychiatric Disorders Associated with Substance Use Among Children and Adolescents

The relationships between specific quantities and frequencies of alcohol, cigarette, and illicit substance use and substance use (SUD) and other psychiatric disorders were investigated among 1,285 randomly selected children and adolescents, aged 9 to 18, and their parents, from the Methods for the Epidemiology of Child and Adolescent Mental Disorders (MECA) Study. Logistic regressions indicated that daily cigarette smoking, weekly alcohol consumption, and any illicit substance use in the past year were each independently associated with an elevated likelihood of diagnosis with SUD and other psychiatric disorders (anxiety, mood, or disruptive behavior disorders), controlling for sociodemographic characteristics (age, gender, ethnicity, family income). The associations between the use of specific substances and specific psychiatric disorders varied as a function of gender. Kandel, D. B., Johnson, J. G., Bird, H. R., Canino, G., Goodman, S. H., Lahey, B. B., Regier, D. A., and Schwab-Stone, M. Psychiatric Disorders Associated with Substance Use Among Children and Adolescents: Findings from the Methods for the Epidemiology of Child and Adolescent Mental Disorders (MECA) Study. Journal of Abnormal Child Psychology, 25 (2), pp. 121-132, 1997.

Psychopathology in Preadolescent Sons of Fathers with Substance Use Disorders

Investigators at CEDAR examined the relationships between offspring and parental psychopathology by comparing the psychiatric disorders of preadolescent boys of fathers with and without substance use disorders (SUDs). Fathers (i.e., probands) of boys 10-12 years old were recruited to represent families of boys with paternal SUD (high risk or HR: n = 113) and boys without paternal SUD (low average risk or LAR: n = 170). These boys (i.e., index cases) and their biological parents were administered structured diagnostic interviews, and diagnoses were determined by the best-estimate method. Disruptive behavior disorders and anxiety disorders were found to be more prevalent in HR than in LAR index cases. Logistic regression analyses indicated that parental childhood psychiatric disorders were more strongly predictive of boys' psychiatric disorders than were parental adulthood psychiatric disorders, including SUDs. These findings suggest that disruptive behavior disorders and anxiety disorders may be important targets for early intervention to prevent the development of SUD, as well as the morbidity associated with these disorders. Clark, D.B., Moss, H.B., Kirisci, L., Mezzich, A.C., Miles, R., Ott, P. Psychopathology in Preadolescent Sons of Fathers with Substance Use Disorders. Journal of the American Academy of Child and Adolescent Psychiatry, 36 (4), pp. 495-502, 1997.

The Influence of Spouses' Behavior and Marital Dissolution on Marijuana Use: Causation or Selection

Similarity between spouses may result from prior similarity (selection) or interpersonal influence (causation) or both. Spouses' mutual influences on marijuana use were studied in a two-wave longitudinal cohort of 490 married pairs, using data obtained twice from each spouse over a 5.5 year interval. To estimate processes during marriage free of sample selection bias, marriages that dissolved during the interval were used, and the impact of divorce on the drug use of the spouse was analyzed using reinterview data. Causation effects of spouse (or event) were distinguished from selection effects involved in assortative mating (or divorce) using models with and without controls for latent individual propensities to use marijuana. Marital selection effects were found to predominate over causation effects, and divorce was found to affect spouses' continued marijuana use. These findings have implications for understanding the persistence of drug use in adulthood, gender differences in the relationship of substance use with marriage and

divorce, and the study of interpersonal influences. Yamaguchi, K., and Kandel, D. The Influence of Spouses' Behavior and Marital Dissolution on Marijuana Use: Causation or Selection. Journal of Marriage and the Family, 59, pp. 22-36, 1997.

Correlates of College Student Marijuana Use

In a study to determine which personal student background and college characteristics are associated with marijuana use, researchers used data from a self-administered survey mailed to a national representative sample of 17592 students at 140 American colleges. One of four (24.8%) students reported using marijuana within the past year. Rates of use among the colleges ranged from zero percent at the lowest use schools to 54 percent at the highest use schools. Multiple regression models, constructed to determine the college and student characteristics predicting marijuana use, suggest that use was higher among students at non-commuter colleges and at colleges with pubs on campus. Student characteristics associated with marijuana use included being single, white, spending more time at parties and socializing with friends, and less time studying. Marijuana use was higher among students who participate in other high-risk behaviors such as binge drinking, cigarette smoking and having multiple sexual partners, and among students who perceived parties as important, and religion and community service as not important. The study points to the social nature of drug use in college, and demonstrates that this behavior is of continuing concern for public health. Bell, R., Wechsler, H., and Johnston, L.D. Correlates of College Student Marijuana Use: Results of a US National Survey. Addiction, 92 (5), pp. 571-581, 1997.

Predictors of Problem Drinking and Alcohol Dependence in a Population-Based Sample of Female Twins

To identify characteristics associated with problem drinking (PD) and alcohol dependence (AD) in women, researchers at Virginia Commonwealth University studied 2,163 white women aged 17-55 from the population-based Virginia Twin Registry. Measures were selected from a clinical interview and questionnaires to reflect five domains associated with alcoholism in prior studies: demographic characteristics, personality, health, and personal and family history of psychopathology. Logistic and linear regression analyses were used to predict PD and DSM-III-R defined AD. Multiple regression models were found to account for 19% of the variance in PD (significant predictors included: higher parental education-particularly among younger women, being the primary breadwinner, less frequent church attendance, higher scores on measures of neuroticism, extroversion and interpersonal dependency, history of major depression and social phobia, paternal PD and maternal treatment for emotional problems); 9% of the variance in diagnosis of AD (predicted by generalized anxiety, paternal depression and maternal PD); and 20% of the variance in number of symptoms of AD (predicted by the interaction of younger age and less-educated parents, higher neuroticism and mastery, lower optimism, generalized anxiety and agoraphobia, and maternal PD). The authors concluded that characteristics and parental psychopathology are important predictors of PD and AD independent of their effect on risk for affective and anxiety disorders. Many characteristics found to be associated with PD and AD in bivariate analyses were not significant when considered in the context of other predictors. Future studies of the etiology of alcoholism among women should simultaneously study measures from a variety of domains. Prescott, C.A., Neale, M.C., Corey, L.A., and Kendler, K.S. Predictors of Problem Drinking and Alcohol Dependence in a Population-based Sample of Female Twins. Journal of Studies of Alcohol, 58 (2), pp. 167-181, 1997.

Weekly Marijuana Use as a Risk Factor for Initial Cocaine Use

The gateway hypothesis argues that adolescents begin experimenting with cigarettes or alcohol, progress to marijuana use and finally to other illicit substance use. Although prior research has supported this hypothesis, studies have not examined the effects of weekly marijuana use on subsequent use of illicit substances such as cocaine and have not attempted to identify psychosocial mediators of relationships among substances. The current study used longitudinal national survey data with six assessment periods and a comprehensive set of psychosocial risk factors for substance use to examine relationships between cocaine and marijuana use using discrete-time survival analysis for multiwave longitudinal data. The results show that weekly marijuana use, as opposed to initial marijuana use, is an independent risk factor for initial cocaine use. Weekly marijuana users were over ten times more likely to initiate cocaine within the next year. The results also show that many psychosocial predictors are not predictive of initial cocaine use after controlling for prior weekly marijuana use. However, the association between weekly marijuana use and cocaine use is, in part, mediated by delinquent attitudes. The authors conclude that weekly marijuana use is a risk factor for cocaine use of equal or greater magnitude compared to other risk factors for initial cocaine use such as deviant peer bonding and attitudes toward deviance. These findings argue for some revision of the gateway

hypothesis and psychosocial theories of substance use. In addition, the current research shows support for clinical observations that suggest that regular use of any illicit substance is likely to spawn experimentation with other illicit substances. Miller, T. Q., and Volk, R. J. Weekly Marijuana Use as a Risk Factor for Initial Cocaine Use: Results from a Six Wave National Survey. Journal of Child and Adolescent Substance Abuse, 5 (4), pp. 55-78, 1996.

Understanding Delinquency and Substance Abuse among Children of Drug Users

Criminological theories and research have stressed the importance of family factors in understanding delinquency and substance use. Much work has documented the elevated risk of various problem behaviors faced by the children of drug users, as well as the factors that mediate their risk. This study examined a unique sample of high-risk children whose parents were receiving methadone treatment for opiate addiction. A model was developed and tested to estimate the impact of positive family management practices, maternal attachment, and deviant peers on delinquency, initiation of substance use, and misbehavior involving school and police sanctions. Positive family management practices showed little effect on reducing problem behaviors among these children of methadone clients, unlike in the general population. Similarly, the effect of maternal attachment was relatively weak and varied with age of the child. Gainey, R.R., Catalano, R.F., Haggerty, K.P., Hoppe, M.J. Deviance Among the Children of Heroin Addicts in Treatment: Impact of Parents and Peers. Deviant Behavior: An Interdisciplinary Journal, 18, pp. 143-159, 1997.

Cigarette Smoking Among Mexican American Youth

A self-report survey of cigarette use among 10th- and 12th-grade Mexican American students found no differences in rates of use by migrant status. Male students reported higher levels of lifetime, experimental, and daily smoking than female students, and 12th-grade students reported higher levels of daily smoking than 10th-grade students. A socialization model of cigarette use based on peer cluster theory was evaluated using structural equation methods, examining the effects of family strength, family tobacco use, school adjustment, religious identification, and peer tobacco associations. The basic latent-structure socialization model was supported in all groups, but final models including specific effects identified both unique and common relationships by gender and migrant status. Common patterns across groups suggest that completely different prevention programs may not be necessary for these youth. However, program elements based on subtle group differences may serve to tailor prevention efforts and make them more effective. Swaim, R.C., Oetting, E.R., and Casas, J.M. Cigarette Use Among Migrant and Nonmigrant Mexican American Youth: A Socialization Latent- Variable Model. Health Psychology, 15, pp. 269-281, 1996.

Predictors of Continued Drug Use During and After Treatment for Opiate Addiction

Many persons treated for opiate addiction continue to use drugs during and after treatment. It may be possible to improve outcomes by addressing patient characteristics that predict continued use. This review uses meta-analytic techniques to identify risk factors for continued drug use in patients treated for opiate abuse. A thorough search of the published literature yielded 69 studies that reported information on the bivariate association between one or more independent variables and continued use of illicit drugs during and after treatment for opiate addiction. Most of the patient variables summarized have weak longitudinal relationships with continued drug use, although several variable display moderate longitudinal associations. Ten variables show statistically significant and longitudinally predictive relationships with continued use, including: high level of pretreatment opiate/drug use, prior treatment for opiate addiction, no prior abstinence from opiates, abstinence from/light use of alcohol, depression, high stress, unemployment/employment problems, association with substance abusing peers, short length of treatment, and leaving treatment prior to completion. Several other variables may be potentially longitudinally predictive. To prevent relapse, treatment interventions should address multiple variables because no single variable strongly predicts continued use. Brewer, D.D., Catalano, R.F., Haggerty, K.P., Gainey, R.R., and Fleming C.B. A Meta-Analysis of Predictors of Continued Drug Use During and After Treatment for Opiate Addiction. Addiction, In press.

Familial Aggregation of Depressive Symptoms, Antisocial Behavior, and Alcohol Abuse

This paper describes results from an ongoing family study of adolescent boys and their families designed to investigate potential risk factors for substance abuse. The sample currently includes 251 individuals: 39 male treatment probands and their families and 34 control families matched by age and geographic location (zip code). The adolescent treatment probands have severe drug and alcohol related problems and were recruited through a

residential rehabilitation program. Probands and participating family members are given a structured interview that assesses alcohol and drug problems, and various psychiatric symptoms. Data were analyzed to examined the coaggregation of depressive symptoms, antisocial behavior, and alcohol misuse. Multivariate pedigree analyses were performed using a model that allowed for the estimation of vertical familial transmission, residual sibling resemblance, and assortative mating. Spouse correlations were estimated at .57, .21, and .31 for antisocial behavior, depressive symptoms, and alcohol abuse, respectively. Residual sibling environment (i.e., sibling resemblance unaccounted for by parent-offspring transmission) was not found for alcohol problem symptoms, but did contribute to resemblance for antisocial behavior and depressive symptoms. The proportion of variance accounted for by vertical familial transmission was estimate at approximately 30 to 40%. More important, correlations among the transmissible family factors for these psychiatric syndromes ranged from .58 to .73, suggesting substantial overlap among the underlying familial antecedents for these disorders. Stallings, M. C., Cherny, S. S., Miles, D. R., Hewitt, J. K., and Fulker, D. W. The Familial Aggregation of Depressive Symptoms, Antisocial Behavior, and Alcohol Abuse. American Journal of Medical Genetics, 74, pp.183-191, 1997.

Intervening with Drug-Addicted Parents

Parents in methadone treatment were offered an experimental intervention, Focus on Families, designed to reduce their risk of relapse and their children's risk of substance use. Experimentally assigned volunteers participated in systematic group training in relapse prevention and parenting skills, and received home-based case management services. Immediate posttreatment outcome results reported here include analyses of covariance controlling for baseline measures. Analyses show experimental parents held more family meetings to discuss family fun, displayed stronger refusal/relapse coping skills, demonstrated stronger sense of self-efficacy in role-playing situations, and had lower levels of opiate use than control subjects. No significant differences in family bonding, family conflict, or other measures of drug use were found. The utility of intervening with drug-addicted parents in methadone treatment is discussed in light of these findings. Catalano, R.F., Haggerty, K.P., Gainey, R.R., Hoppe, M.J. Reducing Parental Risk Factors for Children's Substance Misuse: Preliminary Outcomes with Opiate Addicted Parents. Substance Use & Misuse, 32(6), pp. 699-721, 1997.

Substance Abuse Disorders Among Runaway and Homeless Youth

Systematic sampling methods were used to recruit a sample of 432 homeless youth from both service and natural 'hang-out' sites. According to DSM-III criteria, 71% of respondents were classified as having alcohol and/or illicit 'drug abuse' disorders. The results from multivariate logistic regression analyses indicated that cumulative length of time of use is positively associated with an "abuse" disorder. The implications of these findings and recommendations for service interventions are discussed. Kipke, M.D., Montgomery, S.B., Simon, T.R., and Iverson, E.F. "Substance Abuse" Disorders Among Homeless and Runaway Youth. Substance Use & Misuse, 32(7&8) pp. 969-986, 1997.

Prevalence and Demographic Correlates of Past Year Dependence on Four Substances

Dr. Denise Kandel and her associates conducted secondary analyses based on three aggregated waves (1991, 1992 and 1993) of nationally representative samples of the general population aged 12 and over interviewed in the National Household Survey on Drug abuse (N=87,915). An approximate measure of DSM-IV drug-specific past-year dependence for each drug class was derived from self-reported symptoms of dependence, data on frequency and quantity of use, and drug-related problems. Although the measure of dependence has limitation, the inclusion of cigarettes, the large number of cases and the wide age range of respondents permitted drug, age, gender and ethnic comparisons on liability for dependence not otherwise possible. Five major findings were obtained regarding rates of dependence experienced among last year users of each drug class: (1) nicotine is more addictive than alcohol, marijuana and cocaine; (2) among adolescents, rates of dependence on alcohol, marijuana and cocaine are higher among females than males; (3) among adults, rates of dependence are higher among males than among females for alcohol and marijuana, but lower for nicotine; (4) adolescent females are significantly more at risk for dependence on alcohol and marijuana than any other age group of women; (5) whites are more likely than any other ethnic group to be dependent on nicotine and blacks to be dependent on cocaine. This is the first report in the literature in which the liability for dependence could be compared among adolescents and adults, and nicotine dependence could be systematically compared with dependence on other drugs. Adolescent girls constitute an especially high risk group for drug dependence. Kandel, D.B., Chen, K., Warner, L., Kessler, R., Grant, B. Prevalence and Demographic Correlates of Symptoms of Dependence on Cigarettes, Alcohol, Marijuana and Cocaine in the U.S. Population. Drug and Alcohol Dependence, 44, pp. 11-29, 1997.

Developmental Correlates of Alcohol and Tobacco Use

Since the use of tobacco and alcohol during childhood predicts the heavy use of these substances and use of illicit drugs during adolescence, this cross sectional survey was used to identify developmental correlates of alcohol and tobacco use among elementary school children. Results were based on information obtained from 1470 third and fifth grade students. Children's current alcohol and tobacco use was strongly related to low scores of several measures of child competence; both self report and teacher rated. Use of these substances was also associated with less effective parenting behaviors and with parental use of alcohol and tobacco. The researchers conclude that childrens' early experience with tobacco and alcohol is associated with weak competence development and exposure to socializing factors that promote risk taking. Interventions to prevent early use of alcohol and tobacco is needed. Jackson, C., Henriksen L., Dickinson, D., and Levine, D.W. Early Use of Alcohol and Tobacco: Relation to Child Competence and Parental Behavior. American Journal of Public Health, 87, pp 359-364, 1997.

Family Functioning Can Be Protective Against Narcotic Addiction

A retrospective case-control study of male narcotic addicts, equally divided between White and Black subjects, showed that, during early teen age, intact family structure deterred later addiction at statistically significant levels. Strong attachment to father or father figure, positive home atmosphere, strong parental adherence to traditional ethical norms, and expected weak parental disapproval of misbehavior by subjects were also identified as significant deterrents of later addiction. Nurco, D. and Lerner, M. Vulnerability to Narcotic Addiction: Family Structure and Functioning. Journal of Drug Issues, 26(4), pp. 1007-1025, 1996.

Nicotine Withdrawal in Women

Associations between self-report symptom profiles for nicotine withdrawal, personality (TPQ, EPQ-R), life-time history of psychopathology and smoking history were examined in data obtained from 553 female adult Australian twins (246 regular smokers), ages 32-48 years, who had participated in a telephone interview survey that included life-time assessments of smoking history, nicotine dependence, and symptoms of withdrawal. Two hundred and two respondents were from high-risk pairs where either the respondent or the respondent's co-twin had reported a life-time history of alcohol dependence; 351 were from control pairs. Latent class analysis was used to identify subtypes ('classes') of smokers reporting similar withdrawal symptom profiles. Three major classes were identified which appeared to represent a continuum from mild to severe nicotine withdrawal. Smokers from the severe withdrawal class were best characterized by hands shaking and by the prominence of depressive features. There were marked increases in lifetime alcohol dependence rates as a function of severity class. In contrast, significantly elevated rates of major depression, conduct disorder and anxiety disorder were observed only among smokers from the most severe withdrawal class. Neuroticism was the only personality factor strongly associated with the development of withdrawal symptoms. Madden, P. A. F., Bucholz, K. K., Dinwiddie, S. H., Slutske, W. S., Bierut, L. J., Statham, D. J., Dunne, M. P., Martin, N. G., and Heath, A. C. Nicotine Withdrawal in Women. Addiction, 92 (7), pp. 889-902, 1997.

Maturing Out of Substance Use: Selection and Self-Correction

The third decade of life is a period when individuals are held responsible for taking an active role in controlling and optimizing their developmental prospects and outcomes. It is also a period when most young adults mature out of various problem behaviors including delinquency, illicit drug use, and heavier alcohol use. Self-regulation of development and maturing out of substance use are assumed to be linked to (a) self-correction and (b) selection and differential association. By age 28 to 31, the vast majority of participants in the Rutgers Health and Human Development Project reported significant decreases in their own alcohol and drug use, decreases in their friends' substance use, and increases in the number of married friends. Reductions in use were more pronounced among individuals who remained married since their early twenties, those who became married, and those who became parents. Self-corrective changes in substance use are facilitated by the selection of, and differential association with, friends who are also married and have children by age 30. However, some degree in continuity of use is also evidenced by individuals tending to select friends and/or spouses on the basis of shared behavioral norms. Labouvie, E. Maturing Out of Substance Use: Selection and Self-Correction. Journal of Drug Issues, 26, pp. 457-476, 1996.

Parent Substance Use As A Predictor of Adolescent Use: A Six-Year Lagged Analysis

The present study investigated the role of parental use of alcohol, cigarettes, and marijuana on lagged change in the specific substance abuse of their adolescent offspring over a six year period. The analyses also examined the relative influence of mothers and fathers and their interaction as moderated by marital status and age and gender of the adolescent. A generalized estimating equations approach was employed to estimate regression coefficients through an iterative weighted least squares algorithm. Findings indicated that, when employed as time varying covariates, parental substance use resulted in substance-specific effects on fluctuations in the adolescent's own use. Age, parent marital status, and each parent's marijuana use independently were found to significantly affect adolescent marijuana use. In contrast, the complex relationship between parent and adolescent use of alcohol and cigarettes showed variation by substance, age, and gender text. The results suggest that parent use of substances must be considered risk factors with particular effects on their younger offspring. Thus, prevention efforts should be directed at middle childhood and include components aimed at parents as well as their children. Hops, H., Duncan, T. E., Duncan, S. C., Stoolmiller, M. Parent Substance Use As A Predictor of Adolescent Use: A Six-Year Lagged Analysis. Ann Behavior Medicine, 18 (3) pp. 157-164, 1996.

Intervention and Prevention of Steroid Use in Adolescent Athletes

A study involving high school football players was conducted to test the hypothesis that those with an intent to use steroids had features/characteristics that distinguished them from players who did not. Thirty-one football teams in the Portland, Oregon area participated in the study. One quarter of the participants (n=279) fell into the category of high-intent as measured by a questionnaire. Comparison and evaluation between high and low intent groups uncovered many similarities, such as demographics, physical measurements and knowledge questions about weight training and sports nutrition. They did differ, however, on several variables. A greater number of high intent users currently were using amino acid supplements (27% versus 16%) which has been postulated as a behavior which precedes steroid use. Also, the students with higher intent had higher levels of alcohol and marijuana use. Psychological trait differences were also uncovered with high intent players scoring higher on dimensions of hostility, impulsivity, and a "win-at-all-costs" attitude. Finally, despite similar physical measures, high intent athletes were less satisfied with their current weight. These differences provide a needs assessment to identify curricular components for an intervention to prevent steroid use. Elliott D. and Goldberg L., Intervention and Prevention of Steroid Use in Adolescents. The American Journal of Sports Medicine, 24(6), S-46, 1996.

Testing a Multi-Stage Model for the Adoption of Alcohol and Tobacco Behaviors by Children

A staged model of smoking adoption has been widely applied in studies of adolescent smoking. The present study applied this model to examine the preliminary stages of tobacco and alcohol use by children. Using discriminant analysis, factors associated with abstinence, initiation and experimentation stages of tobacco and alcohol use were compared in a sample of 1272 fourth and sixth grade children. Modeling of use by best friends and the perceived prevalence of use among same-age peers were most strongly related to the initiation and experimentation stages of tobacco and alcohol use. Other key factors were offers from parents and friends, adjustment to school and behavioral self-regulation. The weakest factors were parent modeling and self-esteem. The initiation and experimentation stages were not as highly differentiated among children as other studies have found them to be among adolescents. This suggests that if initiation occurs during childhood, progression to experimentation is more likely than if initiation begins during adolescence. Therefore, development of prevention programs that simultaneously influence children's risk of alcohol and tobacco use by targeting the common risk factors for preliminary use of these substances are suggested. Jackson, C. Initiation and Experimental Stages of Tobacco and Alcohol During Late Childhood: Relation to Peer, Parent and Personal Risk Factors. Addictive Behaviors, 22, pp. 1-14, 1997.

Smokeless Tobacco: Demographic Differences in Prevalence and Place in Drug Involvement Continuum

In a study of 2,525 Southern California high school seniors, Dr. Brian Flay and his affiliates examined patterns of smokeless tobacco (ST) use and the place of ST in a unidimensional model of drug involvement based on latent trait analysis. Among male students, lifetime ST use was reported by 31.9% of Whites, 3.0% of Blacks, and 16.1% of Hispanics; among females, comparable rates were 6.3%, 1.8%, and 1.9% for these respective racial/ethnic groups. In the total sample, the ordering of drugs along the hypothesized involvement continuum was, from least to most involved: alcohol, cigarettes, marijuana, ST, LSD, "uppers", cocaine, "downers", PCP, and heroin. Analyses showed

that although ST use fits the unidimensional model of drug involvement, the place of ST use along the continuum of drug involvement is not stable and differs by gender and ethnicity. Particularly for males, ST use is likely to be preceded by soft drug use and followed by hard drug use; for females, however, ST use is closely associated with hard drug use. The analyses also revealed that the fit of the unidimensional model and the location of ST use along the dimension vary with different ethnic groups. Hu, F.B., Hedeker, D., Day, L.E., Flay, B.R., Siddiqui, O., Sussman, S., and Richardson, J. Patterns of Use of Smokeless Tobacco and the Unidimensional Model of Drug Involvement. Addictive Behavior, 22 (2), pp. 257-261, 1997.

Childhood Abuse and Inhalant Use

Two ethnographic studies of drug-involved adults were analyzed to evaluate the association between child-abuse victimization and levels of involvement in inhalant use. Historical accounts of childhood exposure to physical or sexual abuse were compared among nonusers of inhalants (n = 197), light inhalant users (n = 64), and heavy inhalant users (n = 24). Heavy inhalant use was found to be associated with history of any child abuse (adjusted odds ratio [OR] = 4.6) and physical abuse (adjusted OR = 3.8). Light inhalant use showed no association with child-abuse history. The authors concluded that childhood abuse may be an important correlate of extensive involvement in inhalant use and suggest that carefully designed longitudinal methods be used to further research this relationship. Fendrich, M., Mackesy-Amiti, M.E., Wislar, J.S., and Goldstein, P.J. Childhood Abuse and the Use of Inhalants: Differences by Degree of Use. American Journal of Public Health, 87 (5), pp. 765-769, 1997.

ADHD and Early Initiation of Smoking

The association between attention-deficit hyperactivity disorder (ADHD) and cigarette smoking in children and adolescents was evaluated. Subjects were 6- to 17-year-old boys with DSM-III-R ADHD (n = 128) and non-ADHD comparison boys (n = 109) followed prospectively for 4 years into mid-adolescence. Information on cigarette smoking was obtained in a standardized manner blind to the proband's clinical status. Cox proportional hazard models were used to predict cigarette smoking at follow-up using baseline characteristics as predictors. Findings indicate that ADHD was a significant predictor of cigarette smoking at follow-up into mid-adolescence. ADHD also was associated with an early initiation of cigarette smoking even after controlling for socioeconomic status, IQ, and psychiatric comorbidity. In addition, among children with ADHD, there was a significant positive association between cigarette smoking and conduct, major depressive, and anxiety disorders. Thus, ADHD, particularly the comorbid subtype, is a significant risk factor for early initiation of cigarette smoking in children and adolescents. Considering the prevalence and early childhood onset of ADHD, these findings highlight the importance of smoking prevention and cessation programs for children and adolescents with ADHD. ADHD Is Associated with Early Initiation of Cigarette Smoking in Children and Adolescents. Milberger, S., Biederman, J., Faraone, S.V., Chen, L., and Jones, J. Journal of American Academy of Child and Adolescence Psychiatry, 36 (1), pp. 37-44, 1997.

Profiles of Children as a Function of Aggression

It was hypothesized that reactive and proactive types of antisocial youths would differ in developmental histories, concurrent adjustment, and social information processing patterns. In Study 1, examination of 585 boys and girls who were classified into groups called reactive aggressive, proactive aggressive, pervasively aggressive (combined type) and nonaggressive revealed distinct profiles. Only the reactive aggressive group demonstrated histories of physical abuse and early onset of problems, adjustment problems in peer relations and inadequate encoding and problem solving processing patterns. Only the proactive aggressive group demonstrated a processing pattern of anticipating positive outcomes for aggressing. In Study 2, 50 psychiatrically impaired chronically violent boys classified as reactively violent or proactively violent demonstrated differences in age of onset of problem behavior, adjustment problems and processing problems. Dodge, K.A., Lochman, J.E., Harnish, J.D., Bates, J.E. and Pettit, G.S. Reactive and Proactive Aggression in School Children and Psychiatrically Impaired Chronically Assaultive Youth. Journal of Abnormal Psychology, 106(1), pp. 37-51, 1997.

Protective Factors and Alcohol Abstinence

Two waves of data from a family-focused prevention intervention project were used to test a model of the influence of protective factors on young adolescent's tendency toward alcohol abstinence. Prior theoretical and empirical work guided the specification of hypothesized effects of the protective factors -- affectional relationship with parents,

affiliation with prosocial peers, and mastery-esteem -- on tendency toward alcohol abstinence. The tested model controlled for pre-intervention measures and included specified interrelations of protective factors across time. Structural equation analysis indicated that the model fit the data. The hypothesized relationship between affectional relation with parents and prosocial peer relations was not supported. However, there was support for the cross-time effects of affectional relationship with parents and prosocial peer affiliation on young adolescents mastery esteem. Moreover, participation in the intervention was associated with child's report of a positive affectional relationship with parents. Spoth, R., Redmond, C., and Hockaday, C. Protective Factors and Young Adolescent Tendency to Abstain from Alcohol Use: A Model Using Two Waves of Intervention Study Data. American Journal of Community Psychology, 24(6) pp. 749 771, 1996.

Effect of Parents and Peers on Alcohol Refusal in Adolescents

This paper describes the specification and testing of a model of protective parent and peer factors in peer refusal skills. Two modifiable protective factors suggested by relevant research on adolescent substance use - child attachment with parents and association with peers having prosocial norms--were incorporated as independent variables in the model. The effects of parent and child attendance at skills training interventions were also assessed. Covariance structure modeling of data from a sample of 209 families participating in a controlled study of family-oriented skills intervention was used to test two versions of the model, one version addressing attachment and skills training attendance specific to mothers and one specific to fathers. Following two indicated modifications of the original model, strong fits with the data were achieved for both mother and father versions of the model; hypothesized protective factor effects and skills training effects were significant. Spoth, R., Yoo, S., Kahn, J., and Redmond, C. A Model of the Effects of Protective Parent and Peer Factors on Young Adolescent Alcohol Refusal. The Journal of Primary Prevention, 16(4), pp. 373-394, 1996.

Shared and Unshared Risk Factors in African American and Puerto Rican Youth

A study was conducted to examine the shared and unshared psychosocial risk factors related to stage of drug use and delinquency. The sample consisted of 655 African American and 600 Puerto Rican male and female adolescents. Net regression analysis was used to analyze the data. The results showed that adolescent stages of drug use and delinquency reflect shared and unshared risk factors. Among the shared risk factors were low adolescent and peer achievement, low father identification, and a poor school environment. The magnitude of the risk factors for adolescent delinquency was generally greater than for stage of drug use. Risk factors showing a stronger relationship to delinquency than to drug use included tolerance of deviance, low ego integration, parent-child conflict, low mother identification, and particularly, peer deviance. Only father alcohol use and peer marijuana use had a stronger relationship to adolescent drug use than to delinquency. Since delinquency encompasses a greater variety of behaviors than does drug use, it is easier for more diverse factors to contribute more strongly to delinquency than to drug use. The findings support a socialization hypothesis (from parent to personality to behavior) as well as a dispositional model (from child to parent or peer to behavior). The support of both models suggests that there is a reciprocal influence between adolescent personality and parent or peer factors in their impact on problem behavior. Overall, a reduction in many adolescent risk factors will lead to a decrease in both delinquency and drug use. Brook, J.S., Whiteman, M., Balka, E.B., et al. Drug Use and Delinquency: Shared and Unshared Risk Factors in African American and Puerto Rican Adolescents. Journal of Genetic Psychology, 158(1), pp. 25-39, 1997.

Alcohol, Drugs, and Aggressive Crime among Mexican-American, Black, and White Male Arrestees in Texas

In this study, investigators analyzed existing data from the 1992 Drug Use Forecasting (DUF) system to understand the relationship between aggressive crime and substance abuse among Mexican-American, Black, and White male arrestees in Dallas, Houston, and San Antonio, Texas. The aim of the analysis was to predict the outcome of aggressive crime from drug and alcohol-related and ethnic group variables within the total male sample (n=2,364). Ethnicity was found to be significantly related to aggressive crime. Mexican American arrestees were more likely to be arrested for aggressive crime than Blacks or Whites. Drug and alcohol use effects were found across all ethnic groups. The subgroup of arrestees who drank alcohol frequently and tested positive for drugs was less likely to be charged for aggressive crime than were the other subgroups. Specific ethnic subcultural and ecological influences are discussed which may influence the study findings. The findings indicate the heterogeneous character of the alcohol and drug using population related to aggression. The authors observe that the heterogeneity becomes more obvious when examining differences between the ethnic groups, likely because of the mix of socioeconomic, environmental,

and cultural factors which distinguish ethnic communities independent of the pharmacological effects of the various substances. Such variability between subculturally defined groups requires detailed ethnographic field studies to describe the context of drug taking, drinking, and aggressive behavior. Valdez, A., Yin, Z., and Kaplan, C. A Comparison of Alcohol, Drugs, and Aggressive Crime among Mexican-American, Black, and White Male Arrestees in Texas. American Journal of Drug and Alcohol Abuse, 23(2), pp. 249-265, 1997.

Why Families Decline Program Participation

This study extends a line of programmatic research on families who decline participation in interventions and assessment components of family-focused prevention projects. Parents responding to a brief telephone interview (N=459) identified the most important of 28 barriers concerning project assessments, intervention-related time demands and logistic requirements, beliefs and attitudes about interventions, and family member influences. Results demonstrated that several time-related factors, logistic requirements, and family member influences were important barriers. Findings also showed that socio demographic factors were associated with unfavorable attitudes about interventions and their assessments. Implications for the development of effective recruitment strategies and for future research are presented. Spoth, R., Redmond, C., Hockaday, C., and Shin, C.Y. Barriers to Participation in Family Skills Prevention Interventions and Their Evaluation: A Replication and Extension. Family Relations, 45, pp. 247-254, 1996.

Juvenile Drug Traffickers: Characterization and Substance Use Patterns

Juveniles involved in drug trafficking have been reported to be more likely to be seriously immersed in substance abuse and delinquent behavior than nonsellers. Investigators studied the substance use patterns of juveniles incarcerated for drug trafficking offenses in Virginia (N = 240) and characterized juvenile drug traffickers based upon their delinquent, social, psychological, educational and medical histories, making comparisons with a demographically similar control group (N = 433). The results indicated that the most frequently sold substance was cocaine (93%), either powered or crack, while alcohol and marijuana were the drugs most often used by the juvenile drug traffickers. The juvenile drug traffickers showed lower levels of aggressivity, violence and delinquency when compared to other incarcerated juveniles from their community. In addition, the juvenile drug traffickers had higher ratings on social and psychological functioning. Characteristics that did not correlate well with drug trafficking were physical health, intellectual functioning and academic achievement. The results of this study indicate that juvenile drug traffickers tend to use the drugs that they sell, and generally present as higher functioning and better adjusted in almost every area evaluated, when compared to their incarcerated delinquent peers. McLaughlin, C. R., Smith, B. W., Reiner, S. M., Waite, D. E., and Glover, A. W. Juvenile Drug Traffickers: Characterization and Substance Use Patterns. Free Inquiry In Creative Sociology, 24 (1), pp. 3-10, 1996.

Health Services Utilization by Clinical Homeless, Community Homeless, and Domiciled Clinic Samples

Clinic-based studies on the health of the homeless have often been used to represent the health status of the all homeless people. Although convenient and economical, such studies may not generalize to the wider homeless community. Investigators in this study contrasted 216 homeless and 212 domiciled free clinic users, and 531 community homeless persons on latent variables representing alcohol and drug use, mental and physical health, appearance, life satisfaction, and health services utilization (HSU). Homeless clinic patients were found to equal the community homeless sample in alcohol problems and drug use, poor health, mental illness, mental health services utilization, and life satisfaction but exceeded them in HSU and cleanliness. Homeless clinic users reported more substance abuse, poorer health, greater mental illness and mental HSU, less cleanliness, and lower life satisfaction than domiciled patients. These findings suggest that the homeless subpopulation receiving services in the free clinic resembled to a great extent the greater population of homeless people residing in the area. Thus, researchers may feel comfortable extrapolating to the wider homeless community from homeless clinic attendees, especially those attending a convenient, free facility. Stein, J.A., Gelberg, L. Contrasting Clinical Homeless Samples with Domiciled Clinic Users and Community Homeless Persons: Issues of Comparability and Representativeness. Health Psychology, 16, pp. 155-162, 1997.

Gender and Hostility Effects on Alcohol Use and Aggression

In a study at Rutgers, investigators working with Dr. Robert Pandina used a series of nested structural equation models to examine the interrelationships among alcohol use, aggressive behavior, and episodes of acute alcohol-related aggression. Both prior aggressive behavior and prior alcohol use predicted later episodes of acute alcohol-related aggression. In addition, early aggressive behavior predicted later alcohol use, but alcohol use was not related to subsequent increases in aggressive behavior. Gender interaction effects were significant. Prior alcohol use was a better predictor of alcohol related aggression for females, while prior aggression was a better predictor for males. However, the relationships among alcohol use and aggression did not vary by levels of hostility as measured by the SCL-90R. In sum, these data suggested that the nature and direction of the relationship between alcohol use, aggression, and alcohol-related aggression over time are conditioned by gender. White, H. R., and Hansell, S. The Moderating Effects of Gender and Hostility on the Alcohol Aggression Relationship. Journal of Research on Crime and Delinquency, 33, pp. 451 472, 1996.

Friendships and Violent Behavior During Adolescence

This study investigated the extent to which interpersonal processes within male friendships are associated with violent behavior patterns during adolescence. Researchers observed participants (206 boys) at ages 13 14, 15-16, and 17-18, discussing problem solving situations with a close friend. Although the boys typically brought in different friends for each of the three assessments, considerable continuity in the boys' behaviors were found, most notably in the topics discussed. In particular, the tendency of a dyad to engage in deviant and violent talk was uniquely associated with violence in adolescence, controlling for childhood antisocial behavior and coercive disciple practices in the home. These findings suggest that adolescent violence is embedded within enduring social interactional patterns of friendship, where the faces change but the process remain the same. Dishion, T.J., Eddy, J.M., Li, F., and Spracklen, K. Friendships and Violent Behavior During Adolescence. Social Development, 6(2), pp. 207-223, 1997.

Narcotic Addicts' Parenting Practices

This survey study of male and female narcotic addicts participating in methadone maintenance programs examined self-reported retrospective data on parental behavior experienced by addicts during their adolescent years. These findings were contrasted with the addicts' self-report of their current parenting practices with their own adolescent children. Results showed addicts as perceiving their mothers as significantly more functional in their parenting practices than their fathers on indices of parental involvement, attachment, and responsibility. Significant parenting differences between addicts and their parents were reported for the three indices mentioned, as well as for parent discipline and punitive actions, with the addicts rating their current parenting practices as more effective than those of their parents. Reported parenting practices were further analyzed in the context of how the ratings of parental functioning were related to problems of drug and alcohol abuse exhibited in the home. Findings are discussed in terms of the implications for prevention and treatment approaches with addicts and their children. Nurco, D.N., Blatchley, R.J., Hanlon, T.E., O'Grady, K.E., and McCarren, M. The Family Experiences of Narcotic Addicts and their Subsequent Parenting Practices. The American Journal of Drug and Alcohol Abuse, In press.

Effects of a Localized Antidrug Media Campaign

The authors report a study designed to determine whether antidrug campaigns that have been localized can effect variables associated with adolescent drug use. An experiment was conducted with sets of matched communities with populations between 5000 and 30,000 distributed throughout the United States. Seventh- through twelfth-grade students in experimental communities were exposed to a year-long campaign followed by a survey. The targeted variables were perceived influence of media messages on "favorability" toward substance use and drug-related intentions, perceived harm of substance use, parental sanctions against substance use, parent-child communication about substance use, peer encouragement to use substances, and peer sanctions against substance use. Recall of the media campaign was low. However, adolescents with low and moderate levels of drug use who recalled individual campaign spots showed beneficial effects on targeted variables in comparison to students who did not recall the campaigns and control students who were not exposed to the campaigns. The implications of the findings for further research and public policy are discussed. Kelly, K.J., Swaim, R.C., and Wayman, J.C. The Impact of a \Localized Antidrug Media Campaign on Targeted Variables Associated With Adolescent Drug Use. Journal of Public Policy and Marketing, 15, pp. 238-251, 1997.

Mental Health Distress Among Homeless Youth

This study assessed depression, self esteem, ADHD, suicidality, self-injurious behaviors, as well as alcohol and other drug abuse disorders in a sample of runaway and homeless youth in Los Angeles. Results indicated a high prevalence of mental health problems within the sample; 64% clinically depressed, 62% reporting suicidal ideation, 39% reporting previous suicide attempts and 49%, self-injurous behaviors. Demographically, African-American youth were at lower risk of suicidal ideation and self-injurous behavior than other racial/ethnic groups. Younger youths were at increased risk of self-injurous behaviors while older youth and females were more likely to be clinically depressed. Risk factors for a drug disorder included ethnicity other than African-American, homelessness for a year or more, suicidality, self-injurous behaviors, depression and low self-esteem. For alcohol disorders increased risk is associated with being a white male, being homeless, and reporting suicidality and injurous behaviors. Mental health and substance abuse disorders were found to be highly correlated. The need for service programs and policies to address these problems are discussed. Unger, J. B., Kipke, M.D., Simon, T.R., Montgomery, S.B., Iverson, E. And Johnson, C.J. Homeless Youth in Los Angeles: Prevalence of Mental Health Problems and the Relationship Between Mental Health Distress and Substance Abuse Disorders. American Journal of Community Psychology, In press.

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National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse
September, 1997

Research Findings

Intramural Research

Office of the Director, IRP

During the past year, Intramural Research Program Director Dr. Barry Hoffer's work has focussed on effects of trophic peptides in the GDNF family, and on regulation of GDNF-family receptors. This work, carried out primarily in collaborating laboratories during the past year, will move to DIR labs this summer. In addition, work will be initiated at DIR on Nurr-1, which appears to be a critical factor for the specific development of midbrain DA neurons. New initiatives to be developed during the coming year involve multiunit recording approaches and ultrastructural studies, as well as the electrochemical, electrophysiological, and immunocytochemical protocols traditionally used by this laboratory.

Brain Imaging Section, Neuroscience Branch

Global Brain Glucose Metabolism is not Confounded by Modest Changes in Plasma Glucose following Acute Alpha2 Blockade by Idazoxan

The sympathetic nervous system can modulate glucose levels via several mechanisms, including inhibition of insulin release by alpha2-adrenergic receptors. Such effects could potentially confound measurements of brain glucose metabolism during studies of the central actions of sympathomimetic drugs. To test this hypothesis, plasma glucose, insulin and sympathetic responses following infusion of idazoxan, a selective alpha2 antagonist, or placebo were compared with global brain metabolism obtained from positron emission tomography (PET) scans using [18F]-fluoro-deoxyglucose before and after the infusion. Glucose levels fell and fractional levels of insulin rose after idazoxan, compared to placebo. Relative increases in insulin correlated with increases in epinephrine after active drug, consistent with the role of alpha2-adrenoreceptors in regulating insulin release. Estimates of global brain glucose metabolism did not appear to be influenced by the modest changes in plasma glucose. Schmidt, M.E., Goldstein, D.S., Schouten, J.L., Matochik, J.A., Kim, H.G., Potter, W.Z. Acute Alpha2 Blockade by Idazoxan Increases Insulin and Lowers Plasma Glucose During Positron Emission Tomography. Psychopharmacol Bull, 33, pp. 253-259, 1997.

Anxiety Level Affects Cerebral Glucose Metabolism During Repeated PET Trials

Cerebral glucose utilization was higher during the first positron emission tomography (PET) session than during the second PET session, as assayed using the [18F]fluorodeoxyglucose method in male human volunteers. This difference was due largely to data from subjects with low Trait Anxiety, since subjects with high anxiety showed similar metabolism in both PET sessions. High-anxiety subjects showed greater right/left ratios of cerebral metabolism than low-anxiety subjects, particularly during the second PET session. These findings suggest that the level of anxiety may

be an important variable to consider in PET studies using multiple sessions. Stapleton, J.M., Morgan, J.M., Liu, X., Yung, B.C.-K., Phillips, R.L., Wong, D.F., Shaya, E.K., Dannals, R.F., and London, E.D. Cerebral Glucose Utilization is Reduced in Second Test Session. J. Cereb. Blood Flow Metab. 17, pp. 704-712, 1997.

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[125]I-IPH: A Promising Epibatidine Analogue for Imaging Neuronal Nicotinic Receptors

An analog of epibatidine (EB) was synthesized with an iodine atom in the 2 position of the pyridyl ring. This analog, (+/-)-exo-2-(2-iodo-5-pyridyl)-7-azabicyclo[2.2.1]heptane (IPH), as well as its two stereoisomers, displayed high affinity for neuronal nicotinic acetylcholine receptors (nAChRs). Therefore, radioiodinated IPH, [125I]IPH, was synthesized with specific radioactivities consistently > 1000 Ci/mmol, and its properties as a radioligand for neuronal nAChRs were evaluated. The characteristics of [125I]IPH binding in tissue homogenates appeared to be virtually identical to those reported for [3H]epibatidine binding, but the high specific radioactivity of [125I]IPH greatly facilitated measurements of nicotinic receptors in tissues with relatively low receptor densities and/or where tissues are in limited supply. Autoradiography with [125I]IPH provided clear localization of nAChRs in brain and adrenal gland after film exposure times of < or = 2 days. Investigators conclude that [125I]IPH will be a very useful radioligand for the study of neuronal nicotinic receptors in brain and in peripheral ganglia. Davila-Garcia, M.I., Musachio, J.L., Perry, D.C., Xiao, Y., Horti, A. London, E.D., Dannals, R.F., and Kellar K.J. [125I]IPH, An Epibatidine Analog, Binds with High Affinity to Neuronal Nicotinic Cholinergic Receptors. J. Pharmacol. Exp. Ther. 282, pp. 445-451, 1997.

Molecular Neuropsychiatry Section, Neuroscience Branch

Evidence that Methamphetamine Damages Human DNA

Immortalized neural cells obtained from rat mesencephalon were used to further assess the role of oxidative stress in methamphetamine (METH)-induced neurotoxicity. Investigators tested if the anti-death proto-oncogene, Bcl-2, could protect against METH-induced cytotoxicity. Results suggested that METH can cause cell death in a manner that resembles apoptosis. This was demonstrated by flow cytometry, fluorescence microscopy and DNA gel electrophoreses. Bcl2 protected cells against METH-induced molecular changes. These results are the first to demonstrate the possibility that METH use might cause DNA damage in humans who abuse that drug. Cadet, J.L., Ordonez, S.V., and Ordonez, J.V. Methamphetamine Induces Apoptosis in Immortalized Neural Cells: Protection by the Protoncogene, Bcl2. Synapse, 25, pp. 176-184, 1997.

Increased EEG Beta Activity is Manifested During Cocaine Withdrawal

This investigation shows that the brains of chronic cocaine users have increased beta activity on the EEG. Together with the demonstration of that these subjects have neuropsychological impairment, these data indicate that chronic cocaine abuse results in a brain disorder that can be characterized as a neuropsychiatric syndrome. Herning, R.I., Guo, X., Better, W.E., Weinhold, L.L., Lange, W.R., Cadet, J.L., and Gorelick, D.A. Neurophysiological Signs in Cocaine Dependence: Increased EEG Beta During Withdrawal. Biol. Psychiatry, 41, pp. 1087-1094, 1997.

Molecular Neuroadaptive Changes in the Dopamine Transporter and Cocaine Addiction

Binding of cocaine to dopamine transporters leads to inhibition of dopamine reuptake and plays a pivotal role in its addictive effects. In contrast to cocaine, clinically used dopamine reuptake inhibitors are considered not to possess abuse potential. One factor that may underlie differences between cocaine and other dopamine reuptake inhibitors is pharmacological heterogeneity among dopamine reuptake inhibitors. In this context, we previously demonstrated that following chronic intravenous self-administration of cocaine, cocaine upregulated dopamine transporters, while the dopamine-selective uptake inhibitor GBR12909 lacks this effect. New evidence now demonstrates that the self-administration of bupropion, but not nomifensine upregulated dopamine transporters confirming initial results obtained by NIDA IRP scientists. Since the neuroadaptive changes that gradually develop after chronic exposure to cocaine may relate to addictive and withdrawal states, the elucidation of pharmacological heterogeneity among dopamine reuptake inhibitors by examining the differences in the neuroadaptive molecular changes following chronic exposure to these drugs may have direct relevance to the understanding of the neurobiology of cocaine addiction. Tella, S., Ladenheim, B. and Cadet, J.L. Differential Regulation of Dopamine Transporter following Chronic Self-Administration of Bupropion and Nomifensine. J. Pharmacol. Exp. Ther. 281, pp. 508-513, 1997.

Effects of Marijuana on Visual Responses

The results of a clinical study indicate that marijuana impairs smooth pursuit eye tracking and reduces the response to a flash of light. These effects were previously unrecognized. They offer a potentially important explanation for the detrimental effects of marijuana on complex performance tasks and its role in workplace and automobile accidents.

Drug Delivery

A review of the literature indicates that the reinforcing effects of abused drugs depend on the speed of their delivery to sites in the reward pathway of the brain. Interestingly, therapeutic effects of replacement medications do not depend on the rate of delivery. For example, smoked nicotine is highly addictive but transdermal delivery of nicotine aids in the maintenance of abstinence. A similar situation exists for opiates (smoked or injected heroin versus oral methadone or LAAM). This tenet of drug action may dictate development of medication for the treatment of cocaine and other stimulant abuse.

Nicotine Studies

Acute effects of tobacco withdrawal are diminished by transdermal delivery of nicotine. Although many studies have shown that the nicotine patch and gum increase successful tobacco abstinence this study is unique in that it demonstrates that the patch reduces short-term performance, EEG and cardiovascular measures of tobacco withdrawal. Endocrine and subjective measures of withdrawal were not reduced by the patch. The study also demonstrates the utility of this experimental paradigm for studying tobacco withdrawal.

The acute effects of a proposed treatment for cigarette smoking was evaluated in an outpatient study. Cigarette smoking through an occlusive filter diminishes smoke exposure to men and women. The barrier reduced the plasma nicotine and CO boost ordinarily seen after smoking. Effects on EEG and cardiovascular measures were not significant. Pharmacokinetic examination indicated that men and women have equal exposure (and health risks) to nicotine after smoking and that kinetic properties of nicotine after smoking are similar to those derived from infusion studies.

Mecamylamine, a centrally acting antagonist of nicotine, caused similar EEG and performance effects in non abstinent smokers and in non smokers. These results indicate that nicotinic cholinergic receptors may modulate EEG and performance. The results further suggest a model to study effects of nicotinic cholinergic deficits (as those seen in Alzheimer's disease) in young healthy individuals. Preliminary evidence indicates that the EEG effects of smokeless tobacco use is similar to that after smoke-delivered nicotine. The stimulatory effects of smokeless tobacco may be related to their appeal and addictive properties. These results are from a controlled laboratory study of smokeless tobacco users.

Preliminary studies with a recently developed denicotinized cigarette indicate that smoked delivered nicotine is responsible for many of the physiologic effects of smoking but the short term subjective effects of smoking may be independent of nicotine delivery.

Hair Testing

Hair testing is a new technology that is growing in popularity for use in employment testing and forensic testing for drugs of abuse. Its primary advantage is the long window of detection (months compared to days by urinalysis). There is also interest in use of hair testing in prevalence studies and monitoring drug use during treatment. This technology is controversial because there is little scientific information available on how drugs are deposited in hair. Studies conducted at the IRP revealed that melanin may be the primary site of drug binding. In vitro studies were performed to characterize cocaine binding to dark and light colored ethnic hair types. In vitro binding to hair was selective, reversible and increased linearly with increasing hair concentrations. Scatchard analyses revealed high affinity (6 to 112 nM) and low affinity (906 to 4,433 nM) binding in hair.

Multivariate analysis indicated that significantly greater nonspecific and specific radioligand binding occurred in dark colored hair compared to light hair. Multivariate analysis also demonstrated a significant ethnicity by sex effect on specific and nonspecific binding to hair. These in vitro results suggest there may be significant ethnic bias in hair testing for cocaine.

Saliva Testing

Saliva testing for drugs of abuse may have advantages over traditional urine drug testing because it can be collected easily and in a non-invasive manner. Because of the short time course of drugs in saliva, the presence of drug in saliva may infer recent drug use. A recent study was made of cocaine and metabolites in saliva following administration by the intravenous, smoked and intranasal routes. The smoked and intranasal routes produced local contamination of saliva as evidenced by elevated saliva/plasma ratios. These ratios normalized within two hours of dosing; the presence of cocaine was detectable for about 12 hours. The duration of pharmacologic effects (increase in pulse and subjective effects) was generally equal to or shorter than detection times of cocaine in plasma and saliva. Overall, the study demonstrated the usefulness of saliva as a test matrix for the detection and measurement of cocaine following administration by different routes of administration.

Development of New Drug Testing Technology

New methods are needed for monitoring patients' drug use during treatment. A recent study at the IRP evaluated skin (stratum corneum) and sebum, for use in monitoring drug use and their possible role in deposition of drugs in hair. Skin was collected by light scraping from the back and sebum was collected by applying 'Sebutape' patches for 1-2 hour intervals to the forehead. Specimens were collected periodically from subjects who received cocaine and codeine administrations. Drug content in skin and sebum was analyzed by gas chromatography/mass spectrometry. Cocaine and codeine were the primary analytes in sebum and stratum corneum. After dosing, these drugs appeared in sebum within 1-2 hours and were detected for 1-2 days. Peak drug concentrations in skin occurred one day after completion of dosing; elimination of drugs continued over the next 1-2 weeks following dosing. Overall, no definitive relationship was observed between drug concentrations in sebum and stratum corneum compared to dose. Interpretation of drug distribution and elimination in sebum and stratum corneum was complicated by possible contamination of specimens with drugs from sweat. The mechanism(s) for deposition of cocaine and codeine in sebum and skin appeared to be complex and could involve transfer of drugs between different body fluids (i.e., sebum and sweat) and other matrices (i.e., skin and hair).

Sweat Testing

Improved methods for monitoring illicit drug use are needed in clinical treatment trials. A new technique, sweat patch analysis, was used to determine cocaine and opiate use in methadone maintenance patients enrolled in a voucher-based contingency management trial. The results of thrice weekly urine drug tests (EMIT immunoassay cutoffs;300 ng/mL) from 44 human subjects were compared to results of 355 sweat patches that were applied for 7 days. Sweat was analyzed for cocaine and heroin and metabolites by an ELISA immunoassay (cutoffs 10 ng/mL) and confirmed in a subset of samples by GC/MS (cutoffs 5 ng/mL). The accuracy, sensitivity and specificity of sweat ELISA results was high compared to GC/MS analysis (reference standard method). Data from this field trial suggests that once per week sweat testing may be a viable alternate to the three-times-per-week schedule needed for adequate monitoring by traditional urinalysis for cocaine and heroin.

Clinical Pharmacology Branch

Drug Detection and Evaluation

The Drug Evaluation and Classification (DEC) program is used by police agencies to determine if individuals are behaviorally impaired due to drug use, and if impaired, to determine the class of drug(s) causing the impairment. Although widely used, the validity of the DEC evaluation has not been rigorously tested. The primary goal of this study was to determine the validity of the variables of the DEC evaluation in predicting whether research volunteers had been administered ethanol, cocaine, or marijuana; a secondary goal was to determine the accuracy of trained police officers (Drug Recognition Examiner, DRE) in detecting whether subjects had been dosed with ethanol, cocaine, or marijuana. Community volunteers with histories of drug use received ethanol (0, 0.28, 0.52 g/kg), cocaine (4, 48, 96 mg/70 kg), and marijuana (0, 1.75, 3.55% THC) in a double-blind, randomized, within-subjects design. The ability of the DEC evaluation to predict the intake of ethanol, cocaine, or marijuana was optimal when using 17-28 variables from the evaluation. When DREs concluded impairment was due to drugs other than ethanol, their opinions were consistent with toxicology in 44% of cases. These findings suggest that the DEC evaluation can be used to predict accurately acute administration of ethanol, cocaine, or marijuana, and that predictions of drug use may be improved if DREs focused on a subset of variables.

Subjective and Behavioral Effect Profiles of Alcohol and Marijuana

One study compared subjective and behavioral effect profiles of alcohol and smoked marijuana using technology that controlled puffing and inhalation parameters. Male volunteers with histories of moderate alcohol and marijuana use were administered three doses of alcohol (0.25, 0.5, 1.0 g/kg), three doses of marijuana (4, 8, 16 puffs of 3.55% 9-THC), and placebo in random order under double blind conditions in seven separate sessions. BAC (10-90 mg/dl) and THC levels (63-188 ng/ml) indicated that active drug was delivered to subjects dose dependently. Alcohol and marijuana produced dose-related changes on subjective measures of drug effect. Ratings of perceived impairment were identical for the high dose of alcohol and marijuana. Both drugs produced comparable impairment on digit-symbol substitution and word recall tests, but had no effect on time perception and reaction time tests. Alcohol, but not marijuana, slightly impaired performance on a number recognition test. These data are useful for understanding the relative performance impairment produced by alcohol and marijuana at the delivered doses and the relationship between their subjective and behavioral effects.

In two other studies, researchers investigated the effect of smoked marijuana on four standardized field sobriety tests (FST) that are used to determine whether a person can safely operate a motor vehicle. Subjective effects and D9-tetrahydrocannabinol (THC) plasma concentrations were also measured to correlate with behavioral impairment. In a residential study, 12 volunteers participated in six experimental sessions. At each session, subjects smoked ad lib two half-cigarettes containing 0 or 3.58% THC. Placebo, low, and high doses consisted of two placebo half-cigarettes, one placebo and one active half-cigarette, and two active half-cigarettes, respectively. Subjects received each marijuana dose twice in random order. Marijuana impaired performance on only one FST, the One Leg Stand, by increasing number of hops and times the elevated foot touched the floor to maintain balance. In a nonresidential study, 20 subjects participated in three experimental sessions. At each session, subjects smoked two cigarettes (16 paced puffs) containing 0, 1.75, or 3.55% THC. Marijuana impaired performance on two FST, One Leg Stand and Finger to Nose. The number of times subjects put their foot down and raised their arms to maintain balance and amount of body sway were increased by marijuana in the One Leg Stand test. A dose-dependent increase in number of misses was observed in the Finger to Nose test. In both studies, marijuana produced orderly dose-related increases in subjective ratings of intoxication. THC plasma concentrations peaked immediately after smoking and had declined to 15-28 ng/ml at the time of FST testing (15 min postsmoking). These data suggest a threshold plasma THC level in the 20-25 ng/ml range for marijuana to impair behaviors critical for safe driving.

Nicotine

Research volunteers with histories of drug abuse participated in a single 60-min session. At the start of each session, subjects smoked ad lib one cigarette (own brand) and completed the Questionnaire on Smoking Urges (QSU) and Mood Form (MF). They then listened to six audiotaped scripts that either described a situation in which a person desired a cigarette (urge condition) or contained no mention of cigarettes (no urge). Additionally, each script contained descriptors of positive, negative, or neutral affect. Presentation order of the scripts was counterbalanced across subjects. There was a greater increase in QSU scores after the urge scripts compared to no-urge scripts across all three affect conditions. Urge scripts decreased positive mood and increased negative mood scores across all three affect conditions. In the negative and neutral affect conditions, positive MF scores decreased and negative MF scores increased. In contrast, mood changes were minimal under positive affect conditions. These data suggest that tobacco craving can be experimentally manipulated in a drug-abusing population. This laboratory model of craving will allow further investigation of the factors that modulate tobacco craving.

Clinical Psychopharmacology Section, Clinical Pharmacology Branch

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Discovery of Novel Peptidic Dopamine Transporter Ligands By Screening A Positional Scanning Combinatorial Hexapeptide Laboratory

The reinforcing effects of cocaine are thought to result from cocaine binding to the dopamine (DA) transporter, which inhibits DA uptake and increases synaptic DA levels in the mesolimbic system. One strategy for developing medications for treating cocaine addiction is identifying drugs which bind to the DA transporter (DAT ligands) but which do not inhibit DA uptake as effectively as cocaine. Of the numerous known structural classes of DAT ligands, none convincingly inhibit DAT binding without inhibiting DA uptake. The purpose of the present study was to identify members of a novel structural class of DAT ligands and to characterize their interactions at the DA transporter. A positional scanning hexapeptide D-aminoacid library was screened for inhibition of [125I]RTI-55 binding to rat caudate DA transporters. Based on the results, twelve peptides were synthesized. All twelve peptides inhibited [125I]RTI-55 binding to DA transporters with IC50 values, which ranged from 1.8 B5M to 12 B5M. The two most potent peptides were prepared in larger quantities and will be characterized further in various in vitro assays and in

vivo using the technique of in vivo microdialysis.

Behavioral Pharmacology Section, Preclinical Pharmacology Laboratory

Motivational Effects of Combining Stimuli Associated with Food and Cocaine Self- Administration

In previous experiments, IRP scientists have shown that combining two discriminative stimuli associated with the same reinforcer increases responding for that reinforcer by 2-3 fold, regardless of whether the reinforcer was food, water, shock-avoidance or cocaine. Compounding two stimuli associated with two different appetitive reinforcers such as food and water also increased responding, although not to the same degree. We have recently shown a similar effect with cocaine self-administration, where combining stimuli associated with cocaine and food reinforcement led to increased responding. These results support the hypothesis that the effects of two stimuli associated with reinforcers from the same incentive class (appetitive) are mutually enhancing. Thus, in some situations a stimulus associated with an alternative reinforcer might increase the motivation to self-administer cocaine. Panlilio, L. V., Weiss, S. J., and Schindler, C. W. Motivational Effects of Compounding Discriminative Stimuli Associated with Food and Cocaine. Psychopharmacology, In press.

Alteration of the Reinforcing and Other Behavioral Actions of Nicotine by Chronic Caffeine Exposure

Epidemiological surveys in humans show that smokers tend to smoke more cigarettes while drinking coffee and they also drink significantly more coffee than nonsmokers. It is now generally accepted that this positive correlation can be ascribed to interactions between nicotine and caffeine -the main psychoactive ingredients of coffee and tobacco, respectively. In previous experiments, we have shown that pretreatment with acute injections of caffeine can selectively increase nicotine self-administration responding in monkeys. Recently we have extended these studies to characterize nicotine-caffeine interactions under conditions of chronic caffeine exposure. Effects of nicotine are examined in rats that are chronically exposed to caffeine added to their drinking water and in monkeys that receive repeated daily i.m. injections of caffeine. Researchers are using several behavioral techniques including i.v. self-administration, drug discrimination, and a fixed-interval schedule of food reinforcement that are commonly used to investigate the behavioral effects of psychostimulants. Results have demonstrated that chronic caffeine exposure appears to (1) markedly enhance acquisition of iv nicotine self-administration in rats and markedly increase rates of responding for nicotine and nicotine intake in monkeys, (2) qualitatively change the discriminative cue of nicotine without altering the rate of acquisition of a nicotine discrimination, but (3) has little impact on the effects of nicotine on schedule-controlled food maintained responding. Thus, findings reveal a rather complex pattern of nicotine-caffeine interactions which appears to depend upon the particular aspect of behavior under examination.

Gasior, M., Shoaib, M., Yasar, S., and Goldberg, S.R. Qualitative Changes in the Discriminative Properties of Nicotine Produced by Chronic Caffeine Exposure in Rats. International Behavioral Neuroscience Society, 6; 54 (P2-30), San Diego, CA, April, 1997.
Jaszyna, M., Gasior, M., Shoaib, M., Yasar, S., and Goldberg, S.R. Effects of Chronic Caffeine Exposure on the Effects of Nicotine on Schedule-Controlled Behavior in Rats. International Behavioral Neuroscience Society, 6:54(P2-32), San Diego, CA, April, 1997.
Yasar, S., Shoaib, M., Gasior, M., Gasior, M., and Goldberg, S.R. Intravenous Nicotine Self-Administration in Squirrel Monkeys: Effects of Timeout Duration and Caffeine Pretreatment. International Behavioral Neuroscience Society, 6:54(P2-35), San Diego, CA, April, 1997.
Yasar, S., Shoaib, M., Gasior, M., Jaszyna, M., and Goldberg, S.R. Facilitation of IV Nicotine Self-Administration in Squirrel Monkeys by Caffeine. Journal of Psychopharmacology, Vol. 11(Suppl)(3):A14, 1997. Presented at the British Association for Psychopharmacology, Cambridge, United Kingdom, July, 1997.

Neuroadaptive Changes Resulting From Chronic Methamphetamine Self-Administration

A series of studies are underway to identify neuroadaptive changes in the dopaminergic (DA transporters, D1 and D2 receptors) and opioid (mu, delta , and kappa receptors) systems occurring at the different stages of withdrawal from chronic exposure to methamphetamine self-administration in animals receiving response-dependent (self-administered) and response-independent (yoked) drug administration. Research is carried out in Sprague-Dawley rats using a variety of experimental procedures, including: intravenous self-administration, quantitative autoradiography and immunocytochemistry. Initial findings confirm previous demonstrations that methamphetamine can serve as a reinforcer of self-administration behavior and support the hypothesis that a functional reduction of dopamine neurotransmission is one important consequence of chronic methamphetamine exposure, unmasked when

methamphetamine administration is withdrawn. Findings also indicate a functional reduction in endogenous opioid release, which may be another important component of methamphetamine withdrawal. Stefanski, R., Ladenheim, B., Lee, S.H., Cadet, J.L., and Goldberg, S.R. Neuroadaptive Changes in Rats After 4 Months of Intravenous Methamphetamine Self-Administration. In L.S. Harris (Ed.). Problems of Drug Dependence, 1997: Proceeding of the 59th Annual Scientific Meeting, College on Problems of Drug Dependence, NIDA Research Monograph, Washington, D.C., U.S. Gov't Printing Office, In press.

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National Institute on Drug Abuse

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

September, 1997

Program Activities

Program Announcements/RFAs

Discovery of Novel Pharmacotherapies for Cocaine Dependence RFA

NIDA's Medications Development Division issued an RFA (DA 97-003) entitled "Discovery of Novel Pharmacotherapies for Cocaine Dependence". Twenty-seven (27) applications were reviewed, and it is anticipated that eight (8) will be funded. Three approved applicants are new to the field (no prior NIDA grants) and one applicant is just finishing an R29 (FIRST) award.

Sex and Gender-Related Differences in Pain and Analgesic Response RFA

NIDA will participate in an RFA entitled, "Sex and Gender-Related Differences in Pain and Analgesic Response," RFA No. DE-97-003, P.T. 34, issued in the NIH Guide, volume 26, number 23 on July 18, 1997. Other participants are the National Institute of Dental Research (NIDR), the National Institute of Nursing Research (NINR), and the National Institutes of Health's (NIH) Office of Research on Women's Health (ORWH). This RFA encourages research in sex- or gender- related differences in pain and analgesic response and mechanisms underlying these differences to facilitate targeted, effective, safe treatments for men and women.

B/START-NIDA: Behavioral Science Track Awards for Rapid Transition

(NIH GUIDE March 21, 1997; #PAR-97-046) This announcement has been re-issued as a Program announcement. Newly independent investigators are invited to submit applications for small-scale, exploratory (i.e., pilot) research projects related to NIDA's behavioral sciences mission. B/START-NIDA provides rapid review and funding decisions of applications. Research applications are encouraged across a wide variety of behavioral factors in drug abuse, including neurocognitive, cognitive and perceptual processes, psychosocial, and more broadly motivational, social and community factors in drug abuse. HIV/AIDS applications are especially encouraged. In FY 98 and beyond, there will be two receipt dates per fiscal year: October 1 and February 1.

Other Program Activities

Dissemination of Prevention Research

The NIDA 1998 SBIR Contract Concepts for the first time include a call for proposals to examine mechanisms used to transfer research-based drug abuse prevention information to practitioners, policy makers, and the public. It is anticipated that two contracts will be awarded to examine stages of diffusion. The purpose of this work is to increase the capacity of the research field to disseminate findings in an effective and efficient manner.

Buprenorphine and Buprenorphine/Naloxone Efficacy Trial

The Data Safety Monitoring Board for the Department of Veterans Affairs Cooperative Studies Program reviewed the NIDA Medications Development Division sponsored study (CSP #1008, "A Multicenter Efficacy/Safety Trial of Buprenorphine/Naloxone for the Treatment of Opiate Dependence"). The Board met on June 24, 1997 to review trial data and again on July 17, 1997 to review updated data. On both occasions the Board agreed that the efficacy portion of the study had proven that both buprenorphine alone and the buprenorphine/naloxone combination arms of the trial had conclusively demonstrated that these products were superior to placebo. The differences between these treatment groups on both primary outcomes measures were highly significant ($p<0.001$) and the likelihood of determining no difference if allowed to go to completion was remote ($p<0.005$). Therefore, the Board recommended that the efficacy portion of the trial be terminated and that the transfer of current patients to the safety trial be conducted as quickly, efficiently and orderly as possible. This transfer has been completed. Recruitment of patients to the safety trial is continuing, but is expected to be completed by the end of September 1997. The safety portion of the trial will continue for one year.

NIDA/ALGOS Pharmaceutical Company CRADA

A Cooperative Research and Development Agreement (CRADA) between NIDA and ALGOS Pharmaceutical Company was approved on June 17, 1997. This CRADA will investigate the safety and efficacy of the addition of the low affinity NMDA receptor antagonist, dextromethorphan (DM), to methadone in the treatment of withdrawal and relapse associated with opiate addiction. Initial studies have begun at the Philadelphia VA MDRU.

NIDA'S New/Competing Awards Since May 1997

Aldrich, Jane V. --- University of Maryland-Dept. of Pharmaceutical Sciences
Dynorphin Analogs as Kappa Opioid Receptor Antagonists

Allen, Richard G. --- Oregon Health Sciences University
Regulation of Prepro-orphanin Fq (Ofq)-derived Peptides

Ataabadi, Ali N. --- Affiliated Systems Corporation
Cocaine Use, Psychosocial Factors, & AIDS Risk Behaviors

Barnea, Ayalla --- University of Texas Southwestern Medical Center
HIV and Cocaine Interactions in the Developing Brain

Barr, Gordon A. --- Research Foundation for Mental Hygiene Inc.
Development and Plasticity of Opiate Withdrawal

Bentler, Peter M. --- University of California-Dept. of Psychology
Collaborative Research on Drug Abuse

Bornheim, Lester M.--- University of California-Dept. of Pharmacology
Cannabidiol: Effect on Cytochrome P 450 Isozymes

Botvin, Gilbert J. --- Cornell University Medical College-Dept. of Public Health
Multi-ethnic Drug Abuse Prevention among New York Youth

Butler, Stephen F. --- Innovative Training Systems
Computer-based Vocational Intervention for CD Clients

Carey, Kate B. --- Syracuse University
Enhancing Readiness to Change in Schizophrenics

Chang, Jing-Yu --- Bowman Gray School of Medicine
Electrophysiology of Cannabinoid Action on Rat Behaviors

Chavez, Ernest L. --- Colorado State University
Mexican-American Dropouts & Drug Use

Chou, Chih-Ping --- University of Southern California-Dept. of Preventive Medicine
The Random-Effect Models for Substance Abuse Research

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

Crystal, Stephen --- Rutgers University-Institute for Health
Health Care Use Patterns among Drug Users with HIV/AIDS

Cunningham, Kathryn A. --- University of Texas Medical Branch
FASEB Summer Research Conference: Drug Abuse

D'Aunno, Thomas A. --- University of Chicago-School of Social Services Admin.
The Role of Managed Care Organizations in Drug Treatment

Davis, Thomas P. --- University of Arizona-Dept. of Pharmacology
Blood to CNS Uptake of Opioid Peptide Drugs

Dawes, Michael A. --- University of Pittsburgh Medical Center-Dept. Of Psychiatry
Drug Use Liability During Pubertal Development

Deleo, Joyce A. --- Dartmouth-Hitchcock Medical Center
Alternatives to Opioids for Chronic Pain: Part II

Dey, Sudhansu K. --- University of Kansas Medical Center-Dept.of Physiology
Effects of Marijuana on Early Pregnancy

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

Dunlap, Eloise --- National Development & Research Institute
Co-occurring Drugs & Violence in Distressed Households

Eissenberg, Thomas E. --- Virginia Commonwealth Univ.-Center for Drug & Alcohol Studies
Drug Craving: Pharmacologic and Associative Influences

El-bassel, Nabila --- Columbia University-School of Social Work
Partner Abuse: Minority Women on Methadone

Eldefrawi, Mohyee E. --- University of Maryland-School of Medicine-Pharm and Exp. Ther.
Biosensors of Cocaine and Heroin Abuse

Eldridge, Gloria D. --- Jackson State University
HIV Risk Reduction for Women in Drug Treatment

Ellis, Alicja I. --- Essex Consulting, Inc.
Information System for Substance Abuse Practitioners

Fenaughty, Andrea M. --- University of Alaska
Women, Drugs and Condoms: Ecologies of Risk

Fendrich, Michael --- University of Illinois-Dept of Psychiatry
Secondary Analysis of Substance Use Reporting

Ferguson, David M. --- University of Minnesota-Dept. of Medicinal Chemistry
Modeling Opioid Receptor Structure and Function

Freedman, Jonathan E. --- Northeastern University-Dept. of Pharmaceutical Sciences
Opioid Modulated Ion Channels in Limbic Forebrain

George, Frank R. --- Amethyst Technologies, Inc.
Science Education: Neurobiology for Practitioners

Gibb, James W. --- University of Utah-Dept. of Pharmacology/Toxicology
Neurochemical Alterations by Designer Drugs

Glowa, John R. --- Louisiana State Medical Center
Mechanisms of Inhalant Abuse

Goodman, Allen C. --- Wayne State University
Comorbidities, Time to Treatment, and Episode Costs

Gorman, E. Michael --- University of Washington
HIV, Drugs, Sexual Risk in DUMSM: A Community Study

Greenwald, Mark K. --- Wayne State Univ.-Dept. of Psychology & Behavioral Neuroscience
Behavioral Studies with Methadone Clients

Griffiths, Roland R. --- Johns Hopkins University-Bayview Medical Center
Experimental Analysis of Sedative/Stimulant Abuse

Guttmacher, Sally J. --- New York University-Dept. of Health Studies
Capturing High-Risk Students in Classroom-Based Surveys

Gu, Howard H. --- Yale University School of Medicine-Dept. of Pharmacology
Functions of Biogenic Amine Transporters

Hanson, Glen R. --- University of Utah-Dept. of Pharmacology & Toxicology
Drug Abuse and Regulatory Enzymes of Biogenic Amines

Harper, Gary W. --- Depaul University-Dept. of Psychology
HIV Sexual Risk and Substance Use among Homeless Youth

Hienz, Robert D. --- Johns Hopkins University-Bayview Medical Center
Cocaine: Perceptual and Motor Effects

Higgins, Stephen T. --- University of Vermont-Dept. of Psychiatry
Factors Influencing Cocaine Use in Humans

Hoffmann, John P. --- National Opinion Research Center
Community and Family Context of Adolescent Drug Use

Hollander, Eric --- Mount Sinai School of Medicine
Serotonin/Norepinephrine Function: Pathological Gambling

Hoover, Donald R, III --- Johns Hopkins University-Dept. of Epidemiology
Analytical Methods for Observational Drug User Cohorts

Houlihan, William J. --- Drew University
Mazindol Analogs as Cocaine Receptor Antagonists

Howells, Richard D. --- University of Medicine and Dentistry-New Jersey Medical School
Structure/Function Analysis of Opioid Receptor Subtypes

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

Howlett, Allyn C. --- Saint Louis University
Cannabinoid Receptor Pharmacology & Biochemistry

Ho, Begonia Y. --- University of North Dakota-Dept. of Pharmacology and Toxicology
Cellular Signaling of the Cannabinoid Receptor

Ho, Ing Kang --- University of Mississippi Medical Center
Mechanism of Action of Butorphanol

Hruby, Victor J. --- University of Arizona
New Modalities for Treatment of Pain & Drug Abuse

Iguchi, Martin Y. --- Allegheny University of Health Sciences
Methadone Treatment: Behavioral/Phamacological Variables

Inturrisi, Charles E. --- Cornell University Medical College-Dept. of Pharmacology
Pharmacology and Neuroscience of Drug Abuse

Jainchill, Nancy --- National Development & Research Institute, Inc.
Hispanic American/Venezuelan Youth-Drug Use Risk Factors

Janda, Kim D. --- Scripps Research Institute
Immunopharmacotherapy as a Treatment for Cocaine Abuse

Johanson, Chris-Ellyn --- Wayne State Univ.-Dept.of Psych. and Behavioral Neuroscience
Individual Differences in Bio-behavioral Drug Response

Johnson, Karen C. --- University of Tennessee
Treating Nicotine Addiction in Pregnancy

Jones, Reese T. --- University of California-Langley Porter Psychiatric Institute
Neuropsychopharmacology of Altered Consciousness

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

Kaplan, Howard B. --- Texas A&M University
Drug Abuse & Other Deviant Adaptations: Two Generations

Kauer, Julie A. --- Duke University-Dept. of Neurobiology
Glutamate Synapses in Sensitization to Drugs of Abuse

Kessel, Raymond --- University of Wisconsin-Dept. of Health and Human Issues
Teacher/Scientist Partnerships: Impacting Drug Abuse

Kiyatkin, Eugene A. --- Indiana University- Dept. of Psychology
Dopamine Neurons and Heroin Reinforcement

Kleinfeld, David --- University of California San Diego
Work Group on Neuronal Dynamics

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

Kuhar, Michael J. --- Emory University-Yerkes Primate Research Center
Cocaine Sensitive Dopamine Transporter Synthesis

Laruelle, Marc --- Research Fountation for Mental Hygiene-NewYork State Psych. Inst.
Neurobiology of Cocaine-Induced Sensitization

Latimer, William W. --- Univ. of Minnesota-Division of General Peds. & Adol. Health
A Cognitive-Behavioral Therapy for Drug Abusing Youth

Lester, Henry A. --- California Institute of Technology
Biogenic Amine Transporters: Structure and Function

Leukefeld, Carl G. --- Center for Drug & Alcohol Research
Health Services Use by Chronic Rural Drug Abusers

Levin, Jonathan M. --- McLean Hospital-Brain Imaging Center
Functional Neuroimaging of Drug Abuse

Lipton, Douglas S. --- National Development & Research Institute
Correctional Drug Abuse Treatment Effectiveness

Lipton, Stuart A. --- Childrens Hospital
Cellular/Molecular Pathophysiology of Mental Retardation

Little, Karley Y. --- Veterans Administration Medical Center
Brain DAT/5-htt Dysregulation in Human Cocaine Users

Luborsky, Lester B. --- University of Pennsylvania-Dept. of Psychiatry
Effective Ingredients of Behavioral Therapies for Drug Abuse

Lukas, Scott E. --- McLean Hospital
Pharmacological and Behavioral Indices of Drug Abuse

Lyons, David --- Bowman Gray School of Medicine
Primate Cocaine Abuse and Cytochrome Oxidase Histochemistry

Madras, Bertha K. --- Harvard Medical School
Cocaine: Molecular Targets, Brain Imaging and Medication

Magura, Stephen --- National Development Research Institute
Effectiveness of Self-help for the Dually Diagnosed

Malison, Robert T. --- Yale University School of Medicine
SPECT Imaging of DA Function in Cocaine Dependence

Marley, R. J. --- University of Albany-Dept. of Psychology
Pharmacogenetic Approaches to Cocaine Neuropharmacology

Martin, Billy R. --- Medical College of Virginia
An Investigation of THC Receptors

Martin, Billy R. --- Virginia Commonwealth University
Inhalation of Drugs of Abuse

Matt, George E. --- San Diego State University-Dept. of Psychology
Improving Self-reports of Drug Use: A Cognitive Set Model

Mayes, Linda C. --- Yale Child Study Center
Regulation of Arousal and Attention in Cocaine-exposed Children

McMillan, Donald E. --- University of Arkansas for Medical Sciences
Drugs of Abuse: Chronic Interactions and Behavior

Moises, Hylan C. --- University of Michigan-Dept. of Physiology
Opioid & G-protein Regulation of Calcium Currents

Molitor, Thomas W. --- University of Minnesota-Dept. of Clinical and Population Sciences
Opiate Modulation of Pulmonary Infection

Monti, Peter M. --- Brown University-Center for Alcohol and Addiction Studies
Motivational Interviewing for Teen Smokers

Moody, David E. --- University of Utah-Dept. of Pharmacology & Toxicology
Human Metabolism of L-alpha-acetylmethadol (LAAM)

Mosberg, Henry I. --- University of Michigan-College of Pharmacy
Conformation - Selectivity Relations of Opioid Peptides

Moss, Howard B. --- Western Psychiatric Institute & Clinic
Intergenerational Transmission: Substance Abuse Liability

Murphy, Edward L. --- University of California
Medical Consequences of HTLV-II in Drug Abusers

Murphy, Sheigla --- Institute for Scientific Analysis
AIDS Prevention: Needle Exchange and Ancillary Services

Nagalla, Srinivasa R. --- Oregon Health Sciences University
Xen-dorphins: A New Opioid System

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

Noell, John W. --- Oregon Center for Applied Science, Inc.
Multimedia Program to Prevent Adolescent Sexual Coercion

Oyarce, Ana M. --- Johns Hopkins University-Dept. of Neuroscience
Translational Control of Peptidergic Enzymes by Dopamine

Patkar, Ashwin A. --- Thomas Jefferson University
Serotonergic Dysfunction and Treatment Outcome in Cocaine

Perkins, Kenneth A. --- Western Psychiatric Institute & Clinic
Discriminative Stimulus Effects of Nicotine in Humans

Pickel, Virginia M. ---Cornell University Medical College
Em-transmitter Interactions of Striatal Opioid Neurons

Pierce, Robert C. --- Washington State University
Dopamine, Calcium and Repeated Cocaine

Pintar, John E. --- University of Medicine and Dentistry-New Jersey Medical School
Genetic Studies of Opioid Receptor Function

Razdan, Raj K. --- Organix Inc.-Dept. of Research
Synthesis of Tetrahydrocannabinol Related Compounds

Reinarman, Craig --- University of California
Marijuana Use Careers and Consequences in Three Cultures

Rhodes, Fen --- Center for Behavioral Research Services
HIV Reduction for High Risk Male Drug Users

Ricaurte, George A. --- Johns Hopkins Medical Institute
Safety Assessment of Fenfluramine/Phentermine in Humans

Ries, Richard K. --- University of Washington-Harborview Medical Center
Contingent Benefits in Substance Abusing Mentally Ill

Roache, John D. --- University of Texas Health Science Center
Reinforcing Effects of Benzodiazepines in Anxiety

Roberston, Marjorie J. --- Alcohol Research Group
Drug Problem and Course of Homelessness

Robles, Rafaela R. --- University of Central De Carib
Addressing HIV Risk and Health Care Needs Under Managed Care

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

Rohsenow, Damaris J. --- Brown University-Division of Biology and Medicine
Cocaine Craving and Coping in Treatment and Relapse

Rosenblum, Leonard A. --- State University of New York-Dept. of Psychiatry
Early Adversity and THC/Methamphetamine Vulnerability

Roth, Robert H. --- Yale University-Dept. of Pharmacology
Prenatal Cocaine Alters Cortical Dopamine Function

Roy, Alec --- East Orange VA Medical Center
Retinal Dopamine: Neurobiologic Marker in Cocaine Patients

Schulties, Gerhard H. --- VA Medical Center
CNS Delta Opioid Receptors in Pain and Drug Abuse

Seiden, Lewis S. --- University of Chicago-Pharmacology and Physiological Science
Neuropsychopharmacology Training for Drug Abuse Research

Selley, Dana E. --- Bowman Gray School of Medicine
Transduction Mechanisms of Opioid Agonist Efficacy

Sevarino, Kevin A. --- Yale University School of Medicine
The Role of PreproTRH-derived Peptides in Cocaine Action

Seybold, Virginia S. --- University of Minnesota-Dept. of Cell Biology/Neuroanatomy
Neuroscience Training in Drug Abuse Research

Sheldan, Kamel --- Arizona Institute for Biomedical Research
Neurobiology of Drug Abuse: Science Education

Sigelman, Carol K. --- George Washington University
A Theory-Centered Approach to Teaching Children about Drugs

Simon, Eric J. --- New York University Medical Center
Effects of Morphine and Analogues on Cell Metabolism

Simon, Eric J. --- New York University Medical Center-Dept. of Psychiatry
Postdoctoral Training in Research on Abused Drugs

Snyder, Solomon H. --- Johns Hopkins School of Medicine
Drug Abuse Research Center

Stevens, Sally J. --- University of Arizona-Social & Behavioral Science
Women's-Centered HIV Risk Reduction Research Study

Su, S. Susan --- National Opinion Research Center
Drug Injectors' Risk Networks and HIV Transmission

Tashkin, Donald P. --- UCLA Department of Medicine
Pulmonary Effects of Habitual Use of Marijuana

Taylor, David A. --- West Virginia University-R.S. Byrd Health Science Center
Membrane Potential and Morphine Tolerance

Turner, R. Jay --- University of Miami-Sociology Research Center
Drug Use Trajectories: Ethnic/Racial Comparisons

Walker, Ellen A. --- University of North Carolina-Dept. of Psychology
Neutral Antagonists: Functional Studies

Wang, Qiang --- East Carolina University
Metabotropic Glutamate Regulation of Amphetamine Action

Weiss, Friedbert --- Scripps Research Institute
Novel Treatments for Cocaine Dependence

Wesselmann, Ursula --- Johns Hopkins University School of Medicine-Dept. of Neurology
Opioid Modulation of Mechanisms of Uterine Pain

Wetter, David W. --- University of Texas-M.D. Anderson Cancer Center
Computer-Delivered Treatment for Smoking Cessation

Williams, Mark L. --- Nova Research Company
Intervention Efficacy Targeting Male Prostitutes

Winter, Jerrold C. --- State University of New York
Behavioral and Pharmacologic Analysis of Drug of Abuse

Wong, Dean F. --- Johns Hopkins University School of Medicine-Dept. of Radiology
Imaging Dopamine-Serotonin Mechanisms in Cocaine Craving

Wong, Mamie Mee --- Southwest Regional Lab
Patterns and Correlates of Substance Use among Mixed Heritage

Yu, Xiao-Fang --- Johns Hopkins University School of Public Health
Phenotypic/Genotypic Variation in HIV Infection

Zhang, Jianhua --- University of Cincinnati-Dept. of Cell Biology/Neuroscience
D1 Dopamine Receptor Signaling and Effects of Cocaine

Review Activities

CPDD Presentation on NIDA Review Procedures

Dr. Teresa Levitin, Director, OEPR, in collaboration with NIDA's Office of Science Policy and Communications (OSPC), presented on NIDA review procedures and chaired a "mock review" at the OSPC's grant writing workshop at the College on Problems of Drug Dependence in Nashville, TN in June. Ms. Jackie Porter of OEPR arranged the "mock review" for the workshop. At the same meeting, Dr. Levitin gave a presentation on the integration of NIDA neuroscience applications with the NIH Division of Research Grants (DRG).

Integration of NIDA's Neuroscience Applications Into the DRG Review System

Drs. Teresa Levitin and Rita Liu have continued to meet weekly with staff from the NIH Division of Research Grants (DRG) to plan the integration of NIDA's neuroscience applications into the DRG review system. Each Scientific Review Group (SRG, or "study section") at NIDA has been briefed on the plans for neuroscience integration by either Dr. Levitin, Dr. Khursheed Asghar, or Dr. William Grace of OEPR, and each SRG has been informed of upcoming activities to plan for integration of behavioral science and AIDS-related science.

NIDA Conference Grant Committee

A NIDA-wide committee formed to develop and implement procedures for the review of R13 (Conference Grant) applications met on August 11, 1997. The committee is chaired by Dr. William Grace (OEPR), and members are Drs. Cindy Miner (OSPC), Charles Sharp (DBR), Dorynne Czechowicz (DCSR), and Jamie Biswas (MDD), as well as Ms. Susan David (DEPR), Mr. Noble Jones (OoA), and Ms. Catherine Mills (GMB).

New Criteria for Research Grant Applications

NIH's announcement of new review criteria for unsolicited research grant applications has necessitated NIDA's revision of its own guidelines for, and instructions to, reviewers. OEPR staff are working with the NIH Review Policy Committee to adapt the NIH's guidelines and instructions for NIDA's use, and documents incorporating the new review criteria are being prepared for review of applications received on or after October 1, 1997. NIDA study section members have already been briefed about these new criteria, and they will be discussed again at the October/November scientific review group meetings.

New Study Sections

Plans are underway for the creation of two new study sections, one for medications development applications and one for career development applications. The career development group will review training, career development, and fellowship applications from across all NIDA scientific areas and will begin operation with the February 1, 1998 application receipt date. Dr. Mark Swieter will be the SRA for that committee. The medications development committee will review applications for the development of new pharmacotherapies for drug abuse. Dr. Khursheed Asghar will be the SRA. These changes coincide with the integration of neuroscience applications into DRG.

Review of Center Grant Applications

Plans are underway to revise NIDA's handling of center applications. In addition to the current receipt dates of June 1 and October 1, NIDA will begin to accept applications for February 1 receipt dates, starting February of 1998. Reviewing center applications three times a year will reduce the average length of time from submission to outcome. OEPR is setting up an internal centers steering committee of program and review staff to refine the research center grant guidelines and procedures.

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National Institute on Drug Abuse

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

September, 1997

Congressional Affairs

(Prepared August 25, 1997)

FY 98 Appropriations

By the beginning of the August recess, the House had already passed eight of the 13 FY 98 appropriations bills; the Senate had passed ten. House and Senate floor action on the Labor, HHS and Education and Related Agencies (L/HHS) Appropriations bills is expected to be completed during the first week of September.

Labor/HHS/Education Appropriations Bills:

H.R. 2264 -- The first week of September 1997, floor action may begin on H.R. 2264, the FY 1998 Labor, HHS, Education bill. The full House Appropriations Committee (Chairman Livingston, R-LA) marked up the bill on July 22, as reported out of the House Subcommittee. For NIH, H.R. 2264 provides an increase of $764.4 million or 6% over FY 1997, bringing FY 1998 funding to $13.505 billion, which is $427.1 million more than the President's request. The accompanying report is House Report 105-205. The text of the House bill and report may be obtained at the following Internet site: http://www.aamc.org/research/adhocgp/ news.htm.

S. 1061 -- S. 1061, the FY 1998 Labor, HHS, Education bill, will be the first measure on the agenda when the Senate reconvenes on September 2. The full Senate Appropriation Committee (Chairman Stevens, R-AK) marked up the bill on July 24, with no changes to NIH amounts as reported out of the Senate Subcommittee. For NIH, S. 1061 provides $13.692 billion, which is an increase of $952 million or 7.5 percent over FY 1997, and $187.6 million more than the House. The accompanying report is Senate Report 105-58. The text of the Senate bill and report may be obtained at the following Internet site: http://www.aamc.org/research/adhocgp/ news.htm.

NIDA Appropriations

Appropriations, 1997	$489,160,000
President's Budget Request, 1998	$521,915,000
House Committee recommendation	$525,641,000
Senate Committee recommendation	$531,751,000

House Report Language for the National Institute on Drug Abuse

[House Report 105-205]

"The bill includes $525,641,000 for the National Institute on Drug Abuse (NIDA), an increase of $3,726,000 over the amount requested and $35,528,000 over the comparable 1997 appropriation.

"Mission.-- NIDA-supported science addresses questions about drug abuse and addiction, which range from its causes and consequences to its prevention and treatment. NIDA research explores how drugs of abuse affect the brain and behavior and develops effective prevention and treatment strategies; the Institute works to ensure the transfer of scientific data to policy makers, practitioners, and the public.

"Behavioral and cognitive science.--The Committee commends NIDA for its pursuit of a behavioral science research portfolio to investigate such important questions as why people initiate drug use and why some become dependent on drugs. The Committee commends NIDA's recent efforts to increase the number of cognitive scientists studying issues relating to drug abuse, including the impact of drugs on learning and memory.

"The Committee is pleased with NIDA's child and adolescent research initiative and encourages additional research on the basic behavioral factors in processes such as peer pressure and decision-making at these age levels. The Committee also encourages NIDA to investigate the impact of drugs of abuse on the brains of young people. The effects of long-term drug use on development and behavior as well as the increased risk for HIV infection have a devastating impact on our youth.

"Social work research.--The Committee commends NIDA's support for research on families and drug abuse, behavioral and psychosocial treatment research and health services research. The Committee also supports NIDA's efforts to increase the number of social work researchers conducting drug research and encourages NIDA to explore possibilities to fund social work services research within graduate schools of social work."

Senate Report Language for the National Institute on Drug Abuse
[Senate Report 105-58]

"The Committee recommends an appropriation of $531,751,000 for the National Institute on Drug Abuse [NIDA]. This is $9,836,000 more than the budget request and $42,591,000 more than the fiscal year 1997 appropriation. The comparable numbers for the budget estimate include funds to be transferred from the Office of AIDS Research.

"Mission--Created in 1974, NIDA supports about 85 percent of the world's biomedical research in the area of drug abuse and addiction. The Committee commends NIDA for demonstrating through research that drug use is a preventable behavior and addiction is a treatable disease of the brain. NIDA's basic research plays a fundamental role in furthering knowledge about the ways in which drugs act on the brain to produce drug dependence and contributes to understanding how the brain works. In addition, NIDA research identifies the most effective pharmacological and behavioral drug abuse treatments. NIDA conducts research on the nature and extent of drug abuse in the United States and monitors drug abuse trends nationwide to provide information for planning both prevention and treatment services. An important component of NIDA's mission is also to study the outcomes, effectiveness, and cost benefits of drug abuse services delivered in a variety of settings.

"Behavioral and cognitive science--The Committee agrees that research should inform the Nation's policies on treating and preventing drug abuse and commends NIDA for its aggressive pursuit of an expanded behavioral science research portfolio to investigate such critical questions as why people initiate drug use and why some become dependent on drugs. The Committee commends NIDA's recent efforts to increase the number of cognitive scientists studying issues relating to drug abuse.

"Putting research to work for drug abuse prevention.--The Committee congratulates NIDA for its recently released research based guide. The Committee is pleased that the guide is being distributed to schools and community groups nationwide.

"Information dissemination and education.--The Committee is pleased that NIDA continues to reach out to communities across the country to provide research-based information to scientists, practitioners, policymakers, and the public. The Committee encourages NIDA to continue to develop culturally appropriate research-based materials, work with local community-based networks and hold town meetings at various locations to present the latest scientific information available to prevent and treat drug abuse and addiction.

"Methamphetamine initiative.--Recognizing that methamphetamine abuse is a growing problem of alarming proportions in the Western United States, the Committee is very pleased that NIDA sponsored a regional meeting in

San Francisco to bring together scientists, practitioners, policymakers, and members of the community to discuss the most current research on methamphetamine effects and to identify those research areas that are the most promising.

"Treatment initiative.--Behavioral therapies are often the only available treatments for drug problems where no medication yet exists. The Committee applauds NIDA's treatment initiative which is directed toward transplanting the knowledge in behavioral science into new and useful therapies and for laying the groundwork for the integration of both behavioral and pharmacotherapies.

"Genetic research.--Great strides have been made in understanding of human genetics. The Committee encourages NIDA to continue working to identify genes that contribute to individual vulnerability to drug addiction. This research may ultimately lead to the development of new and more effective prevention and treatment strategies.

"Children and adolescents.--Addiction affects every segment of American society, but nowhere is it more devastating in its consequences than among our Nation's youth. The Committee recognizes that NIDA's research is providing critical insights into the factors that place young people at particular risk for drug abuse. NIDA is also identifying those characteristics that protect against drug abuse, and it is providing the foundation on which to build effective, research-based drug abuse prevention strategies. The Committee is pleased that NIDA has launched a special initiative on children and adolescent research to speed progress in this important area."

NIH Reauthorization

Senator Bill Frist, R-TN, Chairman of the Senate Labor and Human Resources Committee's Public Health and Safety Subcommittee, plans to introduce an NIH reauthorization or revitalization bill some time in late September. According to the Senator, the Subcommittee is pursuing a systematic process that will eventually lead to the introduction of the NIH reauthorization/revitalization bill. The Subcommittee is conducting a series of three hearings to provide forums for discussion and exchange for the Members' consideration, in advance of the time at mark up of the NIH reauthorization/revitalization bill when decisions must be made. The first hearing, held on May 1, 1997, was to provide such a forum for discussion on NIH priority setting in the context of Congressional earmarks. Senator Frist reiterated that this first hearing grew out of discussions at the mark up of the NIH Revitalization Act of 1996, S. 1897, where many Members of the Subcommittee expressed an opinion that the Subcommittee should not micromanage research by establishing legislative mandates for specific areas of research.

The second hearing, on July 24, 1997, was to focus on how the NIH coordinates research. Sen. Frist said that he recognized that scientific research is applicable to many diseases, resulting in multiple institutes involved with a single disease. The Subcommittee heard about how NIH coordinates across Institutes; how NIH promotes special areas of research; and what criteria are applied to determine appropriate mechanisms for coordination and how it should be coordinated. The hearing addressed these through case studies in emerging technologies, such as bioengineering and bioimaging; Parkinson's disease; and research involving special populations such as children. The hearing addressed the need for technology coordination, in particular, bioengineering and imaging, then moved quickly into the areas of Parkinson's disease, which consumed a majority of the three and one half hour hearing. Sen. Frist stated that there will be a third hearing in September on clinical research.

ONDCP Reauthorization

On July 23, 1997, a hearing was held before the Senate Judiciary Committee to consider reauthorization of the Office of National Drug Control Policy (ONDCP). Retired General Barry McCaffrey, Director of ONDCP, testified. Two bills to reauthorize the Office (ONDCP's current authorization ends September 30) have been introduced.

- S. 1053, the Administration's bill, was introduced by Senator Joseph Biden (D-DE) on July 22, and would extend the Office for 12 years (FY 98 through FY 2009): 10 years for implementing its new 10-year Drug Control Strategy, and 2 to evaluate its effectiveness.
- HR 2295, introduced by Rep. Dennis Hastert (R-IL) July 30, is a straight one-year reauthorization bill (through September 30, 1998) and makes no substantive changes in ONDCP existing statutory authorities.

A third, related bill, HR 1641, introduced by Rep. Maxine Waters, D-CA, on May 15, would increase ONDCP's authority to transfer funds from one drug control agency to another from the current 2%, up to 10%.

Miscellaneous Bills of Interest

HR 2212 - On July 22, Representatives Elijah Cummings (D-MD) and Nancy Pelosi (D-CA) introduced HR 2212 [the "HIV Prevention Outreach Act of 1997"], which would require the Secretary of HHS in consultation with the Director, NIH, and Director, CDC, to award grants to states and localities to carry out needle exchange programs without charge. Such a program must be part of an HIV prevention project and must be "carried out consistent with scientific studies that have found that making sterile hypodermic needles available to the public without charge is an effective means of preventing the transmission of HIV and does not encourage the use of illegal drugs." NOTE: The Congressional Quarterly reports that nearly 100 locally-funded needle exchange programs are now operating nationwide.

HR 1345 - In April 1997, Rep. Cummings (D-MD) sponsored HR 1345, which would establish a Commission on National Drug Policy to conduct a comprehensive study and report to the President and the Congress on the unlawful production, distribution, and use of controlled substances. The 13-member panel, appointed by the President and Congressional leaders, would investigate the causes of such unlawful use; evaluate the efficacy of existing Federal laws, including minimum sentences; and analyze present national policy, including an evaluation of what proportion of funds should be dedicated to interdiction, Federal enforcement, education and other forms of prevention, and rehabilitation.

HR 2363 - On July 31, Rep. Pete Sessions (R-TX) introduced HR 2363, which would amend the Controlled Substances Act to provide a mandatory life penalty for trafficking and certain other offenses involving methamphetamine.

HR 2031 - On June 24, Rep. Charles Rangel (D-NY) introduced HR 2031, which would amend the Controlled Substances Act and the Controlled Substances Import and Export Act to eliminate the specified mandatory minimum penalties relating to trafficking, possession, importation, and distribution of crack cocaine.

HR 2158 and S 1034 - The third largest FY 1998 appropriations measure provides funding for all programs under the VA and HUD departments, and a host of independent federal agencies, including the National Science Foundation (NSF). The House bill includes a 6.6% increase over FY 97 for NSF; the Senate bill provides a 3.3% increase. NOTE: The two-year NSF reauthorization passed by the House (HR 1273) and similar legislation (S 1046) approved by the Senate Labor and Human Resources Committee authorize about a 7 percent rise for FY 98.

Senate Forum on Medications Development

Senators Carl Levin (D-MI) and Bob Kerrey (D-NB) co-hosted a Senate Forum on May 9, to examine the progress of research aimed at developing anti-addiction medications to block the craving for illicit drugs. Senator Moynihan (D-NY) also participated. The forum featured three panels of experts including Dr. Alan Leshner, the Director of NIDA, and Dr. Frank Vocci, Director of NIDA's Medications Development Division. Leading academic scientists involved in research and representatives of the pharmaceutical industry also appeared to discuss their research and development activities.

Drug Free Communities Act

On June 27, the President signed into law the "Drug Free Communities Act of 1997" (HR 956-PL 105-20), which authorizes $143.5 million over five years for small grants from the Office of National Drug Control Policy (ONDCP) to local groups that have established effective plans to reduce substance abuse among youth. Community coalitions could receive up to $100,000, but would have to match the amount of the grant with their own money. The new law's bipartisan supporters, including bill sponsor Rep. Rob Portman (R-OH) and Sen. Charles Grassley (R-IA), who introduced the similar Senate counterpart, say local groups are better situated to fight drug use in their communities than the Federal government. NOTE: The pending FY 1998 Treasury, Postal Service and General Government appropriations bills (S. 1023 as passed by Senate/unnumbered draft approved by the House Appropriations Committee) include a $10 million allocation to ONDCP to begin implementation during fiscal 1998.

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International Activities

The second international satellite meeting, **Building International Research in Drug Abuse**, was held in conjunction with the annual scientific meeting of CPDD in Nashville June 19 and 20, 1997. Sponsored by NIDA with support from the U.S. Department of State, the meeting included more than 90 participants from 24 countries interested in or engaged in international collaborative research on drug abuse and drug-related health consequences. The keynote address was delivered by Dr. Michael Merson, Dean of Public Health, Yale School of Medicine, who examined the role of drug abuse in the transmission of infectious diseases, especially HIV infection. Presentations were also made by Dr. Alan Lopez, Acting Programme Manager, WHO Programme on Substance Abuse, and Mr. William Dant, Division Director, Hubert H. Humphrey Fellowship Program, Institute of International Education. Former and current INVEST and Humphrey Fellows, other non-U.S. and U.S. scientists, NIDA grantees and NIDA staff Frank Vocci, Moira O'Brien, Lula Beatty and J.C. Comolli moderated and presented in a variety of workshops, oral and poster presentations and panels.

In early June, NIDA announced the selection of drug abuse researchers from France, Mexico and Russia as awardees for the **1997-98 INVEST Research Fellowship**. Dr. Olivier Manzoni of the Centre National de la Recherche Scientifique, Montpelier, has begun working with Dr. John T. Williams at the Vellum Institute for Advanced Biomedical Research at the Oregon Health Sciences University, Portland. Dr. Guilherme Borges, an epidemiologist with affiliations at the Mexican Institute of Psychiatry, the National Autonomous University of Mexico and the National Council Against Addictions, is working with Dr. Ronald C. Kessler, Professor of Health Care Policy, Harvard Medical School, on an investigation of the relationship between substance use, substance abuse disorders, and suicidal behavior within a cross-national framework. For her INVEST Research Fellowship, Dr. Yulia Lyupina of the State Research Center on Addictions, Moscow, will be working in the laboratory of Dr. James E. Smith of the Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina, on assessing the role of mu and delta opioid receptors in the nucleus accumbens in the self-administration of heroin by rats.

On June 23, 1997, NIDA and the Food and Drug Administration (FDA) hosted a delegation from Vietnam for discussions on the scientific development of the Vietnamese detoxification medication HEA(N)TOS. Dr. Frank Vocci, MDD, provided an overview of MDD's mission and activities, and discussed current treatments for narcotic withdrawal and dependence and current efforts in the development of new treatments. The HEA(N)TOS project is in the preliminary stages; additional data need to be collected before a U.S. scientific review can be carried out.

Drs. Richard Needle and William Bukoski, DEPR, and Dr. M. Patricia Needle, International Program, represented NIDA at the **U.S.-Spain Conference on Theoretical and Methodological Advances in the Prevention of Drug Abuse and the Prevention of HIV Infection among Drug Users** held July 14-15, 1997 in Madrid. Other members of the U.S. delegation included Drs. Gilbert Botvin, Thomas Dishion, Richard Catalano, Mary Jane Rotheram-Borus, Alan Neaigus, and Robert Booth. The binational meeting was cosponsored by the Plan Nacional Sobre Drogas, the USIA office of the U.S. Embassy, Madrid, and NIDA. Dr. Zili Sloboda, Director, DEPR, presented a paper on the epidemiology of drug abuse among adolescents in the United States and on the most recent findings from NIDA-funded prevention models in May 1997 at the **International Symposium on Drug Abuse Prevention and Educ ation**in Taipei, Taiwan. Th e symposium included presentations on the epidemiology of drug abuse in the United States, Hong Kong and Taiwan, on prevention programs and activities in Hong Kong, the United States, Japan,

and Taiwan, and an open discussion about the development of a national epidemiologic and prevention research program for Taiwan.

Dr. Zili Sloboda and Mr. Nicholas Kozel participated in the **Border Epidemiology Work Group (BEWG) meeting** held August 11-12, 1997 in San Diego, CA. The BEWG is a drug abuse surveillance program with the objectives of providing timely quantitative and qualitative data on current patterns and trends, emerging problems and characteristics of vulnerable populations along the U.S.-Mexico border. The program is in the initial stages of development and is attempting to use a "sister city" approach in assessing the status of drug abuse in the area.

Ms. Ann Blanken, Deputy Director, DEPR, represented NIDA at the **26th meeting of the Pompidou Group of substance abuse epidemiologists** June 16-17, 1997 at the Council of Europe in Strasbourg, France. She presented information on recent drug use trends in the United States and on NIDA conferences addressing changing patterns of drug abuse in the United States. The Pompidou group includes representatives from cities in nations in the European Union, Eastern bloc countries of the former Soviet Union, and selected other locations.

Richard H. Needle, Ph.D., M.P.H., Chief, Community Research Branch, DEPR/NIDA, gave a presentation entitled "Overview of Research on HIV Prevention among Injection Drug Users", at the **Conference on Theoretical and Methodological Advances in the Prevention of Drug Abuse and the Prevention of HIV Infection among Drug Users**, held July 14-15, 1997, in Madrid, Spain.

Mr. Nicholas Kozel cochaired a joint meeting of the **East and South Asian Multi-City Epidemiology Work Groups** from April 28 - May 1, 1997 in Penang, Malaysia. These Work Groups are composed of researchers from Malaysia, Singapore, the Philippines, Thailand, Burma, China, Laos, Cambodia, Vietnam, Bangladesh, India, Nepal, Pakistan, Sri Lanka and Turkey. This is one of a series of regional programs being developed to provide assessment and surveillance of drug abuse with the objective of integrating regional data into a global perspective. The project is jointly funded by the U.S. Department of State and the Association of Southeast Asian Nations and is coordinated by staff of NIDA and the Universiti Sains Malaysia.

Dr. Peter Hartsock, DEPR, participated in the annual meeting of the **Federal Interagency Arctic Research Policy Committee** in June. The meeting focused on collaborative research opportunities with the former Soviet Union. At the meeting, NIDA was recognized as the first NIH Institute to sponsor research on HIV/AIDS and drug use in the Arctic (i.e., Alaska). Dr. Hartsock also represented NIDA at the June annual conference of the Arctic Research Council of the U.S.

Dr. Mario de la Rosa, DEPR and Office of Special Populations, presented a paper at the **Third International Conference on Drug Abuse** sponsored by the U.S. Embassy and held in Barquesimento, Venezuela, on July 17, 1997. The title of his presentation was "Drug Abuse Behavior Among Hispanic Youth in the United States." Dr. de la Rosa also presented a paper on the drug use/crime connection in a drug abuse symposium sponsored by Carabobo University in Valencia, Venezuela.

Dr. Steven Goldberg, IRP, gave presentations entitled "Food Deprivation Facilitates Acquisition of Nicotine Self-administration," and "Facilitation of IV Nicotine Self-administration in Squirrel Monkeys by Caffeine," at the **British Association for Psychopharmacology and Canadian College of Neuropsychopharmacology meeting**, Cambridge, United Kingdom, July 13-18, 1997.

Dr. Jeffrey Witkin, IRP, gave a presentation entitled, "A Functional Role for NMDA Receptors in the Control of Cocaine-induced Convulsions," at the September 7-10, 1997 meeting of the **Polish Neuroscience Society Third International Congress**, Lodz, Poland. Dr. Witkin also made a presentation entitled "A Role for Dopamine D3 Receptors in PCP and Cocaine Intoxication," at the University of Groningen, The Netherlands, on September 15, 1997.

Dr. Maciej Gasior, IRP, presented "Does Chronic Caffeine Exposure Change the Behavioral Effects of Psychostimulants?" at the September 3 meeting of the **Lublin Branch of the Polish Pharmacological Society**, Lublin, Poland, and "Neuroactive Steroids as a Treatment for Epilepsy: Current Status and Future Directions," at the Symposium on Seizure Phenomena and EAA Receptors at the September 7-10, 1997 **Third Congress of the Polish Neuroscience Society**, Lodz, Poland.

Drs. Edward Cone and Marilyn Huestis, IRP, attended **The International Association of Forensic Toxicologists** in Padova, Italy, August 24-28, 1997 and made two presentations.

Drs. Robert Battjes and Jack Blaine, DCSR, represented NIDA at the **Steering Committee Meeting of the WHO/NIH Joint Project on the Assessment and Classification of Disablements** on June 24, 1997 in Bethesda. The Steering Committee reviewed the progress on the reliability and validity study of substance abuse disorders

diagnoses made utilizing the CIDI and the SCAN as well as the progress on development of the disability assessment instruments.

Dr. Dorynne Czechowicz, DCSR, represented NIDA at the **WHO Working Group meeting on Identification and Management of Substance Use Problems in Primary Care Settings**, held during July in San Francisco. The WHO Programme on Substance Abuse is planning an international study to develop and test a clinical screening instrument to identify harmful psychoactive substance use in primary care settings along with the development and evaluation of brief therapeutic interventions for such problems.

Dr. Peter Cohen of MDD presented a paper entitled "Is "Fault" Relevant to the Goals of Medicine? Alcoholism and Drug Addiction as a Paradigm Case" at the **International Conference: "The Goals of Medicine. Priorities for the Future"** which was held in June, 1997 and was co organized by the Hastings Center and the Instituto Italiano per gli Studi Filosofici.

NIDA Deputy Director, Richard A. Millstein, attended the **Netherlands Ministry of Health, Welfare and Sport's invitational conference on the Monitoring of Illicit Drugs and Health** held on May 22-23, 1997 in Amsterdam.

Dr. Jean L. Cadet presented "Regulation of Cell Death-Related Genes by Methamphetamine in Immortalized Neural Cells" at the **International Society for Neurochemistry/American Society for Neurochemistry** in Hamilton, Bermuda, July 16-18, 1997.

NIDA, in cooperation with the St. Petersburg State Pavlov Medical University, will cosponsor the bilateral workshop on "Prevention of HIV and Other Infectious Diseases Among Drug Abusers" October 6-8 in St. Petersburg. A delegation of nine NIDA staff and grantees and one person from the Office of AIDS Research, NIH, will join Russian researchers and practitioners to identify existing public health efforts to prevent further spread of HIV and other infectious diseases, including drug abuse treatment; to explore potential research initiatives and public health interventions with practical application to preventing the spread of these diseases; and to develop an action plan for further scientific cooperation between Russian and U.S. drug abuse scientists. The workshop is supported by NIDA, the NIH Office of AIDS Research, and the U.S. Agency for International Development, Moscow.

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September, 1997

Meetings/Conferences

On May 9, 1997, NIDA's Office of Science Policy and Communication (OSPC) held the **"Second Annual Training Directors' Meeting"** in Bethesda, Maryland, cochaired by Dr. Alan I. Leshner, NIDA Director, and Dr. Timothy P. Condon, NIDA Associate Director for Science Policy, Director of OSPC, and NIDA's Research Training Coordinator. This meeting brought together 40 of the 44 NIDA training directors to meet with NIDA staff to discuss administrative and research training issues. This annual meeting was established to facilitate communication and collaboration among the NIDA training directors and NIDA staff in order to enhance the training experience of the next generation of drug abuse researchers.

NIDA organized a "Town Meeting" in Chicago, Illinois entitled **"Understanding Drug Abuse and Addiction: Myth Vs. Reality"** on May 30, 1997. Dr. Leshner and NIDA researchers discussed ways that policy makers, organizations, practitioners, schools and communities can utilize the latest scientific research to assess state and local drug problems and develop programs to meet these needs. In conjunction with the Chicago Town Meeting, Congressman John Porter of the 10th District of Illinois co-sponsored a community meeting with parents, teachers, and community leaders at Glenbrook South High School in Glenview, Illinois. Congressman Porter addressed the community and Dr. Leshner discussed the current state of scientific knowledge on drug abuse and addiction and the implications for prevention and treatment.

The NIDA Office on AIDS (OoA) provided a state-of-the-science review of research on drug abuse and AIDS at the College on Problems of Drug Dependence (CPDD) Fifty-Ninth Annual Meeting June 14-19, 1997 in Nashville. During the five days of the meeting, six invited symposia on HIV/AIDS and drug abuse issues were held, as well as two oral and three poster sessions. An impressive group of National and International experts provided an overview of basic immunology and virology of HIV disease and the status of therapeutic interventions, described the epidemiology of HIV infection and AIDS and its relationship to drug abuse, and summarized research opportunities for drug abuse researchers in the HIV/AIDS area. The 1997 meeting marked CPDD's first integrated focus on the breadth of issues surrounding drug abuse and HIV/AIDS. The AIDS forum successfully highlighted scientific advances and research opportunities. The AIDS focus at CPDD was well-received and the NIDA symposia were extremely well attended, with wide representation from within the drug abuse field as well as from other fields of investigation now linked to drug abuse through AIDS research. The scientific community was receptive to the AIDS-related issues and their relevance, and responsive to NIDA's efforts to address drug abuse-related aspects of the AIDS epidemic.

On July 31, the NIDA OoA and the NIH OAR and OBSSR, representing the NIH Behavioral and Social Sciences Interest Group and the NIH AIDS Interest Group, sponsored an NIH Minisymposium, **"Substance Abuse and AIDS: Research from the Behavioral and Social Sciences"**. National and international experts presented on the epidemiology of HIV, substance abuse, and related risk behaviors; basic behavioral research on addiction, cognitive consequences, impulsive behavior and risk behavior; basic social science research, social network analysis, and ethnography; and intervention research, risk reduction and outreach, needle and syringe access and exchange, and addiction treatment. The minisymposium was well attended and a summary of the proceedings will be published.

A **Northwest Regional Workshop on HIV Prevention for Alcohol and Drug Use among Men Who Have Sex with Men** was sponsored by the National Institute on Drug Abuse, the Centers for Disease Control and Prevention,

the Substance Abuse and Mental Health Services Administration, the University of Washington Alcohol and Drug Abuse Institute, the Seattle-King County Department of Public Health, the Washington State Department of Health, and the Washington State Alcohol and Drug Abuse Agency. The Workshop was held September 3-5, 1997, in Seattle, Washington and included national and Northwest region leaders in substance abuse and human immunodeficiency virus (HIV) prevention as it relates to men who have sex with men (MSM) and their use of drugs, especially methamphetamines.

A Work Group meeting on **"The Development of a POSIT (Problem Oriented Screening Instrument for Teenagers) HIV/STD-Risk Mini-Questionnaire"** was held on July 31, 1997 in Washington, D.C. The Work Group was sponsored by the Treatment Research Branch, Division of Clinical and Services Research and co-chaired by Drs. Elizabeth Rahdert and Dorynne Czechowicz.

The Medications Development Division sponsored a workshop at the College on Problems of Drug Dependence meeting in Nashville, Tennessee. The workshop was co-chaired by Drs. Anna Rose Childress and Frank Vocci. The theme of the workshop was **"Sex, Food, and Drug Incentives: Implications of a Common Substrate for the Development of Anti Craving Medications".**

A Work Group meeting on **"The Development of Early Treatment Strategies for Pre/Early Adolescent Drug Abuse"** was held on September 4-5, 1997 in Rockville, MD. The Work Group was sponsored by the Treatment Research Branch, Division of Clinical and Services Research and co-chaired by Drs. Elizabeth Rahdert, Lisa Onken and Dorynne Czechowicz.

"Drugs of Abuse: the Role of Neural and Behavioral Plasticity in Chronic Drug Abuse" was held at FASEB's Copper Mountain facility in Colorado. The meeting, organized by Drs. Kathryn Cuningham, David Wessinger, and Nancy Pilotte focused on how the brain adapts to chronic drug exposure.

The Medications Development Division presented on **"An Open Label Pilot Safety Study of Lofexidine for the Treatment of Opiate Withdrawal"** at the annual meeting of the College on Problems of Drug Dependence in Nashville, TN in June 1997.

NIDA's Behavioral Science Working Group held a satellite conference at the annual meeting of the American Psychological Society titled **"Cognitive Science Research: More Than Thinking About Drug Abuse"** on May 23, 1997. The conference was organized by Dr. David Shurtleff.

The Behavioral Sciences Research Branch sponsored a symposium entitled **"Cognitive Science Research: Applications to Drug Abuse"** at the annual meeting of the College on Problems of Drug Dependence in Nashville, TN in June 1997.

The Behavioral Sciences Research Branch, DBR has made presentations at various universities to emphasize NIDA's interest in broadening the base of behavioral sciences research. Recent presentations were held at Columbia University, University of Pennsylvania, The Johns Hopkins School of Hygiene and Public Health, and the University of Maryland College Park. Staff included Drs. Jaylan Turkkan, David Shurtleff, and Cora Lee Wetherington.

The Division of Basic Research held a two-day workshop titled **"New Opportunities in Behavioral and Pain Research on AIDS and Drug Abuse"** on July 29-30, 1997. The workshop hosted a number of basic and clinical researchers who discussed their research at the intersection of behavioral sciences, AIDS and drug abuse; a second day of the workshop focused on pain and opiates in AIDS. NIDA's Office on AIDS, The Behavioral Sciences Research Branch and The Behavioral Neurobiology Research Branch were integrally involved in planning this event.

On July 9-10, 1997, the Division of Epidemiology and Prevention Research sponsored a meeting on **Child Psychopathology Risk Factors for Drug Abuse: Features and Mechanisms**, co-chaired by Drs. Naimah Weinberg and Meyer Glantz, held in Gaithersburg, MD. Seventeen experts in the field of child psychopathology and development participated in one and a half days of discussion on features and models of risk, and generated a consensus report.

NIDA's Special Populations Office sponsored a research development workshop on morphine and nitric oxide on June 4 - 6, 1997 in Melville, NY. Participants were women and underrepresented minority postdoctoral fellows and faculty. The scientific chair was Dr. George Stefano of SUNY/Old Westbury, and cosponsors were Nikon, Hewlett-Packard, Image Analytics Corporation, and Morrell Instrument Company.

On June 13-14, 1997 the **Hispanic Work Group** sponsored by NIDA's Special Populations Office held a research meeting on Hispanic issues in drug abuse including a session on AIDS (supported by the Office on AIDS) as part of the CPDD conference in Nashville. NIDA Director, Alan I. Leshner, Ph.D., and Deputy Director, Richard A. Millstein,

participated and spoke.

A workshop, **"The Development and Retention of African American Investigators in Research Careers,"** was sponsored by NIDA's Special Populations Office with support from the Office of Research on Minority Health on June 26 -27, 1997 in Bethesda. Presenters included Dr. Luther Williams from the National Science Foundation, Dr. Edmund Gordon from Yale, Dr. Jerry Bryant from the United Negro College Fund, Dr. Gwendolyn Keita from the American Psychological Association and faculty from Emory, Johns Hopkins, University of Michigan, Howard, and the University of Colorado. A publication is being prepared based on the papers presented.

NIDA's Special Populations Office cosponsored **"Diversity 2000,"** a mentoring program of the American Psychological Association to stimulate interest in research for community college students. It was held August 13-14, 1997 in Chicago during the annual meeting of the Association. NIDA's Special Populations Office initiated a summer research program for students from ethnic/minority populations underrepresented in the biomedical and behavioral research sciences. Twenty-two undergraduates were placed with NIDA grantees for 8 - 10 week research experiences.

On July 24, 1997 NIDA sponsored a meeting to address an initiative raised during the May meeting of the National Advisory Council on Drug Abuse. The topic was disclosure issues for releasing microdata from grant supported research. This meeting was chaired by Andrea Kopstein of the Division of Epidemiology and Prevention Research. Participants included a panel of experts on data confidentiality and disclosure. The panelists were both Federal employees and NIDA researchers.

Dr. Frank Vocci, MDD. presented on "Translating Research into Treatments: Successes and Challenges" at the FASEB meeting at Copper Mountain on August 15, 1997.

Dr. Frank Vocci, MDD presented on Medications Development, Treatment and Prevention at the 1997 ONDCP International Technology Symposium on August 20, 1997 in Chicago, Illinois.

On July 22, 1997 Dr. Peter Cohen of MDD spoke on "Ethical Issues in Treating Cocaine Addicts with a Vaccine" at a miniworkshop, Science, Ethics and Regulatory Issues in the Development of Peripheral Cocaine Blocking Agents for Treating Cocaine Addiction, sponsored by NIDA's Medication Development Division's Treatment Workgroup.

On June 11-12, 1997, Dr. Lisa Onken attended the second National Planning Summit on Scientifically- based Behavioral Health Practice Guidelines. The Summit was held in Minneapolis, MN, and had representatives from both APAs, AABT, AAAPP, nursing organizations, the Center for Mental Health Services, managed care companies, etc. At the meeting, it was agreed to begin work on writing a "guideline for guidelines" on practice. Meeting participants also agreed that practice guidelines must be evidence-based.

On August 20, 1997, Drs. Stephen R. Zukin and Lisa Onken chaired a planning meeting for the National Conference on Drug Addiction Treatment, scheduled for April 1998. Numerous organizations were invited to attend this planning meeting and to serve as collaborating organizations for the Conference.

Dr. Rao S. Rapaka attended the International Cannabinoid Research Society Meeting at Stone Mountain, held in Atlanta, GA June 20-22, 1997 and made a presentation on NIDA's role in drug abuse research.

Drs. Tom Aigner, Jaylan Turkkan, and Jack Blaine promoted NIDA's continuing interest in nicotine research in a Question and Answer session on June 14th in Nashville, TN, at the Third Annual Meeting of The Society for Research on Nicotine and Tobacco, a satellite meeting prior to The College on Problems of Drug Dependence meeting.

On June 12-13, 1997, Ms. Adele Roman, Deputy Women's Health Coordinator, and Dr. Elizabeth Rahdert, DCSR/TRB, participated in the second of four regional workshops sponsored by the NIH Office of Research on Women's Health (ORWH). The meeting, held in New Orleans, LA, focused on sex/gender issues and their influence on research on women's health, continuing or emerging gaps in knowledge about women's health, and career issues of concern to women scientists.

On July 22-23, 1997, Ms. Roman, Deputy Women's Health Coordinator, Dr. Lula Beatty, Chief of the Special Populations Office, and Ms. Katherine Davenny, DCSR/CMB, participated in the third regional workshop sponsored by ORWH. The meeting, held in Santa Fe, NM, focused on women's health research, with particular reference to differences among populations of women, continuing gaps in knowledge, emerging scientific issues, and issues of concern to minority women scientists.

Dr. Jaylan Turkkan attended a conference sponsored by the Robert Wood Johnson Foundation entitled "New Partnerships and Paradigms for Tobacco Prevention Research" in Sundance, Utah in May. Neurobiological and behavioral scientists joined with prevention researchers and marketing experts to explore how interdisciplinary

approaches can be used to prevent teens from smoking.

Dr. Turkkan represented NIDA at a meeting at the Carnegie Mellon University entitled "Neurobehavioral Economics of Craving", a meeting that sought to bring together micro- and non traditional economists with craving and other drug abuse researchers to learn how the brain, visceral and emotional factors may lead to impulsive decision making.

Dr. Lula Beatty presented a paper on African Americans in drug abuse research at the workshop, "The Development and Retention of African American Investigators in Research Careers," sponsored by NIDA's Special Populations Office with support from the Office of Research on Minority Health on June 26-27, 1997 in Bethesda, MD.

Dr. Lula Beatty was a member of the National Convention Committee for the Association of Black Psychologists. The meeting was held August 6-9, 1997 in Washington, DC.

Dr. Lula Beatty chaired three sessions at the annual convention of the American Psychological Association, August 14-19, 1997, in Chicago. They were: Prevention of Tobacco Use and Other Substance Abuse by Teens (a session of the Prevention miniconvention sponsored by OBSSR, NIH), Black Women in Psychology: Old Issues and New Challenges, and Health and Strengths (of African American women).

Dr. Lula Beatty attended the meeting, "Beyond Hunt Valley," sponsored by the Office of Research on Women's Health on July 21- 23, 1997 in Santa Fe. She participated in the career development work group.

Dr. Lula Beatty presented a session on drug abuse and research careers for a high school summer research program at Meharry School of Medicine in Nashville on June 16, 1997.

Dr. Lula Beatty presented a session with Dr. Joseph Frascella of DCSR on research opportunities at NIDA for faculty from Fisk, Meharry, and Tennessee State on June 17, 1997 at Fisk University in Nashville.

Pamela Goodlow presented an overview of NIDA at the Diversity 2000 meeting at the annual convention of the American Psychological Association in Chicago on August 14, 1997.

Mr. Nicholas Kozel, DEPR, chaired the biannual meeting of the Community Epidemiology Work Group (CEWG) which was held in Washington, D.C. on June 24-25, 1997. The CEWG is composed of researchers from 21 metropolitan areas of the United States who meet semiannually to report on patterns and trends of drug abuse in their respective areas; emerging drugs of abuse; vulnerable populations and factors that may place people at risk of drug use and abuse; and, negative health and social consequences. Reports are based on drug abuse indicator data, such as morbidity and mortality information, treatment data and local and State law enforcement data. Additional sources of information include criminal justice, correctional, medical and community health data, local and State survey information and research findings from ethnographic studies. In addition, the fourth meeting of the International Epidemiology Work Group (IEWG) on Drug Abuse was held in conjunction with the CEWG meeting on June 26-27, 1997.

Ms. J.C. Comolli presented an assessment of U.S. patterns and trends in drug abuse and AIDS at the NIDA International Satellite Meeting to CPDD. Ms. Comolli provided an overview of the U.S. perspective and included an update on surveillance data linking the drug abuse and AIDS epidemics.

Dr. Steven Gust presented on NIDA's AIDS Research Program at the Behavioral Science Satellite sponsored by NIDA at the American Psychological Society (APS) Annual Meeting on May 23, 1997.

Drs. Steven Gust and Lynda Erinoff, and Mr. Noble Jones attended the "Research Synthesis Symposium on the Prevention of HIV in Drug Abusers," held in Flagstaff, Arizona, August 3-5. Dr. Gust, Acting Director of NIDA's Office on AIDS, was both a moderator and a presenter on a panel entitled, "Future Directions for Preventing HIV Among Drug Abusers: NIH and NIDA Perspectives.

Dr. Timothy P. Condon chaired a Grant Writing Workshop with Dr. Teresa Levitin, OEPR and Dr. Lucinda Miner, OSPC at the College on Problems in Drug Dependence Annual Meeting held in Nashville on June 17, 1997.

Dr. Timothy P. Condon participated in a nationwide cable broadcast, "The Meth Challenge: Threatening Communities Coast to Coast," produced by the Multijurisdictional Counterdrug Task Force Training program of the Criminal Justice Institute. Dr. Condon was featured as a member of a panel of national drug abuse experts chaired by James Copple, President of the Community Anti Drug Coalitions of America, and provided information on methamphetamine and answered phone in questions from the television audience.

Dr. Timothy P. Condon addressed the Leadership Council of the National Association of Alcoholism and Drug Abuse Counselors (NAADAC) at their July 2 - 3, 1997 meeting in San Francisco. Dr. Condon provided information on

communications research on drug abuse in a presentation titled "Drug Abuse and Communications Research: Lessons for the National Antidrug Campaign." Dr. Condon also conducted a workshop during the conference on "Utilizing Drug Abuse Research to Inform Treatment and Preventions Programs."

Dr. Timothy P. Condon gave a keynote address at the American Psychiatric Association's second annual Research Colloquium for Young Investigators. The aim of the conference was to bring young investigators into contact with peers throughout the country who are also attempting to develop careers in psychiatric research and to help to establish contacts with successful investigators.

Dr. Lucinda Miner, OSPC, represented NIDA at the American Sociological Association annual meeting, August 9 - 13, 1997, in Toronto, Canada. Dr. Miner discussed research funding opportunities from NIDA for sociologists and behavioral scientists.

Dr. Zili Sloboda presented a paper entitled, "Principles for Preventing Drug Abuse," at the NIDA Chicago Town Meeting. Dr. Sloboda also conducted a workshop with Ms. Shelly Coleman, the Director for Prevention of Gateway Youth Care Foundation of Chicago, on "Implementing Prevention Research into Practice." The NIDA Chicago Town Meeting was an opportunity to present NIDA's science within the framework of prevention and treatment practice.

On June 26, 1997 Arthur Hughes, DEPR/ERB made a presentation titled: National Trends and Seasonal Patterns of Drug-related Emergency Room Episodes at the Community Epidemiology Work Group/International Epidemiology Work Group meeting.

On July 2, Andrea Kopstein, DEPR attended the press release of a report produced by the Federal Interagency Forum on Child and Family Statistics entitled "America's Children: Key National Indicators of Well-Being" which included 25 key indicators on critical aspects of children's lives, including behavior and environment. The 25 indicators, which will be updated annually, included two on alcohol and substance abuse.

Dr. Coryl Jones served as one of the NIDA representatives participating in the Fifth Annual Conference on Women's Health, Washington, DC, June 23-25, 1997.

Moira O'Brien, DEPR, served as moderator for a session on Epidemiology Research Methods during the International Research Satellite Meeting of the annual CPDD meeting, June 20, 1997, Nashville, Tennessee.

Dr. Coryl Jones represented NIDA on the Federal Task Force on Child Abuse and Neglect, which met June 4, 1997. She also presented a progress report on NIDA activities at the Federal Interagency Research Committee on Children in Washington, DC, June 4, 1997.

Richard H. Needle, Ph.D., M.P.H., Chief, Community Research Branch, DEPR, presented "An Overview on the History and Evolution of HIV Prevention Research," at the opening of the 4th scientific forum, "Research Synthesis Symposium on Prevention of HIV in Drug Abusers," held August 3-5, 1997, at Northern Arizona University, in Flagstaff, Arizona.

Richard H. Needle, Ph.D., M.P.H., Chief, Community Research Branch, DEPR, participated in the Northwest Regional Workshop, "HIV Prevention for Alcohol and Drug Use among Men Who Have Sex with Men," held September 3-5, 1997 at the University of Washington, in Seattle, Washington.

Richard H. Needle, Ph.D., M.P.H., Chief, Community Research Branch, DEPR, organized and chaired the panel, "Research on Preventing HIV," at the 1997 meeting of the College on Problems of Drug Dependence, held June 14-19, 1997 in Nashville, TN.

Dr. Richard Needle, in collaboration with Zili Sloboda, Ann Blanken, and other senior staff of the Community Research Branch and the Division of Epidemiology and Prevention Research planned and held the 4th scientific forum, Research Synthesis Symposium on the Prevention of HIV Among Drug Abusers, August 3-5, 1997 at Northern Arizona University (NAU) in Flagstaff. The Symposium was jointly sponsored by NIDA, the NIH Office of AIDS Research, and NAU. The purpose of the Symposium was to review the effectiveness of HIV interventions for injection and noninjection drug users, to translate science-based findings into prevention principles that can be applied by prevention planners and practitioners, and to discuss future directions for research on the prevention of HIV transmission among drug abusers. The symposium was the first event in a series of forums to center on HIV prevention among injecting and noninjecting drug users.

Arthur Hughes, Dr. Coryl Jones, Dr. Naimah Weinberg, and Dr. James Colliver of the Epidemiology Research Branch, DEPR participated in the Annual Meeting of the Society for Prevention Research in Baltimore, Maryland May 5-7, 1997.

On May 22, 1997, Dr. Liz Robertson presented at a session on Funding Opportunities for Research on Preventing Drug Abuse Among African American College Students at a conference co-sponsored by NIDA and the Center for Drug Abuse Research at Howard University.

On July 31, 1997, Drs. Liz Robertson and Bill Bukoski participated in a discussion group at the Workgroup on Preventing Substance Abuse and Mental Health Problems in Managed Health Care Settings meeting co-sponsored by the National Mental Health Association and CSAP.

On April 25, 1997 Dr. James Colliver, DEPR/ERB participated in the Center for Education and Drug Abuse Research (CEDAR) Annual Research Conference at the University of Pittsburgh.

On May 6, 1997, Dr. Ro Nemeth-Coslett, PRB/DEPR, chaired a panel entitled Applications of Neuroscience to Drug Abuse Prevention Research at The Society for Prevention Research 5th Annual Meeting, the Hyatt Regency, Baltimore, Maryland. This year's meeting focused on (1) learning about bio-behavioral mechanisms underlying drug and alcohol abuse, (2) methods of conducting preventive trials for psychopathology, and (3) social and behavior determination of the cause and prevention of aggression.

On May 15, 1997, Drs. Liz Robertson and Bill Bukoski represented the DEPR at the DHHS working group on creating partnership plans for the Secretary's Initiative on Youth Substance Abuse Prevention.

Susan Coyle, Ph.D., DEPR/CRB, organized a plenary panel and presented a paper on the effects of outreach-based HIV prevention interventions for out-of-treatment drug users for the 4th Research Synthesis Symposium on the Prevention of HIV in Drug Abusers, August 3-5, 1997, at Northern Arizona University, in Flagstaff, Arizona.

On June 17, 1997, Susan Coyle, Ph.D., CRB/DEPR, presented a paper entitled "Community Based Outreach as an HIV Risk Reduction Strategy for Out-of-Treatment Injection Drug Users," at the annual meeting of the College on Problems of Drug Dependence, in Nashville, TN.

Susan Coyle, Ph.D., Community Research Branch, DEPR, organized a consortium of grantees who are conducting social network research on drug use and HIV transmission with the support of CRB/DEPR. The group, NIDA-NET, met May 20-21, 1997, at Johns Hopkins University in Baltimore, MD, to exchange ideas and information about quantitative and qualitative aspects of conducting network-based HIV research, especially its challenging methodological issues.

Susan Coyle, Ph.D., of CRB/DEPR, gave a presentation on the use of visual anthropology to examine antecedents to drug use and HIV infection, at NIDA's July 29-30, 1997 Workshop on New Research Areas Related to Drug Abuse and AIDS, in Rockville, MD.

Susan Coyle, Ph.D., CRB/DEPR, represented Dr. Needle, Chief, CRB, at the meeting of "HIV Prevention Indicators Consultants," convened by the Centers for Disease Control and Prevention on July 14-15, 1997 in Atlanta, GA. Dr. Coyle consulted in the review of potential core indicators of HIV infection and HIV risk behaviors among injecting drug users.

Dr. Robert Battjes, DCSR, chaired a scientific session entitled "Organizational Factors in the Delivery of Drug Abuse Treatment" at the 14th annual meeting of the Association for Health Services Research, held in Chicago, IL, June 15-17, 1997.

Dr. Robert Battjes, DCSR, presented on future directions for HIV prevention at the "Fourth Science Forum: Research Synthesis Symposium on the Prevention of HIV in Drug Abusers," held in Flagstaff, AZ, August 3-5, 1997.

Bennett Fletcher, Ph.D. Chief, Services Research Branch, attended the Annual Meeting of the National Association of State Alcohol and Drug Abuse Directors (NASADAD) in Portland, ME, June 7-11, 1997.

Bennett Fletcher, Ph.D. attended the Annual Meeting of the Association for Health Services Research in Chicago, IL, June 15-17, 1997. Dr. Fletcher chaired a NIDA pre-meeting symposium on Access and Utilization of Drug Abuse Services on June 15, helped organized an AHSR Research Reports Panel on Organizational Factors in the Delivery of Drug Abuse Treatment, and co-chaired a Research Agenda panel (with Dr. Zili Sloboda, Director, DEPR) to speak about areas in which the Division of Clinical and Services Research hopes to stimulate future health services research.

Bennett Fletcher, Ph.D., presented a paper at a panel on the Drug Abuse Treatment Outcome Study (DATOS) at the Annual Meeting of the American Psychological Association in Chicago on August 15, 1997.

Bennett W. Fletcher, Ph.D., participated in a research agenda development conference on Improving the Quality of Health Care for Children, sponsored by the Association for Health Services Research, at Tysons Corner, VA on May

28-30, 1997.

Dr. William S. Cartwright presented a paper entitled Cost-Benefit and Cost-Effectiveness Analysis of Drug Treatment Services: Review of the Literature at the Western Economics Association on July 12, 1997 in Seattle, WA.

Dr. William S. Cartwright conducted a workshop on cost-benefit analysis and cost-effectiveness for the NIDA funded Treatment Research Center in Philadelphia, PA.

Dr. Peter Delany participated in a conference on Best Practices for Discharge Planning for Homeless Persons with Multiple Disorders on June 19-20, 1997. Dr. Delany helped plan this conference as NIDA's representative to the Interagency Task Force on Homelessness, comprised of participants from DHHS, HUD, OMB, and Departments of Labor, Education, Agriculture, and Energy.

Dr. Mac Horton, ECNB/DCSR, chaired a Symposium entitled "Drug Abuse Research: Selected Clinical Aspects" at the 68th Annual Meeting of the Eastern Psychological Association, in Washington, D.C. on April 12, 1997.

Dr. Horton presented brief remarks at the Symposium entitled "Approaches to the Molecular Genetics of Drug Abuse at the College on Problems of Drug Dependence Meeting in Nashville, Tennessee (CPDD), June 18, 1997.

Dr. Harold Gordon, ECNB/DCSR attended the international Conference on Dopaminergic Disorders: Novel Approaches for Drug Discovery in Boston, Massachusetts, June 1997.

Dr. Joseph Frascella, ECNB/DCSR gave a presentation in a workshop for young investigators in psychiatry at the annual meeting of the Society of Biological Psychiatry in San Diego, California, May 15, 1997.

Dr. Joseph Frascella attended the American Psychiatric Association annual meeting and participated in a Young Investigators Workshop as well as presented a poster on research opportunities within the Division of Clinical and Services Research in San Diego, California, May 1997.

Dr. Joseph Frascella presented a poster on the Etiology and Clinical Neurobiology Branch's research program at the annual meeting of the American Psychological Society annual meeting in Washington, D.C. on May 24, 1997.

Dr. Joseph Frascella was a faculty participant in the "NIDA Special Populations Research Training Workshop on Morphine and Nitric Oxide" held in Melville, New York, June 4 - 6, 1997. He gave a talk entitled "The Neuroscience of Drug Abuse" as well as one entitled "Critical Aspects of the Grant Process."

Dr. Joseph Frascella gave a keynote address entitled "Addiction: A Disease of the Brain" at the 26th Annual Summer Institute on Alcoholism, Drug Abuse and Mental Health held at the University of Delaware, July 28, 1997.

Henry Francis, M.D., Chief, Clinical Medicine Branch, moderated a session: "Linking Biological and Behavioral Prevention Interventions" at a recent NIDA-sponsored symposium, Research Synthesis Symposum on the Prevention of HIV in Drug Abusers, held at Northern Arizona University, Flagstaff, Arizona, August 3-5, 1997.

Dr. Mario De La Rosa of NIDA's Special Populations Office presented a paper at the Community Epidemiology Work Group Meeting held in Washington, D.C. June 20, 1997. The title of the presentation was Drug Abuse Behavior among Colombian Youth.

Dr. Edythe D. London, IRP, presented "Neurobiology of Addiction:What's Craving Got to Do with It?" at the American Society of Addiction Medicine 28th Annual Medical Scientific Conference, San Diego, CA, April 17-20, 1997.

Dr. Edythe D. London, attended Grand Rounds "Imaging Studies in Substance Abusers" at the Medical University of South Carolina, Charleston, SC, May 26-27, 1997.

Dr. Edythe D. London presented a lecture on drug abuse at the University of Minnesota Research Training Retreat, Minneapolis, MN, May 31-June 1, 1997.

Dr. Steven J. Grant, IRP, co-chaired a panel entitled "Interactions between Cocaine, Monoaminergic Systems and Sensory Circuits: Is There a Link to Cue Reactivity and Drug Craving?" at the annual meeting of the College on Problems of Drug Dependence, Nashville, TN, June 13-19, 1997.

Dr. Toni Shippenberg, IRP, presented "Neurobiology of Cocaine and Opioid Abuse" at the annual meeting of the College on Problems of Drug Dependence, Nashville, TN, June 13-19, 1997.

Dr. Alexis Thompson, IRP, presented a poster entitled "Dynorphin 2-17 Alters Striatal Dopamine Dialysate Levels and Cocaine-Induced Behavioral Sensitization" at the annual meeting of the College on Problems of Drug Dependence,

Nashville, TN, June 13-19, 1997.

Dr. Toni Shippenberg, IRP, presented a seminar entitled: "Role of Behavioral and Neurochemical Effects of Cocaine" at East Carolina University Medical School, Greenville, NC, June 19-20, 1997.

Dr. Ronald I. Herning, IRP, presented "Cerebral Blood Flow and EEG Differences in HIV+ and HIV- Cocaine Abusers" at the annual meeting of the College on Problems of Drug Dependence, Nashville, TN, June 13-19, 1997.

Dr. Ronald I. Herning presented "Subclinical Neurovascular Deficits in Cocaine Abusers: Drug and Psychosocial Considerations" at the annual meeting of the College on Problems of Drug Dependence, Nashville, TN, June 13-19, 1997.

Dr. Tsung-Ping Su presented "The Delta Opioid DADLE Attenuated Methamphetamine Neurotoxicity via Opioid and Nonopioid Mechanisms" at the annual meeting of the College on Problems of Drug Dependence, Nashville, TN, June 13-19, 1997.

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National Institute on Drug Abuse

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

September, 1997

Media and Education Activities

Press Releases

July 18, 1997 - Later Criminal Behavior and Drug Use Dramatically Reduced By Drug Treatment Beginning in Prison. In a study published in the *Journal of Drug Issues*, researchers at the University of Delaware's Center for Drug and Alcohol Studies found that comprehensive treatment of drug-addicted prison inmates, when coupled with post-release aftercare, reduces the probability of their being rearrested by 57 percent and reduces the likelihood they will return to drug use by 37 percent.

June 26, 1997 - Effects of Long-Term Marijuana Use on the Brain Shown Similar To Other Addicting Drugs. Long-term use of marijuana produces changes in the brain that are similar to those seen after long-term use of other major drugs of abuse such as cocaine, heroin, and alcohol. Moreover, these changes may increase a user's vulnerability to addiction to other abusable drugs by "priming" the brain to be more easily changed by drugs in the future. This study, conducted by researchers from Scripps Research Institute, is published in the June 27 issue of *Science*.

June 24, 1997 - Medication for Treating Heroin Dependence Proven Safe and Very Effective If Used at High Enough Doses. Heroin-dependent individuals reduced their use of heroin by up to 90 percent using the treatment medication LAAM (levomethadyl acetate hydrochloride). Heroin use was reduced for individuals taking a regimen of low, medium, or high doses of LAAM, with effectiveness increasing substantially at the highest dose. The NIDA funded study is published in the June 25 issue of the *Journal of the American Medical Association*.

June 23, 1997 - Researchers Meet To Discuss Emerging Drug Trends in U.S. Metropolitan Areas and Internationally. Current and emerging patterns and trends in drug abuse will be discussed at the 42nd meeting of the Community Epidemiology Work Group (CEWG) to be held June 24-27 in Washington, D.C.

April 30, 1997 - Chicago Area Town Meeting and School Event to Promote Understanding and Dispel Myths About Drug Abuse and Addiction. NIDA will hold a community Town Meeting ***Understanding Drug Abuse and Addiction: Myths versus Reality*** in Chicago on May 30, 1997. Scientists and community leaders will discuss the problem of drug abuse in the State of Illinois and in the Chicago area, and consider how the results of research can be used to improve the response to the problem. On May 29 from 7:00 p.m. to 9:00 p.m., Dr. Leshner will join parents, students, teachers, and community leaders at Glenbrook South High School in Glenview, Illinois for a discussion on ***Drug Abuse and Our Youth***.

April 29, 1997 - Federal Drug Research Agency Recognizes Entertainment Industry's Efforts Toward Accurate Depiction of Drug Abuse. NIDA and The Entertainment Industries Council, Inc. Recognized outstanding efforts of the entertainment industry to accurately depict violence and drug abuse in entertainment products. Over 60 titles/productions and over 450 entertainment leaders were given the first Annual Prism Awards for their role in making creative choices in the portrayal of substance abuse in television productions, feature film and community service.

April 24, 1997 - Scientists Identify Brain Mechanisms of Cocaine's Euphoric Effects. Researchers at the Brookhaven National Laboratory in Upton, NY, State University of New York at Stony Brook, and Columbia University have found a significant relationship between the intensity and duration of the "high" induced by cocaine and the degree to which the drug blocks one of the major mechanisms to control the amount of dopamine in the brain. The study, using the brain imaging techniques of positron emission tomography (PET), is published in the April 24 issue of *Nature*.

April 22, 1997 - Role Found for Natural Body Opioids in Reproduction and Resistance to Infection. Researchers at the Indiana University School of Medicine have discovered that in addition to being essential to responses to pain and the euphoria from drugs such as morphine, codeine, and heroin, the mu opioid receptor, the cellular target of these drugs, also appears to be involved in regulating the immune and reproductive systems. This NIDA funded study was published in the April 21 issue of the *Journal of Experimental Medicine*.

Other Press Activities

Print Media

June 27, 1997 - Parade Magazine Article - Parade Magazine published an article, "Can They Beat The Odds," written by Bernard Gavzer. The article included a quote from Dr. Leshner and references from NIDA's Pregnancy and Health Study. Babies who were born to crack addicted mothers were considered doomed in the beginning but now they are in schools and the picture seems to be changing.

June 17, 1997 - Washington Post, Health Section Article - "What Addiction Really Means" an article by Dr. Leshner was published in the Washington Post Health Section. The article defines what addiction really is and acts as a guide for the public's understanding of addiction.

June, 1997 - Editorial Board Meeting, Nashville Banner - Dr. Leshner met with editors and reporters of the Nashville Banner while attending the CPDD annual meeting. Dr. Leshner was also a guest on a nightly program on the Nashville CBS Affiliate cable station, talking about drug abuse and addiction.

May, 1997 - Editorial Board Meeting, Chicago Sun Times - Dr. Leshner met with editors from this Chicago newspapers while in Chicago for NIDA's Town Meeting. Dr. Leshner was also interviewed by two local radio stations.

Broadcast Media

August 7, 1997 - On Camera Interview for German ARTE's ARCHIMEDES Television Show: Dr. Leshner was interviewed as well as Drs. Edythe London and David Gorelick of NIDA's Intramural Research Program for a segment that will focus on what we know about addiction, the latest on receptors, and the developing brain.

August 5, 1997 - On Camera Interview for Japanese Primetime Television: Dr. Edythe London, Director of NIDA's Brain Imaging Center was interviewed for a science special on the history of medicine and current day issues. The interviews focused on how drugs work in the brain and how we can treat their effects.

June 26, 1977 - On Camera Interview for CBS Evening News: CBS interviewed Dr. Leshner on the new study on marijuana's effects on the brain. The news segment aired nationally June 26.

June 26, 1997 - On Camera Interview for CNN News: CNN interviewed Dr. Leshner on the new study on marijuana's effects on the brain. The news segment aired nationally on June 26.

June 26, 1997 - On Camera Interview for ABC Nightly News: ABC interviewed Dr. Leshner on the new study on marijuana's effects on the brain. The news segment aired nationally June 26.

May 6, 1997 - On Camera Interview for ABC Discovery News - Dr. Alan Leshner was interviewed by George Strait for a segment on medical use of marijuana for a new program that aired on the Discovery Channel May 30.

Dr. James Inciardi's study on the impact of prison-based Therapeutic Community treatment for criminal justice-involved drug abusers will be the topic of an upcoming NIH Director's Column in the Journal of the American Medical Association.

Planned Meetings

On September 18-19, 1997, Dr. Lisa Onken will chair the second in a series of scientific workshops aimed at linking basic behavioral science with behavioral therapy development research. The papers presented at this workshop, **"Behavioral Therapy Development and Psychological Science-Part II,"** will be written for acceptance in a special issue of the journal, *Behavior Therapy*. The papers from "Behavioral Therapy Development and Psychological Science-Part I" were published in the May, 1997 issue of the journal, *Psychological Science*. Dr. Lisa Onken was the Guest Editor of the *Psychological Science* special section.

NIDA will co-sponsor an NICHD-sponsored conference on **"Smoking and Middle Childhood"**, to be held on September 25-26, 1997.

On September 29-30, 1997 **"Heroin Use and Addiction: A National Conference on Prevention, Treatment and Research"** will be held at the Sheraton Washington. The conference will provide new findings from research that can assist leaders of national drug abuse organizations, prevention and treatment practitioners, the media, criminal justice and law enforcement personnel, and policymakers to respond to the changing problem of heroin addiction. It will also focus on effective, research-based drug abuse prevention and treatment efforts that can be implemented in the local community. In addition to plenary presentations, the conference will offer the opportunity for an active interchange among participants through question-and-answer sessions, workshops, and luncheon topic tables.

NIDA's Genetics Workgroup will sponsor a workshop on October 6-7, 1997 entitled **"Approaches to Drug Addiction Molecular Genetics."** The purpose of this workshop is to inform participants regarding strategies, successes and pitfalls encountered in identifying gene variants that increase disease risk and how these lessons can be applied to identifying variant genes associated with vulnerability to features of addiction. The meeting will focus on issues related to phenotypes and genetic models. In addition, the scope and research efforts necessary for the successful elucidation of gene variants and associated features will be discussed.

On October 6-8, 1997 NIDA and the Pavlov Medical University, St. Petersburg Russia, will convene a meeting in St. Petersburg entitled **"Prevention of HIV and Other Infectious Diseases Among Drug Abusers."** A delegation of NIDA/NIH staff and NIDA-supported scientists will advise scientists, government officials, and community representatives from St. Petersburg regarding monitoring and prevention of HIV and other infectious disease epidemics. Dr. Robert Battjes, DCSR, and Dr. Patricia Needle, International Office, are the U.S. co-chairs of the meeting. The NIH Office of AIDS Research is co-funding the meeting.

NIDA is planning **"Understanding Drug Abuse and Addiction: A Town Meeting"** for Monday, October 20, 1997, in Philadelphia at the Wyndham Frankin Plaza Hotel. This is one of several town meetings held in selected cities to disseminate NIDA-based research to providers, policy makers, and community leaders.

The American Society of Addiction Medicine State of the Art Conference entitled **"Models and Measures of Early Recovery: Implications for New Treatment Strategies"** is co sponsored by NIDA and NIAAA and will be held October 23-25, 1997 at the Marriott Metro Center, 725 12th Street, NW, Washington, D.C. Representatives from the NIDA Treatment Research, Services Research, Behavioral Science and Women and Gender Research Workgroups participated in the conference planning. In addition, NIDA will present a Workshop, entitled "A New Treatment for Heroin Addiction: Buprenorphine Update", chaired by Drs. Frank Vocci and Betty Tai from the Medications Development Division.

NIDA's Neuroscience Consortium will sponsor a satellite symposium on the development of the limbic system for the 1997 Society for Neuroscience Annual Meeting. The symposium will be held on October 25 in New Orleans. Topics will include: transcription factor nurr1 and dopamine neurogenesis; mutations of the homeobox genes, Dlx-1 and Dlx-2, striatal subventricular zones and the differentiation of late born neurons; the functional maturation of the limbic system; specification of limbic cortical circuits; the regulation of topographic projections in the limbic system by Eph family molecules; and the molecular regulation of limbic cell fate and circuit formation.

NIDA's Neuroscience Consortium will sponsor a satellite symposium on the development of research training programs for underrepresented minorities and neuroscience research in drugs of abuse for the 1997 Society for Neuroscience Annual Meeting. The symposium will be held on October 28, 1997 in New Orleans and it will be co-hosted by Xavier University. Accomplishments of students trained under the Minority Institutions Research Development Program and experiences of their mentors will be featured.

NIDA's Behavioral Science Working Group will be sponsoring a satellite symposium at the annual Society for Neuroscience conference entitled **"What Do We Really Know About Mouse Behavior? Classical and New**

Approaches for Phenotyping Transgenic and Knockout Mice." The meeting will be held on Wednesday, Oct 29, 1997 at the New Orleans Marriott Hotel from 5:30 - 8:00 p.m. Dr. Alan Leshner, NIDA Director, will open the meeting which will feature experts in the analysis of mouse behavior. Speakers and their topics are: Geert van Oortmerssen, University of Groningen, The Mouse Ethogram: A Mouse Is Not a Mouse; Jeanne Wehner, University of Colorado, Mouse Strain Differences on Learning and Memory Tasks; Christopher Cunningham, Oregon Health Sciences University, A Mouse May Not Be a Rat: Mouse Behaviors in Substance Abuse; and Jacqueline Crawley, NIMH, Behavioral Phenotyping of Mutant Mice. The meeting will also provide an opportunity for active interchanges among the speakers and audience during a general discussion period lead by Lucinda Miner, Ph.D., of OSPC.

NIDA's Treatment Workgroup will be holding a workshop entitled **"Current and Future Status of Naltrexone"** on November 12-13, 1997 (organized by Drs. Jack Blaine, Peter Cohen, Kenzie Preston, and Betty Tai).

The Glutamate Cascade: Common Pathways of Central Nervous System Disease States. May 4 & 5, 1998, Masur Auditorium, NIH, Bethesda, MD. NIDA (lead Institute) and 7 other NIH Institutes (NINDS, NIMH, NIAAA, NIDR, NICHD, NIAIDS, NIA) participated in formation of the agenda for this meeting. Barbara H. Herman, Ph.D., Medications Development Division chaired the meeting. NIDA Co-Chairs included: Stephen R. Zukin, M.D., DCSR; Jerry Frankeheim, Ph.D., DBR; Dave Thomas, Ph.D., DBR; and Lynda Erinoff, PH.D., Office on AIDS, OD, NIDA. This meeting was an outgrowth of from concepts discussed in NIDA's internal Neuroscience Consortium chaired by Dr. Karen Skinner.

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Publications

Dr. Naimah Weinberg, DEPR/ERB, published a chapter entitled **"Developmental Effects of Parental Alcohol Use"** in the second edition of the Handbook of Child and Adolescent Psychiatry, edited by Joseph Noshpitz, in Volume IV, "Varieties of Development", edited by Norman Alessi, John Wiley & Sons, pp. 171-187, 1997.

Dr. Naimah Weinberg, DEPR/ERB, published an article entitled **"Cognitive and Behavioral Deficits Associated with Parental Alcohol Use"** in the Journal of the American Academy of Child and Adolescent Psychiatry, 36(9), pp. 1177-1186, 1997.

Herman, B.H., Vocci, F. **Understanding Drug Addiction in the Brain**. In: The Medical Prescription of Narcotics, Scientific Foundations and Practical Experiences. Swiss Federal Office of Public Health (Bern, Switzerland). English language edition edited by D. Lewis, C. Gear, M. Laubli Loud, D. Langenick-Cartwritght. Eds. M. Rihs-Middel, A. Uchtenhagen, A. Dobler-Mikols, F. Gutzwiller, P. Affentranger, P.J. Dietschy, P. Frehner, B. Hertli, L. Medioni, Hogrefe & Huber Publishers, Seattle, pp. 216-234, 1997.

A series of eight articles on **"Medications Development for Opiate Addiction"** will appear in the upcoming 1997 issue of Seminars in Neuroscience edited by B.H. Herman and Leslie Iversen.

Vocci, F.J., and London, E.D. **Assessment of Neurotoxicity from Potential Medications for Drug Abuse: Ibogaine Testing and Brain Imaging**. In: Imaging Brain Structure and Function, eds. Lester, D., Felder, C.C., and Lewis, E.N., Annals of the New York Academy of Sciences, vol. 820, pp. 29-40, 1997.

Cohen P.J. **'Off-Label' Use of Prescription Drugs: Legal, Clinical and Policy Considerations**. European Journal of Anaesthesiology, 14: pp. 231-235, 1997.

Cohen, P.J. **Immunization for Prevention and Treatment of Cocaine Abuse: Legal and Ethical Implications**. Drug and Alcohol Dependence, In press.

Egertson, J.A., Fox, D.M., and Leshner, A.I. (Eds). **Treating Drug Abusers Effectively**. Malden, MA: Blackwell (1997). The eleven original articles that comprise this book result from a collaboration organized by NIDA/OSPC and the Milbank Memorial Fund to describe research based knowledge about effective treatment.

Rural Substance Abuse: State of Knowledge and Issues. NIH Publication #97 4177. This monograph provides information about the characteristics of rural setting and the people who live in those settings. Characteristics are then related to drug and alcohol abuse patterns, consequences, and prevention and treatment services.

The NIDA research monograph #165, **Beyond the Therapeutic Alliance: Keeping the Drug-Dependent Individual in Treatment**, has been published. The editors of this monograph are Drs. Lisa Onken, Jack Blaine, and John Boren.

The NIDA research monograph #172, **Treatment of Drug-Dependent Individuals with Comorbid Mental Disorders**, has been published. The editors of this monograph are Drs. Lisa Onken, Jack Blaine, Sander Genser, and

Arthur Horton.

NIDA Research Monograph #173 entitled **"Pharmacokinetics, Metabolism, and Pharmaceutics of Drugs of Abuse "** has been recently published. This Monograph was edited by Drs. Rao S. Rapaka (DBR, NIDA), Nora Chiang (MDD, NIDA) and Billy R. Martin (Virginia Commonwealth University, Richmond).

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Staff Highlights

Honors and Awards

Dr. Lula Beatty received the NIH Director's Award in June, 1997 for "exceptional leadership and service in promoting Institute initiatives on minority research development, and for advancing the needs of under represented minorities and other special populations."

Dr. Alan I. Leshner received the Richard T. Louttit Award for excellence in government service from the Federation of Behavioral, Psychological, and Cognitive Sciences on August 15, 1997 at the annual meeting of the American Psychological Association in Chicago, IL.

Dr. Alan I. Leshner received the American Psychological Association's (APA) 1996 Senior Career Award for Distinguished Contribution to Psychology in the Public Interest on August 16, 1997 at the APA annual meeting held in Chicago, IL.

Dr. Teresa Levitin has been invited to serve on the Society for Research in Child Development's Committee for Ethical Conduct in Child Development Research.

Chanvadey Nhim received the NIH Director's Award in June, 1997 "in recognition of the outstanding efforts displayed in assuming significant responsibilities which enabled the Institute to continue providing critical human resource services without disruption."

Dr. Alexis Thompson received a travel award from the International Narcotics Research Conference (INRC) to present her research at the 1997 INRC meeting which was held in Hong Kong, China, August 3-8, 1997.

Berhane Yitbarek received the NIH Director's Award in June, 1997 "in recognition of the outstanding efforts displayed in assuming significant responsibilities which enabled the Institute to continue providing critical human resource services without disruption."

Staff Changes

Teresa Levitin, Ph.D. was appointed Director of NIDA's Office of Extramural Program Review (OEPR) on June 5, 1997. In February 1997, Dr. Levitin assumed the role of Acting Director, OEPR. Prior to joining NIDA as OEPR's Deputy Director in September 1995, Dr. Levitin held review and program positions with the Division of Research Grants, NIH, and with the National Institute of Mental Health.

William Grace, Ph.D. has been selected as Deputy Director, Office of Extramural Program Review (OEPR). Dr. Grace has been serving as Acting Deputy Director, OEPR since February 1997. Prior to assuming this role he held both program and review positions within NIDA, serving as a scientific review administrator in OEPR from 1995 to 1997

and as a program official in DCSR's Clinical Medicine Branch from 1990 to 1994.

Andrea Baruchin, Ph.D. is OSPC's new Science Policy Branch chief. Dr. Baruchin was previously associate director of science policy at NIMH and has authored and collaborated on numerous publications on topics including molecular neurobiology of stress and biomedical ethics.

Ahmed Elkashef, M.D. has joined MDD's Clinical Trials Branch. Dr. Elkashef, a biological psychiatrist, came to NIDA from the NIMH's Neuropsychiatry Branch where he was a Senior Staff Fellow.

Florence Hammond joined NIDA as a Secretary in the Prevention Research Branch, DEPR on August 17, 1997. Ms. Hammond was formerly a Customer Service Representative with Colonial Distributors.

Jan Lipkin is the new deputy chief for OSPC's Public Information Branch. Ms. Lipkin transferred from a similar position at the NIH Clinical Center where she was responsible for media relations, publications, videos, events, and publicity. Her 20-plus years in communications include serving as senior public relations manager for the American Diabetes Association, co-founding and editing a regional political journal, and creating an employee newspaper.

Ms. Aida Meagher-Klun has recently joined NIDA's MDD. Ms. Meagher-Klun formerly worked at the Fogarty International Center, NIH.

Montrue Nelson joined NIDA's MASB as an Administrative Technician on July 6, 1997. Prior to coming to NIDA Ms. Nelson was with the NIH Office of the Director.

Jacques L. Normand, Ph.D. has joined the Community Research Branch, DEPR, as a Health Science Administrator.

Jack Stein, LCSW is a public health analyst in the OSPC director's office. Before coming to NIDA, Mr. Stein worked for several private firms as a project director on numerous Federal and state-funded training and technical assistance projects on drug abuse and HIV-related topics. A social worker, Mr. Stein has provided direct clinical services to drug abusers with HIV/AIDS and was executive director of a large AIDS service organization in Baltimore. He is currently pursuing a doctoral degree in health services with a focus on drug abuse from Walden University.

Marc Swieter, Ph.D. has recently joined OEPR as a Scientific Review Administrator. Before coming to NIDA Dr. Swieter was a senior staff fellow at the National Institute of Dental Research.

Naimah Weinberg, M.D. has joined the Division of Epidemiology and Prevention Research, Epidemiology Research Branch, as a Medical Officer. Dr. Weinberg formerly served as special expert in DEPR/ERB.

James V. Dingell, Ph.D., Director, Division of Basic Research, will retire in November 1997 after a distinguished career of academic and Federal government service. Dr. Dingell began his career at the National Institutes of Health as a chemist in 1955 at the National Heart Institute, later to become the National Heart, Lung and Blood Institute. After working for various universities, he worked for the National Cancer Institute. Dr. Dingell joined NIDA in January 1990 where he nurtured the development of the Institute's basic biomedical, behavioral and neuroscience research programs.

Gary Palsgrove, a Public Health Analyst with the Services Research Branch and a federal employee for over 37 years, retired in July.

Grantee Honors

John L. Falk, Ph.D. of Rutgers University, is the recipient of the 1997 Solvay Award. The award, given by Solvay Pharmaceuticals and administered by Division 28 of the American Psychological Association, is for "Outstanding Basic Psychopharmacological Research on Affective Disorders."

Perry F. Renshaw, M.D., Ph.D., of Harvard Medical School/McLean Hospital, a NIDA-funded investigator, was recently given the American Psychiatric Association/ SmithKline Beecham Young Faculty Award for Research Development in Biological Psychiatry. The award was primarily based upon Dr. Renshaw's research in the area of depression.

Duncan Stanton, Ph.D., a NIDA grantee and professor, Department of Psychiatry, University of Rochester Medical Center, was selected as the 1997 recipient of the American Family Therapy Academy Award for Outstanding Contributions to Family Therapy Research. The award was presented at the annual meeting in Minneapolis, MN, June 19, 1997 in recognition of Dr. Stanton's outstanding work and its impact on the family therapy field.

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