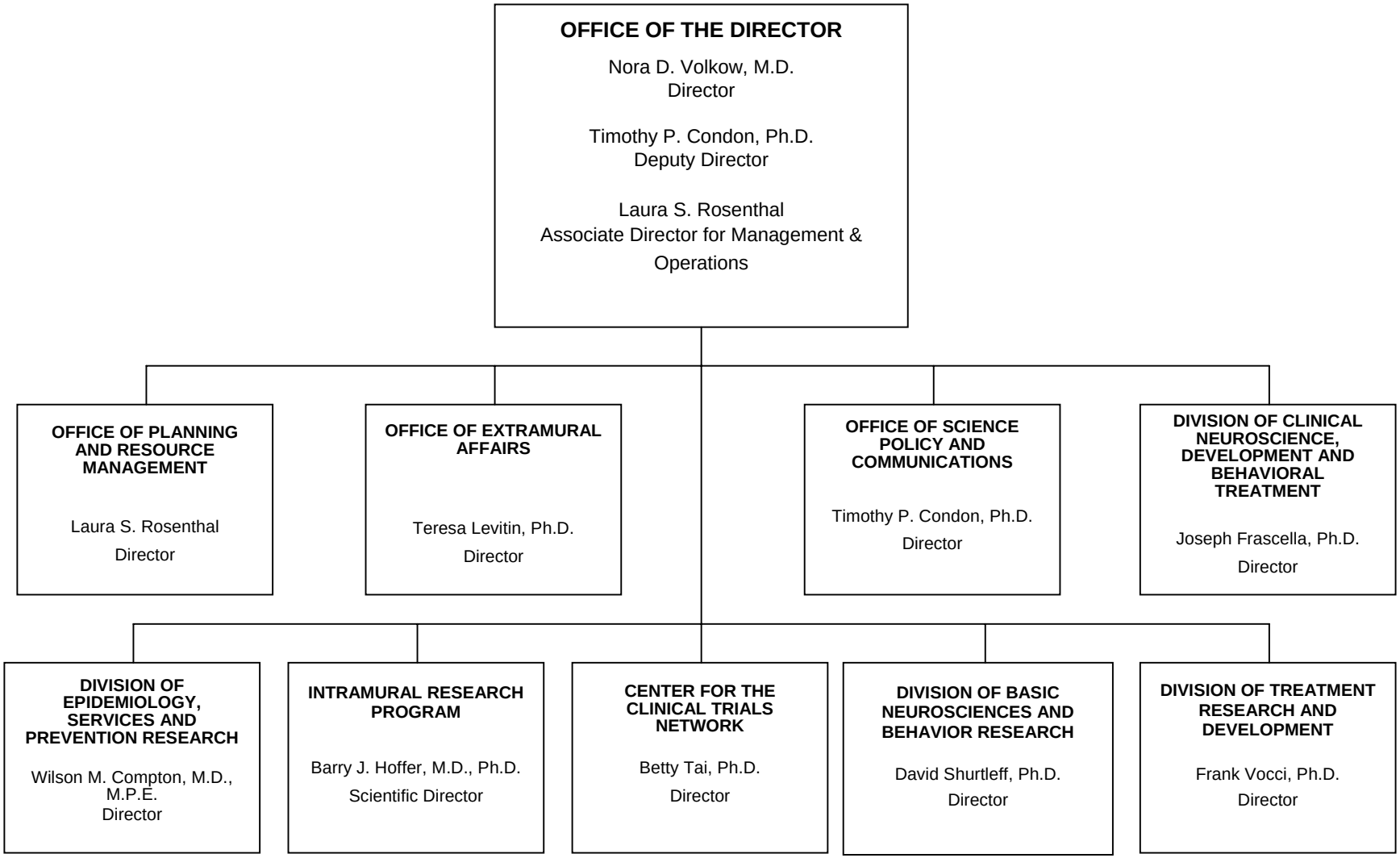
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute on Drug Abuse

National Institutes of Health
National Institute on Drug Abuse
Organizational Structure



NATIONAL INSTITUTES OF HEALTH

National Institute on Drug Abuse

For carrying out section 301 and title IV of the Public Health Service Act with respect to drug abuse, [$1,014,760,000] *$1,010,130,000.*

[Departments of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Consolidated Appropriations Act for Fiscal Year 2005]

National Institutes of Health
National Institute on Drug Abuse

Amounts Available for Obligation 1/

Source of Funding	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Appropriation	$997,414,000	$1,014,760,000	$1,010,130,000
Enacted Rescissions	(6,461,000)	(8,341,000)	0
Subtotal, Adjusted Appropriation	990,953,000	1,006,419,000	1,010,130,000
Real transfer under NIH Director's one-percent transfer authority to other ICs	(3,261,000)	0	0
Real transfer from: Office of National Drug Control Policy	3,818,000	0	0
Comparative transfer to Buildings and Facilities	(119,000)	0	0
Comparative transfer to Clinical Center Program	(47,000)		
Comparative transfer to/from other NIH ICs for NIH Roadmap	3,261,000	0	0
Subtotal, adjusted budget authority	994,605,000	1,006,419,000	1,010,130,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	994,605,000	1,006,419,000	1,010,130,000
Unobligated balance lapsing	0	0	0
Total obligations	994,605,000	1,006,419,000	1,010,130,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2004 - $3,442,000; FY 2005 -$3,282,000; FY 2006 - $3,282,000
Excludes $107,000 in FY 2004 and $110,000 in FY 2005 for royalties.

Justification

National Institute on Drug Abuse

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended.

Budget Authority:

FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
342	$994,605,000	348	$1,006,419,000	348	$1,010,130,000	0	$3,711,000

This document provides justification for the Fiscal Year 2006 activities of the National Institute on Drug Abuse, including HIV/AIDS activities. A more detailed description of the NIH-wide Fiscal Year 2006 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research" (OAR).

INTRODUCTION

Supporting and conducting science that will help prevent and treat drug abuse is the ultimate goal of the National Institute on Drug Abuse (NIDA). The economic burden of drug abuse on our society is estimated to be more than $484 billion per year according to the Office of National Drug Control Policy (ONDCP) and the Robert Wood Johnson Foundation. As the world's largest supporter of research on the health aspects of drug abuse and addiction, NIDA supports a comprehensive research portfolio that continues to bring us new knowledge about addiction and has led to our current understanding of addiction as a disease. From research we know that addiction is a chronic relapsing disease associated with long lasting changes in the brain and the body that can affect all aspects of a person's life. Having more widespread acceptance of the disease model of addiction is a top priority for the Institute, our patient population, and the field. We are making progress in this area by working with others to bring science to communities across the country and convincing them that addiction is a preventable and treatable disease, and in turn reducing the stigma associated with addiction.

New research supported by NIDA and others is revealing that drug addiction is a "developmental disease." That is, it often starts during the early developmental stages in adolescence and sometimes as early as childhood. Last year almost 3 million 12-17 year olds reported using illicit drugs. This is a time when the brain is undergoing major changes in both structure and function. We now know that the brain continues to develop throughout childhood and into early adulthood. Exposure to drugs of abuse at an early age may increase a child's vulnerability to the effects of drugs and may impact brain development. NIDA has increased its emphasis on adolescent brain development (see the "Initiatives" section for more information) to better

understand how developmental processes and outcomes are affected by drug exposure, the environment and genetics. Recent advances in genetic research have enabled researchers to start to investigate what genes make a person more vulnerable, which genes protect a person against addiction, and how genes and environment interact. As part of the prevention portfolio we are also involving pediatricians and other primary care physicians to develop tools, skills and knowledge to be able to screen and treat patients as early as possible, including patients with mental disorders who may be at a high risk to develop addiction. We know that if we do not intervene early, drug problems can last a lifetime, making prevention a high research priority.

Treatment is another priority area for NIDA. Tremendous effort is underway to develop, test, and ensure the delivery of evidence-based interventions to all practitioners and patients across the country. Building on advances from our basic neuroscience and behavioral research program NIDA has introduced a number of effective medications and behavioral treatments.
For example, there are about 60,000 people who are being treated with a medication that NIDA helped to develop. Buprenorphine, sold under the brand name Suboxone is the very first medication that can be prescribed by physicians in their office setting to patients who are addicted to heroin or prescription pain killers. Our increased understanding of the brain mechanisms involved in addiction is providing us with new targets for addiction, including testing new compounds for America's most abused illegal substance -- marijuana. NIDA is developing new treatments for marijuana abuse and addiction, especially for adolescents and those who suffer from co-occurring mental illnesses.

We are also continuing to look for more innovative, efficacious, and cost-effective ways to treat patients for a variety of addictions, including addiction to nicotine. Because data tell us that there are about 46 million people who smoke cigarettes and that about 70% report that they want to quit, NIDA is encouraging more research on smoking cessation quitlines. Quitlines can provide telephone-based counseling, and in some cases nicotine replacement therapies to smokers who want to quit smoking. When they're used as part of a comprehensive tobacco control plan, they can help increase smoking abstinence rates and reach out to new audiences, like pregnant smokers and minority populations. (See our nicotine "Story of Discovery.") We are also trying new approaches, like the Internet, to reach out to new populations and to recruit patients for our clinical trials, particularly adolescents and young adults who may be in need of treatment. For example, we have placed an electronic ad so that individuals who conduct searches for "no prescription Vicodin" and similar requests will now be invited to read the patient recruitment brochure on "Buprenorphine/Naloxone-Facilitated Rehabilitation for Heroin Addicted Adolescents/Young Adults," conducted through NIDA's Clinical Trials Network or to contact the study site nearest to them. This innovative recruitment effort exemplifies how we are using our National Drug Abuse Treatment Clinical Trials Network (CTN) to help respond to emerging public health needs like prescription drug abuse and the increases in patients who are seeking treatment for both substance abuse and mental disorders, like attention deficit hyperactive disorder (ADHD). (See the "Initiatives" section for more information.)

Another important treatment priority for NIDA is curtailing the spread of HIV/AIDS. Because illicit drug use can impact decision-making and increase the likelihood that an individual will engage in risk-taking behaviors, treatment for drug abuse is, itself, HIV prevention. Drug abuse treatment can reduce activities related to drug use that increase the risk of getting or transmitting

HIV. NIDA is especially interested in reducing HIV/AIDS rates in racial and ethnic minority populations, which are disproportionately affected by this disease. Almost half of HIV/AIDS cases occur among African Americans even though they constitute only about 12% of the population according to the latest Census data. Understanding the factors that are driving this epidemic in these populations is an important research area for NIDA.

Recognizing substance abuse as a disorder that can affect the course of other diseases, including HIV/AIDS, mental illness, trauma, cancer, cardiovascular disease and even obesity is critical to improving the health of our citizens. We have launched several efforts to reach out to numerous professions within the medical community. For example, to reach psychiatrists we partnered with the American Psychiatric Association at their annual conference to focus on how to better integrate the science of addiction into psychiatric practice. Topics such as comorbidity of substance abuse and mental illness, the effects of substance abuse during pregnancy on children, and the effects of stress and trauma on substance abuse disorders will help the 30,000 psychiatrists in attendance better diagnose and treat patients with substance abuse disorders.

In these times when science is advancing very rapidly, but resources may not be, it is imperative that we retain the flexibility to address issues of concern and to meet scientific needs. NIDA has initiated a number of activities to ensure we are best utilizing our resources and identifying the most critical research priorities. We are doing this systematically in light of two major factors: National needs and scientific opportunities. We have reached out to our National Advisory Council and others to assist us in our priority setting exercises. Some of the new and expanded initiatives that we think will improve the health of all Americans, especially those directly affected by drug abuse and addiction, are presented here.

NEW AND EXPANDED FY 2006 RESEARCH INITIATIVES

The National Drug Abuse Treatment Clinical Trials Network—Expanding Its Role to Help Meet Emerging Public Health Needs. NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN), which was established in 1999, has grown to include over 17 research centers or nodes spread across the country. The CTN provides us with the infrastructure to test the effectiveness of new and improved interventions in real-life community settings with diverse populations, allowing us to expand treatment options for providers and patients.

To optimize the utilization of this Network, we will begin to expand the mission of the CTN. While we will continue to maintain its important role as a critical bridge between research and practice, where community treatment providers and researchers work side by side, using science to improve the quality of treatment, the CTN will also serve as a platform to help NIDA respond to emerging public health needs. Several areas of national importance have been identified, including the rising use of prescription drugs for non-medical purposes, the effective treatment of patients with concurrent Attention Deficit Hyperactivity Disorder and substance abuse disorders, and determining the effects of some addiction medications on liver function. To help address these emerging public health needs, the researchers and practitioners involved in the CTN are developing and planning to implement several new research protocols.

Reducing Prescription Drug Abuse. There has been a dramatic increase in the number of

people who are taking prescription medications for non-medical purposes, particularly in younger populations, including adolescents. When used for legitimate medical purposes, medications like morphine and Oxycontin, can improve the quality of life for millions of Americans with debilitating diseases and conditions. It is only when these medications are used improperly that they pose a serious health threat. Alarmingly, NIDA's 2003 Monitoring the Future survey of 8th, 10th, and 12th graders found that 10.5 percent of 12th graders reported using Vicodin for non-medical reasons and 4.5 percent of 12th graders reported using OxyContin without a prescription. Vicodin abuse was second only to marijuana abuse among 12th graders. These surveillance findings, coupled with the ease with which individuals can now receive medications without prescriptions over the Internet, and increases in emergency room visits related to prescription drug abuse, continue to make prescription drug abuse a top research priority area for NIDA.

Understanding the potential dangers and health consequences associated with this type of drug abuse and developing effective prevention strategies and treatments to curtail it is critical to our Nation's efforts. NIDA has formed an Institute–wide Working Group and is working with agencies like the Substance Abuse and Mental Health Services Administration and the Office of National Drug Control Policy to address this issue. We plan to reach out to researchers in other disciplines to expand our research efforts. For example, we will encourage researchers to develop and evaluate therapies for individuals who abuse prescription drugs and have comorbid mental disorders, such as depression, anxiety disorders, post-traumatic stress disorder, and eating disorders. We will encourage research studies to identify and address gaps in knowledge and practice by specialty physicians. We will also pursue the development of medications that are unlikely to have addiction liability; and develop prevention and treatment interventions for adolescents who are abusing prescription drugs.

Additionally, NIDA's Clinical Trials Network will also play a key role in addressing this emerging public health problem. The CTN participants are developing a research protocol to treat prescription opioid addiction. In September 2004, the NIDA Director brought in experts to consult with NIDA about the feasibility of conducting clinical trials to treat addiction to opioid analgesics. The consultants advised NIDA that there is a need for information about how to effectively treat these patients. Currently, there are no established guidelines for physicians to rely on to treat patients addicted to prescription opioids. Medications such as methadone and buprenorphine have been shown to be effective in treating chronic heroin abuse, but there is a need to focus on the details of abuse of prescription drugs in addition to illicit, street drugs. The research protocol, to be implemented in the CTN, will help determine if patients who are addicted primarily to prescription opioids, can be stabilized and treated using medications, such as buprenorphine and methadone. The protocol will also have a behavioral counseling component to ensure greater success rates.

Adolescent Brain Development: How Understanding the Brain Can Improve our Prevention Efforts. New research continues to uncover the mysteries of the human brain. Understanding how the human brain works and develops, particularly the brains of adolescents, is critical to prevention efforts. We now know that the brain continues to develop structurally until about the age of 25. Tools like magnetic resonance imaging are showing us the changes occurring in the adolescent brain. These images are showing us how the prefrontal cortex, an

area of the brain critical to decision-making, is among the last areas of the brain to fully develop. They are also showing us how and when the brain's gray (nerve cells) and white matter (nerve pathways) develop. We now know that the brain's gray matter peaks around the age of 11 in girls and 12.5 in boys beyond which other maturational processes that are believed to reflect strengthening and consolidation of connections between brain areas become more prominent. All of these findings have implications for prevention. As we begin to understand how these structural changes affect function, such as thinking, decision-making, sensation and perception, we will be better able to develop more targeted prevention strategies using a brain development perspective. Understanding adolescent motivational processes and decision-making, especially as they relate to the drive and the decision to use drugs is an important research area for NIDA. Also, understanding the neurobiological consequences of environmental stressors during childhood and adolescence as it pertains to drug use and addiction is critical.

To truly understand the effects that drugs of abuse can have on the adolescent brain we need to know what the normal brain anatomy of an adolescent looks like. That is why NIDA is committed to working with the other Institutes to actively support and participate in "the NIH MRI Study of Normal Brain Development." This study uses noninvasive magnetic resonance imaging (MRI) to map brain changes during development. Along with the information obtained from the MRI studies, data on behavioral development are also being gathered. About 500 healthy children and adolescents, ranging in age from 2 weeks to 18 years, are being enrolled in the study and seen at various times over a 6 year period. The result of this study, a database of human neurobiological and behavioral development, will be very useful as we try to discern the effects of drugs of abuse on the human brain and to understand other serious childhood conditions including epilepsy, psychosis and autism.

In addition to utilizing existing technologies and tests to measure "normal" and in many studies "disordered" brain development, NIDA is very interested in improving our capacity to use functional neuroimaging, by both developing and refining techniques, so that neurobiological and behavioral measures can be compared across studies. Building on the progress made in the Centers supported under the "Normal Brain Development" project, NIDA hopes to begin forming a collaborative research network to help establish standardized imaging protocols and behavioral testing paradigms to better understand the relationship between brain and behavioral development, especially in behavioral domains that are commonly affected by exposure to abused drugs, such as impulsivity, attention, memory and emotional regulation.

Addressing Co-Occurring Diseases. A great number of individuals simultaneously suffer from substance abuse, mental illness, and other medical or physical disorders, including chronic pain, hepatitis C, AIDS and other diseases. From research and from experience, we know that patients who suffer from mental illness may be more vulnerable to substance abuse and addiction and vice versa. Unfortunately our current health care system is not set up to adequately address co-occurring health problems. To improve this, NIDA will work with NIMH and others to encourage new research to develop effective strategies, and with the Substance Abuse and Mental Health Services Administration to ensure the timely adoption and implementation of evidence-based practices for the prevention and treatment of co-occurring disorders.

The issue of addressing co-morbidity is especially relevant in children and adolescent

populations. NIDA will encourage researchers to develop prevention programs that are geared toward adolescents who may be at high risk for substance use disorders, because of co-morbidities such as learning disabilities, trauma exposure, conduct disorders and Attention Deficit Hyperactivity Disorder (ADHD). ADHD is one of the most common mental disorders in children. ADHD can impair academic, social, and occupational functioning and can be associated with comorbidity, including cigarette smoking and substance abuse. A significant number of patients in substance abuse clinics have ADHD. NIDA will use the CTN infrastructure to develop more effective treatments to handle the very real problem of patients who suffer from both ADHD and substance abuse. More research needs to be done to evaluate the benefits of treating ADHD to see if it improves substance abuse treatment outcomes. Studies will be conducted in both adolescent (13-18 year-olds) and adult (18-40) populations.

Developing Treatments for Marijuana Abuse and Addiction. Marijuana is the most commonly abused illegal drug in the United States and the most frequent illicit drug for which people receive substance abuse treatment. Marijuana abuse can potentially lead to addiction, the use of other substances, and health consequences. An estimated 974,000 individuals reported in 2002 that marijuana was the drug for which they received substance abuse treatment. Many adolescents report using marijuana, despite its harmful consequences. For example, in 2003 46% of 12^{th} graders had tried marijuana and 21% were current users (i.e., had used within the past 30 days) (Monitoring the Future Survey, 2003). Considering the growing number of adolescents exposed to marijuana, the impact of this substance on the population's overall physical and mental health, needs to be further explored. For all of these reasons, developing new treatments for this illicit drug is a top priority for NIDA.

Last year, NIDA initiated a number of activities to encourage researchers to more rapidly bring new pharmacological treatments for cannabis-related disorders to fruition. In April, we brought together the world's leading experts on this topic to provide recommendations on how to strategically develop safe and effective medications and to let them know of our interest in supporting more research in this area. The field heard our call. We have already begun to fund new grants in this area. Basic research will help us to develop promising compounds; studies in animals will help us determine their safety; and some of the human trials we hope to support will test new compounds as well as those found to be efficacious for other medical conditions, including psychiatric conditions. Approaching medications development from a variety of perspectives, will bring us closer to having pharmacotherapies that are tailored to different patient populations, including adolescents, and those who suffer from co-occurring mental illnesses. Researchers will also continue to look for other marijuana binding sites in addition to the two cannabinoid receptors already showing promise as targets for medications to be developed for marijuana abuse, as well as tobacco addiction, and obesity. Additionally, building on our knowledge from the prevention arena about the role that risk factors play in later substance abuse, researchers will be looking to develop innovative ways to treat factors such as aggressiveness and impulsivity, before addiction to marijuana and/or other drugs sets in.

Blending Research and Practice To Enhance Prevention and Treatment Efforts. NIDA is a strong leader in making sure the comprehensive research that it supports is used. We accomplish this through a number of exemplary and innovative activities (some examples that we will initiate or expanded in FY 2006 follow). Using Data to Ensure Community Prevention Needs

are Being Met**.** NIDA will work with the Substance Abuse and Mental Health Services Administration (SAMHSA) to enhance state substance abuse systems. NIDA is supporting the evaluation of the Strategic Prevention Framework State Incentive Grant (SIG) programs that SAMHSA oversees. This innovative program will use epidemiological data to help identify needs in target populations where evidence-based services will help. Having epidemiological data will also be useful to communities as they make prevention-related funding decisions. Moving Science Based Practices into Communities, State by State. One of the main users of research on drug abuse and addiction, particularly research on efficacious treatment and prevention interventions is the State, Alcohol and Drug Abuse Agencies, commonly referred to as "Single State Authorities." These Single State Authorities know their communities. They also know that there are numerous evidence-based treatments available. They may not however, have the expertise, time or resources to be able to select, implement and sustain the most efficacious, and cost effective prevention and treatment programs for their citizens. To help state's make these important decisions, NIDA is inviting state agencies to team with research organizations in their states to apply for grants that will provide them with resources to improve the delivery of publicly supported drug abuse prevention and or treatment services. NIDA is committed to helping foster a state's ability to adopt evidence-based practices into everyday use and will fund research that encourages State Agencies to conduct research to ensure that science-based approaches reach the people who need them most.

Addressing Health Disparities: Reducing HIV Rates Among African Americans. African Americans comprise about 12% of the US population, but account for a disproportionate amount of health consequences resulting from drug abuse, including HIV/AIDS. In fact, HIV/AIDS is the leading cause of death in African American men ages 35-44 and African American women ages 25-34 (National Vital Statistics Report Vol. 50 No. 16, CDC, 2002). HIV prevention interventions targeting behavioral risk reduction have not been as successful in African American populations as they have been in other populations. NIDA is working to strategically reduce the disproportionate burden of HIV/AIDS among the African American population. Researchers are being encouraged to conduct more studies in this population and to target their studies in geographic areas where HIV/AIDS is high and or growing among African Americans. It is well documented that substance abuse is a major risk factor for contracting HIV/AIDS. Not only can HIV be transmitted through the sharing of contaminated injection equipment, but drugs also can impact decision-making. NIDA will increase its efforts to understand the social and cultural context, as well as the neuobiological mechanisms of impulsivity, including lack of inhibitory control in the context of exposure to HIV and drug abuse.

Utilizing Our Knowledge of Genetics and New Technological Advances to Curtail Addiction. Not everyone who takes drugs becomes addicted. NIDA plans to use the power of science to better understand why some individuals become addicted and others do not. We know from animal studies and human twin studies that genetics plays a critical role in addiction. Although we know that environmental factors are also a significant contributor, we are at a crossroads in the genetics arena, where technological advances are providing us with the tools to make significant breakthroughs in disease research.

For example, we are about to employ a new high-resolution technology which may help us to develop new tailored treatments for smoking. Cigarette smoking is the primary preventable

cause of death in the United States ("The Health Consequences of Smoking" a report by the Surgeon General, 2004). Because we know that genetics plays a significant role in determining an individual's vulnerability to nicotine's effects, it is critical that we begin to identify some of the gene variants that lead to addiction to nicotine. To accomplish this, NIDA has just contracted with Perlegen Sciences, Inc. to perform a whole genome scan for nicotine addiction loci. This new method will allow us to scan or genotype over 1.5 million single nucleotide polymorphisms (SNPs) across the genome and start identifying common genes in smokers that contribute to the heritability of addiction. These SNP variants could then be developed into diagnostic tools for clinicians and as potential targets for new therapeutics. This new method has already shown much success in identifying candidate genes responsible for the increases in HDL cholesterol levels. In addition, we are trying to identify gene variants that confer vulnerability to addiction for illicit substances as well. We expect that many of these gene variants overlap with those that confer vulnerability to nicotine addiction.

Also as part of our effort to better determine the genetic components of addiction and the role that genetics can play in treatment response and treatment outcomes, NIDA will add a pharmacogenetics component to one of its treatment protocols set to begin in 2005 in the Clinical Trials Network. Blood samples from patients enrolled in the Starting Treatment with Agonist Replacement Therapies (START) Study will undergo genetic analysis. The START Study is designed to help evaluate the effects of addiction medications on liver function in opiate addicted populations. The genetic analysis component of the study will help determine how different individuals metabolize and respond to the two addiction medications being tested in this study (buprenorphine and methadone). The researchers will also study individual differences in candidate genes to determine or predict treatment response and outcomes.

We are also taking advantage of new tools to better understand how genes function. We plan to join with other Institutes to acquire a license to have access to more than 750 knockout mouse lines and extensive phenotype data, which will increase our understanding about how genes might function in humans. We also plan to join NIH Institutes in the knockout mouse project to create a null mutation (knockout) in every gene in mouse embryonic stem cells. This is the first step to creating a null mutation for each gene in a living mouse. Additionally, tools like RNA interference (RNAi) are allowing scientists to "knock-down" or "knock-out" specific genes to better understand their function. RNAi shows great promise in helping us to understand the biological mechanisms of many of today's public health problems, including addiction and infectious diseases like hepatitis and HIV. RNAi technologies will be instrumental in helping us develop new therapeutics, and may be especially promising for developing antiviral therapies. NIDA will collaborate with other ICs to bring this new technology to a broad spectrum of researchers.

Reaching out to Primary Care Physicians. Substance abuse in youth and adults is a serious public health problem, with significant morbidity and mortality. The primary care physician can make major inroads into effective prevention and treatment by recognizing and addressing these issues in the outpatient office setting. NIDA has been supporting research to give physicians the tools they need to accomplish this. The response to our recent call to expand this area of research has been impressive, with about eight new grants funded. Researchers will continue to develop brief interventions for both adolescents and adults that are practical for use in busy

office settings where patients receive their routine healthcare. In FY 2006, we will test some of these new interventions in primary care settings. We will also continue to co-fund grants with SAMHSA related to this topic. Additionally, we plan to fund new research that will help develop innovative financing strategies for physicians who do take the time to assist people with substance abuse problems. Primary care physicians need to be reimbursed for treating patients with substance abuse disorders. One of our grantees has set up a system to monitor key practices and treatment services in over 600 treatment sites across the country. Following these practices and sites over time will allow us to see if research-based interventions are being adopted.

Story of Discovery--Addiction and Obesity: Unexpected Commonalities

Amanda sits at home on a Friday night watching her favorite lineup of TV shows. Her week was stressful, and now she just wants to relax and unwind. By her side is an assortment of "comfort foods," most highly caloric and sweet. She cannot stop herself from devouring bags of chips and candy. Unfortunately, Amanda has a 250-pound body, and she cannot seem to control her urges to consume large amounts food, even when she is not hungry.

Ron is out with his college buddies on this same Friday night. For him, there is no time to watch TV. His night will be consumed by smoking crack and getting high. As he sits back with his friends and inhales from the crack pipe, all of his troubles and worries become erased. From that first drag, he is now obsessed with a new problem: where will he get his next fix?

Two different people with very similar problems. Both are experiencing a loss of control – one from food, the other from drugs. For each initially, the consumption of the foods or the smoking of the drug resulted in a clear feeling of pleasure or gratification. We know from addiction research that people take drugs because they like what drugs do to their brains. Drugs make them feel really good, at least in the beginning. All substances of abuse, including cocaine, methamphetamine, heroin, and alcohol, target the brain's pleasure areas. These substances result in a sharp increase in the brain neurochemical known as dopamine. Food, a natural reinforcer, also results in a release in dopamine, albeit somewhat smaller. People have anecdotally spoken about the "addiction" to foods such as sweets; however, it wasn't until very recently, with the advent of brain imaging techniques, that the connection between food, dopamine, compulsiveness, and addiction has become apparent.

Researchers at Brookhaven National Laboratory (BNL) suspected that there might be a connection between food and dopamine. They had done numerous brain imaging studies over the years with patients who were using various drugs of abuse; they found that almost all abusers had low brain dopamine D2 receptor levels. The amount of D2 receptors in the brain correlated to whether an individual would "like" or "dislike" a certain drug. Individuals with high levels of D2 receptors typically found a mild stimulant to be unpleasant; whereas those with low levels found the stimulant to be pleasant. This combined with the fact that animal studies show that D2 receptor levels mediate the reinforcing responses to drugs of abuse, made them wonder whether a similar mechanism might help explain an addiction to food.

In an important series of parallel studies, the BNL group tested the notion that compulsive eaters, who were morbidly obese, might show perturbations of the brain dopamine system much like those of substance abusers. Brain imaging methods of positron emission tomography (PET) were used to see if obese patients also had lower D2 receptor levels. Ten severely obese individuals (five women and five men with body mass indexes (BMI) of 51.2, with 30 or above being considered obese) participated in the study. Ten non-obese subjects also participated. The PET scans revealed that compared to the controls, obese individuals had significantly fewer D2 receptors in the striatum, an area of the brain where dopamine receptors are highly concentrated. The greater an individual's BMI, the fewer available dopamine receptors. This study published in 2001was the first study to show direct evidence of a deficit in D2 receptors in obese individuals. We know from animal studies that other factors such as chronic stress, the hormone known as leptin, the environment, and genetics all contribute to obesity as well. This new insight, coupled with research published in 2003 showing that dopamine and other neurobiological processes influence an individual's motivation to eat, tell us there's more to the obesity and addiction problem, than just willpower.

Researchers found that not all who had low D2 receptor levels abused drugs or food, however. One of the challenging questions to neurobiologists is to determine why some individuals abuse drugs or food and others do not. It is likely that the answer will emerge from a better understanding of the known complex interactions between human biology, behavior, and environment that underlie all compulsive disorders.

From a prevention and treatment perspective the discovery that there is a neurobiological link between addiction

and obesity may help to expedite new interventions. Medications being tested to treat drug-addiction will likely also help control unrestrained food-seeking behavior in some patients. There are some compounds, for example, that work on the brain's cannabinoid receptors that show promise not only for addiction, but for obesity as well. Also, because pharmaceutical companies have prioritized the development of medications for obesity more highly than those for addictions, the drug abuse field is poised to benefit greatly from the identification of common mechanisms underlying these disorders.

Story of Discovery -- New Horizons in the Treatment of Nicotine Addiction

One thousand people die every day, in the United States alone, as a result of cigarette-smoking and related diseases, a figure that is associated with a staggering $80 billion per year in health care costs ("The Health Consequences of Smoking" a report by the Surgeon General, 2004). More than 90 percent of people trying to quit smoking fail within 1 year, with the majority relapsing within a week; and only 2 to 5 percent of those who seek treatment succeed. These figures expose a pressing need to develop new and more effective smoking cessation strategies. Long-term investments in basic and behavioral research, by the National Institute on Drug Abuse (NIDA) and other Institutes and organizations, are coming to fruition in the form of new treatments.

An average smoker is exposed to no less than 4000 chemicals present in tobacco vapors and smoke, 100 of which are known to cause mutations and cancer. While these harmful components play a major role in the etiology of smoking-induced diseases, nicotine has been identified as the main culprit for the rewarding properties of cigarette smoking and the addiction it can cause. Nicotine has the ability to reshape neural circuits, in and around the reward centers of the brain, so that addicts are compelled to take the drug in order to maintain what the brain determines to be an optimal level of nicotine.

Discovering how nicotine works has enabled the development of successful strategies proven to curb its effects and aid in cessation programs. One, referred to as Nicotine Replacement Therapy (NRT), works by intentionally satiating the brain's appetite for nicotine with a lower, yet effective dose of the drug, through safer routes of administration. A second strategy uses Bupropion, a non-nicotinic medication that interferes with the craving impulse. These strategies do relieve some symptoms of nicotine addiction but they are more known for their ability to improve initial abstinence. Fortunately, pharmacotherapies can be strengthened further by concurrent behavioral therapies that provide support and reinforce acquired coping skills, yielding better long-term abstinence rates.

Recent findings point to the interesting possibility that nature itself might have been experimenting with its own version of the NRT concept. It has been reported that CYP2A6, an enzyme that inactivates nicotine, is highly polymorphic. This means that, depending on their genetic background, different persons will display very different levels of CYP2A6 metabolic activity. Preliminary experiments have shown that slow metabolizers of nicotine maintain higher levels of nicotine in their systems, and for longer periods of time. This phenotype could elicit at least two beneficial consequences: an increase in the potential for the aversive reaction to nicotine experienced by new smokers, and a decrease in the number of cigarettes needed to maintain satisfactory brain levels of nicotine.

While it is too early to evaluate the clinical impact of CYP2A6 polymorphisms as a rationale for the development of medications, it is clear that researchers are beginning to look outside of the box for alternative fronts of attack. Such caveats notwithstanding, genetic background is certain to play a prominent role in determining nicotine's behavioral outcome, which reflects its diverse effects upon different subtypes of nicotinic receptors, residing on many functionally different neuronal systems. Indeed, researchers have recently begun to take advantage of specific nicotinic receptor knockout mouse strains to dissect the intricate neural substrates underlying the range of influences of nicotine on the brain. The tantalizing CYP2A6 and nicotinic receptor stories, suggest that accelerating advances in human genetic research will likely yield a rich crop of novel therapeutic targets.

In the meantime, the neuropharmacological approach has produced an expanded menu of non-nicotinic medications, currently in various stages of research and development. One compound, known as Rimonabant, was able to reverse nicotine withdrawal symptoms in rats and block the weight increase frequently seen in participants of smoking-cessation programs. Results with another compound suggest that by targeting a specific subtype of dopamine receptor (D3), one could achieve exquisitely specific behavioral responses, such as reducing the cue-induced motivation without interfering with the primary drug-related reward. Many more examples exist that evince an increased sophistication in the target selection process.

An even more revolutionary approach to stop smoking is now in the works, in the form of a vaccine. NicVAX™, currently under development by NABI, a biopharmaceutical company funded in part by NIDA, is designed to prevent nicotine from ever reaching the brain. If successful, such an approach could prove effective in both the treatment and prevention of nicotine addiction. In pre-clinical animal studies, NicVAX™ reduced nicotine levels in the brain by up to 64% and Phase I clinical trials have shown the vaccine to be well tolerated. The results of a

randomized, double-blind, placebo-controlled Phase II clinical trial are expected soon.

Researchers are taking full advantage of the much deeper understanding of the complex mechanisms underlying nicotine addiction. Their ingenuity and efforts have resulted in a series of both well-established and very promising intervention devices, which should bring new hope to the millions of people afflicted worldwide.

SCIENCE ADVANCES

GENETICS

Addiction to Heroin May be Influenced by the OPRM1 Gene. Based on a variety of research studies, it is estimated that 40 to 50% of the vulnerability to addiction is genetic. However, there is still much to be learned about the specific genes that are involved and the role they play in addiction. The mu-opioid receptor, which binds drugs such as heroin and other opiates, is known to be involved in the rewarding effects of opiates and other drugs of abuse. The OPRM1 gene, which codes for the mu-opioid receptor, has several genetic variants, known as alleles, and thus represents a promising candidate gene for involvement in addiction. In this study, the OPRM1 gene was examined in 139 people who are heroin addicts and compared to 170 people who had never used drugs. It was found that there was a significant association between one of the variants of the OPRM1 gene and heroin addiction and that up to 21% of the attributable risk of heroin addiction can be ascribed to this particular allele. Although this NIDA-supported study took place in Sweden and so only examined people of primarily Swedish descent, it clearly shows that genetics can be a significant factor in the development of addiction. As the first study to demonstrate this genetic association, it is an important, but preliminary finding, which will need to be replicated by other researchers using other populations of heroin addicts. By identifying vulnerability genes for addiction it may be possible to develop prevention efforts targeting those most at risk, as well as treatments that more effectively address the factors that make an individual vulnerable to addictions.

BRAIN DEVELOPMENT AND PREVENTION

Neuroimaging Allows Us to See How the Adolescent Brain Develops and Learns. New research has revealed that the brain continues to grow throughout childhood and into early adulthood, but available technology has, in the past, made it difficult to study that growth in fine detail. Recent advances in the fields of neuroimaging and computational analyses are now making such studies possible. In the current study, 45 children from 5 to 11 years old received magnetic resonance imaging (MRI), a non-invasive, painless neuroimaging procedure, twice, two years apart. The images or brain scans were then used to determine the relative growth of specific areas of the cerebral cortex as well as differences in the growth of gray matter (nerve cells) and white matter (brain pathways) in different cortical regions. The children in the study also received a vocabulary test to determine if changes in their brain structure were associated with changes in test scores. For the first time, researchers demonstrated that changes in brain structure were linked to changes in functional ability in the same individuals during a period of time when cognitive abilities are undergoing rapid development. Performance on the vocabulary test showed a significant improvement over time, which correlated with the changes in brain regions involved in language. This study demonstrates that the rapidly changing brain of children can be studied in detail, making it possible to not only understand normal development, but to also understand how the growing brain may be affected by abused drugs. Understanding how drugs of abuse affect the developing brain is particularly important because drug use often starts early and drugs may have an increased impact on the brains of young people by interfering

with normal brain growth and development.

Adolescents May Respond Differently Than Adults To Drugs Like Nicotine. Nicotine is one of the most widely used drugs during adolescence. Chronic nicotine use produces a withdrawal syndrome upon quitting that includes negative physical and emotional symptoms. Previous research with animal models has demonstrated that adolescent rats display heightened sensitivity to the reinforcing and stimulant effects of nicotine relative to adult rats. Little work has focused on the response of adolescent rats to measures of nicotine withdrawal. The present study sought to understand whether there were differences in withdrawal effects between adolescent and adult rats. After chronic nicotine treatment for seven days, administration of the nicotinic receptor antagonist mecamylamine to adult rats results in physical withdrawal signs. In contrast, mecamylamine did not precipitate similar withdrawal signs in adolescent rats that received chronic nicotine. These results indicate that there are reduced signs of physical dependence in adolescent compared to adult rats, and highlight the need for additional studies examining drug effects at various stages of development in order to optimize developmentally appropriate therapeutic interventions.

MECHANISMS OF ADDICTION

Cocaine-Associated Stimuli: More Powerful Than Previously Thought. The process of becoming addicted to a drug like cocaine is accompanied by a profound remodeling of neural circuits. During this process, and because the brain is influenced by situational context, the effects of drugs of abuse can become tightly linked to specific environmental cues. Such drug-associated cues pose formidable obstacles in front of an individual attempting to abstain from taking a drug, and remain remarkably effective triggers of relapse. Understanding how that association becomes imprinted in the brain is a fundamental goal in substance abuse research today. This study investigates the minimal requirements for the establishment of a persistent association between environmental cues and the self-administration of cocaine. Rats were trained to associate the onset of a sound with the availability of cocaine. This training occurred in a single session in which the rats learned to press a bar in order to self-administer cocaine. The sound signaled the drug's availability. The researchers then removed the animals from the training chamber and tested the persistence of the sound-drug association at various times thereafter. The authors found that the motivating effect of a sound associated with only a single experience of self-administered cocaine was incredibly robust and capable of reestablishing drug seeking behavior, even when measured up to a year later. While there is ample evidence that cues associated with drug use can elicit craving and facilitate relapse in humans, it was assumed that such effects required frequent reinforcement of the association. The present findings indicate that the links established between drug taking and environmental cues are much more powerful and persistent than previously thought. The results show that presentation of a cue that had become associated with a single exposure to cocaine a year before, may be enough to trigger craving, implying that drug-related learning may have a significant role in perpetuating desire for the drug soon after initiation of drug use.

New Insight Into Genes Involved in Addiction to Cocaine. To determine if specific genes (those in the Homer family) are involved in cocaine addiction, researchers used “knockout” technology in mice to delete certain genes to determine their behavioral and biological effects. They found that deleting genes from the Homer family produced the same symptoms seen in withdrawal from cocaine, including affecting the brain chemical glutamate, known to be involved in addiction. This suggests that the Homer genes may be involved in the plastic

changes that accompany the process of addiction. Discoveries such as this provide us with a new level of analysis in our understanding of the cellular processes that underlie addiction and may also lead to new targets for treatment.

Gene PSD-95 May Play A Role in Drug-Related Learning. Researchers embarked on a genome-wide search for genes that become induced or repressed when the reward center in the brain is activated by drugs of abuse. One such gene, PSD-95, stood out among the altered genes. The level of PSD-95, which encodes a protein involved in cellular scaffolding, was significantly reduced in all the models of chronic drug abuse. Reduced PSD-95 expression had previously been found to be associated with the learning process in the frontal cortex. The new findings uncover a previously unappreciated role of PSD-95 in the actions of stimulants and identify a mechanism shared between drug-related plasticity and learning that may lead to new targets for treatments for addiction.

The Longer An Individual Abuses Drugs, The More Extensive the Damage. Researchers investigated the extent to which chronic cocaine use affects diverse areas of the striatum, a brain region involved in the control of pleasure, learning and movement. They showed, in Rhesus monkeys, that the longer the animals self-administered cocaine, the more pervasive the damage to the striatum, in areas beyond the reward center. The results help explain why chronic cocaine use can disrupt not only reward and motivational behaviors, but also learning and motor functions, which also involve the striatum.

NEUROBIOLOGICAL CHANGES IN ADDICTED PATIENTS

Partial Brain Recovery in Methamphetamine Abusers After Protracted Abstinence. Methamphetamine is a particularly problematic drug in that not only is it highly addictive but its administration to laboratory animals results in damage to brain dopamine pathways. Similarly, studies of chronic methamphetamine abusers have shown deficits in brain glucose metabolism, a marker of brain activity, as well as in brain dopamine and serotonin pathways. Some such studies have also shown that markers of dopaminergic activity may recover with abstinence, though this recovery has not been associated with the same degree of functional improvement in motor and memory tasks. By using positron emission tomography (PET) scans, researchers were able to measure brain activity (glucose metabolism) in methamphetamine abusers after short-term (less than 6 months) and long-term (12-17 months) abstinence and compared to non-drug users. Compared to non-drug users, those who had abstained from methamphetamine for 6 months or less showed altered glucose metabolism in several brain regions, including the thalamus and the striatum. Following long-term abstinence, activity returned to levels similar to those in non-drug users in the thalamus. The thalamus is a particularly important area of the brain for creating memories. It filters incoming sensory information and sends the most important messages onto other areas of the brain. This increased activity in the thalamus with prolonged abstinence was associated with improved performance in motor and verbal memory tests. In contrast, there was no recovery of function in the striatum, which may reflect long-lasting changes in dopamine cell activity in this region. Such changes could account for the persistent lack of motivation and inability to experience pleasure observed in detoxified methamphetamine abusers. Therefore, while protracted abstinence may reverse some of the drug-induced alterations in brain function, other deficits persist. These findings have implications in the treatment of methamphetamine abusers, suggesting that protracted abstinence and proper rehabilitation may reverse some methamphetamine-induced alterations in brain function. Longer-term treatment and services may also be required to address persisting deficits

in motivation and mood that can plague chronic methamphetamine abusers.

Structural Abnormalities in the Brains of Human Who Use Methamphetamine. Over 35 million people regularly use amphetamine, including methamphetamine. Studies of chronic methamphetamine abusers have shown deficits in brain dopamine and serotonin pathways as well as in brain metabolism. However, few studies to date have examined whether there is structural damage in the brains of methamphetamine abusers. Using structural magnetic resonance imaging and new computational brain mapping techniques, the current study revealed that chronic methamphetamine abusers have severe decreases in gray-matter density in brain regions that are associated with cognition and emotion. The normal asymmetry between brain hemispheres found in one of these regions, the anterior cingulate gyrus, was erased in methamphetamine abusers. Interestingly, this finding is similar to that observed in the brains of patients with schizophrenia. In addition, compared to non-drug users, methamphetamine abusers showed smaller hippocampal volumes, a region of the brain associated with learning and memory, which was associated with decreased memory performance on a word-recall test. The structural deficits observed in this study may help account for many of the emotional and cognitive problems observed in chronic methamphetamine abusers. Future studies are needed to clarify how these deficits relate to clinical prognosis.

New Clues About Connections Between Cocaine Addiction, Thinking, and Decision-making. Inhibitory control mechanisms play an important role in selecting responses that increase the odds to succeed on a task. Many studies point to the anterior cingulate cortex (ACC), a small frontal brain region associated with the subconscious evaluation of outcomes, as a key component of these inhibitory circuits. Current evidence suggests that the ACC is less active in chronic drug users, a finding that correlates with increased impulsivity. Fifteen active cocaine-abusers and 15 non-addicted individuals were asked to perform a task designed to measure impulsivity and memory. During the task, the participants' brains were imaged via functional Magnetic Resonance Imaging (fMRI), which generates a map of the brains' activity. Cocaine users proved to be less proficient than controls at performing the requested task, an impairment that correlated with reduced ACC activity. When the researchers looked for differences elsewhere in the brain of cocaine addicts, they found an unexpected hyper-activation in the cerebellum, a structure known to contribute to cognitive functions, including certain forms of learning. The results suggest that cocaine's effects on two regions of the brain, known to play critical roles in learning and decision-making, may contribute directly to the chronic abuser's inability to control impulsive behaviors.

Neuropsychological Effects in Heavy MDMA Users. The so-called "club drug" MDMA or "Ecstasy" continues to be used by millions of Americans despite growing evidence of its potential harmful effects. Scientists have shown that MDMA can cause dangerous increases in body temperature, heart rate, blood pressure, and heart wall stress. Animal studies show that MDMA can also damage specific neurons in the brain. As well, a number of studies in humans suggest that long-term heavy MDMA users suffer cognitive deficits, including problems with memory. However, studies involving MDMA abusers present distinct challenges that make it difficult to draw conclusions as to the specific role MDMA plays in neuropsychological deficits. For example, many MDMA users use substantial amounts of other drugs, which make it difficult to determine whether cognitive deficits are due to MDMA use or the concurrent use of other drugs. Additionally, comparison subjects in many studies have not been a part of the "rave" subculture; therefore, differences may be due to sleep and fluid deprivation rather than MDMA use. The present pilot study examined a group of nearly "pure" MDMA users with little

or no exposure to other drugs and a comparison non-MDMA using group from the "rave" subculture, to control for these possible confounding factors in determining the neuropsychological effects of MDMA. Investigators analyzed data from a battery of neuropsychological tests administered to 16 non-users, 12 moderate users (22-50 lifetime episodes of use) and 11 heavy users (60-450 uses), adjusting for age, sex, family-of-origin variables, verbal IQ and depression. Although MDMA users as a whole performed worse than non-users on most test measures, these differences did not reach statistical significance. However, heavy users displayed significant deficits on many measures compared to non-users, particularly those associated with mental processing speed and impulsivity, which persisted when adjusted for potentially confounding variables. These data show that whereas modest MDMA use might cause few visible deficits, heavier or more frequent use may result in functional neuropsychological impairments. More subtle deficits may also occur with moderate use of MDMA that were not detected in the current study because of the small sample size. Moreover, such an examination from an unusual population of "pure" users of MDMA provides evidence that these cognitive deficits in heavy MDMA users are not simply due to the use of other drugs.

THERAPEUTIC INTERVENTIONS

Keeping Criminal Offenders Drug Free and Arrest Free for Five Years: How Specialized Drug Abuse Treatment Leads to a 'Win-win' Situation. Linkages between drug abuse and crime have been well established. With growing numbers of drug-involved criminal offenders, drug abuse treatment is becoming a critical component of the criminal justice system. A multistage therapeutic community program implemented in the Delaware correctional system has as its centerpiece a residential treatment program during work release-the transition between prison and community. In addition, Delaware has also implemented an aftercare program to follow criminal offenders as they negotiate the process of reentry into society. An evaluation was conducted on both programs: the work release and aftercare programs were studied to examine the incidence of criminal offenders who remained drug and arrest free after 5 years after release from prison. Study results indicate that participation in both work-release and aftercare drug treatment programs more than tripled the odds of remaining drug free and reduced the odds of a new arrest by 60% compared to those who did not participate in the multistage treatment approach. The findings of this study indicate that a multistage drug abuse treatment approach, which includes an aftercare component, leads to a long-lasting (at least 5 years) reduction in drug abuse and criminal behavior among criminal offenders. These data suggest that the implementation of such programs could bring about significant reductions in both drug abuse and drug-related crime.

Topiramate, a Promising New Approach for the Treatment of Cocaine Addiction. Cocaine addiction is a serious condition, associated with severe medical, psychological and social problems, including the spread of infectious diseases. Approximately one quarter of the 6.8 million persons in the US classified with addiction or abuse of illicit drugs are addicted to cocaine; that's over 1.7 million people in need of treatment (National Survey on Drug Use and Health, 2003). There is an urgent need to identify and develop a treatment to alleviate this condition, including the need to develop new medications. While cocaine administration primarily stimulates a central "reward system" in the brain, recent studies have linked the rewarding properties of cocaine to the actions of secondary circuits, making them attractive targets for pharmacologic intervention. Topiramate, a compound that affects these circuits, is

currently used for the treatment of epileptic seizures but has recently been hailed as potentially useful for the treatment of alcohol and opiate dependence. This is the first pilot study to examine the potential therapeutic benefits of Topiramate for the treatment of cocaine addiction. Drug or placebo was administered to two demographically similar (N=20) cohorts for 8 weeks. Drug dose was slowly increased from 25 mg to a maximum of 200 mg daily by week 8. Patients were then monitored for 5 additional weeks for rates of abstinence and illness severity and improvement. Topiramate-treated subjects fared significantly better in both measures, achieving 3 or more weeks of abstinence at a rate of 59% (compared with 26% in the placebo group) during the second phase of the trial. The Topiramte-treated group also showed a significant reduction in illness severity and a concomitant improvement in the results of standardized clinical tests. The results of this study are very encouraging. This medication could represent a powerful tool with which to counteract the damage caused by cocaine abuse. This small pilot trial should be viewed, however, as a first step that would warrant the implementation of a much larger, randomized, placebo controlled trial to validate both the safety and efficacy of topiramate for the treatment of cocaine addiction.

Alcohol Treatment Medication and Behavioral Therapy Are Effective for Treating Cocaine Addition. Disulfiram (Antabuse) is a well-known effective treatment for alcoholism. Additionally, previous studies have suggested that it might be useful for treating cocaine addiction among alcoholics. What has been unclear, however, is whether individuals reduce or stop their cocaine use because they have reduced or stopped drinking or whether the Disulfiram acts specifically to reduce cocaine use. Thus, the current study examined whether individuals who were cocaine addicts but not alcoholics would reduce their cocaine use when treated with Disulfiram. It also examined the role of behavioral therapy combined with Disulfiram in treating cocaine addiction. It was found that Disulfiram is able to reduce cocaine addiction and that it is most effective when it is combined with Cognitive Behavioral Therapy. These results indicate that Disulfiram can be used to effectively treat cocaine addiction irrespective of whether or not a person is an alcoholic. Furthermore, they show that behavioral therapy augments the effectiveness of Disulfiram.

CO-MORBIDITY

New Research In Animals Reveals Possible Long-Term Effects of Stimulants On Brain and Behavior. Attention Deficit Hyperactivity Disorder (ADHD) affects an estimated 3 to 6 percent of school-aged children around the world ("Diagnosis and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents," Goldman et al., 1998). Many of these children are properly diagnosed and safely treated with medications such as Methylphenidate (MPH, Ritalin™). However, methylphenidate and other stimulants are often abused, causing unknown risks to brain development and behavior. Animal studies are ideally suited to begin to investigate how these drugs affect the brain and behavior of developing organisms. Three recent studies tested the effects of chronic exposure of rats to MPH. All three studies show changes in the function of brain dopamine (DA) cells, as well as changes in behavior, and indicate that such changes appear to persist into adulthood if young animals are exposed to repeated low doses of MPH. These studies represent a significant advance towards the evaluation and understanding of potential long-term effects of stimulant administration on the brain and behavior of developing animals. Several caveats are important to mention before we can extrapolate these studies to humans. For example, the way in which the drug was administered to rats, namely, by injection into the abdominal cavity rather than orally (by tablet)

as used by humans, could lead to differences in how much and how quickly the drug affects the brain. In addition, the studies were carried out in normal rats, not in an animal model of ADHD. Thus, the results may be less applicable to children and adolescents who have ADHD; they might apply instead to those who take stimulants for non-medical purposes, or to those who are treated with stimulants as a result of misdiagnosis. These observations underscore the importance of proper diagnosis of ADHD and emphasize the need for prospective studies to evaluate whether exposure to stimulant drugs may predispose individuals to addiction and other mental disorders, including anxiety and mood disorders.

Unraveling the Mechanisms of Methylphenidate's Therapeutic Effects in Attention Deficit Hyperactivity Disorder (ADHD). Methylphenidate (MPH, Ritalin™) is the most commonly prescribed drug for ADHD. Its therapeutic effects are thought to derive from its ability to increase dopamine (DA), a multifaceted brain chemical that mediates motivational responses. However, the mechanisms by which MPH selectively enhances attentional processes in patients with ADHD are not well understood. A recent study was carried out to test specifically whether Methylphenidate can enhance the motivational value of an academic task. Using positron emission tomography (PET), researchers assessed the effects of MPH on brain DA in healthy volunteers, and the levels of interest and motivation elicited in the participants while attempting to solve a mathematical problem. The PET scans showed that when participants received methylphenidate and worked through the mathematical tasks, they experienced a significant increase in brain dopamine. These participants were also more likely to describe the mathematical tasks as interesting, exciting, and motivating. The link between MPH's effect on brain DA levels and task saliency sheds new light upon how MPH can be effective in the treatment of ADHD; it can increase the saliency and interest value of complex tasks. MPH may help people with ADHD improve their focus and motivation for performing academic tasks. The study also broadens our understanding of the role of DA in not only reward, but also in stimulus saliency. Patients with addictions have altered dopamine systems, which make them unresponsive to natural rewards and highly focused on seeking and taking drugs.

EPIDEMIOLOGY

Marijuana Abuse and Addiction has Increased in the United States. Marijuana has been the most common illicit substance used in the United States for several decades. Little information is available on whether or not the prevalence of marijuana abuse and addiction is increasing over time and what populations are most affected. Marijuana use was compared between two large national surveys, the National Longitudinal Alcohol Epidemiologic Survey (NLAES) in 1991-1992 and the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) in 2001-2002. In these studies, each of which surveyed approximately 43,000 men and women ages 18 years and older, researchers found that, overall, the prevalence of marijuana use remained stable between these two time periods; however, increases in use were observed in 18-29 year old African American and Hispanic women and among those aged 45-64. They also found that the overall prevalence of marijuana abuse or addiction increased by 22 percent during this time period. This means that there were approximately 800,000 more adults in the United States with marijuana abuse or addiction in 2001 - 2002 compared to approximately 10 years earlier. Moreover, increases in the prevalence of abuse or addiction were most notable among those aged 45-64 and among young African American men and women and young Hispanic men. The results of this study highlight the need to strengthen existing prevention and intervention efforts and to develop and implement new programs that specifically address

marijuana abuse among those aged 45-64 as well as among young minority men and women.
Common Household Products As Drugs of Abuse. Research has shown the abuse of inhalants to be a devastating drug problem that impacts many populations, particularly disadvantaged youth, worldwide. Inhalants are easily accessible in the form of household and office products, which may explain why they are, after marijuana, the second most widely used class of illicit drugs among 8th graders. Commonly abused products include glue, shoe polish, and gasoline. Through the analysis of a representative sample of U.S. adolescents the researchers found that approximately 2 million adolescents aged 12-17 abuse inhalants annually. Use was associated with a number of factors including, a history of incarceration, a history of foster care placement, delinquency, the use of alcohol and other drugs, and participation in mental health treatment. The researchers also found that 80% of inhalant abusers reported using before the age of 15, and that the younger a person is at the age of first use the more likely they are to become addicted. Adolescents that reported first use at 13-14 were six times more likely to become addicted than those who reported first use at age 15-17. This study demonstrates that inhalant abuse is associated with co-occurring problems and that younger users are at higher risk for addiction.

DRUG TESTING

Increased Sensitivity and Convenience In Improved Drug Test For Marijuana. It is generally accepted that drug testing of biological fluids, such as blood and urine, is the most objective means of diagnosis of drug use. There have been remarkable advances regarding the analysis of drugs in unconventional biological specimens such as hair and sweat, which offer the obvious advantage of being almost non-invasive, easy to perform and harder to adulterate or substitute. A sweat patch, for example, has been approved by the FDA for measuring amphetamines, cocaine, heroin, nicotine and marijuana in various drug-use monitoring programs. This study describes the validation of an analytical procedure for the quantitative determination of marijuana in human sweat patches using gas chromatography-mass spectrometry. Optimization of this technique for measuring marijuana resulted in a 10-fold increase in sensitivity over standard procedures. This improved sensitivity provides an adequate margin with which to handle the new marijuana cutoff guidelines established by the Substance Abuse and Mental Health Services Administration without causing unwanted increases in false positives rates. Importantly, no interference was observed after addition of 21 potentially interfering compounds.

HIV AND OTHER MEDICAL CONSEQUENCES OF DRUG ABUSE

Evidence Of Decreased Dopamine Function In HIV Patients With Dementia. Central nervous system complications are a common occurrence in the course of HIV infection. HIV-associated dementia, for example, can affect up to 25% of infected adults, and may result from HIV's ability to invade regions deep in the brain. These regions are home to critical centers that control movement, motivation, emotion and reward, all of which are very sensitive to the brain chemical dopamine (DA). Indirect evidence suggests that a dysfunction in the DA system could be a major contributor to HIV-associated dementia but, to this date, there have been no efforts to directly assess DA function in the brains of patients with HIV. Positron emission tomography (PET) was used to monitor the status of the brain DA system in 15 HIV positive subjects and 13 HIV negative controls. The HIV subjects with dementia showed evidence of a significant functional decline in their DA nerve terminals, when compared to either control or HIV-positive subjects without dementia. This is the first report that evaluates DA function in the living brain

of HIV patients. The results illuminate one aspect of the poorly understood mechanisms of HIV-mediated neurotoxicity; they provide the first direct evidence of damage to the DA system in HIV dementia patients, thereby suggesting that these patients may benefit from treatment with DA modulating agents. Finally, the findings will allow us to categorize and compare HIV-associated dementia with other diseases that target the DA signaling system, such as Parkinson's and methamphetamine addiction.

Early Intervention with Highly Active Antiretroviral Therapy (HAART) Can Delay Progression to AIDS. Research has shown that the use of highly active antiretroviral therapy (HAART) in those with HIV can both delay the progression to AIDS and reduce mortality. One critical piece of information that is used to decide when to start the use of medications, such as HAART, involves the number of CD4 cells in a sample of blood. CD4 cells are a type of white blood cell that fights infection, but HIV destroys CD4 cells, making it harder for the body to fight infections. This study represents the first time researchers have compared the mortality rate in HIV-positive persons receiving HAART to that in HIV-negative persons who were in the same risk category (e.g., injection drug use (IDU)) and found that starting HAART therapy for HIV-infected individuals earlier in the course of their disease than recommended by current standards of care may decrease mortality and progression to AIDS.

Reducing HIV Risk Among Crack-Abusing, African American Women: Women-Focused Interventions Work. Among the 33 areas with integrated HIV and AIDS surveillance systems an estimated 350,000 Americans are currently living with HIV/AIDS (CDC, 2003). The HIV/AIDS crisis particularly has had a devastating impact upon the African American community: The disease ranks as one of the top three leading causes of death for African Americans ages 25-54. The majority of HIV infections are contracted through risky sex behavior, which is strongly correlated to drug use. To determine if a women-focused HIV intervention that promotes positive health choices and self-worth was effective in reducing crack use and risky sexual behavior, researchers recruited and screened 620 out-of-drug-treatment African American women who were users of crack to participate in this study. The findings suggest that individualizing and tailoring interventions to the culture, gender, and unique lifestyle of women with high-risk behaviors who live in highly-stressed environments can lead to reduced risk behaviors and improved self-sufficiency through full-time employment and stable housing, which are also linked to improved health outcomes.

Marijuana Could Disrupt Normal Pregnancy. Cannabis (marijuana) remains the most commonly abused illicit drug, even during pregnancy. These troublesome statistics give way to serious concern when studies on pregnancy-related disorders found an association between high levels of anandamide (an endogenous chemical that affects the same receptors, i.e., cannabinoid receptors, as marijuana) and spontaneous pregnancy loss. A new study strengthens the evidence that the cannabinoid system may play an important role during pregnancy. These researchers discovered that the transport of embryos through the oviduct became abnormal in pregnant mice if one of the two known cannabinoid receptor types was rendered non-functional. The implications of this study are likely to apply to humans since significant levels of both anandamide and cannabinoid receptors can also be detected in the human uterus. Because marijuana can bind to cannabinoid receptors and disrupt their normal function, the findings bring up the disturbing possibility that pregnant women, who abuse marijuana, could be at higher risk for ectopic or developmentally flawed pregnancies.

NIH NEUROSCIENCE BLUEPRINT

The Blueprint is a framework to enhance cooperation among fifteen NIH Institutes and Centers that support research on the nervous system. Over the past decade, driven by the science, the NIH neuroscience Institutes and Centers have increasingly joined forces through initiatives and working groups focused on specific disorders. The Blueprint builds on this foundation, making collaboration on a day-to-day part of how the NIH does business in neuroscience. By pooling resources and expertise, the Blueprint can take advantage of economies of scale, confront challenges too large for any single Institute, and develop research tools and infrastructure that will serve the entire neuroscience community.

FY 2005 - - For fiscal year 2005, the Blueprint participants are developing an initial set of initiatives focused on tools, resources, and training that can have a quick and substantial impact because each builds on existing programs. These initiatives, with the participation of all Blueprint Institutes, include an inventory of neuroscience tools funded by the NIH and other government agencies, enhancement of training in the neurobiology of disease for basic neuroscientists, and expansion of ongoing gene expression database efforts. In FY 2005, the NIH Neuroscience Blueprint Inventory (NNBI), under the leadership of NIDA, will develop a web-based, knowledge-indexed neuroscience resource inventory for the scientific community. While this scientific information exists in various forms both within NIH and other national and international institutions, the activities, resources and tools are not easily accessible from a single site. This inventory will allow neuroscientists the opportunity for "one stop shopping" access to a variety of resources, activities and data that heretofore have been underutilized, and, in some cases, unknown to the many members of the scientific community.

FY 2006 - - Advances in the neurosciences and the emergence of powerful new technologies offer many opportunities for Blueprint activities that will enhance the effectiveness and efficiency of neuroscience research. Blueprint Initiatives for fiscal year 2006 will include systemic development of genetically engineered mouse strains of critical importance to research on nervous system and its disease and training in critical cross cutting areas such as neuroimaging and computational biology. In FY 2006, NIDA will take the lead in supporting three new cross-disciplinary training programs that focus in the areas of neuroimaging, computational neuroscience and on the neurobiology of disease. These areas have been identified as being applicable to understanding basic function and to many diseases that affect the nervous system.

NIH ROADMAP

The NIH Roadmap provides an extraordinary opportunity for drug abuse and addiction researchers to take advantage of new NIH funding mechanisms and to become an integral part of transforming how we approach diseases, like addiction, in this country. NIDA is actively working with the field to take advantage of the tremendous opportunities that the NIH Roadmap provides. During the first year, NIDA recruited over 40 researchers to submit Roadmap proposals for FY 2004 funding. Five NIDA researchers received FY2004 Roadmap funding, two NIDA researchers were co-funded in partnership with OBSSR (Roadmap-Affiliated Grants)

and eight additional Roadmap grants were awarded in FY 2004 that are related to NIDA's research mission.

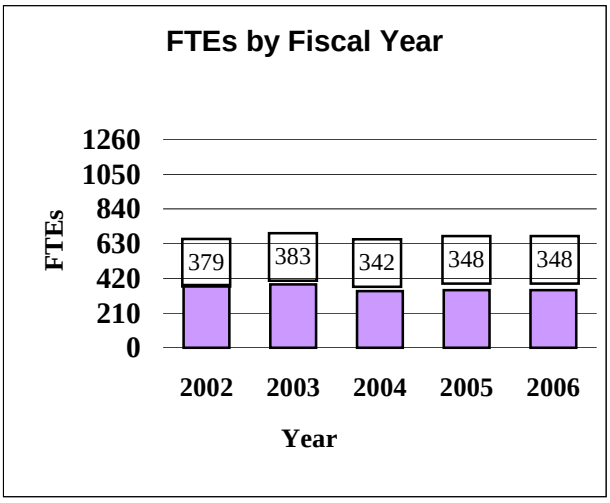
To capitalize on recent discoveries in molecular and cell biology, the research community requires further access to technologies, databases, and other scientific resources that are more sensitive, more robust, and more easily adaptable to researchers' individual needs. NIDA researchers are actively participating in the development of new technologies in metabolomics, for example. These grants will examine the biochemistry occurring within the neurons and supporting cells making up the mammalian brain and researchers will create instruments and protocols to measure the metabolites in neuronal clusters, groups of neurons and even individual neurons. This unique technology promises to enhance our understanding of neurological disorders, including stroke and trauma, and even help deepen our understanding of the neurological effects of the abuse of drugs on the human brain.

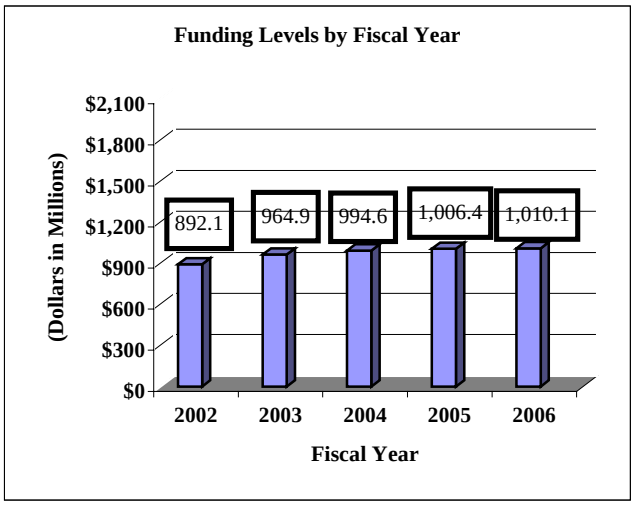
Areas emphasized in the NIH Roadmap, including the Molecular Libraries and Imaging approach is likely to accelerate the development of new medications to treat both common and frequently medicated diseases, as well as common but neglected disorders such as drug abuse that are less likely to be targets for profitable therapeutic development in the private sector. One component of the Roadmap encourages the use of high throughput molecular screening. Multiple research studies related to NIDA's mission were identified. One study will investigate use of this assay system to screen large chemical libraries related to the Hepatitis C virus (HCV), which is the most important cause of chronic liver disease in the US. This research will have two important goals: first – it will serve as an antiviral discovery screen and second, discovery of hit compounds that positively or negatively regulate HCV replication will ultimately help lead to identification of novel cellular targets that can be exploited to further interrupt the viral lifecycle. This research may play an important role in providing critical data to reduce the spread of HCV among injection drug abusers.

Budget Policy

The Fiscal Year 2006 budget request for the NIDA is $1,010,130,000, an increase of $3,711,000 and 0.4 percent over the FY 2005 appropriation Level. Also included in the FY 2006 request, is NIDA's support for the trans-NIH Roadmap initiatives, estimated at 0.89% of the FY 2006 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the NIH Overview.

A five year history of FTEs and Funding Levels for NIDA are shown in the graphs below.





NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. We estimate that the average cost of competing RPGs will be $332,000 in Fiscal Year 2006. While no inflationary increases are provided for direct, recurring costs in non-competing RPG's, where the NIDA has committed to a programmatic increase in an award, such increases will be provided.

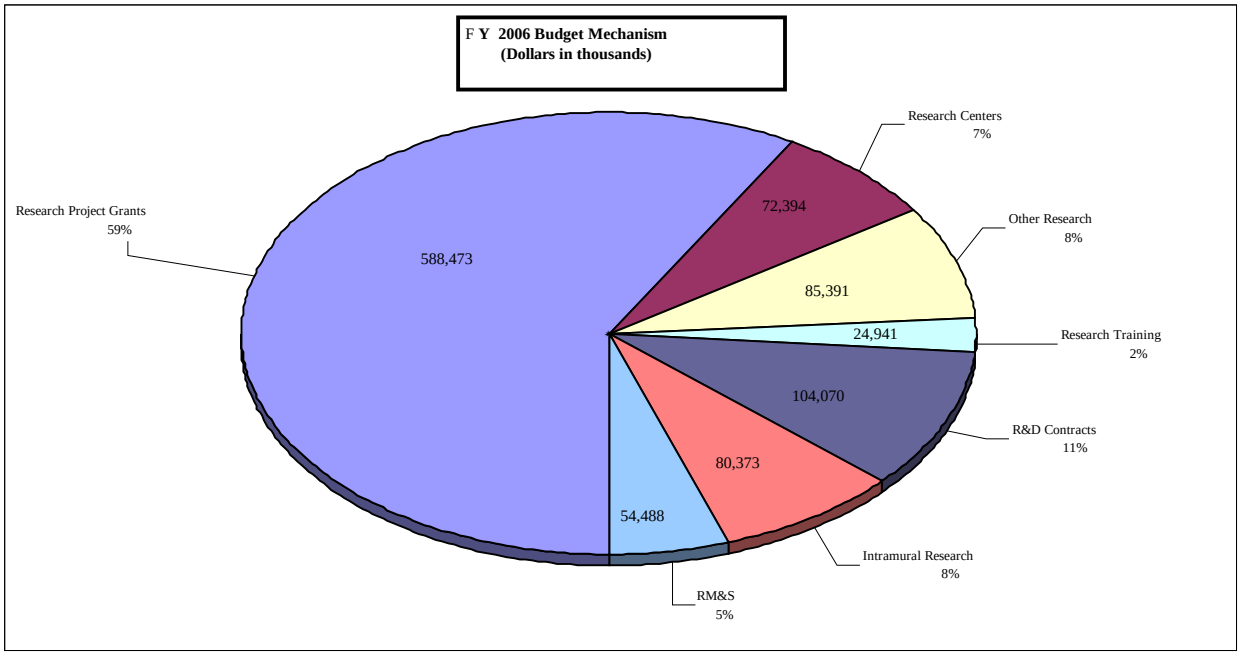
Advancement in medical research is dependent on attracting, training, and retaining the best and the brightest individuals to pursue careers in biomedical and behavioral research. In the Fiscal Year 2006 request, most stipend levels for individuals supported through the Ruth L. Kirschstein National Research Service Awards are maintained at the Fiscal Year 2005 levels. To help prevent the potential attrition of our next generation of highly trained post-doctoral trainees, stipend levels for post-docs with 1-2 years of experience are increased by 4.0%. This will bring these stipends closer to the goal NIH established for post-doc stipends in March, 2000. In addition, individual post-doctoral fellows will receive an increase of $500 in their institutional allowance for rising health benefit costs. The need for increased health benefits is particularly acute for these post-doctoral trainees, who, because of their age and stage of life are more likely to have family responsibilities. The increases in stipends and health insurance are financed within the Fiscal Year 2006 request by reducing the number of Full-Time Training Positions, because NIH believes that it is important to properly support and adequately compensate those who are participating in these training programs, so that the programs can continue to attract and retain the trainees most likely to pursue careers in biomedical, behavioral and clinical research. NIDA will support 599 pre- and postdoctoral trainees in full-time training positions.

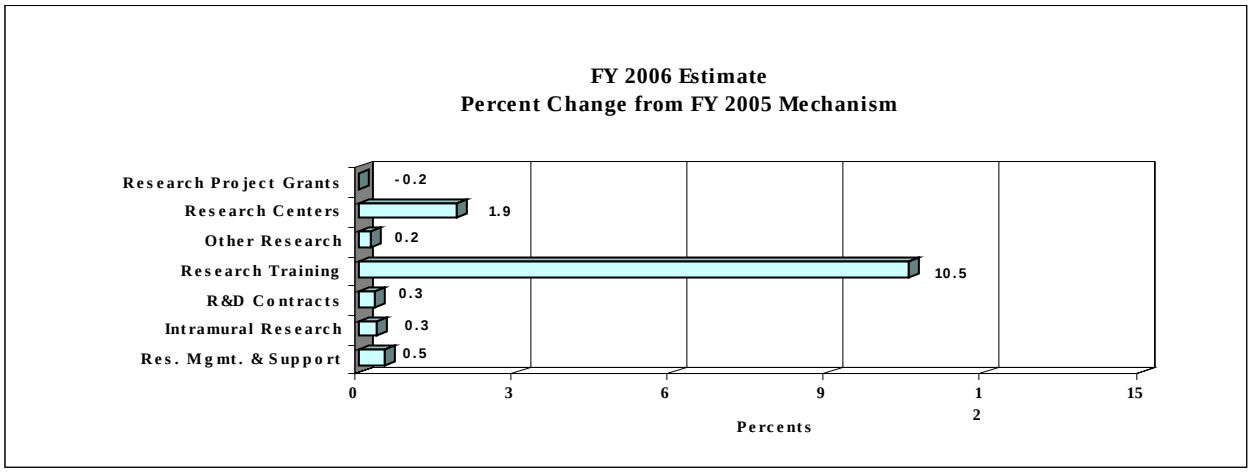
The Fiscal Year 2006 request includes funding for 42 research centers, 324 other research grants, including 253 clinical career awards, and 198 R&D contracts. Research Management and Support increases by 0.5 percent, the same as the NIH total increase. Intramural Research receives an increase of 0.3 percent.

NIDA is participating in the NIH Neuroscience Blueprint. The FY 2006 request includes $3,900,000 for a variety of Neuroscience Blueprint initiatives, including neuroscience cores,

training initiatives, and the Neuromouse project.

The mechanism distribution by dollars and percent change are displayed below:





NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Budget Mechanism - Total

MECHANISM	FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate		2005/2006 % Change
Research Grants:	No.	Amount	No.	Amount	No.	Amount	
Research Projects:							
Noncompeting	1,060	$432,490,000	1,073	$453,360,000	1,032	$434,741,000	-4.1
Administrative supplem	(154)	10,828,000	(80)	4,344,000	(154)	10,823,000	149.1
Competing:							
Renewal	87	32,839,000	76	28,687,000	83	31,329,000	9.2
New	305	93,739,000	268	85,718,000	294	94,095,000	9.8
Supplements	4	1,072,000	2	536,000	2	536,000	0.0
Subtotal, competi	396	127,650,000	346	114,941,000	379	125,960,000	9.6
Subtotal, RPGs	1,456	570,968,000	1,419	572,645,000	1,411	571,524,000	-0.2
SBIR/STTR	62	17,400,000	60	16,886,000	60	16,949,000	0.4
Subtotal, RPGs	1,518	588,368,000	1,479	589,531,000	1,471	588,473,000	-0.2
Research Centers:							
Specialized/compreher	38	66,522,000	41	70,411,000	41	71,508,000	1.6
Clinical research	0	0	0	0	0	0	0.0
Biotechnology	1	413,000	1	646,000	1	886,000	37.2
Comparative medicine	0	0	0	0	0	0	0.0
Research Centers in M	0	0	0	0	0	0	0.0
Subtotal, Centers	39	66,935,000	42	71,057,000	42	72,394,000	1.9
Other Research:							
Research careers	246	32,603,000	248	34,886,000	253	35,278,000	1.1
Cancer education	0	0	0	0	0	0	0.0
Cooperative clinical res	17	39,505,000	17	38,715,000	17	38,469,000	-0.6
Biomedical research sup	0	18,000	0	24,000	0	27,000	12.5
Minority biomedical res	0	0	0	0	0	0	0.0
Other	52	12,904,000	52	11,567,000	54	11,617,000	0.4
Subtotal, Other Rese	315	85,030,000	317	85,192,000	324	85,391,000	0.2
Total Research Grants	1,872	740,333,000	1,838	745,780,000	1,837	746,258,000	
Research Training:	FTTPs		FTTPs		FTTPs		
Individual awards	152	5,279,000	151	5,458,000	169	6,081,000	11.4
Institutional awards	379	15,902,000	393	17,104,000	430	18,860,000	10.3
Total, Training	531	21,181,000	544	22,562,000	599	24,941,000	10.5
Research & development	188	103,413,000	197	103,748,000	198	104,070,000	0.3
(SBIR/STTR)	(17)	(6,428,000)	(19)	(7,000,000)	(19)	(7,000,000)	
	FTEs		FTEs		FTEs		
Intramural research	113	77,230,000	121	80,112,000	121	80,373,000	0.3
Research management an	229	52,448,000	227	54,217,000	227	54,488,000	0.5
Cancer prevention & con	0	0	0	0	0	0	0.0
Construction		0		0		0	0.0
Buildings and Facilities		0		0		0	0.0
Total, NIDA	342	994,605,000	348	1,006,419,000	348	1,010,130,000	0.4
(RoadMap Support)		(3,403,000)		(6,363,000)		(9,026,000)	
(Clinical Trials)		(171,170,000)		(173,910,000)		(174,600,000)	

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2004 Actual FTEs	FY 2004 Actual Amount	FY 2005 Appropriation FTEs	FY 2005 Appropriation Amount	FY 2006 Estimate FTEs	FY 2006 Estimate Amount	Change FTEs	Change Amount
Extramural Research:								
Drug Abuse and Addiction		$864,927		$872,090		$875,269		$3,179
Subtotal, Extramural research		864,927		872,090		875,269		3,179
Intramural research	113	77,230	121	80,112	121	80,373	0	261
Res. management & support	229	52,448	227	54,217	227	54,488	0	271
Total	342	994,605	348	1,006,419	348	1,010,130	0	3,711

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Summary of Changes

FY 2005 Estimate				$1,006,419,000
FY 2006 Estimated Budget Authority				1,010,130,000
Net change				3,711,000
	FY 2005 Appropriaton		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$17,624,000		$241,000
b. Annualization of January 2005 pay increase		17,624,000		163,000
c. January 2006 pay increase		17,624,000		310,000
d. One less day of pay		17,624,000		(72,000)
e. Payment for centrally furnished services		7,846,000		39,000
f. Increased cost of laboratory supplies, materials, and other expenses		54,474,000		1,066,000
Subtotal				1,747,000
2. Research Management and Support:				
a. Within grade increase		27,326,000		470,000
b. Annualization of January 2005 pay increase		27,326,000		252,000
c. January 2006 pay increase		27,326,000		482,000
d. One less day of pay		27,326,000		(104,000)
e. Payment for centrally furnished services		4,979,000		25,000
f. Increased cost of laboratory supplies, materials, and other expenses		21,912,000		418,000
Subtotal				1,543,000
Subtotal, Built-in				3,290,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Summary of Changes--continued

CHANGES	2005 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	1,073	$457,704,000	(41)	($12,140,000)
b. Competing	346	114,941,000	33	11,019,000
c. SBIR/STTR	60	16,886,000	0	63,000
Total	1,479	589,531,000	(8)	(1,058,000)
2. Research centers	42	71,057,000	0	1,337,000
3. Other research	317	85,192,000	7	199,000
4. Research training	544	22,562,000	55	2,379,000
5. Research and development contracts	197	103,748,000	198	322,000
Subtotal, extramural				3,179,000
	FTEs		FTEs	
6. Intramural research	121	80,112,000	0	(1,486,000)
7. Research management and support	227	54,217,000	0	(1,272,000)
Subtotal, program		1,006,419,000		421,000
Total changes	348		0	3,711,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Budget Authority by Object

	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease	Percent Change
Total compensable workyears:				
Full-time employment	348	348	0	0.0
Full-time equivalent of overtime & holiday hours	2	2	0	0.0
Average ES salary	$149,897	$153,794	$3,897	2.6
Average GM/GS grade	11.9	11.9	(0.0)	-0.2
Average GM/GS salary	$94,203	$96,652	$2,449	2.6
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$87,096	$89,360	$2,264	2.6
Average salary of ungraded positions	115,865	118,877	3,012	2.6

OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease	Percent Change
Personnel Compensation:				
11.1 Full-Time Permanent	$24,495,000	$25,058,000	$563,000	2.3
11.3 Other than Full-Time Permanent	5,952,000	6,089,000	137,000	2.3
11.5 Other Personnel Compensation	1,068,000	1,079,000	11,000	1.0
11.7 Military Personnel	1,578,000	1,614,000	36,000	2.3
11.8 Special Personnel Services Payments	3,354,000	3,431,000	77,000	2.3
Total, Personnel Compensation	36,447,000	37,271,000	824,000	2.3
12.0 Personnel Benefits	7,663,000	7,840,000	177,000	2.3
12.1 Military Personnel Benefits	840,000	859,000	19,000	2.3
13.0 Benefits for Former Personnel	0	0	0	0.0
Subtotal, Pay Costs	**44,950,000**	**45,970,000**	**1,020,000**	**2.3**
21.0 Travel & Transportation of Persons	1,349,000	1,320,000	(29,000)	-2.1
22.0 Transportation of Things	170,000	171,000	1,000	0.6
23.1 Rental Payments to GSA	0	0	0	0.0
23.2 Rental Payments to Others	3,738,000	3,757,000	19,000	0.5
23.3 Communications, Utilities & Miscellaneous Charges	1,132,000	1,128,000	(4,000)	-0.4
24.0 Printing & Reproduction	1,001,000	981,000	(20,000)	-2.0
25.1 Consulting Services	8,903,000	8,914,000	11,000	0.1
25.2 Other Services	10,320,000	10,314,000	(6,000)	-0.1
25.3 Purchase of Goods & Services from Government Accounts	98,564,000	99,403,000	839,000	0.9
25.4 Operation & Maintenance of Facilities	8,578,000	8,597,000	19,000	0.2
25.5 Research & Development Contracts	56,889,000	55,969,000	(920,000)	-1.6
25.6 Medical Care	495,000	486,000	(9,000)	-1.8
25.7 Operation & Maintenance of Equipment	1,066,000	1,058,000	(8,000)	-0.8
25.8 Subsistence & Support of Persons	0	0	0	0.0
25.0 Subtotal, Other Contractual Services	**184,815,000**	**184,741,000**	**(74,000)**	**0.0**
26.0 Supplies & Materials	5,514,000	5,490,000	(24,000)	-0.4
31.0 Equipment	5,600,000	5,565,000	(35,000)	-0.6
32.0 Land and Structures	0	0	0	0.0
33.0 Investments & Loans	0	0	0	0.0
41.0 Grants, Subsidies & Contributions	758,149,000	761,004,000	2,855,000	0.4
42.0 Insurance Claims & Indemnities	0	0	0	0.0
43.0 Interest & Dividends	1,000	3,000	2,000	200.0
44.0 Refunds	0	0	0	0.0
Subtotal, Non-Pay Costs	**961,469,000**	**964,160,000**	**2,691,000**	**0.3**
Total Budget Authority by Object	**1,006,419,000**	**1,010,130,000**	**3,711,000**	**0.4**

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Salaries and Expenses

OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease	Percent Change
Personnel Compensation:				
Full-Time Permanent (11.1)	$24,495,000	$25,058,000	$563,000	2.3
Other Than Full-Time Permanent (11.3)	5,952,000	6,089,000	137,000	
Other Personnel Compensation (11.5)	1,068,000	1,079,000	11,000	1.0
Military Personnel (11.7)	1,578,000	1,614,000	36,000	2.3
Special Personnel Services Payments (11.8)	3,354,000	3,431,000	77,000	2.3
Total Personnel Compensation (11.9)	**36,447,000**	**37,271,000**	**824,000**	**2.3**
Civilian Personnel Benefits (12.1)	7,663,000	7,840,000	177,000	2.3
Military Personnel Benefits (12.2)	840,000	859,000		
Benefits to Former Personnel (13.0)	0	0	0	0.0
Subtotal, Pay Costs	**44,950,000**	**45,970,000**	**1,020,000**	**2.3**
Travel (21.0)	1,349,000	1,320,000	(29,000)	-2.1
Transportation of Things (22.0)	170,000	171,000	1,000	0.6
Rental Payments to Others (23.2)	3,738,000	3,757,000	19,000	0.5
Communications, Utilities and Miscellaneous Charges (23.3)	1,132,000	1,128,000	(4,000)	-0.4
Printing and Reproduction (24.0)	1,001,000	981,000	(20,000)	-2.0
Other Contractual Services:				
Advisory and Assistance Services (25.1)	6,970,000	6,923,000	(47,000)	-0.7
Other Services (25.2)	10,320,000	10,314,000	(6,000)	-0.1
Purchases from Govt. Accounts (25.3)	74,257,000	75,096,000	839,000	1.1
Operation & Maintenance of Facilities (25.4)	8,578,000	8,597,000	19,000	0.2
Operation & Maintenance of Equipment (25.7)	1,066,000	1,058,000	(8,000)	-0.8
Subsistence & Support of Persons (25.8)	0	0	0	0.0
Subtotal Other Contractual Services	**101,191,000**	**101,988,000**	**797,000**	**0.8**
Supplies and Materials (26.0)	5,514,000	5,490,000	(24,000)	-0.4
Subtotal, Non-Pay Costs	114,095,000	114,835,000	740,000	0.6
Total, Administrative Costs	**159,045,000**	**160,805,000**	**1,760,000**	**1.1**

NATIONAL INSTITUTES OF HEALTH

National Institute on Drug Abuse

SIGNIFICANT ITEMS IN HOUSE, SENATE, AND CONFERENCE APPROPRIATIONS COMMITTEE REPORTS

FY 2005 House Appropriations Committee Report Language (H.Rpt. 108-636)

Item

Asian American and Pacific Islander (AAPI) populations – The Committee suggests that NIDA take further steps to meet the research needs of the rapidly growing AAPI populations in the fifty states and the six Pacific Island jurisdictions. In particular, AAPI research with respect to substance abuse prevention, treatment, services and training is needed to help address the public health needs of these populations. The NIDA AAPI Workgroup has provided important recommendations to NIDA critical to developing the needed body of scientific knowledge regarding AAPIs, and the Committee encourages NIDA to consider carefully these recommendations and take action where warranted (p.96).

Action taken or to be taken

As mentioned, NIDA established an AAPI Workgroup in 1999, which continues to hold meetings and issue recommendations. The Workgroup is comprised of researchers, scholars, practitioners, and community advocates, who provide guidance to NIDA on drug abuse related issues and needs among AAPI populations, and encourage AAPI students, researchers and community-based organizations to participate in drug abuse research. The Workgroup has made recommendations to imrove the epidemiological and knowledge base on drug abuse in AAPI populations. NIDA is dedicated to implementing the workgroup recommendations in a meaningful way and to this end, throughout the past year, the Institute has sponsored monthly teleconferences with workgroup members in order to maintain open lines of communication between workgroup members and NIDA.

In response to other workgroup recommendations NIDA has taken steps to encourage further research regarding drug abuse in AAPI populations. With the past year NIDA has awarded a professional services contract so that, using existing datasets, researchers will be able to glean useful information specifically regarding AAPI populations. This information will be critical in that it will provide supporting documentation for future grant applications and will help to give researchers a more accurate picture regarding the needs of this diverse population.

NIDA's investment in this area of research recently resulted in the publication of a paper titled "Alcohol, tobacco, and other drug use among Asian American and Pacific Islander Adolescents in California and Hawaii." Prior research suggested that the lowest rates of alcohol, tobacco, and other drug use are often reported for AAPIs, compared to Whites. These low rates are, however, often based upon samples with small representations of AAPIs, or represented by only one or two AAPI groups. This study investigated drug use among specific AAPI subgroups (Chinese, Filipino, Japanese, and Pacific Islander/Native Hawaiian) using data from school surveys

collected from nearly 82,000 9th grade students in California and nearly 5,000 10th grade students in Hawaii. Results showed that rates of alcohol, tobacco, and other drug use were lowest for the Chinese adolescents and highest among the White and Pacific Islanders/Native Hawaiians. In summary, AAPIs clearly constitute heterogeneous groups characterized by a wide range of substance use behaviors, making the treatment needs of each subgroup unique.
In addition to supporting research NIDA has also continues to provide support to the National Asian Pacific American Families Against Substance Abuse, Inc. (NAPAFASA), a national umbrella organization, that has been successful in drawing attention to alcohol and other drug problems in the AAPI populations. During the past year NIDA staff assisted in the design of the research track and presented at the NAPAFASA conference held in June of 2004.

NIDA has also continued to make concerted efforts to increase the number of underrepresented scholars involved in drug abuse research, primarily through the NIH's Minority Supplement Program. This program was established by NIH to increase the numbers of underrepresented minority scientists participating in biomedical and behavioral research. NIDA considers Asians to be underrepresented in behavioral/clinical research. Funding is provided to current NIH research grants to support a minority student or investigator who wants to pursue a career in the biomedical or behavioral research sciences, through research experiences with NIH-funded investigators. This past year NIDA funded three Asian Americans and one Pacific Islander American under the minority supplements program.

FY 2005 Senate Appropriations Committee Report Language (S.Rpt.108-345)

Item

Adolescent Drug Abuse - The Committee is pleased with the Institute's focus on adolescents. The Committee notes that if drug abuse is to be reduced, there must be a better understanding of the adolescent decision-making process so that more effective prevention programs can be developed. NIDA is urged to increase its research to better understand the mechanisms underlying adolescent judgment, decision-making, impulsively and risk-taking (p. 146).

Action taken or to be taken

Adolescent drug abuse is one of the primary challenges facing our nation today. NIDA has long-recognized the importance of supporting research to study the mechanisms associated with adolescent decision-making and risk-taking behaviors involved in drug abuse. NIDA has launched multiple research initiatives during the past year on this topic. One research area focuses on adolescent cognitive processes including decision-making, motivation and judgment, which influence choices to abuse or avoid drugs. Recently funded studies will examine suboptimal decision-making, adolescent impulse control, neurocognitive precursors and decision-making among adolescents in inner-city neighborhoods. To enhance our understanding on how developmental changes in the adolescent brain may increase vulnerability to drugs, NIDA is also using animal models to explore neurological maturation. Recently awarded studies are investigating adolescent reward and motivation, brain vulnerability related to binge drug exposure and gender differences in drug-seeking behavior.

NIDA has also partnered with others Institutes, including NIMH, NICHD and NINDS to support the NIH MRI Study of Normal Brain Development, which is the world's first large-scale database on normal brain development in children and adolescents. The study is using aMRI (anatomic magnetic resonance imaging) and other tools to establish a baseline for normal brain development which will help examine the formation of reward and decision-making processes, chart normal growth curves of brain structures, examine the development of circuitry for language, thinking, and other functions. Imaging and extensive clinical and behavioral data may be able to enhance early diagnosis and differentiation of various disorders, including adolescent drug abuse and speed up the development of targeted prevention and treatment approaches.

Additional NIDA research is illuminating the cognitive and behavioral processes experienced by boys and girls who begin using drugs in adolescence. Further research may help clinicians, teachers and parents to identify problems early, structure environmental conditions and tailor drug abuse prevention programs for children and adolescents to avoid the path to drug abuse.

NIDA convened a science meeting in January 2004 to enhance our understanding of patterns of initiation, risk-taking that results in escalation, and protective factors that contribute to cessation of drug abuse among adolescents and young adults. To further address this area, NIDA issued an RFA titled: "Prevention Research for the Transition to Adulthood" to examine the developmental period of late adolescence into early adulthood and to test the efficacy of preventive interventions to reduce the initiation and progression of drug abuse during this transitional period.

NIDA also launched a new educational tool to empower adolescents to make informed decisions about drugs. "NIDA for Teens: The Science Behind Drug Abuse" is an interactive Web site (http://teens.drugabuse.gov) for teenagers and delivers science-based facts about how drugs affect the brain and body. Animated illustrations, quizzes, and games are used to clarify concepts, test knowledge, and make learning fun.

Item

Collaboration with SAMHSA - The Committee commends NIDA for its outreach and work with State substance abuse authorities to reduce the current 15- to 20-year lag between the discovery of an effective treatment or intervention and its availability at the community. In particular, the Committee applauds NIDA for working with SAMHSA on a recent RFA designed to strengthen State agencies' capacity to support and engage in research that will foster statewide adoption of meritorious science-based policies and practices. The Committee also encourages NIDA to continue collaborative work with States to ensure that research findings are relevant and adaptable by State Substance Abuse systems. In addition, the Committee encourages NIDA to work with SAMHSA, NIAAA, and NIMH to develop more recent and accurate data on persons with co-occurring mental health and substance use disorders, with an emphasis on individuals with mild to moderate mental health disorders (p.146).

Action taken or to be taken

NIDA is continuing to work with SAMHSA, and others, including State Alcohol and Drug Abuse Agencies to bridge the gap between science and services to ensure that substance abuse research is both accessible and used by local communities. NIDA accomplishes through a

number of activities, including continuing to be an active participant in the "Science to Services" Workgroup that SAMHSA initiated in Spring 2002 to enhance collaboration between NIH Institutes (NIDA, NIMH, NIAAA) and SAMHSA. NIDA also collaborated with SAMHSA in April 2004, to issue an RFA titled, "Enhancing State Capacity to Foster Adoption of Science-Based Practices." NIDA has committed approximately $1.35 million in FY 2005 to fund grants from this RFA. This RFA encourages state agencies to team with research organizations in their states to apply for grants that will provide them with resources to support research that should help to improve the delivery of publicly supported drug abuse prevention and or treatment services. Eighteen applications have been received for consideration.

Because NIDA recognizes the important role that State Substance Abuse (SSA) Directors play in helping patients who have substance abuse disorders get treatment, NIDA is working more closely with them. NIDA co-sponsored with NASADAD and SAMHSA four SSA Director meetings, including a pre-conference meeting at the National Association of State Alcohol and Drug Abuse Directors (NASADAD) annual conference in Portland, Maine on June 5, 2004. All meetings have proven to be a great success in terms of disseminating information and facilitating important linkages necessary for the efficacy of drug abuse treatment programs throughout the country. Another SSA meeting is scheduled for June 2005.

NIDA also worked with SAMHSA and others to support the "Blending Clinical Practice & Research: Forging Partnerships in the Great Lakes States to Enhance Drug Addiction Treatment" at the Renaissance Marriott in Detroit, Michigan September 27-28, 2004. This conference provided an opportunity for clinicians and researchers to examine cutting-edge findings about drug use and addiction and their application to clinical practice.

Additionally, the NIDA and SAMHSA partnership has expanded to include collaboration with other agencies and Institutions to address issues like adequately addressing co-occurring health problems. NIDA will work with the National Institute of Mental Health (NIMH) and others to encourage new research to develop effective strategies, and with SAMHSA to ensure the timely adoption and implementation of evidence-based practices for the prevention and treatment of co-occurring disorders. Also, NIDA and the NIMH issued a 3-year program announcement titled: "Effectiveness, Practice, and Implementation in the Center for Mental Health Services Children's Service Sites." The PA encourages research grant applications on services delivered to children, adolescents and their families through the Center for Mental Health Services (CMHS) Comprehensive Community Mental Health Services for Children and their Families Initiative.

To further enhance the likelihood of research adoption and implementation, NIDA has collaborated with SAMHSA and other federal agencies in supporting a number of health service research studies, including: The National Criminal Justice Drug Abuse Treatment Research System (CJ-DATS) Course of Problems in Adolescent Drug Treatment Intakes; Early Family-Centered Prevention of Drug Use Risk; and Science-Based Prevention: Testing Communities that Care. Specifically, in 2004, NIDA co-sponsored the Juvenile Justice Policy Academy with CMHS to provide select jurisdictions with the opportunity to develop improved, collaborative strategies to identify and respond to youth with mental health and co-occurring substance use disorders who come in contact with all aspects of the juvenile justice system.

Item

Co-morbidity – Co-morbidity between drug abuse and mental illness is common and may reflect common contributing factors. The Committee urges NIDA to expand research efforts to better understand the neurobiological underpinnings of these co-occurring disorders; to elucidate risk and protective factors for development of mental health and substance abuse problems; and more specifically to explore the impact of stimulant therapies for mental disorders such as ADHD on later drug use disorders. The Committee also encourages NIDA to examine how treatment services can best accommodate the co-morbid nature of these disorders (p. 147).

Action taken or to be taken

NIDA remains committed to generating new advances to address the complex issues of co-morbidity. Understanding the neurobiological underpinnings of the co-occurring disorders, elucidating the risk and protective factors, and understanding the impact that mediations can have on later drug use disorders, as well as understanding how treatment services can improve treatment outcomes for both conditions, are all important research areas for NIDA.

To address some of these issues, NIDA initiated a number of new activities, including partnering with NIMH to award over a dozen studies to address the neurobiological components of co-morbidity and to spur the development of new imaging compounds that will enable further exploration of the neurochemical receptors and brain regions associated with drug abuse and mental disorders. This important research could pave the way for the development of new medication strategies to treat both conditions.

To explore the links between childhood psychopathology, behavior and subsequent drug abuse, NIDA funded several new studies to enhance our understanding of how biological vulnerability, risk and protective factors and environmental challenges in these children's lives contribute to coexisting mental health and substance abuse disorders. This information will provide the basis for new and more effective prevention and treatment strategies. NIDA has also joined with NIMH, NIAAA, and NCI to develop and test new medications and treatments for mental health disorders and nicotine addiction.

In an effort to encourage more research to optimally design innovative prevention and treatment strategies for comorbidity, NIDA partnered with NIMH and NIAAA, to issue a Program Announcement (PA) to examine how factors related to organization, management, dissemination and financing of services influence the quality, access, utilization, outcomes, and cost effectiveness of treatment. Research in these areas can enhance our understanding of how pharmacological, psychosocial, behavioral and environmental approaches can be combined or tailored to maximize treatment for persons suffering from comorbid disorders.

NIDA co-sponsored a major conference in June 2004 with NIMH, NIAAA, SAMHSA, HRSA and AHRQ titled: “The Complexities of Co-occurring Conditions” to showcase new cutting-edge research about the management, economics, and outcomes of service delivery for co-occurring disorders and to encourage collaboration among the disciplines and professionals involved in this issue. To reach psychiatrists, NIDA sponsored a major addiction research track, comprised of

over 40 scientific sessions, at the American Psychiatric Association (APA) Annual Meeting in New York titled: "Integrating the Science of Addiction Into Psychiatric Practice."

An important research area for NIDA is to better understand the impact that medications for ADHD can have on brain development, behavior and later substance use. Several studies have found that treating children diagnosed with attention-deficit/hyperactivity disorder (ADHD) with stimulant medications reduces their likelihood of developing substance abuse disorders later in life. However, findings are not conclusive and more research needs to be conducted to evaluate whether exposure to stimulant drugs may predispose individuals to addiction and other mental disorders. NIDA also plans to begin studying this issue in its Clinical Trials Network.

Item

Drug Abuse and HIV/AIDS--The Committee understands HIV/AIDS continues to disproportionately affect vulnerable populations in the United States (e.g., criminal justice populations, pregnant women, minorities and youth) and that drug abuse is often a factor in transmission of HIV/AIDS. Therefore, the Committee urges NIDA to continue its support of research that is focused on the development and testing of drug-abuse related interventions designed to reduce the spread of HIV/AIDS in these populations (p. 147).

Actions taken or to be taken

An estimated 40 million people were living with HIV/AIDS in 2002 with 5 million new infections that year. Within the U.S. approximately 40,000 new cases of HIV are contracted annually. NIDA recognizes the need to support innovative research that is aimed at reducing the burden that this devastating condition places on the U.S. healthcare system. Within the past year NIDA has issued three requests for applications (RFAs) that specifically address HIV/AIDS in vulnerable populations and supported the development of a number of research protocols on the topic.

In January 2004, NIDA and NIMH issued a joint RFA entitled *HIV/AIDS, Drug Use and Highly Vulnerable Youth: Targeting Research Gaps* (RFA-DA-04-012) to address critical gaps in research on HIV/AIDS prevention, treatment and related health issues among highly vulnerable youth. In September 2004 six grants were awarded under this RFA. These projects will address a range of issues such as the development of behavioral interventions for minority women; marijuana use, gender, and adolescent HIV sexual risk; as well as HIV risk and substance use among adolescent couples.

In addition to youth it is a well-established fact that those involved in the criminal justice system are often at increased risk for HIV. NIDA is currently supporting three projects within the National Criminal Justice Drug Abuse Treatment Study (CJ-DATS) that will address HIV risk in juvenile offenders, as well as adult men and women. The goal of CJ-DATS is to establish and utilize a research infrastructure to develop and test models for an integrated approach to the treatment of incarcerated individuals with drug abuse or addictive disorders, including both treatment in jail or prison and treatment as part of re-entry into the community. One NIDA supported study under the CJDATS will evaluate the use of family-oriented HIV/AIDS interventions in comparison to the standard HIV prevention program as a part of a family-based intervention for substance abuse juvenile offenders. NIDA is also currently developing two

projects for offenders leaving prison and re-entering the community related to decreasing HIV risk--one for men and one for women.

In December 2003, NIDA issued an RFA entitled *Targeted Integrative Research in Drug Abuse and HIV/AIDS in Pregnancy* (RFA-DA-04-010). Through this RFA, NIDA invited targeted integrative research on epidemiological, prevention and treatment service approaches that focus on drug abuse, HIV/AIDS and other medical consequences of drug abuse specifically relevant to pregnant women and females of childbearing age. One grant awarded under this RFA will evaluate a combined motivational and cognitive behavioral intervention for substance using pregnant women that is designed to simultaneously reduce their substance use and other HIV risk behaviors.

In November 2003, NIDA, in collaboration with NIAAA and NIMH, issued a PA entitled *HIV/AIDS, Severe Mental Illness and Homelessness* (PA-04-024). The goal of this PA is to focus research on persons with severe mental illness, either before or after HIV infection, and to expand HIV-related research to homeless persons. NIDA looks forward to reviewing future submissions under this PA.

Item

Emerging Drugs – The Committee is concerned regarding the abuse of over-the-counter medications, including dextromethorphan [DXM] and steroids. Recognizing the significant role that NIDA has played in monitoring drug trends and responding to emerging drug problems like methamphetamine and prescription drugs, the Institute is encouraged to continue to increase its research and dissemination efforts on emerging drug problems (p.147).

Actions taken or to be taken

The National Institute on Drug Abuse (NIDA) recognizes that the landscape of drug abuse is never static. NIDA is committed to monitoring drug trends, through mechanisms such as the Community Epidemiology Work Group and NIDA's Monitoring the Future Study. NIDA also continues to rapidly share information on emerging drug problems, while maintaining a comprehensive research portfolio that will reduce the burden of drug abuse on society, including increasing our ability to be proactive in responding to emerging drug problems.

Specific areas of concern:

Dextromethorphan: More than 80 over-the-counter cold medicines contain dextromethorphan (DXM), which can be an effective cough suppressant when taken as directed. However, DXM is also a chemical that produces psychedelic and harmful effects when taken in large quantities. NIDA is currently supporting research focused on the neuropharmacology of DXM; including an investigation of the pharmacology of DXM with regard to its actions as a drug of abuse and a study on DXM's detrimental effects on the developing brain. In March 2004, NIDA brought in the world's leading experts to share their knowledge on this subject. The misuse of DXM was also discussed when NIDA's long-standing Community Epidemiology Workgroup members met this past summer.

Steroids: NIDA is currently supporting about numerous projects focused on various aspects of anabolic steroid abuse. Scientists are investigating a variety of topics, including a link between

steroid use and mood swings ranging from periods of violent, even homicidal, episodes known as "roid rages" to bouts of depression when the drugs are stopped. Other studies investigate the effect of sex steroids on cognition, the specific effect of androgenic anabolic steroids (AAS) in girls, and the extent of drug-drug interactions when used in conjunction with other drugs of abuse, such as cocaine or opiates. NIDA dissemination efforts on this topic continue unabated, including the development of publications on this issue, a steroid specific website, press conferences and several press releases highlighting new science findings. In November 2004, NIDA issued a press release and did media interviews on a NIDA study, published in the November issue of the *Archives of Pediatrics and Adolescent Medicine* that focused on reducing steroid and other drug use among high school girls. The curriculum, named ATHENA (Athletes Targeting Healthy Exercise and Nutrition Alternatives), is sport-team centered and taught by coaches and student leaders during 8 weekly 45-minute sessions that are incorporated into team practice activities. This ATHENA program is modeled after the successful ATLAS (Adolescents Training and Learning to Avoid Steroids) Program developed by the same researchers to reduce risk factors for use of anabolic steroids and other drugs in male high school athletes.

Prescription drugs: The numbers of Americans who use prescription drugs for non-medical purposes has increased in recent years at a staggering rate. Opiates/narcotics (excluding heroin) appear increasingly in drug indicator data from emergency rooms, particularly hydrocodone and oxycodone products. In response to this emerging threat NIDA has issued a PA on prescription drug abuse to encourage more research on this topic. A public outreach campaign also has been launched to educate individuals on this topic. NIDA is working with other Federal Agencies, like SAMHSA to reduce the abuse of prescription drugs. NIDA staff continues to share new science on this topic making presentations to both public and scientific audiences. A new Community Drug Alert Bulletin addressing the issue of prescription drug abuse is under development and a special issue of the CEWG Report focusing on prescription drug abuse was released in November 2004. Additionally, in August of 2004 NIDA issued an update of its InfoFacts on "Prescription Pain and Other Medications", with emphasis on their abuse liability.

Item

***Long-Term Consequences of Marijuana Use*--**The Committee is concerned with the continuing widespread use of marijuana. Research shows that marijuana can be detrimental to educational attainment, work performance, and cognitive function. However, more information is needed in order to assess the full impact of long-term marijuana use. The committee urges NIDA to support increased efforts to assess the long-term consequences of marijuana use on cognitive abilities, achievement, and mental and physical health (p. 147).

Actions taken or to be taken

NIDA continues to actively pursue research on the cognitive, and mental consequences of long-term use of marijuana. Most of the recent NIDA grants awarded on this topic focus on the basic neurocognitive effects of chronic use of cannabinoids (the principal psychoactive constituents of marijuana) on neural plasticity, sensory function, memory and behavior. NIDA also supports research on a range of withdrawal symptoms associated with the abrupt cessation of chronic marijuana use, such as anxiety, irritability, somatic complaints and difficulty sleeping, as well as research on the impact of chronic marijuana use in adolescence on school dropout and truancy. A recent NIDA-funded epidemiological study has shown that long-term cannabis use is

associated with lower college completion rates and household incomes in addition to subjective perceptions of impaired cognitive abilities, social life, physical and mental health. This is consistent with the results of another study in which heavy cannabis users (both current and former) differed markedly on various measures of life accomplishment from controls.

NIDA's portfolio on the clinical consequences of chronic marijuana use has increased in response to evidence showing significant effects of marijuana use in the human body. These include an increase in NIDA-supported research on the potential long-term effects of marijuana on the immune, endocrine, reproductive and cardiovascular systems, and potential carcinogenic effects as well. The recent observation that the cannabinoid system plays an important regulatory role in the establishment and maintenance of normal pregnancy in a mouse model offers a window into the novel and far-reaching implications of research on chronic marijuana use.

NIDA issued two RFAs aimed at either developing treatments for, or understanding the developmental impact of chronic marijuana use. RFA-DA-04-014 supports the development of medications for cannabis-related disorders, such as delirium, psychosis, and anxiety, with special emphasis on the treatment of children and adolescents and the medical consequences of long-term use. RFA-DA-04-016 seeks to support investigations on the effects of exposure to marijuana on the developing brain, from the prenatal period through the transition to adulthood. The focus is on influences on brain biochemical, physiological, morphological, and functional parameters, and/or on cognitive, behavioral, and social outcomes resulting from such influences. NIDA will continue to support efforts designed to promote a better understanding of the consequences of chronic marijuana use in the belief that such efforts are critical for the development of effective intervention strategies and intelligent public policy decisions.

Item

Medical Consequences—The Committee recognizes that addiction is a disorder that affects the course of other diseases such as cancer, cardiovascular and infectious diseases. Therefore, the Committee urges the NIDA to continue to support research on the medical consequences associated with drug abuse and addiction (p.147).

Action taken or to be taken

The impact of addiction can be far reaching. It often occurs with other medical diseases, including infectious diseases and mental illnesses. The consequences can even impact children who were prenatally exposed to drugs during pregnancy. Cardiovascular disease, stroke, cancer, HIV/AIDS, hepatitis, lung disease, and even obesity are all impacted by addiction. To address this NIDA is supporting a comprehensive research portfolio that is looking at the medical consequences that each drug brings in it wake, and is also engaging in a large outreach and education campaign to inform patients, the public and primary care physicians about these consequences.

Of particular importance is the link between drug abuse and HIV/AIDS. It is now known that injection drug use directly or indirectly accounts for more than one-third (36%) of AIDS cases. Even more alarming is that an estimated 80-90% of HIV-infected injection drug users are also infected with hepatitis C. To address this problem, NIDA continues to support a wide spectrum

of research on the link between substance abuse and HIV/AIDS, as well as the epidemiology, natural history, underlying pathogenesis, prevention and treatment of HIV/HCV coinfections among drug abusers.

NIDA research has also shown that while chronic drug abusers can comply with medication regimens, a large percentage of them do not. We still need to learn much more about both adapting medication regimens for drug abusers and techniques for increasing their adherence. Moreover, some illicit drugs and drug abuse medications can interact with medications used for treating diseases, resulting in possible loss of efficacy and adverse effects. NIDA will support research that works toward the identification of such interactions and the development of alternative regimens.

NIDA is also committed to supporting research that will help us better treat patients who suffer from both substance abuse and mental illnesses. It is estimated that 6 out of 10 substance abusers also suffer from mental illnesses.

Many of the health consequences of drug abuse also have implications for the health of the non-drug-abusing public. Tuberculosis (TB) is an important example. Chronic drug abusers have higher rates of TB infection and disease than the general population, largely because inadequate nutrition, HIV/AIDS, and other factors lower their resistance. Reducing this high prevalence by screening and treating infected drug abusers is an important strategy in efforts to control TB. NIDA serves as an active member on a Federal Task Force on TB, working to design strategies to eliminate TB from the US.

Item

***Medications Development*--**The Committee applauds NIDA for over a decade of leadership in working with private industry to develop anti-addiction medications and is pleased this collaboration has resulted in a new medication for opiate addiction. The Committee encourages NIDA to continue its work with the private sector to develop anti-addiction medications, particularly for cocaine, methamphetamine, and marijuana (p.148).

Action taken or to be taken

The National Institute on Drug Abuse is committed to working with the private sector to develop medications to be used in conjunction with behavioral therapies for the treatment of drug addiction. NIDA continues to pursue collaborations with pharmaceutical companies in an effort to move their novel and promising compounds forward to clinical evaluation in the treatment of addictive disorders. Currently, NIDA is discussing a number of potential medications. For example, compounds that can dampen the stress response (CRF-1 antagonists) may be useful because of the important role that stress plays in relapse to addiction to drugs of abuse, alcohol, and nicotine. These medications are currently being developed for the treatment of anxiety disorders and depression, but they may also have a role in the treatment of drug abuse. NIDA is also working with pharmaceutical companies in the development of compounds that block the dopamine D3 receptor, a receptor that may block the rewarding effects of drugs, but not other pleasures like food or sex.

Examples of Existing Medications with Potential Utility in Treating Addiction:

- Topiramate (TOPAMAX), a marketed anti-epileptic medication that affects both glutamate and GABA mechanisms, has been shown to reduce alcohol drinking and assist smokers to quit. A recent NIDA funded study at the University of Pennsylvania showed that topiramate was effective in blocking a return to cocaine use. Confirmatory studies will begin place in the next year. NIDA is also interested in evaluating this interesting medication in the treatment of methamphetamine dependence.

- Baclofen, A GABA B agonist, was shown to reduce cocaine use in a clinical trial conducted at UCLA. NIDA is funding a multi-center trial of baclofen to confirm these results.

- Disulfiram (Antabuse), marketed for treating alcoholism, is also showing promise in the treatment of cocaine dependence. Several NIDA sponsored studies conducted at Yale University documented interaction of disulfiram with cocaine in humans. Five efficacy trials conducted with different populations of cocaine- dependent individuals suggest that disulfiram in combination with each of three different therapeutic interventions (cognitive behavioral treatment, 12 step facilitation, or clinical management) might be effective in treating cocaine dependence. NIDA is planning a multi-center trial to commence in the next fiscal year.

- Gamma vinyl-GABA (GVG, vigabatrin) is an anti-epileptic medication, used in Europe and other nations (but not in the U.S.), which increases the amount of an inhibitory chemical in the brain (GABA), thereby reducing the incidence of convulsions in people who have epilepsy. Basic research on GVG revealed that it also alters the reward circuitry of the brain that is affected by nearly all drugs of abuse. NIDA-funded researchers conducted a small clinical study in Mexico to assess whether GVG could be useful in the treatment of cocaine addiction. Participants reported that their cravings for the drug disappeared within 2-3 weeks after starting GVG treatment. The study completers also reported increased self-esteem, improved relations with family members, and increased employment or attempts to obtain jobs. The results of this study indicate the need for a larger, more rigorous clinical trial to ascertain its efficacy and/or to determine under what circumstances GVG can be most useful.

Also, because marijuana is the most commonly abused illegal drug in the United States, NIDA has increased its emphasis on identifying treatments for marijuana addiction. Several RFAs were issued. One in particular, RFA-DA-04-014 "Medications Development for Cannabis-Related Disorder," sought grant applications focusing on the identification, evaluation and development of safe and effective pharmacological treatments for cannabis-related disorders (CRDs), and their comorbidity with other medical and psychiatric disorders (e.g., depression), with special interest in the treatment of children and adolescents.19 applications were received in response to this RFA.

Item

Methamphetamine Abuse – The Committee continues to be concerned with the rate of methamphetamine abuse across the Nation. The problem is especially acute in Midwestern

States. The Committee again urges NIDA to expand its research on improved methods of prevention and treatment of methamphetamine abuse.

Action taken or to be taken

In 2004, methamphetamine abuse continued to be a problem in many states, including those in the Midwest. For example, in Missouri, methamphetamine, along with alcohol, remained a primary drug of abuse in both the outlying rural and statewide areas. Moreover, in a recent NIDA-funded survey of homeless and runaway youth in Denver, Colorado (74% of which were 16-25 years of age), 18% reported use of methamphetamine within the past 9 months, compared to 1.7% past year use for 18-25 year olds in the National Survey on Drug Use and Health that same year (Van Leeuwen JM et al., 2004 - J Community Health 29: 217-229). NIDA recognizes the multi-faceted problems posed by methamphetamine abuse and addiction and is continuing to increase its research efforts accordingly.

A recent NIDA funded study demonstrating structural abnormalities in regions of the brain associated with cognition and emotion, highlights the need for continued efforts in all aspects of methamphetamine research (Thompson PM et al., 2004 - J Neurosci 24: 6028-36). Therefore, NIDA has recently funded new grants to better understand methamphetamine neurotoxicity, its cognitive effects, and potential mechanisms of neuroprotection as well as studies that develop and test new prevention and treatment interventions. In the prevention arena, NIDA-supported researchers are evaluating drug abuse prevention programs, which typically target elementary and intermediate school students, to determine their potential for reducing methamphetamine abuse in older adolescents.

As part of its efforts in developing promising pharmacotherapies to treat methamphetamine abuse and addiction, the NIDA Methamphetamine Treatment Discovery Program (MTDP) was established to identify, evaluate, and recommend potential treatments for the medical management of methamphetamine dependence and in reversing neurotoxicity and cognitive impairment using a preclinical approach. Through the MTDP, NIDA recently awarded a contract to test compounds for their effects in animal models of methamphetamine-induced cognitive impairment.

NIDA also established the Methamphetamine Clinical Trials Group (MCTG) to conduct phase I (safety) and phase II (efficacy) clinical studies. It has sites in geographic areas in which methamphetamine abuse is particularly high, including San Diego, Kansas City, Des Moines, Costa Mesa, San Antonio, and Honolulu. A number of protocols are underway at various stages of investigation. Compounds and medications like bupropion, selegeline, Aripiperazole, GBR 12909, and lobeline are all undergoing testing.

NIDA is also conducting research on behavioral therapies that might be effective for treating methamphetamine addiction. The "Matrix Model," a 16-week program that includes group and individual therapy, has recently been tested by NIDA grantees for efficacy in treating methamphetamine abuse.

It is important to realize that no single type of treatment will be effective for everyone. It is expected that, as with other types of addiction, combining pharmacotherapies with behavioral

therapies will be the most effective method to treat methamphetamine abusers in this country. NIDA will continue with these efforts to bring to the citizens of the Midwest and across the Nation new ways to combat methamphetamine abuse.

Item

Outreach -- The committee commends NIDA for its outreach and work with State substance abuse authorities to reduce the current 10- to 20-year lag between the discovery of an effective treatment of intervention and its availability at the community level. The Committee is pleased with NIDA's collaboration with SAMHSA on strengthening State agencies' capacity to support and engage in research that will foster statewide adoption of science-based policies and practices. The Committee also encourages NIDA to continue collaborative work with States to ensure that research findings are relevant and adaptable by State Substance Abuse systems (p.148).

Action taken or to be taken

NIDA is continuing to work with SAMHSA and others to bridge the gap between science and services to ensure that substance abuse research is both useful and used by local communities. NIDA has taken a multi-pronged approach in this endeavor, as exemplified by the Drug Abuse Treatment Clinical Trials Network (CTN), the NIDA-SAMHSA-ATTC Blending initiative, and, most recently, efforts to engage Single State Authorities.

Established in 1999, NIDA's CTN has grown to include over 17 research centers or nodes spread across the country as a critical bridge between research and practice. Through this network, community treatment providers and researchers work side-by-side, using science to improve the quality of treatment. The CTN infrastructure is used to directly test the effectiveness of new and improved interventions in real-life community settings with diverse populations, allowing us to expand treatment options for providers and patients.

In collaboration with SAMHSA, NIDA has developed a Blending initiative, comprising teams of NIDA researchers, community treatment providers, members of CSAT's ATTCs. These "blending teams" work to develop dissemination materials and implementation strategies for community practitioners based on NIDA research findings and CTN results. Current projects include: buprenorphine awareness for non-physician practitioners; addiction severity index (ASI) as a case management tool; motivational interviewing training materials. Teams are now forming to develop a dissemination plan for positive results obtained in the CTN using buprenorphine as a detoxification medicine for heroin addiction, and motivational incentives to enhance and sustain treatment effects.

SSAs are uniquely positioned to raise the quality of drug abuse treatment services in their States; therefore NIDA is working with SAMHSA and NASADAD to facilitate communication between the SSAs, NIDA's CTN, and ATTC (Addiction Technology Transfer Center) representatives. Four SSA Director meetings have been convened, which have proven to be very successful in terms of bi-directional discussion and information dissemination. Another SSA meeting is scheduled for June 2005 in conjunction with the larger, treatment-oriented NIDA Blending Conference in Miami, Florida. NIDA also invited Single State Agency Directors to participate in the most recent "Blending Clinical Practice & Research: Forging Partnerships in the Great Lakes States to Enhance Drug Addiction Treatment" meeting in Detroit, Michigan September 27-28,

2004. This conference provided an opportunity for clinicians and researchers to examine cutting-edge findings about drug use and addiction and discuss their application to clinical practice. Outreach efforts like this will continue to strengthen State agencies ability to adopt science-based interventions.

In April 2004, NIDA and SAMHSA issued an RFA titled, "Enhancing State Capacity to Foster Adoption of Science-Based Practices." NIDA has committed approximately $1.35 million in FY 2005 to fund grants from this RFA. This RFA encourages state agencies to team with research organizations in their states to apply for grants that will provide them with resources to support research that will help improve the delivery of publicly supported drug abuse prevention and or treatment services.

NIDA is also actively engaged in the "Science to Services " Initiative that SAMHSA leads, which also helps in outreach efforts.

Item

Primary Care Settings and Youth--Primary care settings, such as offices of pediatricians and general practitioners, are potential key points of access to prevent and treat problem drug use among young people; yet primary care and drug abuse services are commonly delivered through separate systems. The Committee encourages NIDA to expand support for health services research on effective ways to educate primary care providers about drug abuse; develop brief behavioral interventions for preventing and treating drug use and related health problems, particularly among adolescents; and develop methods to integrate drug abuse screening, assessment, prevention and treatment into primary health care settings (p.148).

Actions taken or to be taken

New ways of coordinating primary care and drug abuse prevention and treatment services hold promise for the implementation of more holistic, integrated, and cost-effective approaches in the provision of health care for individuals with problem drug use, abuse, and related health problems. Over the course of the past year NIDA has engaged in multiple activities to not only advance the research in the field, but also to coordinate a number of activities to educate the public on this topic. These activities have included issuing a Request for Applications (RFA), holding meetings to encourage a dialogue on the topic among professionals, as well as taking part in a large public outreach campaign.

In December 2003, NIDA, in collaboration with the Substance Abuse and Mental Health Services Administration, the Agency for Healthcare Research and Quality, and the Health Resources and Services Administration, issued an RFA entitled *Screening and Intervention for Youth in Primary Care Settings* (RFA-DA-04-006). This announcement encourages research to develop brief behavioral interventions that can be used in primary care settings to prevent and treat problem drug use and related health problems in youth. As a result of this announcement seven grants were funded to assess the effectiveness of using brief interventions in primary care settings. These grants will be researching topics such as the utilization of a brief intervention among specific populations (e.g., adolescent female marijuana users), the development and evaluation of approaches to screen and assess adolescents seen in primary care settings, as well as research on the technology used to deliver these interventions.

NIDA has also launched an initiative to help educate healthcare professionals on the topic of drug abuse. As a part of this initiative drug abuse information kits were sent to Baltimore area pediatricians, encouraging them to discuss the dangers of drugs and tobacco with their adolescent patients. Together with the Maryland chapter of the American Academy of Pediatrics and the Sheppard Pratt Health System, a nonprofit treatment facility, NIDA held an innovative seminar in December of 2003 to train physicians and other health care practitioners in methods for recognizing the signs and symptoms of tobacco and drug use, as well as how to ask questions related to the prevention, intervention, and treatment of drug and tobacco use. In order to capitalize on the momentum created by this event NIDA has recently initiated a contract to further develop outreach activities for primary care physicians regarding the topic of drug abuse. NIDA has also included in its Prescription Drug Abuse PA a focus on health professional education and outreach in primary care settings.

Also, as a part of this outreach effort and with the assistance of coalition partners, such as the Office of the Mayor and the Maryland Department of Health and Mental Hygiene, NIDA cosponsored the drug free and alcohol free New Year's Spectacular event in Baltimore's Inner Harbor. During this event NIDA representatives conducted extensive outreach efforts to educate attendees about the health consequences of drug abuse, especially among children. In addition to these activities NIDA is also planning to take part in a conference in conjunction with the National Center on Addiction and Substance Abuse (Columbia University) on substance abuse and primary care settings in Washington D.C. in April 2005.

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2005 Amount Authorized	FY 2005 Appropriation	2006 Amount Authorized	2006 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$983,857,000	Indefinite	$985,189,000
National Institute on Drug Abuse	Section 41B	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	22,562,000		24,941,000
Total, Budget Authority				1,006,419,000		1,010,130,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1997	$312,014,000 2/	$487,341,000	$317,936,000 2/	$489,375,000 3/
1998	358,475,000	525,641,000	531,751,000	527,175,000
1999	393,934,000 2/4/	527,426,000	603,274,000	603,274,000
Rescission				(400,000)
2000	429,246,000 2/	656,551,000	682,536,000	689,448,000
Rescission				(3,667,000)
2001	496,294,000 2/	788,201,000	789,038,000	781,327,000
Rescission				(331,000)
2002	907,369,000	900,389,000	902,000,000	888,105,000
Rescission				(372,000)
2003	960,582,000	968,013,000	968,013,000	968,013,000
Rescission				(6,292,000)
2004	995,614,000	995,614,000	997,614,000	997,614,000
Rescission				(6,461,000)
2005	1,019,060,000	1,019,060,000	1,026,200,000	1,014,760,000
Rescission				(8,341,000)
2006	1,010,130,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.
3/ Excludes enacted administrative reductions of $215,000.
4/ Reflects a decrease of $1,195,000 for the budget amendment for bioterrorism.

NATIONAL INSTITUTES OF HEALTH

National Institute on Drug Abuse

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Office of the Director	21	18	18
Office of Extramural Affairs	16	16	16
Office of Planning and Resource Management	38	38	38
Office of Science Policy and Communications	33	32	32
Division of Epidemiology, Services & Prevention Research	33	35	35
Division of Basic Neurosciences & Behavior Research	26	26	26
Division of Pharmacotherapies & Medical Consequences of Drug Abuse	38	38	38
Center for the Clinical Trials Network	11	11	11
Division of Clinical Neuroscience, Development and Behavioral Treatment	13	13	13
Intramural Research Program	113	121	121
Total	342	348	348
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2002	11.4
2003	11.4
2004	11.9
2005	11.9
2006	11.9

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Detail of Positions

GRADE	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Total - ES Positions	4	4	4
Total - ES Salary	$578,196	$599,589	$615,178
GM/GS-15	62	62	62
GM/GS-14	85	86	86
GM/GS-13	33	34	34
GS-12	37	37	37
GS-11	12	12	12
GS-10	1	1	1
GS-9	13	14	14
GS-8	13	20	20
GS-7	8	11	11
GS-6	1	8	8
GS-5	4	5	5
GS-4	0	0	0
GS-3	3	3	3
GS-2	0	0	0
GS-1	0	0	0
Subtotal	272	293	293
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	13	12	12
Director Grade	3	3	3
Senior Grade	2	2	2
Full Grade			
Senior Assistant Grade			
Assistant Grade			
Subtotal	18	17	17
Ungraded	49	49	49
Total permanent positions	311	311	311
Total positions, end of year	364	364	364
Total full-time equivalent (FTE) employment,end of year	342	348	348
Average ES salary	$144,549	$149,897	$153,794
Average GM/GS grade	11.9	11.9	11.9
Average GM/GS salary	$90,842	$94,203	$96,652