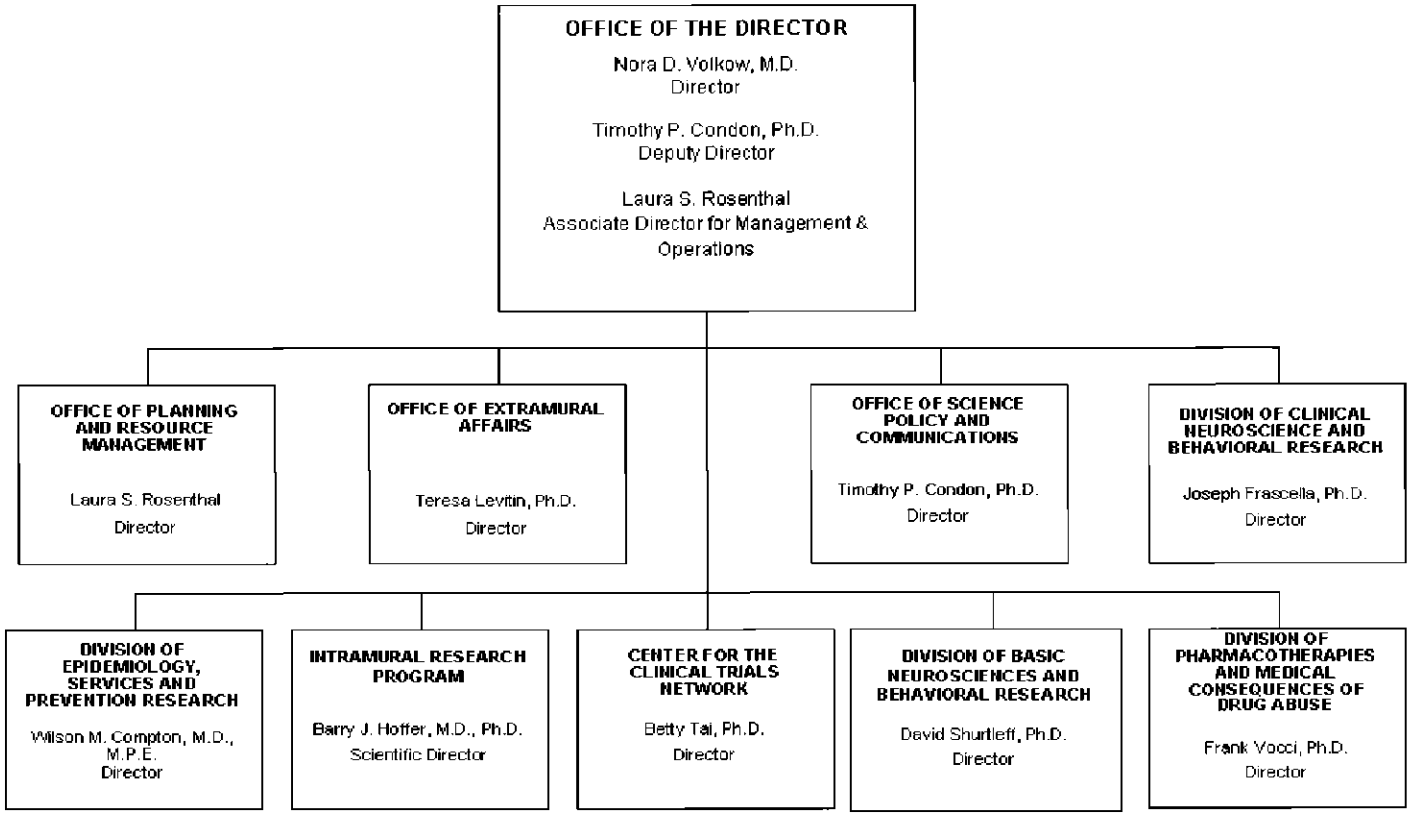
DEPARTMENT OF HEALTH AND HUMAN SERVICES+

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, [$1,010,130,000] *$994,829,000.*

[Departments of Labor, Health and Human Services, Education, and Related Agencies Appropriations Act, 2006, as enacted by Public Law (109-149)]

National Institutes of Health
National Institute on Drug Abuse

Amounts Available for Obligation 1/

Source of Funding	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Appropriation	$1,014,760,000	$1,010,130,000	$994,829,000
Enacted Rescissions	(8,341,000)	(10,101,000)	0
Subtotal, Adjusted Appropriation	1,006,419,000	1,000,029,000	994,829,000
Real transfer under NIH Director's one-percent transfer authority for Roadmap	(6,363,000)	(8,937,000)	0
	0	0	0
Comparative transfer from OD for NIH Roadmap	6,363,000	8,937,000	0
	0	0	0
Subtotal, adjusted budget authority	1,006,419,000	1,000,029,000	994,829,000
Unobligated Balance, start of year	0	0	0
Revenue from Breast Cancer Stamp 2/	0		
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	1,006,419,000	1,000,029,000	994,829,000
Unobligated balance lapsing	0	0	0
Total obligations	1,006,419,000	1,000,029,000	994,829,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2005 - $9,329,000 FY 2006 -$11,324,000 FY 2007 - $11,772,000
Excludes $56,000 in FY 2006 and $141,000 in FY 2007 for royalties.

Justification

National Institute of

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

Budget Authority:

FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
336	$1,006,419,000	362	$1,000,029,000	364	$994,829,000	2	-$5,200,000

This document provides justification for the Fiscal Year 2007 activities of the National Institute on Drug Abuse, including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2007 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)." Detailed information on the NIH Roadmap for Medical Research may be found in the Overview section.

INTRODUCTION

NIDA is the world's largest supporter of research on drug abuse and addiction. Our scientific research addresses the most fundamental and essential questions about drug abuse, including how drugs work in the brain, who is most vulnerable to becoming addicted, and how we can best develop and test new drug treatment and prevention approaches. We also track emerging drug use trends—and this year we have some good news to report. Our Monitoring the Future survey (MTF) revealed a 19 percent decline in overall illicit drug use among 8th, 10th, and 12th graders combined over the last four years. However, the MTF survey also reports that inhalant abuse has risen among 8th graders between 2002 and 2005 and the abuse of prescription painkillers is continuing at alarming rates, especially among 12th graders, for whom Vicodin and OxyContin are among the most commonly abused drugs. Also, while methamphetamine abuse is decreasing in teens, it appears to be growing in popularity in a number of new locations and populations around the country. Therefore, much remains to be done.

Drug abuse is costly to Americans, tearing at the fabric of our society and taking a huge financial toll on our resources. Beyond its inextricable link to the spread of infectious diseases, such as HIV/AIDS, sexually transmitted diseases (STDs), tuberculosis, and hepatitis C, drug abuse is often implicated in family disintegration, loss of employment, failure in school, domestic violence, child abuse, and other crimes. The 2004 National Survey on Drug Use and Health puts the number of people addicted to illicit drugs and tobacco at approximately 5.4 million. Placing dollar figures on the

"The inability to stop drug use is the essence of addiction....It's like riding in a car with no brakes." —Nora Volkow, NIDA Director

"Drugs hijack the survival hierarchy of the brain to the point where they are not just drugs—they are life itself."—Kevin T. McCauley, MD, former Demerol addict

problem, smoking and illegal drugs cost this country about $338 billion a year, with illicit drug use alone accounting for about $180 billion in crime, productivity loss, health care, incarceration, and drug enforcement.[a]

Scientific knowledge is the best tool for addressing the disease of addiction.

Decades of leading edge research have advanced our progress in achieving the goal of preventing and treating drug abuse. Now, with new tools, techniques, and knowledge, we are poised to take advantage of what we know to change the course of drug addiction in this country. We aim to address the nation's most important research needs while remaining sufficiently flexible to respond to new scientific opportunities. Through innovative use of brain imaging technologies, for example, we can now literally see into the brains of people addicted to drugs and discover how drugs are impacting brain function. Advances in genetics are letting us begin to identify genes of vulnerability or protection so we can tailor our interventions to have the greatest impact. And growing knowledge about the dynamic interactions of genes with environment confirms addiction as a complex and chronic disease of the brain with many contributors to its expression in individuals.

Understanding the brain is key to understanding and preventing addiction.

The basic and clinical research NIDA has sponsored for more than 30 years has led to an ever-increasing body of knowledge about how drugs of abuse exert their effects in the brain. Recent studies have illuminated many of the cellular, molecular, and basic brain circuits involved in addiction, revealing detailed cascades of cellular events, some of which lead to long-lasting structural and functional changes caused by drug abuse. This knowledge has helped us to zero in on potential molecular targets for addiction medications and will allow us to see whether our treatments are working as intended. Neuroimaging tools such as functional magnetic resonance imaging (fMRI) allow us for the first time to study how the human brain functions and how it is affected by drugs during the transition from childhood to adolescence to adulthood.

"The addiction process often begins in early adolescence, when teens may unknowing place themselves on the fast track to long-term drug addiction, perhaps at a point already beyond their control."—Don Kurth, Board of American Society of Addiction Medicine

Addiction is a developmental disease.

We know now that the brain continues to develop into early adulthood. Recent imaging data reveal that the prefrontal cortex—the region of the brain involved in judgment, decision-making, and control of emotional responses—is one of the last areas of the brain to mature. This

a The Health Consequences of Smoking: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2004.

Office of National Drug Control Policy (2004). The Economic Costs of Drug Abuse in the United States, 1992-2002. Washington, DC: Executive Office of the President (Publication No. 207303).

knowledge suggests that age matters when it comes to drug abuse: exposure to drugs of abuse during adolescence or childhood may adversely affect brain development and increase vulnerability to drug effects and addiction. Yet, the inherent plasticity during this period of continued development might also present opportunities for resiliency and for receptivity to intervention that can alter the course of addiction. NIDA's enhanced capacity to investigate the motivational processes at work in the young brain can give us valuable insight into teen decisions whether to use drugs, and help us to develop prevention messages and intervention strategies that are more likely to succeed with them.

Additionally, NIDA has been supporting a number of longitudinal studies on cohorts of children prenatally exposed to drugs, which gather information about their cognitive and emotional development, as well as their vulnerability to addiction later in life. The application of high-resolution brain-imaging technologies and new genetic databases to these cohorts will reveal more about the trajectory of addiction and the contribution of social-environmental factors, including stress in childhood (e.g., physical or sexual abuse, poverty). As we gain knowledge of the individual differences in genes and the gene-environment interactions that make a person more vulnerable to addiction, we can tailor interventions for those at high risk.

We must continue to translate knowledge into effective treatments for drug abuse.

As a chronic disease, drug addiction for many people requires some level of continuous care, just like other chronic diseases, such as diabetes, asthma, and hypertension, which have similar rates of relapse (50-75 percent).[b] Treatment can help people stay off drugs and recover function of compromised brain systems that enable motivation, memory, and initiation of drive. Unfortunately, most people who need drug abuse treatment do not receive it.

In response, NIDA is creating an infrastructure for translating science into real-world treatment settings, to enable evidence-based treatments to move from "bench to bedside to community". We are taking an aggressive approach, reaching out to physicians, judges, law enforcement, and other pivotal members of society to educate them about substance abuse disorders and to promote a more integrated and compassionate system that addresses the reality of co-occurring diseases and other drug abuse consequences.

It is not enough merely to have the infrastructure needed to address our ambitious goals of blending science and practice. We must also now use it to translate our findings into effective community-based prevention and treatment programs. Our landmark "Blending Initiative" aims to do just that. NIDA has partnered with SAMHSA, and with researchers, clinicians, practitioners, and state alcohol and drug abuse directors to share strategies for incorporating research-based treatment findings into community settings (see Story of Discovery). Further, a recent evaluation of our dissemination efforts showed that the substance abuse information we convey to the public

"We must continue our important work aimed at advancing the science and erasing the stigma to solve the problem of drug abuse in this country."—Nora Volkow, NIDA Director

[b] Volkow N. Presentation for ASAM, Washington, DC (10-26-05).

through multiple publications and websites is being applied across a variety of settings, extending our outreach efforts.

The selected initiatives summarized below are those that we feel best represent the areas we will continue to emphasize. NIDA is proud of these efforts and of our strategic planning approach that focuses resources on those areas that could make the greatest difference to Americans directly or indirectly affected by drug abuse and addiction. Through sponsoring pivotal research and working with others, we are bringing new insights into the mechanisms of addiction to communities around the country, helping to reduce associated stigma and suffering. Our initiatives also support two of the three goals of the President's National Drug Strategy: (1) stopping use before it starts and (2) healing America's drug users.

NEW AND EXPANDED 2007 RESEARCH INITIATIVES

New Pharmacotherapies for Methamphetamine and Other Addictions. Research has confirmed that addiction is a treatable, though chronic and relapsing, disease of the brain. NIDA research shows that comprehensive treatments (i.e., those that include a combination of available medications, behavioral treatments, and job training and referral services) tailored to the needs of the individual patient have the highest success rates.

Since the establishment of a Medications Development Program by Congress in 1992, we have advanced a series of research initiatives aimed at finding medications for people addicted to cocaine, opiates, methamphetamine, marijuana, and other drugs of abuse. This push is particularly important to NIDA, as efforts to enlist the private sector to help develop effective medications have been only partially successful, largely because of financial disincentives for the pharmaceutical companies as well as the continuing stigma associated with medications for treating addiction.

We will continue to support the development of novel pharmacotherapies through a variety of mechanisms intended to encourage research at all stages. Two innovative programs will be expanded or initiated in FY07. The first, Strategic Program for Innovative Research on Drug Addiction Pharmacotherapy (SPIRDAP), will support preclinical (animal and cellular) and clinical (human) research to identify promising compounds for treating addiction to cocaine, methamphetamine, or cannabis. The program requires applicants to form collaborations between basic and clinical scientists and encourages commercial participation. The second initiative focuses on pilot clinical trials of new medications to reduce or eliminate substance use disorders. It will invigorate the field by helping investigators generate sufficient safety and efficacy data to gain support for full-scale clinical trials of novel therapeutic medications, expediting their possible progression to real-world use.

One of our strategies in developing pharmacotherapies for addiction is to explore medications that are already FDA-approved to see if they could benefit patients being treated for addiction. For example, modafinil, a treatment for narcolepsy (a sleep disorder), promotes wakefulness and enhances memory, a quality potentially useful for ameliorating the cognitive dysfunction

associated with long-term use of stimulants, especially methamphetamine. We are aggressively pursuing medications to treat methamphetamine addiction, testing both the safety and efficacy of compounds potentially useful for treating various aspects of methamphetamine abuse.

NIDA's continued exploration of pharmacotherapies to help treat the disease of addiction responds to HHS strategic objectives (SOs) 1.4 to reduce substance abuse and to SOs 4.1 and 4.2 by advancing understanding of basic biomedical science to prevent and treat addiction and by accelerating private sector development of new drugs.

HIV/AIDS Among African Americans. Drug abuse and HIV/AIDS are intertwined epidemics with daunting health and social consequences. And while intravenous drug use is well known in this regard, less recognized is the role that drug abuse plays more generally in the spread of HIV, by increasing the likelihood of high-risk sex with infected partners. This is because of the addictive and intoxicating effects of many drugs, which can alter judgment and inhibition and lead people to engage in impulsive and unsafe behaviors. Drug abuse may also weaken the immune system, causing people to be more vulnerable to infection, and to experience a more severe progression of the illness and its consequences.

Thus, NIDA's response is multifaceted, including support of research to learn more about the pivotal role of drug abuse in the spread of HIV/AIDS and the differential impact of both drug abuse and HIV on certain racial and ethnic minorities, particularly African Americans. Effective prevention and treatment strategies must recognize drug abuse as an important contributor to the ongoing HIV/AIDS epidemic and should target those populations most at risk. African Americans, for example, comprise just 12 percent of the U.S. population, but accounted for half of the total AIDS cases diagnosed in 2003.[c] Moreover, African-American females accounted for 69 percent of the female HIV/AIDS diagnoses from 2000 through 2003—19 times the rate for White females and 5 times the rate for Hispanic females.[d] HIV/AIDS, in fact, is now the leading cause of death among all African-Americans ages 25-44, ahead of heart disease, accidents, cancer, and homicide.[e]

NIDA has recently issued a call for research, which will begin in FY06, to address these disparate rates of HIV/AIDS infection among African Americans. We are encouraging studies on HIV infection rates and disease progression in light of psychological factors, criminal justice involvement, and availability and use of treatment and services among African Americans. This important initiative will help identify risk and protective factors so as to develop culturally sensitive prevention interventions to reduce HIV acquisition and transmission and minimize associated health consequences, including diseases such as the hepatitis C virus (HCV).

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[c] Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report Vol. 15. Atlanta: US Department of Health and Human Services, Center for Disease Control and Prevention, p. 12 (2004). Available at: http://www.cdc.gov/hiv/stats/2003SurveillanceReport.htm.

[d] Morbidity and Mortality Weekly Report (MMWR). "Diagnosis of HIV/AIDS–32 States 2000–2003" 53(47):1106–1110, CDC, 2004. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5347a3.htm.

[e] Anderson RN, Smith BL, Deaths: Leading Causes for 2001, National Vital Statistics Reports 52(9):27-33, 2002.

Our planned initiative supports HHS SOs 1.1, 1.2, and 1.4 by addressing the behavioral and other factors contributing to the chronic disease of drug abuse (1.1), by seeking to reduce the incidence of HIV infection, a sexually transmitted disease (1.2), and by reducing substance abuse (1.4).

Prescription Opioid Abuse and Pain. Opioid analgesics, the most powerful medications available for the treatment of most pain conditions, enable many of the estimated 90 million Americans suffering from chronic pain to lead relatively normal and productive lives. However, opioid treatment of pain can also result in negative health consequences, such as intoxication and physical dependence and can sometimes lead to opioid abuse and addiction. Moreover, diversion or illicit acquisition of opioid medications is common, given that nearly three-fourths of the estimated 6 million people aged 12 and older who reported use of prescription psychoactive drugs non medically abused pain relievers, with young adults (18-25) showing the greatest increases in lifetime use from 2002 to 2004.[f] Younger populations are also involved, as revealed by findings from NIDA's 2005 Monitoring the Future Survey.

To combat these trends, NIDA's new Prescription Opioid Use and Abuse in the Treatment of Pain initiative will solicit a broad range of both human and animal studies from across the sciences. These include clinical neurobiological investigations using genetics, molecular biology, and brain imaging methods to reveal differences in addiction vulnerability among patients, as well as studies to yield information about the changes in brain cells and circuits that occur with sustained opioid treatment. Because opioid medications are prescribed for all age groups, NIDA is encouraging research that assesses the effects of chronic use over the lifespan.

Through this initiative, NIDA hopes to gain information on how to optimally treat patients with pain so that they do not become addicted. To that end, we are encouraging research on formulations to reduce abuse potential and diminish intoxicating effects, and on screening and diagnostic tools that primary care physicians can use to assess the potential for prescription drug abuse in their patients. We also intend to fund research to discover whether drugs can be prescribed or their use monitored so as to limit their abuse liability; to develop strong analgesics with minimum abuse potential; and to elucidate those factors (genetic, biological, and environmental) that predispose patients to, or protect patients from, opioid abuse and addiction.

NIDA's Prescription Opioid Abuse and Pain Initiative supports SO 1.4 to reduce substance abuse, as well as SO 4.1 by enhancing knowledge of prescription drug effects on brain processes, thereby advancing biomedical science to prevent the disease of addiction.

[f] National Survey on Drug Use and Health, Substance Abuse and Mental Health Services Administration, 2004.

STORIES OF DISCOVERY

Decades of marijuana research uncover a whole-body communication network with big therapeutic potential

Marijuana is the most commonly abused illicit substance in the United States, with an estimated 14.6 million Americans aged 12 and older reporting use of marijuana at least once in the month prior to the 2004 survey.[g] Marijuana use can produce adverse physical, mental, emotional, and behavioral changes and impair memory, learning, judgment, and perception. Its smoke can also harm the lungs and, contrary to popular belief, marijuana can be addictive, with profoundly negative consequences for young teens' development. These findings underlie NIDA's longstanding commitment to researching the addictive effects of marijuana on the brain and body, and the best ways to treat and prevent its abuse. Conversely, since 1839, when cannabis was introduced into the Western pharmacopoeia, there have been published reports suggesting that marijuana may also have pain-relieving, anticonvulsant, and appetitive stimulant properties. Thus, there's been a constant drive to use scientific tools to better understand marijuana's many effects and exploit the good ones for the public's benefit.

Unlocking marijuana's mystery

The body of evidence gathered on marijuana has revealed a complex signaling network capable not only of modulating reward, abuse, and addiction pathways, but also of influencing many other phenomena, such as memory, anxiety, pain, obesity, immunity, brain development, and pregnancy.

In 1964, in the first of what would be a long chain of breakthroughs, delta-9-tetrahydrocannabinol (THC) was identified as the compound that accounts for nearly all the pharmacological activities of marijuana. More than two decades later, two receptors (called cannabinoid 1 [CB1] and 2 [CB2] receptors) that can bind THC were discovered in quick succession. The discovery of THC receptors and the subsequent mapping of their locations throughout the brain provided a satisfactory explanation of marijuana's diverse effects. At the same time, it set off a race to find the natural compounds in the brain and body that could recognize and activate these receptors.

NIDA research stimulates development of cannabis-based therapies

Beginning in 1992, NIDA-supported research eventually zeroed in on a family of related lipid molecules that were structurally and functionally similar to THC. These endocannabinoids (as they came to be known), their receptors, and a retinue of activating enzymes form an intricate network responsible for many of marijuana's beneficial effects as well as its addictive potential.

Emboldened by this new knowledge, the pharmaceutical industry moved to invest significant resources in research and development of cannabis-based therapies for the treatment of obesity and other ailments. This move led Sanofi Recherche in 1994 to develop a promising cannabinoid receptor antagonist called SR141716 (aka Rimonabant). NIDA research conducted in 2001 and 2003 showed that Rimonabant can block the subjective "high" elicited by marijuana in humans,[h] and that it blocked the reinstatement of drug-seeking for cocaine and heroin in animal models,[i] suggesting that cannabinoid antagonists may also be useful in preventing relapse to a variety of drug use.. Now second generation medications are being developed that target other points in the endocannabinoid network.

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[g] NSDUH 2004.

[h] Huestis MA, Gorelick DA, Heishman SJ, Preston KL, Nelson RA, Moolchan ET, et al. Blockade of effects of smoked marijuana by the cb1-selective cannabinoid receptor antagonist sr141716. *Arch Gen Psychiatry* 58(4):322-328 (2001).

[i] Fattore et al. Cannabinoid mechanism in reinstatement of heroin-seeking after a long period of abstinence In rats. *Eur J Neurosci* 17(8):1723-26 (2003).
De Vries et al. Cannabinoid modulation of reinforcing and motivational properties of heroin-associated cues in rats. *Psychopharmacology* (Berl) 168(1-2):164-69 (2003).
De Vries et al. A cannabinoid mechanism in relapse to cocaine seeking. *Nat Med* 7(1):1151-54 (2001).

In 2003, NIDA-supported research helped establish the fact that endocannabinoids utilize a new mode of cellular communication in which the messenger molecules are not stored but are produced as needed.[j] Once released, they modulate how information is processed within and between cells. The final outcome of their actions depends on the type of endocannabinoid involved and the variety and location of the receptor being activated. Also in 2005, a NIDA study demonstrated that, like THC, specific endocannabinoids can serve as effective reinforcers of drug-taking behaviors.[k] Such developments provide direct evidence for the involvement of the endocannabinoid system in brain reward processes, and the basis for its rational exploitation toward the development of drug addiction therapies.

Researchers continue to tap marijuana's potential

While we still lack a full understanding of the physiological roles played by the endocannabinoid system, its ability to affect so many functions has been embraced by researchers eager to tap into a reservoir of novel targets with a wide range of therapeutic potential. Indeed, several studies in the past decade have uncovered robust links between the endocannabinoid system and the regulation of emotion, anxiety, appetite, and pain perception[l].. For example, recent studies have identified CB2 receptors expressed mostly in the periphery as promising targets for a new approach to the treatment of chronic pain from nervous system injury,[m] a difficult and often disabling problem for some 5 million Americans. The development of novel CB2-based medications *without abuse liability* to treat chronic pain would present an attractive alternative to current opiate-based medications with high abuse and addiction potential and would avoid the adverse events seen with marijuana extracts or natural cannabinoids.

Over the past 30 years, NIDA has supported a large number of scientific projects aimed at unraveling the neurobiology of cannabis and the mechanisms underlying marijuana's effects on the human mind and body. The resulting knowledge has provided valuable insights into the brain processes that mediate perception, emotion, and reward, and is helping to shape new cures for challenging diseases of the brain such as addiction.

Changing the culture: translating research from bedside to community

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In 1998, the Institute of Medicine reported that it takes 17 years on average for research results to affect treatment delivery. This astounding lag in diffusion of innovation is costly for society, devastating for individuals and families, and wasteful of knowledge and investments made to improve the health and quality of people's lives. NIDA is working to change this culture by bridging the divide between scientific findings and their implementation by the practitioner community. We have come far in this endeavor.

NIDA takes a multi-pronged approach to more rapidly move promising science-based drug addiction treatments into community settings. This approach includes using our research infrastructure to put effective treatments into the hands of community-based providers, working with our colleagues from other agencies and organizations to build capacity, and promoting ongoing dialogue among all stakeholders involved in moving substance abuse research to the community.

Integrating effective treatments in communities

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[j] Kreitzer AC. Neurotransmission: Emerging roles of endocannabinoids. *Curr Biol* 15(14):R549-551 (2005).
[k] Justinova Z, Solinas M, Tanda G, Redhi GH, Goldberg SR. The endogenous cannabinoid anandamide and its synthetic analog r(+)-methanandamide are intravenously self-administered by squirrel monkeys. *J Neurosci 25*(23): 5645-5650 (2005).
[l] Piomelli D. The molecular logic of endocannabinoid signalling. *Nat Rev Neurosci* 4(11):873-884 (2003).
[m] Ibrahim MM, Deng H, Zvonok A, Cockayne DA, Kwan J, Mata HP, et al. Activation of cb2 cannabinoid receptors by am1241 inhibits experimental neuropathic pain: Pain inhibition by receptors not present in the CNS. *Proc Natl Acad Sci USA* 100(18):10529-10533 (2003).

Two examples of our research infrastructure—the National Drug Abuse Treatment Clinical Trials Network (CTN) and the Criminal Justice Drug Abuse Treatment Studies (CJDATS)—offer in-field vehicles for testing and disseminating evidence-based practices to treatment settings. The first pushes treatment innovations out to affect the larger community, while the second more recent effort seeks to effect change in the criminal justice system.

NIDA's CTN has as its overriding mission to improve the quality of drug abuse treatment, applying innovative approaches that include new treatment methods as well as new syntheses of therapies proven effective in other realms. Everett Rogers, a pioneer in the field of innovation dissemination and communication (having studied the process for 50 years) called the CTN "an ideal 'communication scaffold' in light of the link already in place between researchers and practitioners." By facilitating buy-in from treatment providers, the CTN promotes the adoption of effective research-based treatments in real world settings. CTN facilities not only test the effectiveness of new and improved interventions with diverse community-based populations, but also train community treatment providers in the delivery of such treatments. This provides a continuous improvement loop through practitioner feedback, which helps identify dissemination products needed by the field and inform strategies to surmount noted barriers.

Research supported through CJ-DATS is designed to improve outcomes for offenders with substance use disorders by improving the integration of drug abuse treatment with other public health and public safety forums. CJ-DATS represents a collaboration with other NIH Institutes, including the National Institute on Alcohol Abuse and Alcoholism, and other Federal Agencies, such as SAMHSA, Centers for Disease Control and Prevention, and several Department of Justice agencies. Because many substance abusers receive no treatment for their substance use disorders while imprisoned, CJ-DATS is targeting the criminal justice system as offering valuable opportunities for intervention, especially at the point of re-entry when prisoners transition back into the community.

Working with our colleagues to continue the dialogue and build capacity

NIDA works closely with SAMHSA and many other partners to build capacity in the field and to help streamline the incorporation of effective treatments at the community level. Our "Blending Initiative" takes what we know (not what we *think* we know) from science, identifies needed products, and disseminates them to providers for use with their patients. Our science-based research supports and informs the training that SAMHSA provides through its Addiction Technology Transfer Center (ATTC) Network, facilitating state-of-the-art education and training for addiction treatment practitioners nationwide. Blending teams composed of researchers, practitioners, and trainers develop products from NIDA-supported and CTN-developed research and disseminate them to the field. Regularly scheduled Blending conferences bring together the best scientific minds, community practitioners, and State representatives and substance abuse directors, to share findings, identify effective solutions, and bring research-based practices to the field to help those struggling with the disease of addiction.

How Far We Have Come

Culture change takes time, but we have come a long way in closing the 17-year lag between research and practice. As a result of the community research infrastructure NIDA has developed and our extensive collaborations with SAMHSA and State decision makers, we have reached a point where our research publications and dissemination products are reaching fruition at nearly the same time. Moreover, many programs formerly unwilling to consider medications for addiction have now discovered, and are in fact using, buprenorphine to assist detoxification in opioid-addicted patients. In addition, community treatment providers have learned how to effectively apply motivational incentives or prizes to promote abstinence and treatment retention; a finding well established in the research literature, but not previously considered practical or optimal by the field. Building on these innovations, Blending teams have developed products designed to raise awareness among community treatment providers about their use. For example, completed products on buprenorphine treatment include a full training package (e.g., informational manual, PowerPoint presentations, CDs, and annotated bibliography), as well as a more recently developed product for instructing treatment providers about a unique 13-day buprenorphine detoxification intervention for opioid-dependent patients.

By supporting research-based training for multidisciplinary addiction professionals, including non-physicians, NIDA's CTN is facilitating real culture change. The example of expanding opioid treatment from methadone clinics to physicians' offices and treatment centers in communities nationwide will result in greater access to and choices for opioid addiction treatment, which in turn can bring different patients into care and reach communities that previously did not have access to appropriate treatment.

We are hopeful that as we move the science forward, our positive results and practice innovations will continue to be broadly disseminated and effect lasting change in the treatment of substance abuse and addiction.

SCIENCE ADVANCES

Stress-sensing brain releases cannabinoids to block pain. Scientists have long known of the brain's ability to block pain during times of great stress, a phenomenon called stress-induced analgesia (i.e., insensitivity to pain without loss of consciousness). Researchers have also known that naturally occurring marijuana-like compounds (cannabinoids) can play an important role in pain relief, but it was not clear what natural circumstances would trigger their release in the brain. Now NIDA-supported scientists have discovered that the rat brain responds to stress by increasing the level of some endogenous (naturally occurring) cannabinoids, simultaneously suppressing the perception of pain. More importantly, when these newly made cannabinoids were prevented from reaching their targets, the stress inhibition of pain was also prevented.

Implications: This study demonstrates for the first time that stress may trigger the release of natural marijuana-like compounds to block pain. This finding complements studies of novel cannabinoid-based pain medications already under development to replace, complement, or expand the use of available painkillers.

Does a tipsy brain maintain an acceptable performance by switching to cheaper fuel? It is estimated that half of the American population 12 years of age or older drinks alcohol at least once a month.[n] While most Americans drink in moderation, even one or two alcoholic beverages have been shown to reduce the rate at which the brain burns glucose, its main energy source. A reduction in brain glucose metabolism has typically been viewed as reflecting a decrease in brain activity and, hence, performance. In a study supported by NIDA and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), investigators imaged brain glucose metabolism and measured performance in 20 healthy human volunteers who were administered low to moderate doses of alcohol (equivalent to either one or two drinks). Consumption of alcohol at these doses significantly decreased whole-brain glucose metabolism but, surprisingly, did not impair cognitive performance. This paradoxical result raises the possibility that large reductions in brain glucose utilization could actually signal a shift toward the use of alternative sources of energy, such as acetate, which has been shown to increase markedly during alcohol intoxication and to be a source of energy for the brain.

Implications: This study clearly establishes that relatively low to moderate doses of alcohol can lower brain glucose metabolism just like high doses. However, failure to observe a parallel drop

[n] NSDUH 2004, http://oas.samhsa.gov/nsduh.htm#NSDUHinfo.

in cognitive performance suggests that lower glucose metabolism may not be tightly linked to compromised brain activity and that other brain effects related to alcohol dosage (over time or on a single occasion) might more directly determine level of cognitive impairment. The proposed hypothesis that the alcohol-exposed brain shifts to burning acetate may be one explanation for why low to moderate drinkers do not show cognitive deficits. Moreover, this shifting mechanism could be more efficient in some individuals than in others, which could explain different people's responses to one or two drinks. This finding might help explain alcohol withdrawal symptoms as being the brain running out of glucose *and* acetate, although more research is needed.

Shining the light on complex behaviors. Neuroscientists, like most other biologists, can generally take three basic approaches with a system they are trying to understand: they can measure it, they can block it, and they can manipulate it in order to learn from its responses. In neural systems, the latter approach has been traditionally accomplished by stimulating neurons with electrodes or with chemicals. This method can be directed at neurons in a specific place but cannot target groups of neurons that share features other than location. Now NIDA-supported researchers at Yale University have found a way to introduce genetic changes in selected neurons of the fruit fly, allowing them, by illuminating the whole fly, to stimulate only the changed neurons. Because the modified neurons were part of functional circuits, the researchers could use light to coax the flies to either jump, beat their wings, or take flight. The scientists could also activate cells that produce the brain chemical dopamine, affecting the flies' movements.

Implications: The ability to induce a particular behavior simply by shining light on an awake, behaving animal offers a novel, noninvasive tool for studying the connections and dynamics of brain circuits. This advance may be the first step toward the development of light-based techniques for studying how specific neural circuits influence normal and diseased behaviors in the brains of more complex animals.

Thrombospondins rediscovered as early brain's IT managers. The brain circuits that direct our behaviors rely on the huge number of connections among neurons. Trillions of these "synapses" form during development and most are modified in strength and position as a result of life experiences. Unfortunately, many weaken, decay, and disappear as the result of normal aging or brain diseases, such as Alzheimer's and drug addiction. Investigators supported by NIDA have identified thrombospondins (TSPs), long-known proteins secreted by helper cells in the brain (called glia) as playing a crucial role in creating new synapses, or contacts, between neurons.

Implications: By revealing a previously unsuspected role of TSPs in the process of normal synapse formation, this study may explain why the adult brain, which contains lower levels of TSPs, has a diminished ability to form new synapses. This advance may lead to improved treatment of brain conditions in which the number of synapses is either too high or too low, signaling an era when the judicious administration of TSPs or TSP-like factors might help to reverse the deleterious effects of brain diseases like Alzheimer's, Parkinson's, and chronic drug addiction.

Expanding HIV Screening: It's Cost Effective. According to the Centers for Disease Control and Prevention (CDC), an estimated 1 million people in the U.S. are living with HIV/AIDS, nearly one-third of whom are unaware of their status.[o] Two NIDA-supported multi-center research teams independently determined through computer models that routine screening for HIV in health care settings is as cost-effective as screening for other common medical conditions (e.g., breast cancer, diabetes, high blood pressure) and can provide important health and survival benefits. The studies also suggest that screening which leads to a diagnosis of HIV infection may further lower health care costs by preventing high-risk practices and decreasing virus transmission.

Implications: These studies suggest that routine HIV counseling, testing, and referral should be extended and that voluntary screening for HIV is justified in certain populations for the substantial clinical and cost benefits it confers. Further research could reveal the best ways to implement HIV screening programs, reduce existing barriers to screening, and boost cost-effectiveness and the influence of counseling on patient knowledge.

ATHENA Program Reduces Body-Shaping Related Drug Abuse. High school is a time in which adolescents undergo many changes both biologically and socially. It is also a time when drug abuse approximately doubles. Following upon the highly successful intervention designed to reduce the abuse of anabolic steroids among high school *male* athletes, ATHENA (Athletes Targeting Healthy Exercise and Nutrition Alternative) targets female athletes with the goal of increasing healthy behavioral choices and preventing drug abuse. Researchers enrolled 928 students from 40 participating sports teams in 18 high schools to either a control group or to the ATHENA intervention. Program activities, delivered during a sports team's usual practice schedule, focused on the benefits of healthy sports nutrition and effective exercise training, as well as the dangers associated with drug abuse and other unhealthy behaviors. The intervention correlated with reduced drug abuse, including abuse of diet pills, stimulants, and steroids, as well as with other positive changes, such as healthier eating behaviors.

Implications: ATHENA allows for the incorporation of a prevention program, designed specifically for female athletes, into existing sports training programs, a format that could fit well into many schools' organized sports programs for males and females. It is also an effective multi-dimensional prevention program, addressing a constellation of risk behaviors ranging from disordered eating habits and associated drug use to safe driving.

Gene Identified that Determines Vulnerability to Drug Abuse. Modern molecular biology techniques can be powerful tools in identifying hundreds of genes involved in drug abuse. One gene, NrCAM, is known to be important for normal brain development as well as normal functioning in the adult brain. Studies have also suggested relevant to that the NrCAM gene plays an important role in neuronal connections and functions drug reward and addiction. Researchers identified differences in the NrCAM gene in the post-mortem brains of individuals

[o] Centers for Disease Control and Prevention. Division of HIV/AIDS Prevention. Basic Statistics. http://www.cdc.gov/hiv/stats.htm#hivest.

who were addicted to abused drugs versus those without any significant lifetime use. They also noted that in mice, reward from abused drugs such as morphine, cocaine, and amphetamine was diminished when the animals had reduced expression of the NrCAM gene and was totally eliminated when the animal's NrCAM genes were eradicated or "knocked out." Additionally, NrCAM expression was found in brain regions linked to reward and memory, also involved in drug abuse and addiction.

Implications: Together, these results demonstrate that the NrCAM gene plays an important role in drug abuse and addiction and may contribute to differences in addiction vulnerability in humans. Differences in how the NrCAM gene is expressed in individuals may determine whether or not a person has a predisposition to drug use. This information provides researchers and clinicians with a valuable tool both for understanding and treating substance abuse. It also provides evidence that a propensity to use illicit drugs may be genetically influenced.

Vaccine May be an Effective Treatment for Cocaine Addiction. Although cocaine addiction affects 2.5 million Americans and accounts for 30-40 percent of illicit drug-related emergency room visits, currently no pharmacological treatments exist to effectively treat people addicted to cocaine. Research has suggested that while behavioral therapies are critically important for treating cocaine addiction, concomitant pharmacotherapy may offer the most effective combined method of treatment. For the first time, researchers have found that a vaccine against cocaine is effective in reducing drug abuse. Current cocaine addicts were given the vaccine at either a high or low dose and then followed for several months. Although both the high and low doses reduced drug use, the high dose resulted in the greatest reduction.

Implications: Although this study was small and will need additional larger scale investigations, it provides the first evidence that a cocaine vaccine is effective for treating cocaine addicts.

The National Drug Abuse Treatment Clinical Trials Network (CTN) Demonstrates that Methamphetamine and Cocaine Addiction Can Be Effectively Treated. The CTN is a national network of drug abuse researchers and community treatment providers that tests research-based approaches in multiple-site, real-world conditions. A total of 415 individuals who abused methamphetamine and/or cocaine participated in this study, most of them from CTN sites in the Western United States. Individuals addicted to methamphetamine and/or cocaine experience difficulty remaining in drug treatment, reducing their chances of abstaining from drug use. In this study, approximately half of the 415 study participants were randomly assigned to receive low-cost rewards or motivational incentives for drug abstinence, in addition to 12 weeks of standard care. Findings revealed that those assigned to the incentive condition remained in treatment for a longer period than individuals assigned to standard care. They also submitted more drug-free urine samples and were more likely to achieve 4, 8, and 12 weeks of continuous abstinence than those participating in standard care alone.

Implications: Study results indicate that treatment for both methamphetamine and cocaine can be enhanced through the use of tangible incentives, contingent on abstinence. Moreover, the approach proved to be a low-cost, viable, and acceptable one to the community treatment

providers who used it. These findings are important in increasing the adoption of evidence-based treatments into community settings.

Unraveling the Mechanisms by which Stress Leads to Relapse in Drug Abusers. It is well known that stress is a major precipitant of relapse to drug abuse in recovering drug addicts. The neurochemical, corticotrophin releasing factor (CRF), which is released during stressful events and coordinates the body's response to stress, has been shown to play a role in this relapse, although the precise mechanism has not been known. In this study, researchers compared rats who had previously received cocaine (cocaine-experienced) to rats who had not (cocaine-naïve) to determine the brain areas and chemicals involved in stress-related relapse. The study showed that although stress can cause levels of CRF to increase in both cocaine-naïve and cocaine-experienced rats, its actions differed in the cocaine-experienced rats and led to a re-initiation of drug seeking. Importantly, this occurred 3 weeks after animals received their last exposure to cocaine.

Implications: Researchers have identified for the first time that the same neural pathways typically activated by other triggers of relapse become activated by stress in the brains of drug-experienced but not drug-naïve animals. Moreover, these results identify persistent changes in the brain that leave individuals vulnerable to certain relapse triggers like stress. By revealing the precise brain mechanisms involved, researchers can develop treatments that interfere with them, thus preventing drug relapse.

Maternal Use of Tobacco or Marijuana Heightens Risk of Use in Offspring. Cigarettes and marijuana are two of the most common non-medicinal drugs that are taken during pregnancy, with marijuana the illicit drug most commonly abused by pregnant women. The present study draws its data from the Ottawa Prenatal Prospective cohort, part of an ongoing longitudinal study begun in 1978 and designed to examine the neurobehavioral and developmental effects of maternal cigarette and marijuana use in a cohort followed from birth through adolescence. Researchers sought to determine if maternal cigarette and marijuana smoking during pregnancy were associated with an increased risk of initiation and regular use of cigarettes and marijuana among 152 16 to 21-year-old adolescents. The study shows that offspring who were born to women reporting marijuana use during pregnancy were at increased risk for initiating marijuana use and smoking. A dose-response relationship was also observed between prenatal exposure to marijuana and offspring's use of marijuana and cigarettes.

Implications: The findings presented here have implications for how prenatal smoking and drug abuse prevention programs are constructed and may add a needed perspective regarding the long-term health consequences of in utero exposure to marijuana and cigarettes. This study also suggests that smoking cessation programs could provide long-term benefits in breaking a use cycle that is sometimes established before birth.

Can Brain Images Predict Relapse in Methamphetamine Addicts? Relapse is a serious problem in methamphetamine addicts that can lead to dangerous medical and psychiatric symptoms. Although studies suggest that multiple factors underlie relapse occurrence, the contribution of specific brain circuits has not yet been thoroughly examined. This NIDA-

supported study attempted to "tell the future" by determining whether brain images taken shortly after drug cessation could predict relapse in stimulant-addicted individuals. Specifically, 40 treatment-seeking methamphetamine-addicted males underwent a brain imaging procedure during a simple brain performance task, 3 to 4 weeks after cessation of drug use. A year later, 18 had relapsed and 22 remained abstinent. Amazingly, the brain images of regions involved in decision-making, taken early in the recovery period, predicted who would relapse and who would not with an accuracy rate exceeding 90 percent.

Implications. This study is the first demonstration that brain imaging can identify specific brain activation patterns as accurate predictors of relapse. These findings need to be replicated in other patients, but understanding such patterns could provide an important first step towards developing targeted treatment approaches that increase a patient's chances of long-term abstinence.

Finding the Pathways Responsible for Craving in Drug Addicted Individuals. By their very nature, drugs of abuse can make people feel good or feel better. But, for individuals who are addicted to drugs, exposure to even very small amounts of a drug, or cues associated with it, can trigger intense craving and the desire to get more. The question of how drugs can exert this differential control over the behavior and emotions of addicted vs. non-addicted individuals is an important one if we are to develop improved therapeutic tools to counter these aspects of addiction. Using non-invasive brain imaging techniques, investigators compared glucose metabolism in the brains of detoxified cocaine-addicted and non-addicted controls, following intravenous administration of methylphenidate (Ritalin), which is pharmacologically similar to cocaine in terms of its brain targets. Exposure to methylphenidate resulted in *increases* in metabolism in two regions of the prefrontal cortex in cocaine-addicted individuals, while controls responded with *decreased* metabolic activity in these same regions. The changes in brain activity were linked to craving for cocaine in addicted individuals and increased desire for methylphenidate in both groups.

Implications. Findings suggest that specific brain regions involved in emotion and motivation are differentially affected by drug exposure in cocaine-addicted compared to non-addicted individuals, which could underlie the addicted person's strong emotional response to the drug and intense desire to obtain it. This information is a critical step towards identifying the brain circuits that are targets for rehabilitation by successful therapeutic tools to treat substance abuse and addiction.

Genetic Screen Boosts Nicotine Addiction Treatment's Success Rate. Pharmacogenetics research is about pinpointing genetic variations (alleles) that can predict treatment outcome. For addiction, variations in the dopamine system have been a main focus, given dopamine's major role in modulating reward and motivation. In a NIDA-supported clinical trial, researchers at the University of Pennsylvania investigated the influence of two dopamine receptor alleles on the patient's response to bupropion and nicotine replacement therapy (NRT), two standard treatments for tobacco addiction. By the end of the trial, it became evident that carriers of a dopamine receptor variant referred to as "Ins C" had a much better response to bupropion than carriers of the "Del C" version. The exact opposite pattern was observed with NRT treatment.

Implications. Results suggest that bupropion may be the treatment of choice for smokers with the "Ins C" type of dopamine receptor, while NRT may be more beneficial for those who carry the "Del C" variety. These findings provide a glimpse of a future in which a patient's genetic background will be a major factor in selecting the most appropriate therapeutic course of action.

Small Protein Controls Eating and Drug Seeking. The hypothalamus is a small area of the brain above and behind the roof of the mouth that controls many vital functions, such as eating, body temperature, fat metabolism, and proper balance of fluids, hormones, and sugar. Small regions at either side of the hypothalamus appear to be capable of blocking pain, stimulating feeding, and modulating motivation and reward. Although the connections between these regions and reward centers have long been known, the chemicals that carry information along the pathways had not been fully characterized until now. This research showed that when rats were conditioned to prefer cocaine, orexin-secreting brain cells in the hypothalamus became activated, the same cells that are activated when food is the conditioning stimulus. Furthermore, rats injected with an orexin blocker prior to the training sessions failed to establish drug-seeking behavior. Combined with previous knowledge about orexin's role in modulating eating behaviors, these results highlight the close relationship between the molecular mechanisms that control both eating and drug-seeking, two behaviors located along a reward continuum.

Implications. Results of this study suggest that orexin may be an important factor in tempering the reward-seeking traits of the substance abuser. The identification of new neural pathways and brain chemicals involved in drug abuse, craving, and relapse is a key step in developing more effective therapies.

Pooled DNA Brings New Power to Search for Addiction Genes. Now that the human genome project has been completed, the identification of genetic differences that confer vulnerability to complex disorders and risky behaviors has become an achievable goal. Neuroscientists have been testing and steadily improving new approaches to harness the power of genetic databases to understand, prevent, and treat brain disorders such as addiction. But because of the vast amount of information involved, progress requires reliable, fast, and affordable screening techniques. Investigators from the NIDA Intramural Research Program have validated a new, more powerful method to search the human genome to identify genes that might predispose a person to substance abuse and addiction. Results from screenings of 10,000 well-defined gene forms with pooled genomic DNA samples obtained from heavy substance abusers or well-characterized control individuals revealed 38 genes that show significant variations between drug abusers and control individuals.

Implications: The identification of a first group of drug abuse vulnerability candidate genes supports previous findings of gene variations linked to addiction, and represents a promising direction for future research. Scanning the genome with DNA samples pooled from carefully selected and well-characterized populations provides a powerful and relatively inexpensive tool for elucidating the molecular and genetic underpinnings of complex disorders. It also identifies both well-known and unanticipated mechanisms for addiction vulnerability.

Unraveling the Molecular Bases of Nicotine Addiction. The nicotine found in tobacco leaves is the addictive compound that drives smoking behavior. Nicotine's powerful effects on reward, mental alertness, and memory suggest a direct action on the central nervous system, an action mediated by different forms (alleles) of nicotine receptors. Two recent studies have uncovered important new information about how particular alleles contribute to the addictive properties of nicotine, and represent significant progress in unraveling the molecular bases of nicotine addiction. NIDA-supported researchers found that mice expressing a mutant α4 nicotinic receptor protein displayed a greater sensitivity to the effects of nicotine, with lower doses required to increase locomotor activity, sensitization (increased responsiveness to nicotine's motor effects with repeated exposure), and reward. A different group of researchers discovered that mice with a mutant version of the β4 nicotinic receptor subunit displayed a much milder form of nicotine withdrawal.

Implications. By illuminating underlying molecular mechanisms, these studies provide important information for understanding how nicotine promotes addiction, increasing the likelihood of identifying additional genetic variations that lead to susceptibility. In addition, because some of nicotine's cognitive effects appear to be beneficial in neurodegenerative disorders, a better understanding of these effects at the molecular level may lead to new therapies for diseases like Alzheimer's and Parkinson's.

Human Male Brain More Susceptible to In Utero Marijuana Exposure. A large national survey, published by NIDA in 1996, shows that an estimated 5.5 percent, or 221,000 of the 4 million women who gave birth in the United States in 1992 used illegal drugs while they were pregnant. Marijuana was the illicit drug most frequently used (2.9 percent), followed by cocaine (1.1 percent).[p] The major psychoactive component in marijuana (cannabis) is THC, which readily crosses the placenta and can thus affect the fetus. By examining 42 postmortem fetal brain samples from mid-gestation term (weeks 18-22), this study was the first to examine the neurobiological impact in the human brain of in utero exposure to cannabis. Findings indicate, particularly for male fetuses, a specific reduction in one type of dopamine receptor in the amygdala, a part of the brain involved in emotion, with no significant cannabis-related alterations detected in other brain regions. The reduction was related to the amount of maternal marijuana intake during pregnancy.

Implications. Importantly, a consequence of maternal cannabis use may be (1) to alter distinct neural systems that regulate emotional behavior and (2) to specifically alter gene expression in the male fetal brain. Given the significant gender difference, this study suggests that greater attention should be paid to the sex of the participants in both clinical and preclinical studies of prenatal cannabis exposure.

Prescription Drug Abuse Goes to School. Prescription drug abuse is a growing problem in the United States, especially abuse of opioids or painkillers. And while recent surveys show increased usage among all age groups, young adults report the greatest increase in lifetime and

[p] National Institute on Drug Abuse: National pregnancy and health survey, National Institutes of Health, Rockville, MD, Publication No. 96-3819, 1996.

current use. Addressing this trend, NIDA-supported researchers investigated current and past year illicit use of various prescription medications within several different cohorts of high school and college students. Prescription drugs included sleeping, anxiety, stimulant, and pain medications. Three separate studies examined (1) sources for students' obtaining medications and the relationship to other substance abuse, (2) prevalence rates and correlates of nonmedical use of prescription painkillers, and (3) factors associated with illicit use of opioids among high school seniors. The first two studies expand and support the third earlier study identifying a problem with illicit use of opioid analgesics among American high school seniors and a correlation between greater usage and the desire to join a fraternity or sorority once in college.

Implications. The results of these studies provide useful information for better targeting prevention efforts and therapeutic strategies to mitigate the growing problem of illicit prescription drug use among young adults. For example, the finding that socialization contributes to abuse behaviors suggests a need to focus prevention efforts on high school students who express an interest in fraternities or sororities. Further, the knowledge that college students are getting their prescription drugs from peers will spur prevention efforts to reduce the illicit use and diversion of prescription medication. Finally, the desire to improve performance as a rationale for abusing drugs suggests interventions aimed at reducing stress for this group.

Shedding Light on HIV-Associated Dementia. HIV infection is often complicated by central nervous system dysfunction because of HIV's tendency to invade certain brain regions, leading to a condition known as HIV-associated dementia (HAD). About 10 to 15 percent of people living with HIV eventually develop HAD, characterized by a loss of mental functioning with notable motor effects. Core symptoms of HAD are similar to those seen in patients with Parkinson's disease, believed to be caused by a dopamine deficiency. In this study, researchers used PET to compare the integrity of the dopamine system in HIV patients with dementia to HIV patients without dementia and to controls who did not test positive for HIV. They found that dopamine nerve endings were decreased in the brains of patients with HIV dementia, but not in those without dementia, relative to the controls.

Implications: This finding is consistent with previous work suggesting that dopamine nerve cells may be vulnerable to damage in HIV-infected individuals and suggest further that this damage may contribute to HAD.

New Clinical Trial of Opioid Addiction Treatment Brings Focus and Hope to Adolescents. The past decade has seen a significant increase in opioid abuse among adolescents. The decline of heroin use since the year 2000 has apparently occurred at the expense of increasing rates of nonmedical use of other opioids in the same age group.[q] The signs are even more ominous when we consider that the proportion of heroin-using adolescents who inject the drug intravenously has been rising steadily over the same period, increasing their risk for contracting HIV/AIDS and other blood-borne infectious diseases. It is therefore imperative that we develop age-appropriate and scientifically validated treatments for opioid-addicted adolescents. Now, the first clinical

[q] Monitoring The Future Study, 2004 (http://www.monitoringthefuture.org/pubs/monographs/overview2004.pdf).

trial combining behavioral and pharmacological treatment for adolescent opioid addiction, NIDA-supported researchers assessed the efficacy of two common opioid withdrawal medications as part of a multipronged detoxification protocol. Thirty-six opioid-addicted patients between the ages of 13 and 18 underwent 28 days of behavioral therapy, combined with either buprenorphine or clonidine. While both groups reported similar withdrawal relief and reductions in HIV risk behaviors, the buprenorphine-assisted treatment garnered nearly twice the retention and abstinence rates compared to clonidine, and led to a six-fold increase in the commitment to seek further long-term addiction treatment.

Implications. This study addresses a serious deficit of information regarding the efficacy or even the safety of current addiction treatments when used in adolescent populations. Results demonstrate that a buprenorphine-assisted detoxification program can be safe and highly efficacious, providing hope to many teens and their families in urgent need of help.

HIV and METH: Adding Insult to Brain Injury. Individuals with HIV-associated dementia and those who are chronic methamphetamine abusers can suffer similar reductions in cognitive function. Moreover, post-mortem studies show that both conditions are associated with neuronal loss in the brain. It would seem reasonable then that people suffering from HIV infection who also have a history of methamphetamine abuse could compound the severity of neurotoxic effects. A NIDA-supported study has just completed a test of this hypothesis using a non-invasive imaging method. Researchers used proton magnetic resonance spectroscopy (H-MRS)—a brain imaging technique that can evaluate brain health—to monitor the brains of long-term methamphetamine users, with or without concomitant HIV infection. They discovered that co-occurrence led to an exacerbation of the abnormalities associated with each disease individually.

Implications. The findings suggest that the brains of individuals with a combined history of HIV infections *and* methamphetamine abuse activate a more intense inflammatory response and suffer increased neuronal injury. This information sheds light on some key physiological changes on which researchers can now focus when monitoring whether a pharmacological or behavioral treatment alters either brain function or disease course in this co-morbid population.

NIH NEUROSCIENCE BLUEPRINT

The Neuroscience Blueprint (http://neuroscienceblueprint.nih.gov/) is a collaboration among 15 NIH institutes and centers, established to create and support cooperative activities with broad impact in neuroscience. Scientific programs implemented under the Blueprint are intended to accomplish goals that strengthen the neuroscience enterprise and make it more effective, and that also impact many or all of the individual disciplines within neuroscience. These goals include pooling of resources and expertise, establishing economies of scale, addressing large and complex challenges within neuroscience, and developing tools and infrastructure to serve the entire neuroscience community. NIDA is the lead on developing the FY06 Blueprint Research Training initiatives, which focus on neuroimaging, computational neuroscience, and the neurobiology of disease.

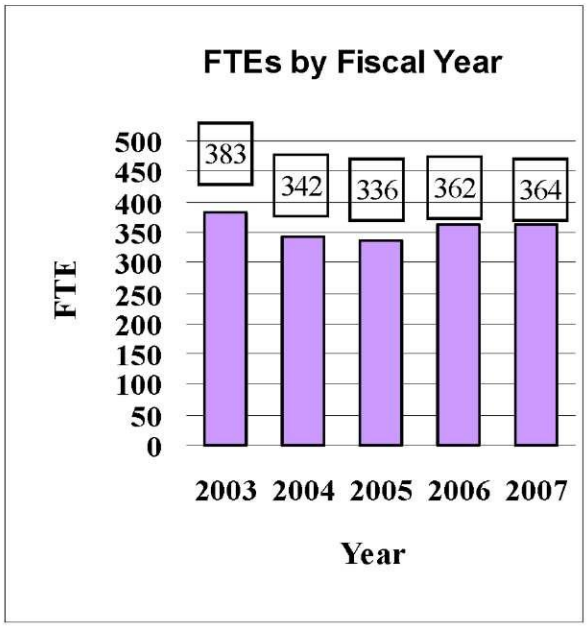
NIH ROADMAP

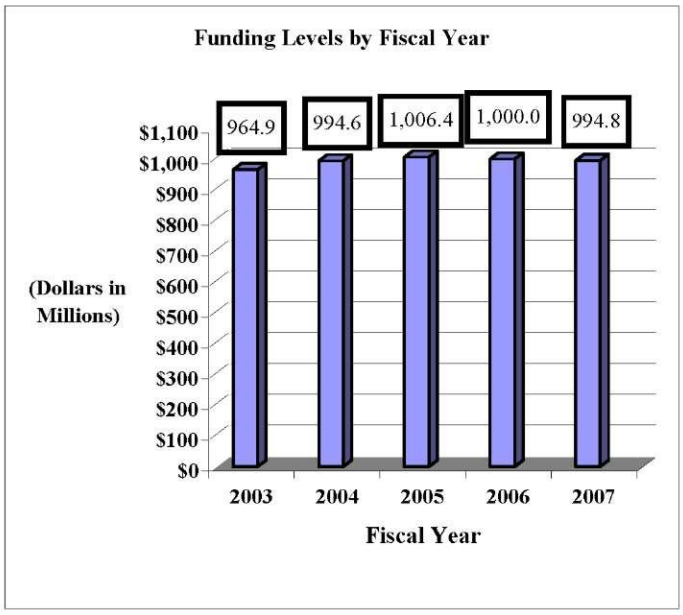
NIDA is participating in Roadmap initiatives that most closely align with our mission to support scientific research on drug abuse and addiction and its related consequences. These include the Molecular Libraries and Imaging initiative, likely to expedite the development of new medications to treat common diseases, including drug abuse and addiction. Similarly, Research Teams of the Future provide the opportunity for drug abuse and addiction researchers to address the application of disparate fields such as neurodevelopmental toxicology, behavioral epidemiology, and transdisciplinary imaging genetics. Findings will enhance our knowledge of the complex interplay between genetics, behavior, environment, and brain function, and contribute to our understanding of how drug abuse and addiction impacts the human brain. NIDA also has a leadership role in the NIH Director's Pioneer Award Program, which supports exceptionally creative scientists who bring their talents, expertise, and perspectives to bear on some of the biggest challenges in biomedical research.

Budget Policy

The Fiscal Year 2007 budget request for the NIDA is $994,829,000, a decrease of $5,200,000 and 0.5 percent below the FY 2006 Appropriation. Included in the FY 2007 request is NIDA's support for the trans-NIH Roadmap initiatives, estimated at 1.2% of the FY 2007 budget request. A full description of this trans-NIH program may be found in the NIH Overview.

A five year history of the FTEs and Funding Levels for NIDA are shown in the graphs below. Note that as the result of several administrative restructurings in recent years, FTE data is non-comparable.





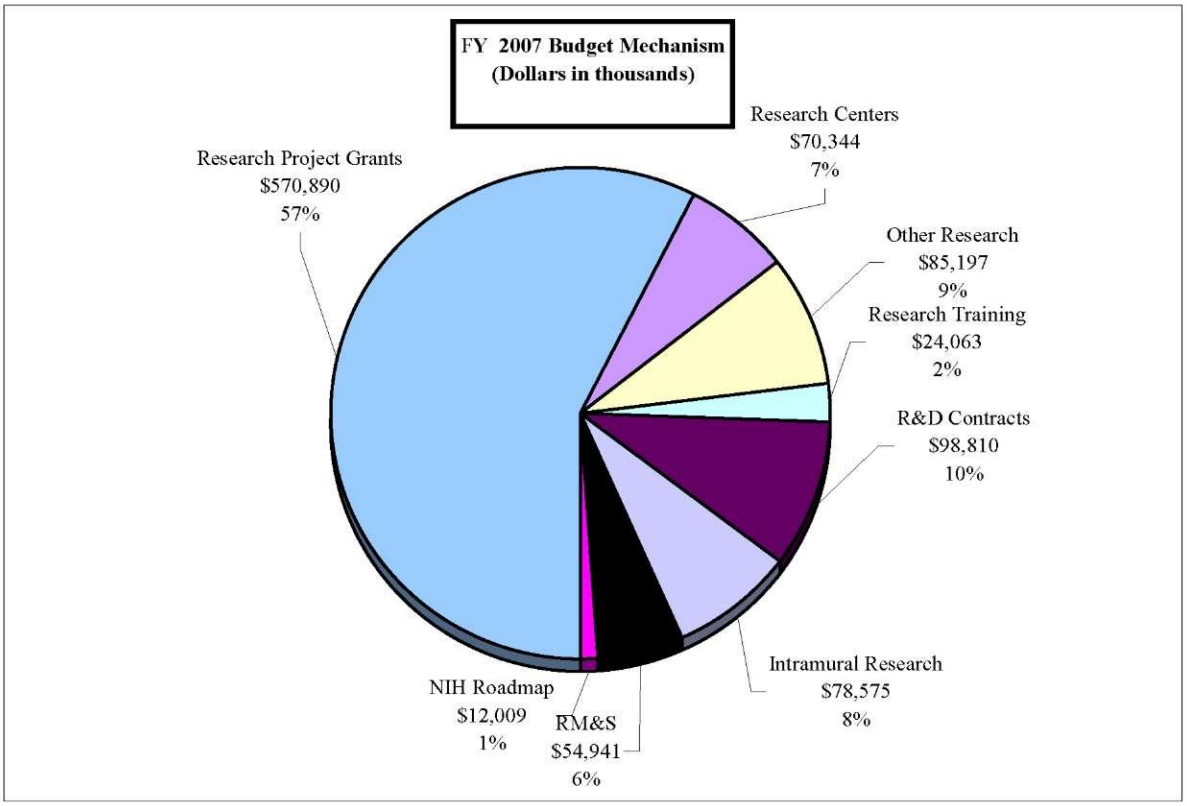
NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. We estimate that the average cost of competing RPGs will be $383 thousand in FY 2007. While no inflationary increases are provided for direct recurring costs in noncompeting RPGs, where the NIDA has committed to a programmatic increase for an award, such increases will be provided.

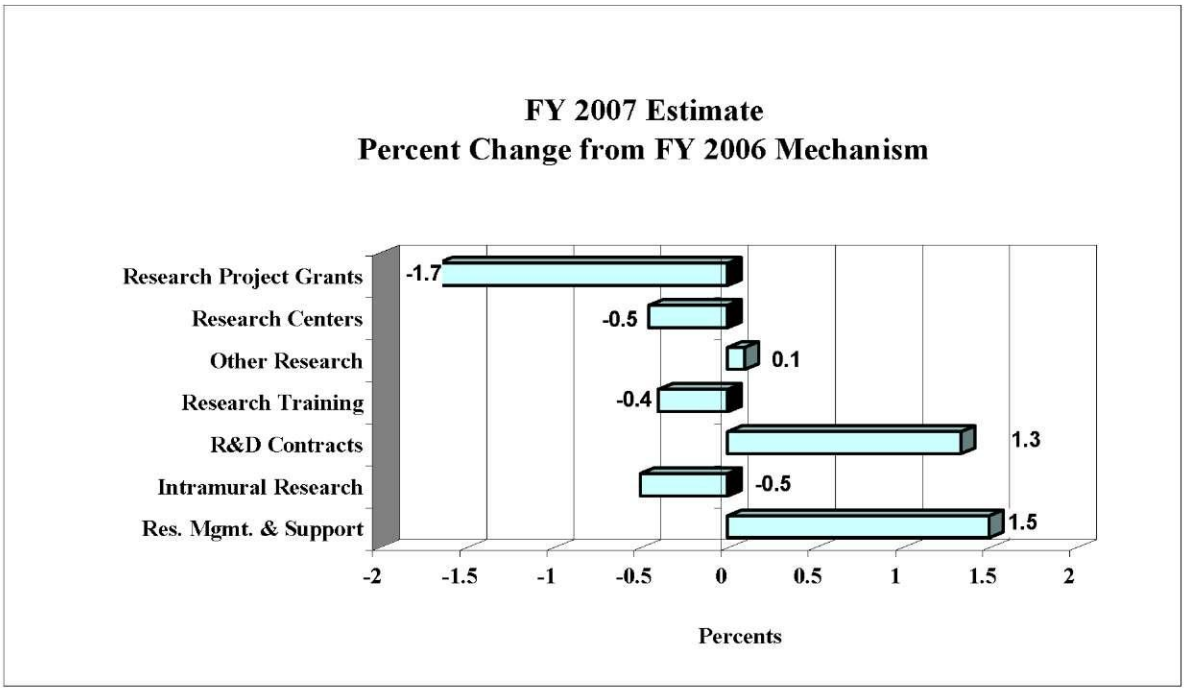
NIDA will also support the Genes, Environment, and Health Initiative (GEHI) to: 1) accelerate discovery of the major genetic factors associated with diseases that have a substantial public health impact; and 2) accelerate the development of innovative technologies and tools to measure dietary intake, physical activity, and environmental exposures, and to determine an individual's biological response to those influences. The FY 2007 request includes $1,205,000 to support this project.

In the FY 2007 request, stipend levels for trainees supported through the Ruth Kirschstein National Research Service Awards will remain at the FY 2006 levels.

The FY 2006 request includes funding for 42 research centers, 312 other research grants, including 251 career awards, and 183 R&D contracts. Intramural Research decreases by 0.5 percent. Research Management and Support increases by 1.5 percent.

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




FY 2007 Estimate
Percent Change from FY 2006 Mechanism
Research Project Grants
Research Centers
Other Research
Research Training
R&D Contracts
Intramural Research
Res. Mgmt. & Support
-1.7
-0.5
0.1
-0.4
1.3
-0.5
1.5
-2
-1.5
-1
-0.5
0
0.5
1
1.5
2
Percents

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Budget Mechanism - Total

MECHANISM	FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	1,070	$436,788,000	1,074	$441,689,000	1,021	$410,834,000
Administrative supplements	(135)	12,482,000	(114)	10,823,000	(139)	12,800,000
Competing:						
Renewal	72	29,993,000	64	26,687,000	75	31,335,000
New	300	94,183,000	269	84,193,000	264	98,914,000
Supplements	4	630,000	2	315,000	2	315,000
Subtotal, competing	376	124,806,000	335	111,195,000	341	130,564,000
Subtotal, RPGs	1,446	574,076,000	1,409	563,707,000	1,362	554,198,000
SBIR/STTR	55	17,500,000	53	16,847,000	52	16,692,000
Subtotal, RPGs	1,501	591,576,000	1,462	580,554,000	1,414	570,890,000
Research Centers:						
Specialized/comprehensive	40	68,680,000	42	70,662,000	42	70,344,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	40	68,680,000	42	70,662,000	42	70,344,000
Other Research:						
Research careers	247	34,789,000	247	35,976,000	251	36,336,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	17	38,875,000	17	37,710,000	17	37,433,000
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	0	0	0	0	0	0
Other	47	14,221,000	45	11,428,000	44	11,428,000
Subtotal, Other Research	311	87,885,000	309	85,114,000	312	85,197,000
Total Research Grants	1,852	748,141,000	1,813	736,330,000	1,768	726,431,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	148	5,352,000	158	5,904,000	156	5,880,000
Institutional awards	385	16,548,000	411	18,255,000	410	18,183,000
Total, Training	533	21,900,000	569	24,159,000	566	24,063,000
Research & development contracts	180	98,553,000	180	97,504,000	183	98,810,000
(SBIR/STTR)	(17)	(6,608,000)	(17)	(6,751,000)	(17)	(6,751,000)
	FTEs		FTEs		FTEs	
Intramural research	116	79,450,000	120	78,970,000	120	78,575,000
Research management and support	220	52,012,000	242	54,129,000	244	54,941,000
Cancer prevention & control						
Construction						
Buildings and Facilities						
NIH Roadmap for Medical Research		6,363,000		8,937,000		12,009,000
Total, NIDA	336	1,006,419,000	362	1,000,029,000	364	994,829,000
(Clinical Trials)		(175,733,000)		(174,679,000)		(173,805,000)

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2005 Actual FTEs	FY 2005 Actual Amount	FY 2006 Appropriation FTEs	FY 2006 Appropriation Amount	FY 2007 Estimate FTEs	FY 2007 Estimate Amount	Change FTEs	Change Amount
Extramural Research:								
Drug Abuse and Addiction		$866,747		$857,993		$849,304		($8,689)
								0
								0
								0
								0
Subtotal, Extramural research		866,747		857,993		849,304		(8,689)
Intramural research	116	79,450	120	78,970	120	78,575	0	(395)
Res. management & support	220	53,859	242	54,129	244	54,941	2	812
NIH Roadmap for Medical Research		6,363		8,937		12,009	0	3,072
Total	336	1,006,419	362	1,000,029	364	994,829	2	(5,200)

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Summary of Changes

FY 2006 Estimate				$1,000,029,000
FY 2007 Estimated Budget Authority				994,829,000
Net change				(5,200,000)
	FY 2006 Appropriation		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$18,537,000		$251,000
b. Annualization of January 2006 pay increase		18,537,000		144,000
c. January 2007 pay increase		18,537,000		312,000
d. One less day of pay		18,537,000		
e. Payment for centrally furnished services		7,839,000		246,000
f. Increased cost of laboratory supplies, materials, and other expenses		52,494,000		1,144,000
Subtotal				2,097,000
2. Research Management and Support:				
a. Within grade increase		28,729,000		494,000
b. Annualization of January 2006 pay increase		28,729,000		223,000
c. January 2007 pay increase		28,729,000		486,000
d. One less day of pay		28,729,000		
e. Payment for centrally furnished services		527,600		164,000
f. Increased cost of laboratory supplies, materials, and other expenses		20,124,000		434,000
Subtotal				1,801,000
Subtotal, Built-in				3,898,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Summary of Changes--continued

CHANGES	2006 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	1,074	$452,512,000	(53)	($28,878,000)
b. Competing	335	111,195,000	6	19,369,000
c. SBIR/STTR	53	16,847,000	(1)	(155,000)
Total	1,462	580,554,000	(48)	(9,664,000)
2. Research centers	42	70,662,000	0	(318,000)
3. Other research	309	85,114,000	3	83,000
4. Research training	569	24,159,000	(3)	(96,000)
5. Research and development contracts	180	97,504,000	183	1,306,000
Subtotal, extramural				(8,689,000)
	FTEs		FTEs	
6. Intramural research	120	78,970,000	0	(2,492,000)
7. Research management and support	242	54,129,000	2	(989,000)
8. Cancer control and prevention	0	0	0	0
9. Construction		0		0
10. Buildings and Facilities		0		0
11. NIH Roadmap for Medical Research	0	8,937,000	0	3,072,000
Subtotal, program		1,000,029,000		(9,098,000)
Total changes	362		2	(5,200,000)

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Budget Authority by Object

	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	362	364	2
Full-time equivalent of overtime & holiday hours	1	1	0
Average ES salary	$157,580	$162,300	$4,720
Average GM/GS grade	12.6	12.6	0.0
Average GM/GS salary	$96,574	$98,505	$1,931
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$91,409	$93,237	$1,828
Average salary of ungraded positions	124,447	126,936	2,489

	OBJECT CLASSES	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
	Personnel Compensation:			
11.1	Full-Time Permanent	$25,097,000	$26,469,000	$1,372,000
11.3	Other than Full-Time Permanent	6,772,000	7,034,000	262,000
11.5	Other Personnel Compensation	1,230,000	1,260,000	30,000
11.7	Military Personnel	1,522,000	1,567,000	45,000
11.8	Special Personnel Services Payments	3,835,000	3,920,000	85,000
	Total, Personnel Compensation	38,456,000	40,250,000	1,794,000
12.0	Personnel Benefits	8,295,000	8,542,000	247,000
12.2	Military Personnel Benefits	848,000	874,000	26,000
13.0	Benefits for Former Personnel	0	0	0
	Subtotal, Pay Costs	**47,599,000**	**49,666,000**	**2,067,000**
21.0	Travel & Transportation of Persons	1,383,000	1,341,000	(42,000)
22.0	Transportation of Things	119,000	115,000	(4,000)
23.1	Rental Payments to GSA	0	0	0
23.2	Rental Payments to Others	12,000	12,000	0
23.3	Communications, Utilities & Miscellaneous Charges	668,000	647,000	(21,000)
24.0	Printing & Reproduction	763,000	740,000	(23,000)
25.1	Consulting Services	4,366,000	4,342,000	(24,000)
25.2	Other Services	12,155,000	12,407,000	252,000
25.3	Purchase of Goods & Services from Government Accounts	100,003,000	100,376,000	373,000
25.4	Operation & Maintenance of Facilities	9,721,000	9,531,000	(190,000)
25.5	Research & Development Contracts	53,821,000	53,388,000	(433,000)
25.6	Medical Care	191,000	187,000	(4,000)
25.7	Operation & Maintenance of Equipment	1,025,000	1,006,000	(19,000)
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**181,282,000**	**181,237,000**	**(45,000)**
26.0	Supplies & Materials	5,100,000	4,957,000	(143,000)
31.0	Equipment	3,818,000	3,752,000	(66,000)
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	750,346,000	740,351,000	(9,995,000)
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	2,000	2,000	0
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	**943,493,000**	**933,154,000**	**(10,339,000)**
	NIH Roadmap for Medical Research	**8,937,000**	**12,009,000**	**12,009,000**
	Total Budget Authority by Object	**1,000,029,000**	**994,829,000**	**3,737,000**

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Salaries and Expenses

OBJECT CLASSES	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$25,097,000	$26,469,000	$1,372,000
Other Than Full-Time Permanent (11.3)	6,772,000	7,034,000	262,000
Other Personnel Compensation (11.5)	1,230,000	1,260,000	30,000
Military Personnel (11.7)	1,522,000	1,567,000	45,000
Special Personnel Services Payments (11.8)	3,835,000	3,920,000	85,000
Total Personnel Compensation (11.9)	**38,456,000**	**40,250,000**	**1,794,000**
Civilian Personnel Benefits (12.1)	8,295,000	8,542,000	247,000
Military Personnel Benefits (12.2)	848,000	874,000	
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	**47,599,000**	**49,666,000**	**2,067,000**
Travel (21.0)	1,383,000	1,341,000	(42,000)
Transportation of Things (22.0)	119,000	115,000	(4,000)
Rental Payments to Others (23.2)	12,000	12,000	0
Communications, Utilities and Miscellaneous Charges (23.3)	668,000	647,000	(21,000)
Printing and Reproduction (24.0)	763,000	740,000	(23,000)
Other Contractual Services:			
Advisory and Assistance Services (25.1)	1,575,000	1,551,000	(24,000)
Other Services (25.2)	12,155,000	12,407,000	252,000
Purchases from Govt. Accounts (25.3)	53,412,000	52,387,000	(1,025,000)
Operation & Maintenance of Facilities (25.4)	9,721,000	9,531,000	(190,000)
Operation & Maintenance of Equipment (25.7)	1,025,000	1,006,000	(19,000)
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**77,888,000**	**76,882,000**	**(1,006,000)**
Supplies and Materials (26.0)	4,058,000	3,936,000	(122,000)
Subtotal, Non-Pay Costs	84,891,000	83,673,000	(1,218,000)
Total, Administrative Costs	**132,490,000**	**133,339,000**	**849,000**

NATIONAL INSTITUTES OF HEALTH

National Institute on Drug Abuse

SIGNIFICANT ITEMS IN HOUSE AND SENATE APPROPRIATIONS COMMITTEE REPORTS

FY 2006 House Appropriations Committee Report Language (H.Rpt. 89-107)

Item

Drug abuse and HIV/AIDS – The Committee understands that one of the most significant causes of HIV virus acquisition and transmission is drug taking practices and related risk factors in different populations. Drug abuse prevention and treatment interventions have been shown to be effective in reducing HIV risk. Therefore, the Committee encourages NIDA to continue its support of research focused on the development and testing of drug abuse related interventions designed to reduce the spread of HIV/AIDS in these populations.

Action taken or to be taken

Domestically and internationally, drug use continues to play a prominent role in the HIV/AIDS epidemic. Recognizing the urgent need for research-based prevention interventions, NIDA continues to support studies of both HIV-negative and HIV- positive drug users. Interventions to prevent the acquisition and transmission of HIV as well as interventions to reduce the impact of HIV/AIDS among infected drug abusers are high-priority research areas at NIDA.

NIDA research has demonstrated that drug abuse treatment *is* HIV prevention and will continue to support research on the interface between drug abuse treatment and HIV, including new pharmacotherapy applications for heroin addiction and studies to improve linkages with primary care and to develop treatment interventions that can be used in prisons and jail settings. This portfolio also includes research on behavioral treatment approaches to HIV risk reduction.

NIDA is encouraging more research regarding the disproportionate effects of HIV/AIDS among African Americans, who account for half of the HIV/AIDS cases in this country.[r] To this end, a Program Announcement (PA) was issued in late 2005 to encourage research on the relationship between drug abuse and prevalence of HIV/AIDS among African Americans, as well as the intersection of criminal justice involvement. Given the huge impact of HIV/AIDS on African Americans, interventions with this population will also affect the overall transmission rates of HIV in the United States.

Additionally, given the continuing high rates of HIV infection among women of childbearing age, in January 2005, NIDA issued a Request for Applications (RFA) inviting applications for

[r] Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report, 2003 (Vol. 15). Available at: http://www.cdc.gov/hiv/stats/hasrlink.htm.

studies testing interventions to prevent or reduce HIV risk among pregnant women in drug abuse treatment. NIDA is also participating with other NIH ICs in a collaborative research project entitled Pediatric HIV/AIDS Cohort Study (PHACS) to continue long-term follow-up of infants exposed to HIV and antiretroviral treatment, as well as in utero illicit drugs and Hepatitis C. A new RFA, issued in February 2005, will extend findings from PHACS to improve intervention efforts in this group of children. NIDA has renewed its participation in the Women's Interagency HIV Study, an ongoing NIH collaborative effort to improve outcomes for women infected with HIV through biomedical and behavioral approaches aimed at reducing negative consequences.

In addition to supporting research NIDA also supports multiple mechanisms to encourage information dissemination on the topic of HIV. In late 2005, NIDA issued a Research Report regarding the linkages between HIV/AIDS and drug abuse. This publication was issued in conjunction with the release of a new HIV/AIDS public service announcement designed for adolescents. (p. 89)

Item

Translation of research findings – The Committee commends NIDA for its outreach and work with state substance abuse directors, also known as Single State Authorities (SSAs), to reduce the current 15- to 20-year lag between the discovery of an effective treatment intervention and its availability at the community level. In particular, the Committee applauds NIDA for working with SAMHSA on a recent RFA designed to strengthen state substance abuse 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 SSAs to ensure that research findings are relevant and adaptable by state substance abuse systems.

Action taken or to be taken

NIDA continues to build and enhance the productive partnership with state directors of substance abuse agencies, also known as "Single State Authorities" (SSAs). SSAs are charged with managing our country's publicly funded substance abuse system and are considered to be primary consumers of drug abuse and addiction research. SSAs look to NIDA to obtain credible information about selecting, implementing, and sustaining science-based and cost-effective treatment and prevention interventions. NIDA continues to strengthen this partnership through multiple activities to close the 15-20 year lag between research and practice.

One collaborative initiative is the recently funded NIDA-SAMHSA RFA, "Enhancing State Capacity to Foster Adoption of Science-Based Practices." This RFA encourages state agencies to team with research organizations to optimize their research infrastructure to examine delivery of publicly supported drug abuse treatment or prevention services. Seven grants were recently funded to develop new resources to facilitate the statewide adoption of meritorious science-based policies and practices.

Other activities aimed at reducing the gap between research and practice include the landmark NIDA-SAMHSA Blending Initiative, designed to accelerate the dissemination and adoption of recently tested, evidence-based treatment findings into mainstream drug abuse and addiction practice. Blending teams comprising practitioners and researchers are developing "products" from NIDA research, including studies conducted within NIDA's Clinical Trials Network (CTN) and disseminating them to the field. These blending initiative products include training curricula, self-study programs, supervisory manuals, and distance-learning opportunities to provide the treatment providers the necessary tools to access and adopt NIDA research protocols. NIDA's successful history of collaboration with SSAs has been facilitated by the productive partnership with the National Association of State Alcohol and Drug Abuse Directors (NASADAD). NIDA continues to work with NASADAD and SAMHSA to fortify communication with the SSAs, NIDA's CTN, and Addiction Technology Transfer Center (ATTC) representatives. In 2005, NIDA and SAMHSA co-sponsored the most recent all-day meeting designed for NASADAD members titled: "Forging Federal-State Collaborations to Blend Research and Practice" to provide an update of Federal and state research-practice blending activities and to enhance the adoption of evidence-based practices by state-based systems, a strong NIDA commitment. This will continue to be a top priority at NIDA since it ensures that new scientific discoveries are translated into prevention and treatment interventions that are adopted by the community. (p. 89)

Item

Prevention Research – The Committee remains interested in research on preventive medicine and encourages NIDA to conduct research on prevention of drug abuse by focusing on the role environment plays on neurobiological factors such as gene expression.

Actions taken or to be taken

NIDA supports a wide range of both investigator-initiated and RFA-supported research projects examining the many ways in which the environment, including exposure to drugs of abuse and social stressors, can alter neurobiology. NIDA also supports research that furthers understanding of the role of environment and gene confluence in drug abuse. Knowledge in these areas will allow development of more targeted prevention interventions to counter negative environmental consequences. (Please refer to the significant item Genetics of Addiction on page NIDA-18 of this document to learn more about NIDA's innovative efforts in prevention research.)

A FY06 RFA, the "Epigenetics of Neurobiology and Addiction," will bring a new approach to the study of the consequences of drug abuse by elucidating the role and effect of epigenetic modifications. Epigenetics refers to heritable and long-term changes that occur without a change in DNA sequence. Little is known about how epigenetic mechanisms contribute to short- and long-term changes in cell function during an individual's lifespan after the brain is exposed to drugs and other environmental stimuli. Another FY06 RFA, "Social Neuroscience," calls for both animal and human investigations of the effects of alcohol and drug abuse on social behavior and decision-making over the life course, particularly the underlying cognitive/behavioral processes and neurobiological mechanisms. A FY04 Program Announcement (PA), "Epidemiology of Drug Abuse," is stimulating research to advance understanding of the

interplay of social interactions, social environments, and individual behavioral characteristics and genetic vulnerability. Funded projects are looking at the effects of stress and stressors on vulnerability to drug abuse, the social structure of drug markets, and the risks of children exposed to methamphetamine use and manufacture. A FY05 RFA titled "Consequences of Drug Abuse and Alcohol Exposure on Brain and Behavioral Development" has funded seven projects, several studying how the adolescent brain is predisposed to or affected by cannabis use. Topics include prenatal exposure, early brain development, and neurocognitive risks and consequences of adolescent drug use. NIDA is also supporting additional basic research using animal models to see how the integration of neurobiological and behavioral approaches can best be used to study adolescent brain development and brain alterations from drug abuse. (p. 90)

Item

Drug-induced liver injury – The Committee notes that the mechanisms and causes of drug-induced liver injury related to over-the-counter and prescription medications are not well understood and merit further research. The Committee encourages NIDA to work collaboratively with National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Food and Drug Administration (FDA), industry, and the liver research community to address these priorities.

Action taken or to be taken

Drug-induced liver injury is the most common reason that medications are not approved by the FDA, or are removed from the market after they have been approved. And, while this sort of drug-induced liver disease is not an area that falls under NIDA's primary mission, NIDA does conduct studies on Hepatitis C (please refer to page NIDA-6 in this document for the significant item Hepatitis and Drug Abuse), and is currently conducting one study in response to a request for information from the Food and Drug Administration (FDA), concerning a new medication for the treatment of opioid addiction.

NIDA is currently using our National Drug Abuse Treatment Clinical Trials Network to compare the effects of buprenorphine/naloxone with methadone, two pharmacotherapies used to treat opioid addiction, on indices of liver function. A secondary aim of this study is to determine risk factors at baseline (e.g., Hepatitis C infection) and during treatment that could either independently or through an interaction with either medication, cause liver dysfunction.

To address the problem of medication-induced liver injury, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) established and supports the Drug-Induced Liver Injury Network (DILIN), which is studying patients who suffered a severe liver injury caused by over-the-counter or prescription medications, as well as herbals and dietary supplements. DILIN hopes to discover why some people have unwanted liver reactions and others do not. The objective of the study is to help develop the means to prevent, detect, and treat liver disease stemming from toxicity caused by these agents. DILIN includes a retrospective study of four prescription drugs that commonly cause liver injury; a prospective study of prescription drugs, over-the-counter medications, and herbal medications; and the development of instruments to improve diagnosis.

Additionally, within the trans-NIH Action Plan for Liver Disease Research, recently developed with broad stakeholder input—NIDDK, NIDA, FDA, industry, and others in the liver research community—several research goals have been identified in the area of drug-induced liver injury. These goals focus on elucidating the mechanisms of common forms of drug-induced liver disease, developing better tools to diagnose liver toxicity and those vulnerable to it, and identifying effective treatments. The goals are being pursued through support of research initiatives, such as DILIN and by developing collaborations among all stakeholders through workshops and meetings, such as those focusing on implementation of the NIH Action Plan for Liver Disease Research, published in January 2005. (p. 90)

Item

Impact of prescription drugs – The Committee encourages NIDA to conduct research on the use of prescription psychoactive medication in children and adolescents and their impact on the development of mental health and substance abuse problems across the life span of individuals.

Action taken or to be taken

The most commonly used psychotherapeutic medications in children and adolescents are stimulants, such as methylphenidate and amphetamine. Stimulant medications are used in treating attention-deficit hyperactivity disorder (ADHD) because of their well documented efficacy in reducing ADHD symptoms. A meta-analysis examining vulnerability to substance abuse in ADHD children who were treated with stimulants versus those who were not indicated a protective effect during late adolescence and young adulthood. However, given the limited sample sizes and restricted age at follow-up, more surveillance and study are needed, particularly since use of these medications is growing. (For a discussion of opioid abuse and addiction, see page NIDA-25 of this document and the significant item on Reducing Prescription Drug Abuse).

The Multimodal Treatment Study of Children with ADHD (MTA) being conducted by the National Institute of Mental Health (NIMH), of which NIDA is a co-sponsor, will continue to seek answers to determine the best kind of help to offer children with ADHD over the long term. Children in the study are being tracked into adolescence to document and evaluate long-term outcomes, including impact of stimulant medications on mental health and substance abuse. Researchers are conducting an extended follow-up study of about 500 ADHD patients who have been treated with stimulant medications or psychosocial intervention from 7-9 years of age.

The potential link to greater drug use in later years by early users of psychoactive medication is important, given the significant increase in use of stimulant medications to treat ADHD over the past 10 years and the grave problem of all prescription drug abuse among adolescents. NIDA's Monitoring the Future (MTF) survey of 8th, 10th, and 12th graders reports that 9 percent of 12th graders used amphetamines (e.g., Dexedrine) nonmedically in the year prior to the survey. Support of research targeting prescription drug abuse includes a recently reissued Program Announcement (PA), with several funded studies looking at abuse liability with ADHD medications, as well as diversion, and web access. Questions about treatment with stimulant medications have been added to the MTF survey, which will allow tracking of whether increases

in prescription stimulant medications are associated with changes in the patterns of drug abuse in school children.

Many young people also report using prescription medication not necessarily to get high, but to try to improve academic or athletic performance. Use of anabolic steroids by high school students is a part of this trend. While past year use decreased between 2004 and 2005 among 12th graders, declines in use were not observed among 8th and 10th graders. NIDA is supporting basic and clinical research to help illuminate the brain circuitry responsible for abnormal steroid-related behaviors and to find treatments to mitigate the negative effects of steroid abuse. In addition, NIDA supports the development of two highly effective prevention programs: Athletes Targeting Healthy Exercise and Nutrition Alternatives (ATHENA) and Athletes Training and Learning to Avoid Steroids (ATLAS). Recent results from ATHENA show that girls taking part in the program were less likely to use diet pills or performance-enhancing substances. (p. 90)

Item

Hepatitis and drug abuse – The Committee is concerned about the prevalence of hepatitis and substance abuse and urges NIDA to work with voluntary health organizations to promote liver wellness, education, and prevention of both hepatitis and substance abuse.

Actions taken or to be taken

Current incidence and prevalence data reveal hepatitis C virus (HCV) infection as a substantial health problem in this country that is likely to linger for some time. Nearly 4 million people in the U.S. are believed to be infected with HCV, the leading cause of liver disease; approximately 400,000 are also co-infected with HIV.[8] Chronic HCV and HIV co-infection results in an accelerated progression to end stage liver disease and death, compared to HCV infection alone.

NIDA is committed to expanding its substantial research portfolio on HCV, particularly among drug using populations. For while therapeutic programs and treatment models have been developed for drug users with chronic HCV infection, multiple treatment barriers prevent most active or recovered drug abusers from receiving HCV therapy. NIDA supports efforts to develop integrated models of care to better manage co-occurring HCV infection, substance abuse, and psychiatric illness, and has held workshops and developed reports on the state of the science with regard to successful medical management and treatment approaches for co-occurring conditions. These reports have been adapted for medical journals and association publications, expanding the dialogue on the linkages between HCV and substance abuse and how to best address them.

For example, NIDA recently published a special supplemental issue to *Clinical Infectious Diseases* on the medical management of HIV-HCV co-infection. This journal, sponsored by the Infectious Diseases Society of America and the HIV Medicine Association, strives to improve

[8] Romeo R, Rumi MG, Donato MF, Carnel MA, Vigano P, Mondelli M, Cesana B, Colombo M, Hepatitis C is more severe in drug users with human immunodeficiency virus infection. J Viral Hepat (4):297-301, 2000.

the health of individuals, communities, and society by promoting quality care, education, research, and prevention relating to infectious diseases.

Working with its partners, NIDA continues to promote HCV treatment, overcome related obstacles, and educate the community about prevention measures. To this end, outreach to partners, voluntary organizations, and grassroots groups is critical. NIDA has relationships with several organizations (e.g., the Liver Foundation) with whom it works to translate science research on HIV and co-occurring problems into user friendly information for community coalitions. One notable example is CADCA, or the Community Anti-Drug Coalitions of America. NIDA worked closely with CADCA to develop the next issue of *The Practical Theorist*, which discusses drug abuse and related infectious diseases, such as HIV and HCV. This magazine encapsulates field research on drug abuse, along with strategies for using the data to mobilize communities, inform policy, and support coalitions at the community level. CADCA represents more than 5,000 community anti-drug coalitions nationwide, which work at the grassroots level as local partnerships between parents, teachers, young people, law enforcement, health providers, the faith community, business and civic leaders, elected officials, and concerned citizens. (p. 90)

Item

Drug treatment in criminal justice settings – The Committee is very concerned about the well-known connections between drug use and crime. Research continues to demonstrate that providing treatment to individuals involved in the criminal justice system decreases future drug use and criminal behavior, while improving social functioning. Blending the functions of criminal justice supervision and drug abuse treatment and support services creates an opportunity to have an optimal impact on behavior by addressing public health concerns while maintaining public safety. The Committee supports NIDA's efforts in this area, particularly the Criminal Justice Drug Abuse Treatment Studies (CJ-DATS), a multi-site set of research studies designed to improve outcomes for offenders with substance use disorders by improving the integration of drug abuse treatment with other public health and public safety systems.

Actions taken or to be taken

The connection between drug use and crime is well known, with the number of adults incarcerated in Federal, state, and local prisons and jails having soared to 6.9 million. Many of those convicted of drug-related crimes have substance abuse problems; one recent study reported drug addiction rates of 44.3 percent for male inmates and 51.8 percent for female inmates.[t] However, only 13 percent of those in need of treatment services receive them while incarcerated; and each year approximately 650,000 inmates are returned to the community, often without receiving drug abuse treatment or being linked to community-based drug treatment and services.[u] Left untreated, drug-abusing offenders have high rates of relapse to drug abuse and to criminal

[t] Karberg J and James D, *Bureau of Justice Statistics Special Report: Substance Dependence, Abuse, and Treatment of jail Inmates, 2002.* Washington, DC: U.S. Department of justice: Office of Justice Programs, Bureau of justice Statistics, 2005.

[u] Mumola, CJ, *Substance Abuse and Treatment: State and Federal prisoners, 1997.* Washington, DC: U.S. Department of justice: Office of Justice Programs, Bureau of justice Statistics, 1999.

behavior, re-arrest, and incarceration. This cycle jeopardizes public health and public safety and further taxes an already over-burdened criminal justice system.

NIDA's integrated public health-public safety response to counter this cycle includes an initiative to educate judges on the science of drug addiction and its treatment to help them better understand the consequences of drugs to the brain and the effects on behavior of individuals, including their sensitivity to punishment. This initiative also supports grants to evaluate outcomes from drug courts, so as to achieve optimal dissemination and improve outcomes.

NIDA supports a robust research portfolio examining the integration of drug treatment into criminal justice settings, including Criminal Justice Drug Abuse Treatment Studies (CJ-DATS). CJ-DATS is a multi-site set of research studies designed to improve outcomes for offenders with substance use disorders by improving the integration of drug abuse treatment with other public health and public safety systems. CJ-DATS is the result of numerous collaborative relationships between NIDA and other NIH Institutes and Federal agencies.

Concerned about the disproportionate impact of drug abuse and criminal justice involvement in African Americans, NIDA has issued a FY06 Program Announcement (PA) to encourage studies on interventions. In October 2005, NIDA's Health Disparities conference in Atlanta hosted presentations on health disparities and drug courts and other criminal justice issues. (p. 142)

Item

Reducing health disparities – The Committee notes that the consequences of drug abuse disproportionately impact minorities, especially African American populations. The Committee is pleased to learn that NIDA formed a subgroup of its Advisory Council to address this important topic. The Committee applauds NIDA for working to strategically reduce the disproportionate burden of HIV/AIDS among the African American population. Researchers should be 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, including in criminal justice settings.

Action taken or to be taken

In May 2004, NIDA created a Minority Health Disparities Work Group to review the Institute's current racial/ethnic minority health disparities research portfolio and provide strategies to best address these issues. As a result, NIDA created an Institute-wide Health Disparities Committee to address racial/ethnic and other health disparity research and monitor the implementation of NIDA's Health Disparities Strategic Plan.

As the Committee recognizes, HIV/AIDS and criminal justice involvement as a result of drug abuse disproportionately affects African Americans. HIV/AIDS is the leading cause of death in African American men and the second leading cause of death in African American women between the ages of 25-44. Although African Americans comprise 12-13 percent of the U.S. population, they account for the majority (over half) of new cases of AIDS. Moreover, since the

1970s African Americans have experienced one of the greatest increases in representation among prison and jail populations, with about 75 percent of this increase estimated to be drug-related.

In October 2004, the NIDA Minority Health Disparities working group convened a scientific meeting "Reducing HIV and Criminal Justice Involvement in African Americans as a Consequence of Drug Abuse," in which experts discussed the current state of the science regarding these issues and developed a research agenda for the future. As a result, NIDA issued an administrative supplement solicitation in 2005 to give NIDA-funded researchers the opportunity to clarify the relationship between drug abuse and criminal justice involvement in the African American population.

To address the issue of the disproportionate prevalence of HIV/AIDS among African Americans and to further research on the over-representation of African American involvement in the criminal justice system, NIDA will invite applications in FY06 to investigate the basic behavioral, epidemiological, prevention, and treatment sciences associated with HIV/AIDS and criminal justice involvement as a consequence of drug abuse among the African American population. (p. 90)

Item

Child abuse and neglect research – The Committee recognizes the magnitude and significance of child abuse and neglect as a serious public health problem claiming an estimated 896,000 victims in 2002, according to data reported by the Department of Health and Human Services. The Committee applauds NIH for developing a coordinated research agenda for child abuse and neglect involving relevant NIH institutes, including NIMH, NICHD, NIDA, NINR, and NIAAA, the Office of Behavioral Social Science and Research and other appropriate agencies, and the continued collaborative and cooperative efforts in child abuse and neglect research. In response to recommendations in the 1993 National Research Council report which examined the current state of research in this area, the NIH child abuse and neglect initiative first addressed the knowledge gaps in child neglect. The Committee encourages NIH to examine current gaps that exist in research on the abuse of children, including research on treatment interventions with substantiated cases of child maltreatment. The Committee requests that the Director be prepared to report on current and proposed NIH efforts in this area at the fiscal year 2007 hearings.

Action taken or to be taken

Childhood physical, sexual and emotional abuse and neglect is one of the primary social problems affecting families and communities today. NIDA is working to address critical research areas where new knowledge is needed on child maltreatment and drug abuse. NIDA has participated in multiple research initiatives during the past year and recently funded a 2-year pilot study to look at the medical and developmental problems of children exposed to methamphetamine manufacture and use. This study will explore the medical and developmental problems of methamphetamine-exposed children and placement outcomes of children removed from home-based methamphetamine laboratories.

Another area where NIDA is interested in building new knowledge is the link between the chronic stress experienced by maltreated children and subsequent drug abuse. Chronic stress has been documented as a primary factor in the development of substance abuse and addiction, including increasing vulnerability for escalation from use to abuse/addiction, and relapse. NIDA has funded research to study pathways in which child abuse and neglect and posttraumatic stress disorder (PTSD) lead to drug abuse and related problems. Specific attention will be given to exploring how child abuse and neglect lead to increased risk for drug use and abuse in adulthood. NIDA will also examine the association between PTSD and drug abuse. Additional research will investigate the effects of chronic stress on nervous system regulation, attention networks, executive function abilities, and emotion regulation capacities.

NIDA is an active member of the NIH Child Abuse and Neglect Working Group, which meets monthly to coordinate NIH research efforts in child abuse and neglect. Activities include clarifying Institute responsibilities in areas of overlap, identifying research needs, and planning future activities. NIDA is also partnering with four NIH Institutes, SAMHSA, CDC, the Department of Education, and the Administration on Children, Youth and Families to co-fund an RFA titled: "Children Exposed to Violence." Recently funded research will investigate the long-term consequences of exposure to family violence to identify the mechanisms through which exposure to violence in the family might disrupt individual development in adolescence, with consequences that cascade over the life course and affect subsequent public health objectives with drug use, HIV/AIDS risk, and future violence. (p. 109)

FY 2005 Senate Appropriations Committee Report Language (S.Rpt. 141-143)

Item

Adolescent Brain Development – The Committee notes neuroimaging research by NIDA and others showing that the human brain does not fully develop until about age 25. This adds to the rationale for referring to addiction as a 'developmental disease.' The Committee encourages NIDA to continue its emphasis on adolescent brain development to better understand how developmental processes and outcomes are affected by drug exposure, the environment, and genetics.

Action taken or to be taken

NIDA recognizes that adolescence and early adulthood are periods of growth, exploration, and, often, the emergence of drug abuse and addictive behaviors. Understanding normal brain development and its contribution to decision-making will aid in developing effective prevention interventions. NIDA has therefore continued its active participation in the NIH Magnetic Resonance Imaging Study of Normal Brain Development, designed to reveal more about how the brain develops in normal, healthy children and adolescents. To increase understanding of how neurobiological mechanisms and responses—genetic, hormonal, and physiological—underlie, motivate, and guide social behaviors related to abuse and addiction, NIDA has again joined with other Institutes to encourage new animal and human research that applies an emerging social neuroscience perspective to alcohol and drug abuse, highlighting the developmental trajectory.

Research that expands our understanding of the specific effects of drug exposure on developmental trajectories, including the influence of environmental and genetic factors, is critical to developing new, evidence-based prevention and treatment approaches. In 2005, NIDA, in conjunction with NIAAA, issued a Request for Applications (RFA) to encourage diverse research on the consequences of drug exposure to brain and behavioral development. Funded projects will study the effects of cannabis and other drug use on the developing adolescent brain; attention, memory, and executive function; and neurocognitive deficits. Several active projects from previous NIDA RFAs are also investigating various developmental aspects of drug abuse, from identifying characteristics of brain function that may predict risk for addiction to understanding the effects of drug use on brain structure and function.

NIDA is also supporting studies to better understand how genetics and environmental factors affect the impact of drug abuse on adolescent development and behavior. One multi-site study is conducting a genome-wide search among 900 families to identify genetic regions that influence drug dependence in antisocial or conduct-disordered adolescents. Another long-term study is examining the role of family and culture in substance use and related problems in Latino youth.

NIDA continues to sponsor and participate in scientific meetings that address issues of brain development and drug exposure. The 2004 Neurobehavioral Teratology Society annual meeting featured a symposium on neuroimaging of prenatal drug exposure, which allowed scientists to exchange ideas and experiences about the use of brain neuroimaging technology with drug-exposed children, some just entering adolescence. Another symposium, held in October 2005 at the annual meeting of the American Academy of Child and Adolescent Psychiatry, examined the neurobiology of the adolescent brain and increased risk for experimentation. (p. 141)

Item

Clinical Trials Network – The Committee is pleased with the success and progress of NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN). The CTN provides an infrastructure to test the effectiveness of new and improved interventions in real-life community settings with diverse populations, enabling an expansion of treatment options for providers and patients. The Committee suggests that NIDA develop ways to use the CTN as a vehicle to address emerging public health needs.

Action taken or to be taken

NIDA established the CTN in 1999 to underscore its commitment to reduce the current 15 to 20-year gap between research findings on effective treatment interventions and their application in community settings. Now in its sixth year, the CTN has grown to include 17 research centers or "nodes" and 150 community treatment programs across the country. The CTN is composed of university drug abuse researchers, and community treatment providers who work closely and blend their expertise to test research-based treatments in real-life, community-based settings.

Since its inception, CTN protocols have tested pharmacological and/or behavioral interventions for a range of public health issues, including drug abuse and addiction, AIDS/HIV, HCV, and Post Traumatic Stress Disorder (PTSD) among various target groups: adolescent drug abusers,

pregnant drug-abusing women, and Spanish-speaking drug abusers. To date, the CTN has served nearly 6,400 people participating in 21 different research protocols.

One example of the utility of a CTN-tested behavioral treatment intervention is Motivational Incentives for Enhancing Drug Abuse Recovery (MIEDAR), an incentive-based method for promoting cocaine and methamphetamine abstinence. This protocol has yielded promising results for treating both addictions. Information on the successful motivational incentives approach is being prepared for dissemination to community treatment providers through NIDA's collaborative Blending Initiative with SAMHSA.

NIDA is also marshalling the CTN infrastructure to address the emerging public health concern of prescription drug abuse. The misuse and abuse of prescription medications has increased across all segments of the population, and NIDA is responding by designing and conducting a large-scale clinical study of treatment for prescription opioid abuse—an urgent need given the dramatic increase in people addicted to opioid analgesics yet no standardized treatment available. The Prescription Opiate Addiction Treatment Study (POATS) will soon be under way to see if patients addicted to prescription pain killers improve after participating in a treatment intervention that evaluates use of buprenorphine in combination with behavioral therapy.

NIDA is also concerned about the growing public health problem of comorbid drug abuse and mental disorders. For instance, an estimated 15-30 percent of patients with substance abuse problems also suffer from comorbid ADHD. It is believed that in some of these cases, drug abuse may reflect an attempt to self-medicate. Given the urgent need for more research in this area, NIDA is planning to examine whether treating ADHD adolescent and adult drug users with medication will enhance the benefits of concurrent substance abuse treatment. In this and similar ways, NIDA's CTN will continue to mobilize its national infrastructure to help solve challenges to public health across diverse populations and communities. (p. 141)

Item

Collaboration with Single State Authorities – The Committee commends NIDA for its outreach and work with SAMHSA's Center for Substance Abuse Treatment (CSAT) and state substance abuse directors, also known as Single State Authorities (SSAs), to reduce the current 15 – 20 year lag between the discovery of an effective treatment intervention and its availability at the community level. In particular, the Committee applauds NIDA for working with SAMHSA on a recent RFA designed to strengthen state substance abuse 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 SSAs, including its "blending activities," to ensure that research findings are relevant and adaptable by state substance abuse systems. (p. 141)

Action taken or to be taken

Please refer to page NIDA-2 of this document for NIDA's response to the significant item regarding Translation of Research Findings.

Item

Co-occurring disorders –The committee recognizes that addiction is a disorder that can affect the course of other diseases, including HIV/AIDS, mental illness, trauma, cancer, cardiovascular disease, and even obesity. To adequately address co-occurring health problems, the Committee encourages the Institute to work with other agencies to stimulate new research to develop effective strategies and to ensure the timely adoption and implementation of evidence-based practices for the prevention and treatment of co-occurring disorders.

Actions taken or to be taken

Many individuals simultaneously suffer from mental illness or other physical disorders and problem alcohol and drug abuse, resulting in levels of individual suffering and societal costs magnified well beyond those associated with substance disorders alone. Substance abuse can also cause or affect the progression of diseases impacting virtually every system of the body, as well as increase the risk for traumatic injuries—drug and alcohol intoxication being one of the most prevalent precursors to violence and other causes of injury. NIDA's support of research and outreach initiatives to increase physician use of screening and referral services to identify substance abusers and refer them for treatment can help break the cycle. NIDA is also supporting 12 projects investigating possible interactions between substance abuse and post-traumatic stress disorder and 3 studies designed to assess the effects of drug addiction on cancer progression and vulnerability. Six active projects are studying the cardiovascular effects of such addictive drugs as nicotine, cocaine, and methamphetamine. Other linkages under study include those between drug abuse and obesity, recent research revealing more details about shared neural pathways involved in eating and in modulating motivation and reward. To provide regular updates on all these areas and more, NIDA developed a new Medical Consequences website in 2005 (http://www.nida.nih.gov/consequences/)

(Note: see the "HIV/AIDS and drug abuse" significant item on page NIDA-1 for additional relevant information).

A Program Announcement (PA) issued in collaboration with NIMH and NIAAA seeks to examine how the organizational aspects of services influence the quality, cost effectiveness, and treatment outcomes for comorbid disorders. In collaboration with NIMH and SAMHSA, NIDA has issued a FY05 RFA, "Enhancing Practice Improvement in Community-Based Care for Prevention and Treatment of Drug Abuse or Co-occurring Drug Abuse and Mental Disorders," to solicit rigorous test designs for adopting, implementing, and continuing to use science-based policies and practices. NIDA is also working with NIMH to re-issue a PA to establish long-term partnerships between NIH, academia, and industry to advance development and testing of new medications and treatments for mental disorders and nicotine addiction; five nicotine groups have already been funded. Research results will be disseminated at a symposium in February 2006 as part of the annual meeting of the Society for Research on Nicotine and Tobacco. Because most treatment of mental disorders does not address co-morbid addiction problems, NIDA has systematically approached the psychiatric community to educate them on co-morbidity. Initiatives include the publication of a special section of articles in the August 2005 *American Journal of Psychiatry* (the most widely read journal by U.S. psychiatrists) on advances in the understanding of addiction and its treatment. NIDA also actively participates in the annual

meetings of the American Psychiatric Association and the American Academy of Child Psychiatry, and has fellowships available to train psychiatrists on drug abuse research. (p. 141)

Item
Drug Abuse and HIV/AIDS – The Committee understands that one of the most significant causes of HIV virus acquisition and transmission is drug taking practices and related risk factors in different populations. Drug abuse prevention and treatment interventions have been shown to be effective in reducing HIV risk. Therefore, the Committee urges NIDA to continue supporting research that focuses on developing and testing drug-abuse related interventions designed to reduce the spread of HIV/AIDS. (p. 141)

Action taken or to be taken
Please refer to page NIDA-1 of this document for NIDA's response to the significant item regarding Drug Abuse and HIV/AIDS.

Item
Drug-Induced Liver Injury – The Committee notes that the mechanisms and causes of Drug-Induced Liver Injury (DILI) related to over-the-counter and prescription medications is not well understood and therefore merits further research. The Committee is aware that NIDDK currently funds five centers in the Drug-Induced Liver Injury Network (DILIN) and encourages increased support for the DILIN to help identify the underlying mechanisms and patterns in DILI to better obtain data and find patterns in DILI. The Committee also encourages NIDA to work collaboratively with NIDDK, FDA, industry, and the liver research community to address these priorities. (p. 141-142)

Action taken or to be taken
Please refer to page NIDA-4 of this document for NIDA's response to the significant item regarding Drug-Induced Liver Injury.

Item
Drug treatment in criminal justice settings – The Committee is very concerned about the well-known connections between drug use and crime. Research continues to demonstrate that providing treatment to individuals involved in the criminal justice system decreases future drug use and criminal behavior, while improving social functioning. The Committee strongly supports NIDA's efforts in this area, particularly the Criminal Justice Drug Abuse Treatment Studies. (p. 142)

Actions taken or to be taken
Please refer to page NIDA-7 of this document for NIDA's response to the significant item regarding Drug Treatment in Criminal Justice Settings.

Item

Emerging Drug Problems – The Committee recognizes that drug use patterns are constantly changing and is pleased with NIDA's efforts to monitor drug use trends and to rapidly inform the public of emerging drug problems. The Committee encourages NIDA to continue supporting research that provides reliable data on emerging drug trends, particularly among youth and in major cities across the country.

Action taken or to be taken

NIDA recognizes the need to disseminate information regarding the most recent drug abuse related trends in a timely and effective manner. To this end NIDA has invested a significant amount of resources in two major systems of data collection: Monitoring the Future Survey (MTF) and the Community Epidemiology Work Group (CEWG).

Established by NIDA in 1976, the CEWG is a network composed of researchers from major metropolitan areas of the United States and selected foreign countries, which meets semiannually to discuss the current epidemiology of drug abuse. Within the past year, work group members met twice to report on significant developments in their geographical locations. The January 2005 meeting was focused primarily on the abuse of stimulant drugs, but members also reported on the abuse of other drugs as well. Two resulting publications became available in the fall of 2005, summarizing the data presented at the meeting. These data were enhanced with qualitative information gathered through various means, providing invaluable insight into emerging drug use trends, such as the spread of methamphetamine abuse indicators to new populations and localities across the country.

Even though the MTF again reported declines in overall illicit drug use, there remain important areas that need our increased attention, including inhalant abuse and the abuse of prescription painkillers and stimulants.

In response to these findings, this past year NIDA has held a number of meetings to increase awareness of the abuse of inhalants, including convening a seminar, *Inhalant Abuse: An Increasing Problem in Youth*, as part of the Community Anti-Drug Coalitions of America's (CADCA's) National Leadership Forum. NIDA sponsored a similar workshop as part of a special research track at the PRIDE World Drug and Violence Prevention Conference in April of 2005. In addition, NIDA released a Community Alert Bulletin focused on the dangers of inhalant abuse; updated its Research Report on this topic; and issued a Program Announcement (PA) indicating NIDA's interest in supporting additional research on inhalant abuse.

In view of findings from both MTF and CEWG that abuse of prescription pain killers is a major concern, NIDA has taken steps to reinforce, among the public, the dangers associated with taking these drugs without a physician's guidance. Within the past year, NIDA has issued an updated Research Report on prescription drug abuse as well as posted a message from the director on the NIDA web page. NIDA will also increase its support of research to develop treatments for those addicted to prescription pain killers, using the Clinical Trials Network and an RFA aimed at achieving a better understanding of who is at risk of addiction and how to prevent it. NIDA is also investigating strategies to obtain reliable and timely information through use of web-based surveys, and is currently evaluating the reliability of these methods. (p. 142)

Item

Genetics of Addiction – The committee recognizes that not everyone who takes drugs becomes addicted. Research has shown that genetics plays a critical role in addiction, and that the interplay between genetics and environment is crucial. The Institute is urged to further investigate this phenomenon.

Action taken or to be taken

It is NIDA's goal to advance the field by applying and increasing knowledge of human genetic variation in drug responses. It is estimated that about 50 percent of the risk for addiction is influenced by the actions of specific genes and their interaction with environmental factors. Thus NIDA maintains an active portfolio in this area, which includes projects that use epidemiologic approaches to study the role of family genetic and environmental influences in the trajectory of abuse and addiction. To ensure continued quality, in 2005, NIDA convened outside experts to review its portfolio of grants on the genetic epidemiology of drug abuse.

Over the past few years, NIDA has issued or participated in six relevant initiatives on this topic. A 2005 RFA, on which the National Institute of General Medical Sciences (NIGMS) was the lead Institute, provides access to and encourages the mining of new databases for predicting effects of a medication or drug based on an individual's genome. One study awarded by NIDA under this RFA will study the pharmacogenetics of nicotine addiction and treatment. NIDA-supported research to identify vulnerability or protective genes for addiction has resulted in a contract award to Perlegen Sciences. Access was granted to Washington University to collaborate on a whole genome scan to identify nicotine addiction vulnerability genes. Additionally, under a Program Announcement titled "Genetic Epidemiology of Substance Use Disorders," NIDA is funding two projects that include a family study of substance use and conduct disorder and a study of statistics applied to the genetics of substance use.

Discussions of key findings and developments (e.g., on gene-environment interactions), as well as continuing gaps and challenges help guide NIDA's future programs and initiatives. In May 2005, NIDA hosted a symposium on "Translational Research on Drug Abuse: Linkages between Genetics and Prevention" at the Society for Prevention Research to discuss potential ways of integrating epidemiological studies with genetics and prevention research on drug abuse. And in August, NIDA organized the panel, "Behavior Genetics of Drug Abuse in the Molecular Genetics Era," to stimulate discussion on how to combine behavioral and molecular genetics approaches in the search for risk genes.

Also, the First Annual Meeting of the NIDA Phenotype Consortium in November 2005 disseminated findings pertaining to the "Novel Approaches to Phenotyping Drug Abuse" Initiative, as well as provided a forum for grantees to share their findings. This consortium is designed to stimulate innovative approaches for finding better markers of underlying genetic and environmental risk for drug abuse and addiction.

Finally, NIDA is partnering with social scientists to help develop methods to quantify social environments, including family dynamics and parenting practices for use in conjunction with genetic studies of drug addiction. The aim is to be able to understand how the environment and genes interact. (p. 142)

Item

Long-Term Consequences of Marijuana Use – The Committee is concerned with the continuing widespread use of marijuana. The committee urges NIDA to continue support for efforts to assess the long term consequences of marijuana use on cognitive abilities, achievement, and mental and physical health, as well as work with the private sector to develop medications focusing on marijuana addiction.

Actions taken or to be taken

Smoking marijuana (the most commonly used illicit drug among teenagers in the U.S.) can produce adverse physical, mental, emotional, and behavioral changes, and—contrary to popular belief—it can be addictive. Scientists are still learning about the ways in which marijuana affects the brain and other organs. In general, the acute effects of marijuana use are better studied and understood than the consequences of chronic use; therefore, NIDA is committed to better understanding the long-term consequences of marijuana use, including its effects on cognition, health, and behavior.

NIDA's portfolio on the potential consequences of chronic marijuana use has evolved in response to animal studies showing the potential long-term effects on the immune, endocrine, reproductive, and cardiovascular systems, and human studies that indicate possible associations between heavy marijuana use and mental illness. Several existing NIDA grants investigate the effects of chronic use of marijuana, including neuroimaging studies that assess whether marijuana abuse caused measurable long-lasting changes in the brain. Seven projects under the broad RFA, "Consequences of Marijuana Use on the Developing Brain," will investigate the drug's effects from the prenatal period to adulthood.

NIDA also supports research on withdrawal symptoms associated with the abrupt cessation of chronic marijuana use, such as anxiety, irritability, somatic complaints and difficulty sleeping. Other projects focus on the impact of chronic marijuana use in adolescence on school dropout and truancy, and on the development of medications to treat marijuana addiction and withdrawal symptoms. A number of protocols being conducted by NIDA's CTN include patients who abuse marijuana, such as the Brief Strategic Family Therapy, which is testing the effectiveness of a family intervention approach in addressing adolescent drug abuse.

NIDA is committed to engaging in productive collaborations with the private sector to develop medications for the treatment of marijuana addiction. In response to growing evidence suggesting Rimonabant as a promising medication for treating abusers of marijuana and other drugs, NIDA will continue its efforts engage industry in assessing this and related medications as possible addiction treatments. NIDA is supporting seven investigators to evaluate medications for the treatment of marijuana abuse and addiction, in collaboration with pharmaceutical

companies. In FY07, NIDA plans to expand its Strategic Program for Innovative Research on Drug Addiction Pharmacotherapy to support preclinical (animal and cellular) and clinical (human) research to identify and expedite the testing of promising compounds for short- and long-term treatment of cocaine, methamphetamine, or cannabis addiction. Ten projects funded under a FY04 RFA, "Medications Development for Cannabis-Related Disorder" will investigate medications for relapse prevention, withdrawal, and comorbid mental disorders. (p. 142)

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.

Action taken or to be taken

NIDA continues its commitment to working with the private sector to develop medications to use with behavioral therapies to treat drug addiction. NIDA also continues to pursue and form collaborations with pharmaceutical companies to move novel and promising compounds forward to clinical evaluation. NIDA will expand its innovative Strategic Program for Innovative Research on Drug Addiction Pharmacotherapy (SPIRDAP) in FY07 to identify potential compounds for treating addiction to cocaine, methamphetamine, or cannabis. The program requires applicants to form collaborations with basic and clinical scientists and encourages commercial participation to expedite testing and availability of drug addiction treatments.

In the past year, NIDA has made significant progress in identifying potential medications for treating drug addiction. For example, a multi-center trial of baclofen as a treatment for cocaine abuse was completed and is currently undergoing analysis, with outcomes expected soon. NIDA is also initiating a multi-center clinical trial with modafinil, a medication initially developed for the treatment of narcolepsy, which has shown to be beneficial in preliminary studies for the treatment of cocaine addiction. Similarly, topiramate (TOPAMAX), a marketed anti-epileptic medication, has been found to block relapse to cocaine use in a NIDA-funded pilot study among cocaine outpatients at the University of Pennsylvania. Several single-site studies of topiramate have recently been funded, with a multi-center confirmatory study just starting. NIDA has also continued to actively support studies of disulfiram (Antabuse), marketed for treating alcoholism, for the treatment of cocaine addiction. Several single-site trials are ongoing, with a multi-center trial planned. Finally, NIDA has advertised for CRADA partners to study gamma vinyl-GABA (GVG) for treating cocaine and methamphetamine addiction, based on research showing its ability to alter the reward circuitry of the brain.

Because of its growing impact on the public's health, NIDA has made substantial investments in research to develop medications for treating methamphetamine addiction. Through its Methamphetamine Clinical Trials Group (MCTG), NIDA has several medications under development, most of which are already approved for treating other disorders. These medications target various neurotransmitter systems in the brain that play a role in the action of

methamphetamine or are impacted by methamphetamine abuse. NIDA has also expanded its portfolio on development of medications for the treatment of marijuana addiction (see p. NIDA-19 for NIDA's response to the significant item Long-Term Consequences of Marijuana Use).

Recognizing the need for novel compounds to be developed as medications to treat multiple substance-related disorders, NIDA has just released a Request for Applications, "Pilot Clinical Trials of Pharmacotherapies for Substance Related Disorders," which will screen a variety of different medications and provide much needed information that can be used to support continued testing in future trials. (p. 142)

Item

Primary Care Settings and Youth – The Committee recognizes that primary care settings are potential key points of access to prevent and treat problem drug use among young people. The Committee encourages NIDA to support health services research on effective interventions for preventing and treating drug use and related health problems; and develop methods to integrate drug abuse screening, assessment, prevention and treatment into primary health care settings.

Action taken or to be taken

Based on a report by a Blue Ribbon Task Force convened by NIDA to review its Health Services Research portfolio, which recommended that NIDA boost the relevance and use of drug abuse research in practice and policy, NIDA has taken a number of steps, including the reissuing of a Program Announcement (PA) to solicit health services research on the prevention and treatment of drug abuse. Funded studies will examine impediments to delivering interventions, methods of blending science-based practices with community services, and research tools that enable higher quality health services research on drug and alcohol abuse (please see p. NIDA-26 of this document for NIDA's response to the significant item on Translational Research). A second FY05 PA, "Drug Abuse Prevention Intervention Research," encourages studies of cognitive, behavioral, and social processes as they relate to novel approaches to drug abuse prevention, processes associated with empirically validated interventions, and methodologies for studying complex aspects of prevention science.

NIDA's health services research portfolio also includes a collaboration with SAMHSA to fund seven grants under a FY04 RFA, "Screening and Intervention for Youth in Primary Care Settings," in areas ranging from brief interventions for nicotine and cannabis use to brief positive image communications for adolescents. In addition, NIDA is currently funding 10 other grants that deal with primary care and drug abuse, but do not deal with youth.

In April 2005, NIDA, together with CASA, Morehouse School of Medicine, and Kaiser Foundation, hosted the meeting "Missed Opportunity: Substance Abuse and Primary Care." The focus of this meeting was primarily to address the gap between primary care, substance abuse interventions, and treatment services. The target audience included physicians, physician organizations and health insurance/managed care organizations, as well as selected health service researchers.

In 2003, NIDA started the Physician Outreach Initiative, designed to develop strategies to enhance primary care physicians to better serve drug-abusing patients through use of science-based screening and brief intervention. A foundation for this initiative is now being built, which involves recruiting physician work group members, drafting a literature review, conducting initial research into how physicians prefer to receive health information, as well as developing plans for surveying physicians and submitting the required paperwork for permission to conduct surveys and assessments. (p. 142)

Item

Reducing Health Disparities – The Committee notes that the consequences of drug abuse disproportionately impact minorities, especially African American populations. The Committee is pleased to learn that NIDA formed a Subgroup of its Advisory Council to address this important topic. Researchers should be 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, including in criminal justice settings. (p. 142-143)

Action taken or to be taken

Please refer to page NIDA-8 of this document for NIDA's response to the significant item on Reducing Health Disparities.

Item

Reducing Inhalant Abuse – The Committee understands and is alarmed that, for the second year in a row, NIDA's Monitoring the Future Survey has shown an increase in the use of inhalants by 8th graders. The Committee urges the Institute to continue its support of research on prevention and treatment of inhalant abuse, and to enhance public awareness on this issue.

Action taken or to be taken

Inhalants are often among the first drugs that young children use, and NIDA recognizes the need to increase the public's awareness of the dangers associated with these drugs. About 6 percent of children in the United States have tried inhalants by the time they reach fourth grade. Although the most recent Monitoring the Future Survey (MTF; 2005) did not show a continued rise in inhalant abuse among 8th graders, it also did not show a decline; thus, past year and lifetime inhalant abuse in 8th graders remains significantly increased between 2002 and 2005, with 17 percent reporting in 2005 having purposely inhaled potentially toxic vapors often found in common household products at some point in their lives. In response to the increasing use of inhalants among youth, NIDA supports a diverse research portfolio on the topic and has increased its efforts to inform the public about the damaging effects of inhalant abuse.

In May 2005, NIDA issued a Program Announcement titled, "Inhalant Abuse: Supporting Broad-Based Research Approaches," which will remain active until July 2008. It is designed to complement NIDA's existing portfolio in this area, as well as encourage research on all aspects of inhalant abuse. NIDA's existing portfolio supports research from the cellular to the behavioral to the epidemiological level. NIDA-supported researchers have recently employed positron emission tomography (PET) to observe the effects of acetone, butane, and toluene in animal

models, and NIDA-sponsored epidemiological studies have also provided valuable information regarding the use of inhalants by youth. For example, one study showed that youth who used inhalants before age 14 were twice as likely to use opiates compared to those who never used inhalants.

NIDA has also enhanced public awareness regarding this topic this year through meetings and through the development and dissemination of science-based materials on inhalant abuse. In March, NIDA published a new *Community Drug Alert Bulletin* on inhalants, providing a synopsis of some of the latest information on inhalants and inhalant abuse. Nearly 150,000 copies were distributed to Regional Alcohol and Drug Awareness Resource centers, medical libraries, constituent groups, and exhibits. NIDA also updated a *Research Report* on inhalant abuse, which details current research findings, and NIDA staff joined the Director of ONDCP and others in a 2-hour press conference at the National Press Club in Washington, DC, as part of the *National Inhalants and Poisons Awareness Week* activities in March 2005.

NIDA has held a number of meetings to increase awareness of the abuse of inhalants, including convening a seminar, *Inhalant Abuse: An Increasing Problem in Youth*, as part of the Community Anti-Drug Coalitions of America's (CADCA's) National Leadership Forum. NIDA also sponsored a workshop on inhalants as a part of a special research track at the PRIDE World Drug and Violence Prevention Conference in April 2005, where researchers presented the latest information regarding the effects of inhalants on the body as well as the prevention of inhalant abuse among youth. (p. 143)

Item

Reducing Methamphetamine Abuse – The Committee is very concerned about the continued abuse of methamphetamine across the United States. The Committee urges NIDA to continue supporting research to address the medical consequences of methamphetamine abuse.

Action taken or to be taken

Methamphetamine abuse continues to be a problem in many states, persisting at high levels in the western United States and increasing in several areas through 2003–2004. NIDA recognizes the myriad problems posed by methamphetamine abuse and addiction and has been increasing its research efforts accordingly, almost 150 percent from 2000 to 2004. To further ensure that it remains on the cutting edge of research on methamphetamine abuse and addiction, NIDA held a Methamphetamine Working Group meeting in March 2005 to review basic, clinical, prevention and treatment research; identify gaps; and set a research agenda for the future.

NIDA supports a comprehensive research portfolio on the effects of methamphetamine abuse, including its behavioral, cognitive, physiological, and medical consequences, as well as developmental outcomes associated with prenatal and childhood exposure. NIDA-supported research has demonstrated that methamphetamine causes structural and functional changes in brain areas associated with emotion and memory and that with prolonged abstinence, some of these changes may be reversible. Moreover, a recent NIDA-funded pilot study of children prenatally exposed to methamphetamine showed a reduction in the volumes of specific brain

structures that correlated with poorer performance on certain attention and memory tasks. However, caution must be exercised in interpreting these findings due to their preliminary nature and potentially confounding methodological issues. To further increase knowledge in this area, NIDA has launched the first large-scale study of the developmental consequences of prenatal methamphetamine exposure, comparing outcomes to well-matched controls for socioeconomic status and other variables. Also, given the hazardous environments created by home-based methamphetamine labs, in 2005 NIDA funded a study to better understand the medical and developmental outcomes of children removed from these homes.

Methamphetamine abuse is also linked with HIV and other sexually transmitted diseases, not only from the use of contaminated injection equipment, but also due to increased risky sexual behaviors it engenders, as well as physiological changes that may favor HIV transmission. NIDA supports research to better understand this relationship. Recent NIDA-funded studies showed that methamphetamine and HIV may have additive effects in the brain, possibly related to cognitive impairment. In addition, because very little is known about the role of methamphetamine in HIV disease progression or on the prevalence of drug-resistant virus in methamphetamine abusers, in March 2005, NIDA solicited supplemental applications to existing NIDA grants to investigate the emergence and characterization of drug-resistant HIV strains in methamphetamine abusers. Five applications will be funded under this announcement.

Given the devastating consequences of methamphetamine abuse, NIDA will continue to support research not only on its medical consequences, but also on prevention and treatment interventions for methamphetamine abuse and addiction. (p. 143)

Item

Reducing Prescription Drug Abuse – The Committee notes the recent increases in the numbers of people who use prescription drugs for non-medical purposes. Research targeting a reduction in prescription drug abuse, particularly among our Nation's youth, should continue to be a priority for NIDA.

Action taken or to be taken

Abuse of prescription medications has increased in all segments of the population, with sharp increases occurring in the abuse of prescription painkillers among all age groups. In the 2004 Monitoring the Future Survey, more than 9.5 percent of 12th graders reported using the pain medicine Vicodin; and 5.5 percent reported using Oxycontin, making these among those most commonly abused substances by adolescents, after marijuana and alcohol. (Please see page NIDA-5 of this document for a discussion of stimulants and anabolic steroids in NIDA's response to the significant item on Impact of Prescription Drugs).

NIDA continues to sponsor research to counter these negative trends. For example, NIDA-sponsored research revealing substantial non-medical use of prescription opioids tied to socialization among college students suggests that prevention efforts should be focused on high school students who express an interest in fraternity membership. To re-emphasize our interest in prescription drug abuse prevention, education, and treatment, NIDA has recently revised and

reissued a Program Announcement encouraging research on prevention approaches, service delivery, and behavioral and pharmacotherapies targeted to particular populations. Six grants have been funded thus far focusing on a range of issues, from recreational opioid use to mortality rates to the role of prescription drug websites in the use of non-prescribed opioids. Clinical neurobiological investigations using modern brain imaging methods will further understanding of how prescription drugs affect brain processes and systems over the life span.

Because research is also needed to determine whether pain patients are more or less vulnerable to the addictive effects of these drugs and how best to treat co-occurring pain and addiction, NIDA has issued a Request for Applications (RFA), "Prescription Opioid Abuse and Pain." NIDA's intensified investigation will help ensure that pain patients have the treatment they need, encouraging research on the development of pain medications that carry the smallest possible risks for abuse and addiction.

Finally, building on efforts begun last year with its Clinical Trials Network (CTN), NIDA is progressing with a Prescription Opioid Addiction Treatment Study (POATS) in outpatient treatment settings to determine whether adding individual drug counseling to the prescription of buprenorphine/naloxone for subjects addicted to prescription opioid analgesics improves treatment outcomes. Additionally, NIDA collaborated with SAMHSA and the American Society of Addiction Medicine on developing and implementing a day-long symposium entitled "Prescription Drug Abuse: Science to Practice," where several NIDA staff and grantees were among the featured speakers. A separate symposium organized by NIDA—"Increases in Opioid Analgesic Abuse: Concerns and Strategies"—was held as part of the American Psychiatric Association's Annual Meeting in 2005. NIDA also released two new publications for the public on the topic of Prescription Drug Abuse: a Community Alert Bulletin aimed at healthcare providers and an updated Research Report. (p. 143)

Item

Translational Research – The Committee commends NIDA for its broad and varied information dissemination programs. The Committee also understands that NIDA is focused on stimulating and supporting innovative research to determine the components necessary for adopting, adapting, delivering, and maintaining effective research-supported policies, programs, and practices. As evidence-based strategies are developed, the Committee urges NIDA to support research to determine how these practices can be best implemented at the community level.

Action taken or to be taken

Research supports the effectiveness of different approaches and interventions for preventing and treating drug abuse and addictive disorders. Many of these strategies are not widely used in clinical practice, however, and NIDA has begun to focus increasingly on the change processes that occur within organizations seeking to improve their prevention and treatment services. Attention has shifted from viewing the translational process as a one-time linear transfer of innovation from researchers to providers, toward viewing it as a complex multidirectional process of continuous practice improvement that involves the interaction of multiple individual-

and systems-level factors. In order to facilitate understanding how to improve the technology transfer process, NIDA has developed a number of recent initiatives, described briefly below.

A Request for Application (RFA) to enhance state capacity to foster adoption of science-based practices, issued in April 2004, seeks to strengthen state alcohol and drug abuse agencies' capacity to support and engage in research to foster statewide adoption of meritorious science-based policies and practices. Initial research will serve as a foundation for more in-depth services research to be conducted in the future by state agencies and their collaborators to enhance continuous practice improvement in the prevention and treatment of drug abuse and to foster implementation of proven, innovative therapeutic and management policies and practices.

Another RFA, issued in August 2005, seeks to create capacity to conduct practice improvement research among community-based providers of drug abuse prevention and treatment services. The ultimate goal is to foster implementation and sustained use of proven, innovative therapeutic and business policies and practices. This NIDA-sponsored research initiative will receive support from NIMH, as well as from SAMHSA.

A 2005 Program Announcement, co-sponsored by NIAAA, describes key research areas in NIDA's (and NIAAA's) ongoing health services research program. It encourages research to translate evidence-based drug and alcohol abuse treatment interventions into community practice. Investigators are advised to collaborate with public health administrators and agencies responsible for resource allocation and for adoption and rapid infusion of innovative models into existing therapeutic and business practices.

Several meetings also addressed translational goals. For example, a 1-day scientific meeting titled "Enhancing Linkages with the Drug Abuse Treatment System: The Role of Faith Leaders, Communities, and Organizations," held in November 2005, developed a research agenda and focused on translating research-based practices into faith-based treatment services. (p. 143)

FY 2006 Conference Report (C.Rpt. 109-300)

Item
The conferees encourage NIDA to move expeditiously on a cooperative research and development agreement (CRADA) regarding the use of vigabatrin for the treatment of cocaine and methamphetamine addiction.

Action to be taken
As there are currently no medications approved by the U. S. Food and Drug Administration for the treatment of cocaine and/or methamphetamine dependence, both of which have substantial negative public health impacts, the National Institute on Drug Abuse is interested in evaluating the safety and efficacy of vigabatrin for the treatment of cocaine and methamphetamine dependence.

The dependence-producing properties of stimulants have been associated with their actions on the reward pathways in the central nervous system. The neurotransmitter gamma-amino butyric acid (GABA) inhibits stimulant effects on this pathway. Therefore, increasing brain GABA levels with medications such as vigabatrin is a potentially effective treatment strategy for cocaine and methamphetamine dependence. Studies in animal models have shown that vigabatrin can reduce cocaine self-administration. There are also anecdotal reports that vigabatrin prevents the ''high'' associated with cocaine intake in humans addicted to cocaine and can, therefore, result in decreased cocaine consumption. As an initial step in the clinical development of vigabatrin for stimulant dependence, it is important to assess the potential efficacy and safety of this compound in cocaine and methamphetamine dependent subjects.

On May 20, 2005, NIDA solicited proposals through the Federal Register for a CRADA to test the hypotheses that vigabatrin may be a safe and effective medication for the treatment of cocaine and methamphetamine dependence. NIDA received three proposals in response to this announcement, which have undergone peer review. NIDA is currently in negotiations to award the CRADA.

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2006 Amount Authorized	FY 2006 Appropriation	2007 Amount Authorized	FY 2007 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$975,870,000	Indefinite	$970,766,000
National Institute on Drug Abuse	Section 41B	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	24,159,000		24,063,000
Total Budget Authority				1,000,029,000		994,829,000

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 1/
1998	358,475,000 2/	0	0	(0)
1999	393,934,000 2/ 3/	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	997,414,000
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	1,010,130,000	1,035,167,000	1,010,130,000
Rescission				(10,101,000)
2007	994,829,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research
3/ 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 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Office of the Director	19	19	19
Office of Extramural Affairs	16	16	16
Office of Planning and Resource Management	38	52	52
Office of Science Policy and Communications	32	32	32
Division of Epidemiology, Services & Prevention Research	30	32	32
Division of Basic Neurosciences & Behavior Research	26	28	28
Division of Pharmacotherapies & Medical Consequences of Drug Abuse	38	37	37
Center for the Clinical Trials Network	11	12	13
Division of Clinical Neuroscience, Development and Behavioral Research	10	14	15
Intramural Research Program	116	120	120
Total	336	362	364
Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research			
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2003	11.4
2004	11.9
2005	12.7
2006	12.7
2007	12.7

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

Detail of Positions

GRADE	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Total - ES Positions	4	4	4
Total - ES Salary	$611,972	636,450	651,088
GM/GS-15	55	61	61
GM/GS-14	80	83	83
GM/GS-13	34	50	52
GS-12	41	42	42
GS-11	8	8	8
GS-10	1	1	1
GS-9	14	14	14
GS-8	14	15	15
GS-7	6	6	6
GS-6	1	1	1
GS-5	4	4	4
GS-4	0	1	1
GS-3	1	1	1
GS-2	0	0	0
GS-1	0	0	0
Subtotal	259	287	289
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General			
Director Grade	12	12	12
Senior Grade	4	4	4
Full Grade	1	1	1
Senior Assistant Grade			
Assistant Grade			
Subtotal	17	17	17
Ungraded	54	54	54
Total permanent positions	277	300	302
Total positions, end of year	334	362	364
Total full-time equivalent (FTE) employment,end of year	336	362	364
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$152,993	$157,580	$162,300
Average GM/GS grade	12.7	12.7	12.7
Average GM/GS salary	$92,860	$96,574	$98,505

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH
National Institute on Drug Abuse

New Positions Requested

	FY 2007		
	Grade	Number	Annual Salary
Health Scientist Administrator	GS-13	2	$78,900
Total Requested		2	