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NIDA

NATIONAL INSTITUTE ON DRUG ABUSE

*1974–2004*

**ADVANCING THE FRONTIERS OF DRUG ABUSE RESEARCH**

# NIDA Celebrates a Record of Achievement

NIDA
NATIONAL INSTITUTE
ON DRUG ABUSE

These pages celebrate 30 years of progress in drug abuse research sponsored by—and often accomplished at—the National Institute on Drug Abuse, or NIDA. In commemorating the tremendous scientific accomplishments highlighted in these pages, it is important to note that these NIDA-sponsored advances in knowledge of drug abuse have transformed society's attitudes toward drug addiction. For much of its history, addiction has been characterized as a moral failing, a disorder of flawed character and failed willpower. These attitudes have hindered efforts to prevent drug abuse and develop effective treatments for those who suffer with the disease of drug addiction.

In the last 30 years, NIDA has replaced myth and misperceptions about drug abuse with scientific understanding of the true nature of drug addiction. Today, thanks to the accomplishments of thousands of NIDA-supported scientists, there is widespread recognition that drug addiction is similar to diseases such as cancer, heart disease, and diabetes that involve a complex mix of biology and behavior. All are marked by a degree of heritability and biological vulnerability that can interact with external events to engender unhealthy behaviors that eventually trigger disease. Research supported by NIDA has demonstrated conclusively that drug abuse is a preventable behavior, drug addiction is a brain disease marked by compulsive abuse of drugs, and research-based approaches can prevent drug addiction from occurring or treat it effectively once it develops.

With an annual budget approaching $1 billion, NIDA now supports intramural and extramural research on all aspects of drug abuse and addiction. NIDA's in-house research program, which traces its origins to a small research unit created in 1935 to study and treat heroin addiction among Federal prisoners, carries out a comprehensive program of multidisciplinary research studies that complements the Institute's more extensive extramural program. The extramural program supports hundreds of scientists in universities and research centers around the country and abroad in conducting a wide range of basic, clinical, and epidemiological studies to increase understanding of drug addiction and develop improved strategies for preventing and treating it.

Today, NIDA's comprehensive research programs are positioned to accelerate the discovery of new scientific information on the causes and consequences of drug abuse and addiction, develop more effective ways to prevent and treat the disease, and foster the rapid integration of these science-based solutions into clinical practice in communities across America. As it has since its inception, the Institute is advancing the frontiers of drug abuse research as it fulfills its vital mission—reducing the devastating and costly individual, social, and public health consequences of this pervasive disorder.

Nora D. Volkow, M.D., Director
National Institute on Drug Abuse

NIDA
NATIONAL INSTITUTE ON DRUG ABUSE
1974-2004 30 Years

# A Record of Achievement

## ASSESSING THE NATION'S DRUG ABUSE PROBLEMS

Discovering and disseminating useful information on the nature and extent of drug abuse has always been a major focus of NIDA's epidemiological research program. Soon after its inception, the Institute launched the Community Epidemiology Work Group (CEWG) and the Monitoring the Future (MTF) surveys to track nationwide trends and patterns in drug use.

Keeping a pulse on the Nation's drug use has yielded critical information. For instance, CEWG, a nationwide epidemiological network that monitors trends in drug abuse in 21 U.S. cities, sounded an early alarm in the 1990s: MDMA, a dangerous drug also known as ecstasy, was becoming the drug of choice for many young patrons of nightclubs and large parties called raves. MTF, an annual survey of drug abuse among America's students, confirmed the threat, noting that while abuse of most illicit drugs was leveling off or declining slightly among youth, ecstasy use was rising among 10th- and 12-graders. In response, NIDA launched the Club Drug Initiative to boost MDMA research and broadcast the dangers of this drug. The effort culminated in 2001 with a NIDA-sponsored conference that focused international research attention on worldwide increases in young people's use of ecstasy.

*Annual student surveys track use of drugs like ecstasy, a popular dance party drug.*

Since its founding, CEWG has helped establish State and international work groups to extend its critical early drug-warning systems to individual States and most regions of the world. Meanwhile, MTF, which began collecting data on drug use among high school seniors in 1975, broadened its scope in 1991 to include data on 8th- and 10th-graders. Augmenting these data are biennial followup surveys of selected samples of college students and young adults from each senior class.

Policymakers and researchers rely on this information to assess the need for and effectiveness of community- and school-based drug prevention programs. To supplement CEWG and MTF data, NIDA has


*NIDA launched the "Stop Shooting Up AIDS" campaign in 1988 to warn IV drug users of HIV/AIDS risks.*

built a program of ethnographic, cross-sectional, and long-term studies that provides continuous detailed information on patterns of drug use by gender, sexual orientation, race and ethnicity, age, and region.

## ADDRESSING THE HEALTH IMPACTS OF DRUG ABUSE

HIV/AIDS and other infectious diseases—such as hepatitis B and C, tuberculosis, and sexually transmitted diseases—multiply the devastation drug abuse and addiction wreak on individuals, their families, and communities. In the past decade, NIDA has provided worldwide leadership in demonstrating how drug abuse spreads these diseases and in developing effective approaches to reducing behaviors that feed transmission.

NIDA-supported research shows that drug abuse treatment reduces the spread of infectious diseases among drug abusers and their contacts. For instance, patients in methadone treatment programs reduce or eliminate heroin injection, thus greatly lowering their risk of acquiring and transmitting HIV infection via contaminated injection apparatus. Similarly, behavioral treatments reduce high-risk sexual behaviors that often accompany cocaine and methamphetamine abuse and constitute another means of transmitting HIV.

Along with drug treatment, two national NIDA-developed community outreach programs have demonstrated they can reduce disease-transmitting drug-use practices and sexual behaviors among the 7 of 10 injection drug users not in treatment for their addiction. This research has helped NIDA develop a model community-based AIDS prevention program, whereby street-based outreach workers encourage abusers to enter treatment, offer them HIV testing and counseling, and inform them about ways to reduce sharing drug-injection equipment and engaging in high-risk sexual practices, such as unprotected sex.

Current studies on social interactions among drug abusers and their impact on initiation into injection drug use and other high-risk drug use and sexual behaviors hold great promise for further reducing transmission of infectious diseases. This research points to more effective interventions linked to gender, race, and ethnicity factors to help reduce the risk of disease transmission among specific abuser groups and those they know. For example, recent research suggests that counseling African-American women who inject drugs or smoke crack cocaine on strategies

## TRACING THE EFFECTS OF PRENATAL EXPOSURE TO DRUGS

Addressing maternal drug abuse and its effects on infants and children has always been a key NIDA concern. Basic research begun in the 1970s demonstrated that prenatal exposure to heroin, cocaine, and marijuana can impair the physiological and behavioral development of animals. New animal studies are assessing the effects of prenatal exposure to methamphetamine and MDMA (ecstasy)—drugs increasingly used by women of childbearing age. Several of these studies suggest that prenatal exposure to MDMA can lead to cognitive and behavioral impairments among juvenile offspring, particularly males.

The last decade has found NIDA funding long-term clinical studies to determine how prenatal exposure to illicit drugs interacts with environmental factors to affect the development of infants and children. More than 20 studies have been tracking urban, rural, and suburban infants and children prenatally exposed to narcotics, cocaine, or marijuana. Employing sensitive new assessment tools developed to measure neurobiological and behavioral development, these studies are yielding critical data on how drug-exposed and unexposed children develop, respond to stimuli, play, behave, and learn.

Evidence suggests that prenatal cocaine exposure may produce subtle neurobiological, behavioral, and cognitive impairments in early childhood that may affect later intellectual development. Adequate pre- and postnatal care, a nurturing home environment, and supportive parenting appear to help reduce or compensate for drug-induced damage. More seriously impaired children may require educational intervention when they enter school.

Many questions remain about the future of children prenatally exposed to cocaine, marijuana, and opiates. Thus, NIDA's long-running clinical studies will track these children into adolescence, enabling researchers to identify how biological, behavioral, and environmental factors interact to increase or reduce vulnerability to drug abuse in adolescence. This knowledge will contribute to the development of more advanced prevention strategies.

to negotiate less risky sexual behaviors with their partners can increase the effectiveness of NIDA's standard AIDS risk-reduction program.

## UNDERSTANDING THE ADDICTED BRAIN AND BEHAVIOR

People with drug addiction compulsively seek and use drugs, despite harmful personal, medical, family, and legal consequences. Three decades of NIDA-supported research has shown that repeated drug abuse causes structural and functional brain changes that drive these destructive choices and behaviors. Rewarding feelings occur the first time a person uses drugs, promoting continued use. In time, more extensive brain changes occur as chronic drug abuse damages nerve

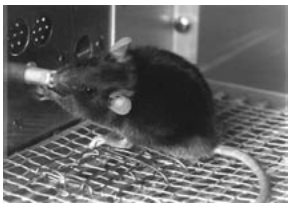
*Dr. Christopher Evans, Duane Keith, and Dr. Robert H. Edwards were part of the UCLA team that cloned the delta opioid receptor, one brain site where morphine binds.*

cells and alters biochemical signaling mechanisms and communications pathways between networks of these cells. These changes allow abused drugs to hijack basic cognitive and emotional functions that motivate people to pursue normally rewarding activities and redirect them toward one overwhelming goal—experiencing the pleasurable effects of abused drugs.

NIDA's molecular, neuroscience, and behavioral research in animals and humans first revealed in the 1970s the primary role the brain plays in drug abuse and addiction. The discovery that both naturally occurring brain chemicals and opiates, such as heroin, act at the same sites in the brain, called receptors, to modulate mood and pain revolutionized thinking about drug addiction and brain function. Building on this insight, NIDA-supported researchers established that drug addiction is a chronic brain disease marked by compulsive drug-seeking, craving during abstinence, and—for many—recurring relapse to drug use during recovery. Discoveries of how abused drugs work in the brain to influence mood, thought, and compulsive drug abuse provide a scientific basis for medications and cognitive-behavioral approaches proven to reduce drug-induced biological and behavioral disruptions, addiction, and its consequences.

In the last decade, NIDA research produced important discoveries about the brain, drug abuse, and other compulsive behaviors at an unprecedented and accelerating pace. Seizing opportunities presented by rapidly advancing research technologies and methodologies in molecular biology and neuroscience, NIDA-supported researchers cloned the genes for the brain receptors through which all major drugs of abuse initiate the complex chain of neurochemical events that produce their addictive effects.

Applying new genetic techniques, researchers reproduced these receptors and used them to develop and test experimental treatment

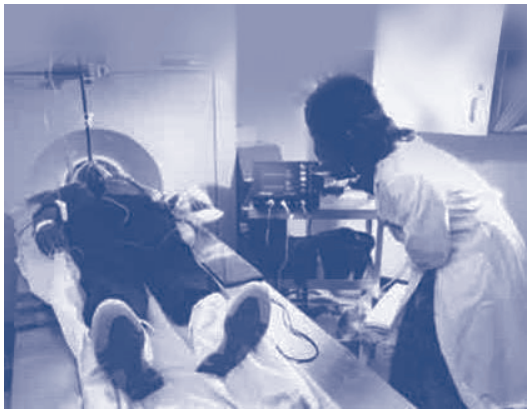


compounds and existing medications for their ability to block or modify the biochemical effects of abused drugs. Scientists also genetically engineered animals that lacked or overproduced these receptors to clarify their role in controlling addictive behaviors, examine how different drugs and compounds affect these behaviors, and mark for possible development as addiction treatment medications those that stop animals from self-administering abused drugs.

The last decade also saw NIDA develop major intramural and extramural programs to apply rapid advances in brain imaging technologies to increase understanding of drug abuse and addiction. Using new positron emission tomography (PET), magnetic resonance imaging (MRI), and electroencephalogram (EEG) techniques, NIDA

scientists can view the human brain in action, assess its moment-to-moment responses to drugs, and show the brain damage chronic drug abuse causes. Imaging studies have located large concentrations of receptors linked to drug abuse in specific areas of the brain and detailed how drug addiction changes the structure of these cells and how they function. By linking acute and long-term, drug-induced changes in brain activity to patients' descriptions of their feelings, choices, and behavior, scientists have made large strides in tracing the brain circuitry, structures, and mechanisms by which abused drugs evoke initial reward, compulsive drug abuse, and craving for drugs when use stops.

NIDA is now opening new vistas in brain imaging drug abuse research. Studies assessing the ability of potential treatment medications and behavioral treatments to moderate the effects of abused drugs on the brain early in treatment and over the long term will accelerate development of new therapies. Other research examining how genetic



*PET scans and other imaging techniques show how drugs affect brain activity.*

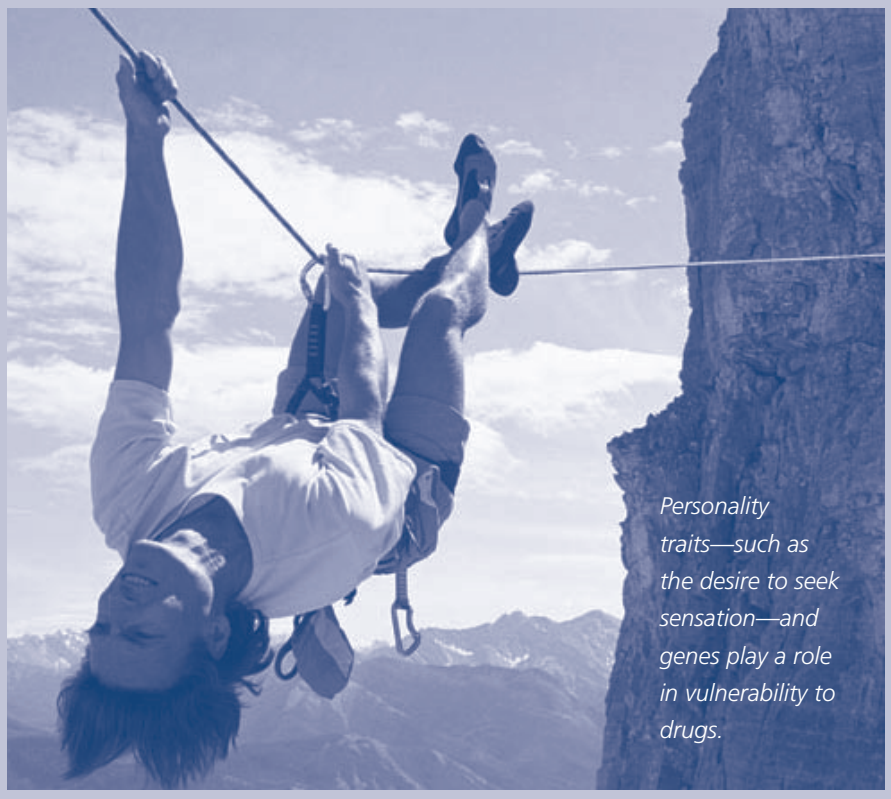
## MOVING TREATMENT FOR OPIATE ADDICTION INTO MAINSTREAM MEDICINE

In 2002, the Food and Drug Administration approved buprenorphine, a new medication that is revolutionizing treatment for opiate addiction. Previous opiate treatment medications, such as methadone, can be dispensed only in federally licensed addiction treatment clinics. Buprenorphine is safer than methadone in case of an overdose, can be discontinued more easily, and is less likely to be abused or diverted to illicit use. As a result, patients addicted to heroin and other opiates can be treated by private physicians in their offices—a first in drug abuse treatment.

NIDA-supported basic and clinical studies dating from the early 1970s made possible buprenorphine's development as a medication. Early findings established that heroin and other opiates achieve their euphoric effects by stimulating brain receptors where neurochemicals act to alleviate pain and modulate mood. The concept of drug-receptor interactions provided the basis for a neurobiological understanding of drug addiction and identified molecular targets for medications that could counter the effects of abused drugs at these brain sites.

In 1993, NIDA-supported scientists cloned the mu opiate receptor, the primary brain site where opiates, including heroin, initiate euphoria. Subsequent research showed that buprenorphine, unlike heroin, only partially activates the mu receptor, while blocking other opiates from binding there. Clinical trials showed that buprenorphine reduced opiate use, had a low potential for abuse, and could be administered safely by physicians to patients in their offices. Additional pharmacological research engineered a combination tablet that blends buprenorphine with naloxone, a medication that completely blocks the mu receptor. The naloxone in this tablet can trigger withdrawal in opiate-dependent individuals but is activated only if the tablet is crushed and injected in an attempt achieve a more potent effect. This safety feature enables physicians to prescribe buprenorphine for long-term use in helping opiate-addicted patients reclaim stable, productive lives.

## WHY ARE SOME PEOPLE MORE LIKELY TO BECOME ADDICTED TO DRUGS?



*Personality traits—such as the desire to seek sensation—and genes play a role in vulnerability to drugs.*

Even as NIDA's drug abuse prevention research continues to expand the range of programs that prevent initial drug use from early childhood to young adulthood, basic research and large-scale human studies are increasing knowledge of how genetic and environmental factors interact to increase or reduce the likelihood that someone will make the transition from drug use to abuse and addiction. This research pursues an ongoing question in drug abuse research: Why can some people stop using drugs after initial use, while others progress to drug abuse and addiction?

In the last decade, NIDA's vulnerability research program, which investigates the interaction of genetic and environmental factors that contribute to drug abuse and addiction, focused on this question. One major finding: Risk factors for experimenting with drugs and initial use differ from those that increase the risk of drug abuse and addiction. While social factors are more important in initial drug use, individual factors—genetics, personality, and certain mental disorders—are more important determinants of vulnerability to drug abuse and addiction.

Genetic research and brain imaging studies have identified genetically controlled variations in the neurobiology and chemistry of the brain reward system that affect whether individuals experience pleasant or unpleasant effects when first exposed to abused drugs. For some people, a heightened response to the rewarding effects of an abused drug on initial exposure may increase the likelihood of subsequent abuse and addiction. In addition,

epidemiological research suggests certain childhood personality characteristics, such as shy-aggressive personalities, and preexisting mental disorders—including untreated attention-deficit/hyperactivity disorder, conduct disorder, depression, and anxiety—also increase the risk that an adolescent who begins to use drugs will transition from drug use to abuse and addiction.

This knowledge could dramatically increase the effectiveness of tomorrow's drug abuse and addiction prevention strategies. New research funded by NIDA and the National Institute of Mental Health will help determine if early treatment of mental disorders that make children more vulnerable to drug abuse can preclude that abuse.

variations affect responses to abused drugs will increase knowledge about vulnerability to addiction. Pediatric studies will increase understanding of how prenatal drug exposure, abuse, and addiction affect the developing brain from early childhood through adulthood.

## PREVENTING DRUG ABUSE AND ADDICTION

In 1992, the science of drug abuse prevention came of age. That year, NIDA-supported scientists published the first systematic classification of individual, family, neighborhood, and school factors that can increase or reduce a child's risk of drug abuse.

*Minimizing risk factors—such as having drug-using friends—and strengthening protective factors—like being successful in school—drive drug prevention programs.*

Identifying risk and protective factors for drug abuse gave NIDA researchers the information they needed to develop broad science-based family, school, and community drug abuse prevention programs. These programs have shown they can reduce rates of initial drug abuse among adolescents, the age group most vulnerable to drug experimentation. The benefits of these programs appear to be long-lasting, reducing the likelihood that children will develop more serious drug abuse problems. Researchers have enhanced the menu of broad drug abuse prevention programs with intensive approaches that help prevent drug abuse among adolescents who are at greater risk than their peers or to reduce use among those who have begun abusing drugs.

With a broad range of effective prevention approaches in hand for middle-schoolers, NIDA researchers are expanding the scope of prevention interventions to cover youths from early childhood through young adulthood. They are examining how the biological, behavioral, and social factors that influence the choice to abuse or avoid drugs change as children develop and mature.

Some interventions appear to mitigate personality traits or behaviors among younger children that are risk factors for later drug abuse, such as antisocial and aggressive behaviors. These interventions also appear to improve academic performance, a protective factor for later drug abuse. Future research will determine whether modifying risk and protective factors can prevent later abuse. At the other end of the developmental spectrum, another set of interventions is addressing social situations and factors most associated with alcohol and drug abuse among high school and college students.

# Developing Effective Addiction Treatments

## PURSUING NEW MEDICATIONS

In recent years, people from all walks of life have sought treatment for addiction to powerful narcotic pain-relieving medications, such as OxyContin and Vicodin, that they have abused outside of a medical regimen. These medications share many properties with heroin, which currently ensnares more than a million people nationwide in the web of addiction. Those who become addicted to legal painkillers or street opiates now have a new medication to help them reclaim their lives. Approved by FDA in 2002, buprenorphine joins two other approved opiate treatment medications—methadone, used in long-term treatment, and the NIDA-developed opiate blocker naltrexone, used to help patients remain drug-free after they have stopped using opiates.

Buprenorphine is the first medication for opiate addiction treatment that can be prescribed by private physicians in offices and clinics. Use of this medication in mainstream medicine should help reduce the stigma still associated with drug abuse treatment, while encouraging more patients to seek treatment for addiction to heroin and other opiates. NIDA also is pursuing medications for cocaine and methamphetamine abuse and addiction, for which no medications are yet available. To fill this void, the Institute is applying the same scientific medications development methodologies that put effective opiate treatment medications into the hands of clinicians and their patients.

On one research track, clinical researchers are screening medications previously approved to treat other disorders. In these small-scale trials, several agents have appeared to weaken the addictive cycle of drug-craving, drug-seeking, and drug-taking. Among them are amantadine (currently used for Parkinson's disease), disulfiram (Antabuse), baclofen (an antispasticity agent), tiagabine and topiramate (antiepileptics), and modafinil (used in narcolepsy). Disulfiram and naltrexone, both effective in treating alcoholism, may fill a critical need for medications that can help cocaine-abusing individuals who also abuse alcohol. Propranolol, a medication used to lower blood pressure, may help substance abuse patients stay the course during the critical

early days of treatment, by alleviating their unpleasant withdrawal symptoms. Researchers are now conducting larger, longer studies to confirm these encouraging results. Because the medications work by a variety of different mechanisms, some of which may complement each other, researchers also will examine whether they may be more effective in combination than alone. Some may also work optimally with specific behavioral therapies.

On another track, researchers in NIDA's cocaine and methamphetamine treatment discovery programs are working to identify new chemical compounds whose pharmacological actions modulate the effects of psychostimulants on the brain and behavior. They already have shown that one compound that blocks a brain cannabinoid receptor can prevent animals from reinitiating cocaine use after exposure to drug-related cues and stressful events. Other compounds that curb the drug-induced flooding of the brain's reward pathways with dopamine may be able to treat addiction to all abused drugs. Still other compounds counter psychostimulants' ability to activate receptor molecules, nerve networks, and neurochemical mechanisms to create pleasure and craving.

Another NIDA initiative is focusing on new medications for treating nicotine addiction. Launched in the 1970s, NIDA's basic research in this area provided the scientific basis for nicotine replacement therapies, such as the transdermal patch, that today help many patients overcome nicotine dependence. The Institute is now pursuing several approaches to medications that could intercept and neutralize nicotine, cocaine, and methamphetamine in the bloodstream before they can act in the brain. In one approach, vaccines containing the abused substance are linked with a larger carrier molecule and stimulate the body to produce antibodies to the drug. Another approach enhances the rate at which the body's enzymes break down the drug molecules into inactive byproducts.


*NIDA uses art cards, displayed in restaurants and other public places, to warn smokers that nicotine, like other drugs, can be addictive.*

## IDENTIFYING EFFECTIVE BEHAVIORAL THERAPIES

Therapies that help drug abuse patients overcome erroneous thought patterns and behaviors that reinforce their abuse and addiction are critical in treating drug abuse and preventing its harmful consequences. Cognitive-behavioral therapies can stand alone as front-line interventions that help many patients stop using drugs and remain drug-free. And they can increase the effectiveness of treatment medications by boosting patients' motivation to remain in treatment, take their medication as scheduled, and learn strategies to avoid relapse and lead drug-free lives. NIDA-supported research has demonstrated that combining

medications, as available, with behavioral treatments is the best way to enhance success for most patients.

Over the last decade, NIDA's Behavioral Therapies Development Program established a three-stage process to develop and introduce new behavioral approaches into clinical practice, similar to that required by the Food and Drug Administration to establish the safety and efficacy of medications. Building on research that suggests avenues for developing new therapies or refining existing ones, pilot studies explore the potential of each new or refined treatment. Those showing promise are then tested in research settings in small- and large-scale clinical trials. Finally, clinical trials can be done in community settings for those therapies that demonstrate therapeutic efficacy.

NIDA behavioral therapy researchers have designed several cognitive-behavioral therapies to help methamphetamine abusers. One innovative therapy gives patients a voucher each time they submit a drug-free urine sample. Vouchers may be exchanged for goods or services that provide pleasurable, legal alternatives to drug use or, as in methadone treatment programs, for special privileges, like reducing the number of required visits to a treatment clinic. Studies show that providing vouchers for drug-free urine tests can help patients stop cocaine and methamphetamine use and remain abstinent for extended periods. Variations of voucher-based therapies that use lower cost vouchers or involve family and other community resources in treatment can be matched to the resources of treatment programs and needs of cocaine-addicted individuals.

*Family therapies tailored to the ethnicity or race of substance-abusing teens have proven successful.*

In the last 10 years, behavioral treatments have demonstrated their potency in improving the health of diverse individuals with many types of drug abuse and other mental disorders. Proven treatments include individual cognitive-behavioral therapy, family therapies for Hispanic and African-American adolescent substance abusers, combination behavioral and medication therapies for adult smokers, and couples therapy for opiate-addicted men and women in methadone treatment programs. The benefits of many of these treatments endure long after treatment has ended. And with individual cognitive-behavioral therapy, the benefits appear to increase over time.

# Research and Practice Partnerships

## TESTING NEW TREATMENTS IN THE NATION'S CLINICS

In NIDA's first 30 years, its research programs produced many promising new medications and behavioral treatments. Yet, as in other areas of medicine, new and improved treatments for drug abuse have often taken too long to make their way into wide clinical use. In 1999, NIDA acted to bridge the critical gap between research and practice by launching the largest initiative in its history—the National Drug Abuse Treatment Clinical Trials Network (CTN).

The CTN embraces an ambitious plan to accelerate the transfer of new science-based behavioral and pharmacological approaches into treatment: to create a national research-practice infrastructure to test and modify promising treatments in community treatment programs, rather than specialized research settings, and rapidly transfer those

proven effective into clinical practice. The network also seeks to develop new treatments that reflect the practical knowledge of the clinic, thus accelerating their acceptance and application in practice.

Beginning with 5 regional research and training centers, each linked to as many as 10 community treatment programs, the CTN brought researchers into community clinics to work alongside practitioners in testing research-based treatments. In little more than a year, NIDA and the pioneering group of university researchers, treatment programs, and practitioners built the organizational and procedural foundation for the CTN, selected promising pharmacological and behavioral approaches, developed standardized clinical protocols, and began testing them in trials with a variety of patients at multiple sites.

The CTN now encompasses 17 regional research and training centers and 115 community treatment programs across the Nation. Minorities, pregnant women, adolescents, and drug abuse patients suffering from post-traumatic stress disorder or depression are among the pool of nearly 9,000 drug abuse treatment patients in 27 States who have or will soon participate in 22 clinical protocols—some under way, some still being refined—for a variety of new treatment approaches. Medication trials range from assessing the effectiveness of buprenorphine in detoxifying opiate-dependent patients to determining whether a combination buprenorphine/naloxone tablet can help treat heroin-addicted adolescents. Behavioral treatment trials take many approaches: tests using motivational enhancement techniques or tangible incentives for staying drug-free to enhance standard counseling approaches, several HIV risk-reduction interventions, and an intervention to help patients in drug abuse treatment stop smoking.

## TAKING PREVENTION PROGRAMS INTO OUR COMMUNITIES

*Community-based prevention programs teach children strategies to avoid drug initiation and other harmful behaviors.*

Although a relatively new science, drug abuse prevention has already yielded a bounty of programs capable of steering many young people away from drug use. As with drug abuse treatments, however, many of these research-proven programs stayed on the shelf, while simpler, less effective approaches were used. Even when such approaches were selected, they often were not delivered to maximum effect.

Taking a cue from the CTN, NIDA began to partner prevention researchers and practitioners to establish research-based programs in the Nation's communities. A major component of NIDA's recently launched broad-based National Prevention Research Initiative instituted four

large-scale field trials of proven drug abuse prevention approaches. These trials find scientists and practitioners collaborating to deliver a research-tested intervention to diverse groups of children and adolescents in urban, suburban, and rural sites. Each trial examines factors with potential impact on a program's effectiveness, such as how different training methods affect its delivery or how accurately community service programs deliver an intervention to different groups in various settings.

Results of these joint research-practice studies will reveal practical barriers to widespread dissemination and implementation of research-tested programs. Equally important, they will point to how programs can be adapted to meet the needs of local communities while still reducing drug use. Ultimately, blending science-based knowledge with community realities will produce more practical prevention programs that will be used by more communities to divert children and adolescents from initiating drug use.

## ADVANCING THE FRONTIERS OF ADDICTION RESEARCH AND PRACTICE

The first three decades of NIDA leadership ushered drug abuse science toward full maturity. The result: profound and practical insights into the complex biological, behavioral, cognitive, and environmental interactions that influence every aspect of drug abuse and addiction. Practitioners now have many effective tools for preventing and treating drug abuse and addiction and their costly public health and social consequences. Yet, much work remains. Too many children and adolescents continue to experiment with drugs, putting themselves at risk for addiction. Research to speed the development and application of prevention strategies stands at the forefront of NIDA's priorities.

Additional NIDA research initiatives continue to address the critical need for treatments for drug abusers who suffer from mental illnesses or abuse multiple substances, including nicotine and alcohol. And more broadly effective prevention and treatment approaches will enable NIDA to fulfill its public health mission of reducing the severe health consequences of addiction, including increased risk of contracting and transmitting infectious diseases.

NIDA is applying revolutionary new techniques in molecular biology, brain imaging, and cognitive neuroscience to these outstanding issues in drug abuse etiology, prevention, and treatment. For example, neuroscientists in the Institute's proteomics program are using 3-dimensional imaging technology to map how distinct proteins in different regions of the human brain function, interact, and change from initial drug use through the transition to addiction. Such research promises new understanding of the molecular mechanisms of drug addiction and the underlying processes of normal and diseased brain function. While offering important new targets for the next generation

## COLLABORATING TO COMBAT TOBACCO USE AND NICOTINE ADDICTION

In July 1998, NIDA, with the National Cancer Institute (NCI), the Centers for Disease Control and Prevention, and The Robert Wood Johnson Foundation (RWJF), sponsored "Addicted to Nicotine," a national research conference on tobacco use and nicotine addiction. This event shed new light on the complexity of research challenges posed by nicotine addiction. Informal conversations among researchers and policymakers highlighted the need for an innovative research approach to meet these challenges. Within a year, this dialogue yielded a proposal: develop Transdisciplinary Tobacco Use Research Centers (TTURCs) to foster collaborations among scientists across many disciplines and allow them to investigate tobacco use and nicotine's effects at levels ranging from molecular genetics to peer interactions. By October 1999, NIDA and NCI announced the first TTURC awards and committed about $70 million to the effort over 5 years. RWJF committed an additional $14 million.

*The transdermal patch, based on early NIDA research, has proven helpful to many smokers trying to overcome nicotine dependence.*

Today, investigators at seven TTURCs across the country are carrying out the research agenda that gave birth to the centers. Their collaborations have produced scores of published studies that advance our understanding of nicotine's addictive effects and the scope of influence smoking has on the Nation's health. Consider the following research accomplishments and initiatives:

**Brown University**—described intergenerational effects, including maternal smoking during pregnancy, that influence smoking initiation and increase the risk for nicotine addiction among adolescents.

**University of California, Irvine**—elucidated the neurobiological impact of nicotine, particularly on the developing brain.

**University of Pennsylvania/Georgetown University**—shed new light on how inherited variations in enzymes increase or decrease the likelihood of becoming addicted to nicotine or contribute to the effectiveness of smoking cessation treatments.

**University of Southern California**—expanded understanding of the role of cultural, ethnic, and peer influences on smoking behavior.

**Yale University**—identified sex differences that contribute to differential success of treatment for men and women and is developing treatments to help smokers who have had the most difficulty quitting.

**University of Minnesota**—began developing and evaluating new smoking cessation treatments, including vaccines to prevent nicotine from reaching the brain.

**University of Wisconsin**—is pursuing strategies to expand access to and increase use of smoking cessation programs and identify measures that reduce the risk of relapse.

of therapeutic approaches, this research may someday allow clinicians to match an intervention to a patient's physiological or genetic traits.

The role that interactions between genetic factors and the environment play in vulnerability to addiction is another area of promise recently opened up through advances in scientific technologies. For while genes and the proteins they produce may increase or reduce the risk of addiction, they do not function in isolation. Using brain-imaging techniques, researchers recently found that social environment can modify monkeys' neurobiology, thereby reducing their likelihood of self-administering drugs. In the study, housing conditions and social interactions altered the genetic expression of proteins in the brain that enable animals, including humans, to experience pleasure and the effects of drugs.

The complexity of drug abuse questions that have come to the fore requires investigation from multiple perspectives. To achieve this goal, NIDA has launched broad research initiatives involving Federal, State, and local government agencies; scientists from many different fields; public and private health service providers; prevention and treatment professionals; and private pharmaceutical companies. One key feature of these collaborations is their emphasis on the resources and practical needs of communities at all research stages—from basic discovery through intervention development to actual trial and integration in community prevention and research programs. Examples of collaborative initiatives include the following.

*Environmental factors, such as a positive home life, may boost brain chemicals that offer resistance to drugs' reinforcing effects.*

**Transdisciplinary Research Centers.** Teams of researchers pool their expertise to search for new knowledge about the interplay of individual, cognitive, social, and environmental circumstances in fostering drug abuse and its many harmful consequences. NIDA currently supports transdisciplinary centers in prevention and tobacco use research. In the tobacco use centers, NIDA, with the National Cancer Institute and the Robert Wood Johnson Foundation, supports investigation of all aspects of tobacco use, from factors that influence initiation through those that aid cessation. The goal is to discover new ways to prevent and treat nicotine addiction, particularly in adolescents.

**Collaborating With Other Federal Agencies.** NIDA is participating in research initiatives with other NIH Institutes, including those that research allergy and infectious diseases, neurological disease and stroke, mental health, alcoholism and alcohol abuse, cancer, and child health and development. Studies funded under these initiatives will help the biomedical research and practice community better understand the links between addiction and comorbid mental and physical disorders. This research will accelerate discovery of prevention and treatment interventions for such disorders as hepatitis, HIV, mood and conduct disorders, and other problems often associated with drug abuse as cause, consequence, or both.

**Working With Private Industry and Practice.** Research partnerships with private pharmaceutical companies are fostering new approaches to treat drug abuse and addiction, including vaccines currently in clinical trials. Agreements negotiated with pharmaceutical companies are enabling NIDA's Medications Development Program to explore the potential of patented compounds in treating cocaine, methamphetamine, and nicotine addiction. NIDA also is working to raise private medical practitioners' awareness that they can play a critical role in improving their patients' health by being alert to the signs and symptoms of substance abuse and aware of treatment options for addiction and related medical and psychiatric problems.


*Fostering research-clinician partnerships is a focus of* Science & Practice Perspectives, *NIDA's peer-reviewed journal.*

**Strengthening Research-Practice Partnerships.** To broaden the research-practice partnership that the CTN has initiated, NIDA has organized regional blending conferences to extend the reach of treatment research into the Nation's community treatment programs. The conferences allow clinicians and researchers to examine how to apply cutting-edge findings about drug use and addiction in clinical settings. NIDA also supports the Substance Abuse and Mental Health Services Administration (SAMHSA) in developing, deploying, and evaluating evidence-based treatment approaches for drug abuse in community-based clinics. These efforts bring research and practice closer together, inform development of more effective and useful interventions, accelerate adoption of research-tested approaches, and improve the quality of drug abuse prevention and treatment.

**Improving Criminal Justice Drug Abuse Treatment Services.** The majority of the 600,000 inmates who return to their communities from prison each year have untreated substance abuse problems that can quickly lead to relapse to drug abuse and criminal behavior. Thus, NIDA has taken the lead in building a multi-agency consortium to develop integrated approaches to the treatment of incarcerated individuals with drug abuse and addictive disorders and test them at multiple sites throughout the Nation. Joining the Institute in this much-needed National Criminal Justice Drug Abuse Treatment Study to improve drug abuse treatment services for offenders are SAMHSA, the Centers for Disease Control and Prevention, and the Department of Justice.

# Key NIDA Accomplishments

## THE ADDICTED BRAIN AND BEHAVIOR

- Developed animal models that scientists use to explore human drug abuse and addictive behaviors and conduct initial screening of potential treatment compounds.
- Discovered that naturally occurring neurotransmitters act at opioid receptors in the brain and that heroin and other opiates activate the same sites to produce addictive effects.
- Identified and cloned the dopamine transporter, the primary brain site where cocaine acts to initiate biochemical events that result in euphoria and addiction; later cloned the brain receptors through which every major abused drug initiates the complex chain of neurochemical events that produce addictive effects.
- Demonstrated that drug-induced flooding of the brain's nucleus accumbens with dopamine is ultimately involved in producing the addictive effects of abused drugs.
- Revealed an intricate network of interrelated biological mechanisms and neurotransmitters that inhibit or increase dopamine release in the nucleus accumbens, providing new biological targets for treatment medications.
- Identified genetic variations that affect the rate of metabolism of nicotine linked to risk of initial abuse and addiction to smoking.
- Used brain imaging studies to document and characterize brain damage from long-term methamphetamine and cocaine abuse in humans.

## DRUG ABUSE PREVENTION

- Established the scientific basis for development of effective prevention programs by identifying individual, family, and neighborhood factors that put children at risk for drug abuse and addiction.
- Synthesized the findings of the initial two decades of prevention research in the first research-based guide to drug abuse prevention, Preventing Drug Abuse Among Children and Adolescents: A Research-Based Guide (updated in 2003). The booklet describes the elements of successful drug abuse prevention programs, explains what research has uncovered about risk and protective factors for drug abuse, and answers questions on designing, implementing, and assessing drug abuse prevention programs.
- Issued Assessing Drug Abuse Within and Across Communities: Community Epidemiology Surveillance Networks on Drug Abuse, which helps communities select drug abuse prevention and treatment programs tailored to their needs.

## MEDICATIONS DEVELOPMENT

- Demonstrated the effectiveness of using adequate doses of methadone administered in a comprehensive treatment program to manage heroin addiction and reduce transmission of infectious diseases.
- Partnered with pharmaceuticals to develop and secure FDA approval of the opiate treatment medications naltrexone, an opiate blocker; LAAM, a long-lasting form of methadone; and buprenorphine, a safer medication with less potential for abuse.
- Defined the central role of nicotine in cigarette smoking and dependence and provided the scientific basis for the development of nicotine replacement therapies—the transdermal nicotine patch, nicotine gum, and the nicotine inhaler—that have helped smokers overcome their addiction to cigarettes.

## BEHAVIORAL THERAPIES

- Established a rational model for developing behavioral therapies, enabling researchers to take new treatments from concept to clinical application.
- Demonstrated the effectiveness of a broad range of behavioral therapies for drug abuse, described in NIDA's research dissemination booklet, Principles of Drug Addiction Treatment.
- Developed detailed manuals for clinicians on how to implement five research-tested cognitive-behavioral treatments for cocaine abuse.
- Supported research to develop and test treatments for patients suffering from coexisting mental and addictive disorders, such as post-traumatic stress disorder and cocaine abuse.

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