STRATEGIC PLAN EXECUTIVE SUMMARY

For the past three decades, the National Institute on Drug Abuse (NIDA) has led the way in supporting research to prevent and treat drug abuse and addiction and mitigate the impact of their consequences—particularly the spread of HIV/AIDS and other infectious diseases. To confront the most pressing aspects of this complex disease and to tackle its underlying causes, our strategic approach is necessarily a multi-pronged one that takes advantage of research programs in the basic and clinical neurosciences, including genetics, functional neuroimaging, and social neuroscience; medication and behavioral therapies; prevention; and health services. Our burgeoning portfolio has given us a large and growing body of knowledge that informs our strategic directions for the future. These directions are grouped into four major goal areas, reflected in the chapters that follow:

I. Prevention
II. Treatment
III. HIV/AIDS
IV. Cross-cutting Priorities

I. Prevention: ***to prevent the initiation of drug use and the escalation to addiction in those who have already initiated use.*** Our prevention research has led to today's improved understanding of addiction and has positioned NIDA to build upon solid epidemiological findings and new insights from genetics and neuroscience, including those revealing the myriad contributors to addiction and the involvement of multiple brain circuits in addictive processes. A major focus of our efforts will be the determined pursuit of why some people get addicted while others do not. To that end, we will support research that strives to identify the factors that put people at increased risk of drug abuse or protect them from it. We are already getting answers to questions we were unable even to ask before, taking advantage of new knowledge about the interaction of interconnected brain circuits and our rich data sources to learn more about how people become addicted and why. Results will allow us to foster more effective counter strategies, particularly to prevent young people from ever using drugs in the first place. We plan to apply modern technologies (e.g., new genetics and brain imaging tools) to our prevention studies and to devise creative and targeted communications strategies to bring about more effective prevention interventions.

NIDA's Prevention objectives include:

1. To identify the characteristics and patterns of drug abuse.
2. To understand how genes, environment, and development influence the various risk and protective factors for drug abuse.
3. To enlarge our understanding of basic neurobiology as it relates to the brain circuitry underlying drug abuse and addiction.
4. To use this knowledge towards the development of more effective strategies to prevent the initiation of drug use and the continued abuse that can lead to addiction.

II. Treatment: ***to support research to develop successful treatments for drug abuse and addiction, and to improve their accessibility and implementation.*** Given the complex interactions of biological, social, environmental, and developmental factors that underlie this disease, NIDA acknowledges the need to take a "whole systems" approach to treating it. We will take advantage of recent discoveries that have uncovered an expanded range of possible targets within these interconnected brain systems to potentially affect craving, euphoria, motivation, learning, memory, and inhibitory control—key contributors to addiction and relapse. To bring about more customized treatments, we will leverage our comprehensive therapeutic research portfolio to advance more effective medication and behavioral therapies. Innovative approaches will take into account genetic variation, comorbid conditions (e.g., mental illness, chronic pain), and the addicted person's changing needs over time. We will make the most of promising compounds being developed as well as medications already on the market, testing their efficacy in counteracting drug-induced changes in the brain and in enhancing the utility of behavioral therapies. We will also apply a scientific approach to understand how to best test and disseminate research-based treatments and how health services systems and settings can optimize treatment implementation. This objective requires that we continue to strengthen our productive partnerships—with treatment practitioners, State substance abuse programs, and other Federal agencies—to help move proven treatments into clinical practice at the community level.

NIDA's Treatment objectives include:

1. To develop effective medications and behavioral interventions to treat drug abuse/addiction and to prevent relapse.
2. To support the design of treatments that target specific aspects of drug abuse and addiction, including an addicted person's changing needs over time.
3. To develop treatments for abuse/addiction in association with comorbid conditions.
4. To develop the knowledge that will lead to personalized or customized treatments.
5. To translate research-based treatments to the community.

III. HIV/AIDS: ***to support research that seeks to diminish the spread of HIV among drug abusers and their partners, and minimize the associated health and social consequences of the disease.*** Drug abuse continues to be a major vector for the spread of HIV/AIDS through its connection with other risky behaviors, such as needle sharing and unprotected sex. Our research has advanced the less acknowledged link between drug abuse in general and the resulting impaired judgment that can lead to risky sexual behavior and HIV transmission, highlighting the value of drug abuse treatment in preventing HIV spread. We plan to continue to support primary prevention research to find the most effective HIV risk-reduction interventions for different populations. Young people are a major focus for these efforts, calling for strategies that start early and can adapt with age. NIDA will also support research to develop effective secondary prevention strategies designed to reduce HIV transmission. Our strategy includes seeking out the best ways to incorporate HIV education, testing, counseling, and treatment referral and supporting research to identify and overcome barriers including stigma and HIV and drug abuse treatment access. NIDA also plans to sponsor research to learn more about the multiple interactions that occur with neurological complications of HIV, substance abuse, other comorbid psychiatric disorders, and their treatment so that more responsive counter interventions may be

developed. We will also strive to target HIV/AIDS-related health disparities and integrate HIV/AIDS initiatives worldwide.

NIDA's HIV/AIDS objectives include:

1. To support research to better understand the etiology, pathogenesis, and spread of HIV/AIDS among drug abusing populations.
2. To help prevent the acquisition (primary prevention) and transmission (secondary prevention) of HIV among drug abusers and their partners.
3. To decrease the health disparities associated with HIV/AIDS.
4. To support international research on the intertwined epidemics of drug abuse and HIV/AIDS.
5. To improve HIV treatment and outcomes in drug abusers through a better understanding of interactions with drugs of abuse, HIV/AIDS disease processes, and the medications used to treat both.

IV. Cross-Cutting Priorities. Several additional priority areas span NIDA's portfolio and greatly contribute to our overall goal of reducing drug abuse and addiction. We will draw on the quality infrastructures we have in place today to pursue knowledge across different agencies and fields, nurturing productive relationships with our many stakeholders. We plan to support research and initiatives to accomplish the following goals:

- To decrease **health disparities** related to drug addiction and its consequences.
- To ensure a **diverse and highly trained workforce** able to assume leadership roles in the research agenda on substance abuse and related disorders.
- To promote collaborative **international research** activities, including training and dissemination of science-based information on drug abuse.
- To promote a more **rapid translation of research findings** into clinical application and practice.
- To **educate a variety of audiences** (e.g., children, parents, teachers, media, legislators, and others) about the science underlying drug abuse.
- To **leverage NIDA resources across the entire NIH research community** to expand our knowledge base and increase awareness of the import of drug abuse on other health issues.

I PREVENTION

Overall Goal

To improve drug abuse prevention efforts through scientific research: To prevent the initiation of drug use and the escalation to addiction in those who have already initiated use is the best way to avoid the myriad adverse health, social, and economic consequences of addiction.

Objectives

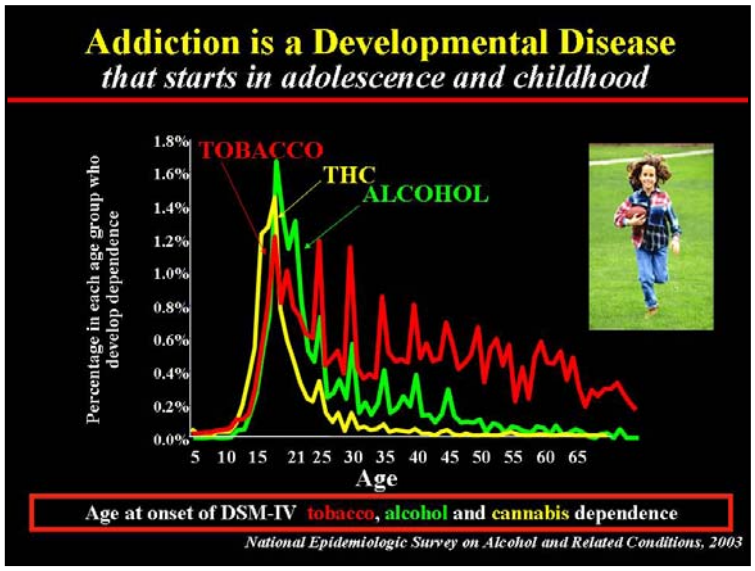
1. To identify the characteristics and patterns of drug abuse.
2. To understand how genes, environment, and development influence the various risk and protective factors for drug abuse.
3. To enlarge our understanding of basic neurobiology as it relates to the brain circuitry underlying drug abuse and addiction.
4. To use this knowledge towards the development of more effective strategies to prevent the initiation of drug use and the continued abuse that can lead to addiction.

Introduction––The Value of Research–Based Prevention Approaches

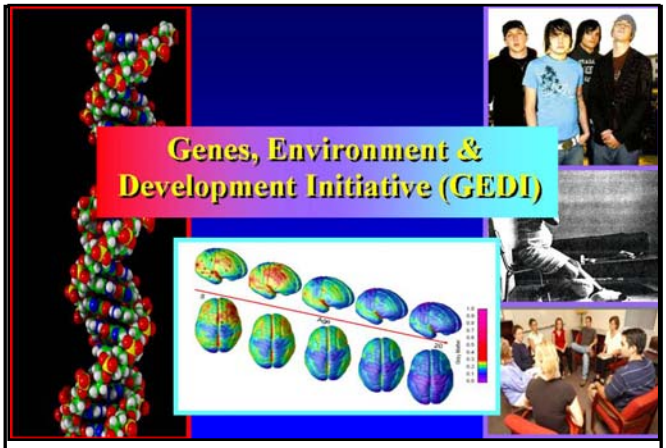
The basic and clinical research NIDA has sponsored for more than 30 years has led to a vast and growing body of knowledge that informs NIDA's strategic directions for the future. For while multiple challenges remain, NIDA will continue to capitalize on opportunities to meet our short- and long-term goals, which are, respectively: to prevent those who are abusing drugs from intensifying their abuse and becoming addicted, and to develop and deploy the best strategies to prevent people from ever starting.

This expanding body of knowledge is leading to evidence-based prevention strategies that build upon solid epidemiological, genetic, and neuroscience research. NIDA's prevention research is assessing the impact of both micro (e.g., family, peers) and macro (e.g., poverty, stigma) environments, using a data-driven approach for preventing drug abuse and addiction in all populations.

Although NIDA recognizes that abuse and addiction only affect a subset of those exposed, any illicit or inappropriate drug exposure can place an individual at risk for serious health consequences. Even a one-time drug experience could lead to accidents or disease stemming from the risky decision-making that can result from drug intoxication. Since experimentation is a common motivation for adolescents to use drugs, our prevention messages must be aimed at keeping young people from ever trying drugs in the first place.



Indeed, the adolescent population is of particular interest for NIDA because drug abuse typically begins during this period of heightened risk-taking. By supporting **epidemiological studies**, such as the Monitoring the Future (MTF) survey, we are able to identify emerging trends among adolescents, and guide responsive national prevention efforts. For example, MTF revealed that in 2007, prescription medications, along with over-the-counter drugs (cough medicine), accounted for five of the top six drug abuse categories reported by 12th graders, marijuana still the most frequently abused illegal drug. Second in frequency of abuse was the prescription painkiller Vicodin, with roughly one in ten seniors reporting abuse during the past year. NIDA has therefore featured prescription drug abuse in calls for research studies and as the topic of national conferences.



Addiction results from the complex interaction of drugs, genes, and environmental and developmental factors. NIDA has therefore made the study of these interactions a priority, joining with other Institutes and organizations to advance a Genes, Environment, and Development Initiative (GEDI).

NIDA is vigorously pursuing research on the effects of abusable substances and how multiple factors—genes, the environment, developmental variables, and their interactions—influence **vulnerability to and protection from addiction**. Because the impact of drug abuse varies at different points along the lifespan**,** NIDA is supporting research from prenatal development to older adulthood to uncover how life transitions influence the likelihood and trajectory of drug abuse and addiction. New studies will examine how these developmental shifts interact with genes and environment to influence disease vulnerability and progression (figure).

Adding to this understanding is our growing knowledge of the **multiple brain circuits** associated with drug abuse and addiction, such as those implicated in reward, inhibitory control, emotional states, and learning and memory. In addition, basic research on brain development (which continues into young adulthood) is illuminating how the plastic brain can influence the response to drugs and affect addiction propensity and progression. Using the powerful tools of modern neuroimaging we can finally "see" how various brain mechanisms interact with drugs of abuse to influence the decision-making process (e.g., willingness to take risks) and the neurobiological effects of a drug—even in real time, throughout development, and as people engage socially (e.g., over the Internet).

Finally, NIDA envisions the application of this research to the **development of more effective prevention interventions**. More than 30 years of research has shown that specific target audiences—such as adolescents, young adults, pregnant women, older adults—require tailored prevention approaches to more effectively reduce risk and enhance protective factors.

Strategic Approaches to Prevention Research

The following section is organized according to four guiding questions to describe NIDA's approach of using basic, clinical, and health services research to improve drug abuse and addiction prevention.

1. How can NIDA research inform the focus of prevention efforts?

Supporting epidemiological research to elucidate the changing patterns and course of drug abuse and addiction:

NIDA continues to identify areas of particular concern and to spot trends early through our scientific studies and epidemiological work in the field. We monitor national and regional substance abuse trends through instruments such as our nationwide Community Epidemiology Work Group (CEWG) and the Monitoring the Future Survey, and others. These mechanisms help us identify the who, what, where, and when of drug abuse trends as well as the attitudes associated with them and their consequences.

We also encourage research that capitalizes on other databases available through our sister Institutes and Federal agency partners, such as the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), sponsored by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Survey of Parents and Youth (NSPY), sponsored by the White House Office of National Drug Control Policy (ONDCP). In addition, we support a number of longitudinal studies (e.g., on cohorts of children prenatally exposed to drugs), which gather information on children's cognitive and emotional development, as well as their vulnerability to addiction later in life.

To continue to make the most of these rich data sources and to improve upon them, NIDA is encouraging researchers to add a genetic component to epidemiological analyses, whenever relevant, to try and zero in on gene-environment interactions at different developmental stages. The potential bounty of genetic information, combined with brain imaging data, will reveal even more about the trajectory of addiction and the contribution of social-environmental factors, which will lead to customized interventions for those at risk.

2. *Why do some people become addicted while others do not?*

Identifying risk and protective factors to achieve a better understanding of vulnerability to drug abuse and addiction throughout the lifespan:

Our research has already identified many factors that can either enhance or mitigate an underlying propensity to initiate or continue drug abuse. Advances in genetics are allowing us to identify genetic polymorphisms (normal genetic variations) that confer increased vulnerability or protection. Recent discoveries about the dynamic interactions of genes with the environment, along with developmental factors, confirm that addiction is a multifactorial, complex, and chronic disease of the brain. A better understanding of the many contributors to drug abuse and addiction, and the different ways they operate at the individual, group, and community levels, is critical to designing more effective prevention messages.

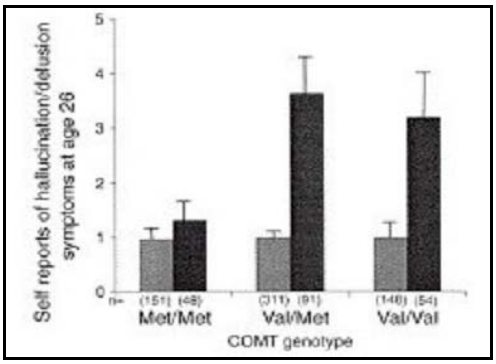
How does a person's biological makeup influence their risk of addiction?

Numerous biological factors confer risk of or protection against drug abuse and addiction, including genetics, developmental stage, gender, comorbid diseases, and pharmacological response or sensitivity to a drug's effects. As particular risk and protective factors emerge from epidemiological and clinical studies, they can be put to the test in animal models (and possibly even *in vitro*) to help validate, trace, and explore the biological correlates of addiction risk.

The use of animal models allows the manipulation of genetic, environmental, and developmental conditions to investigate related changes in brain and behavior. NIDA researchers have developed relevant models in different species to investigate the various behavioral components of addiction. These models can help tease apart the determinants of a susceptibility to drug-taking and its various consequences; the role of stress and social factors in triggering drug-taking behaviors; and the transition from controlled intake to compulsive drug self-administration.

People with particular gene variants may suffer more harmful effects from drugs of abuse

In a longitudinal study of a representative group followed from birth to adulthood, a particular subtype of the catechol methyltransferase (COMT) gene was found to affect the impact of adolescent cannabis use on development of adult psychosis. Carriers of this particular COMT gene variant were most likely to exhibit symptoms of psychosis (e.g., hallucinations, delusions) and to develop schizophrenic-type disorders if they used cannabis; no effect was seen in those who did not carry this allele.



Why it's important. This study reveals a new approach for understanding how genetics, environment, and development interact to increase vulnerability to drug-related consequences.

Caspi et al., 2005 Biol Psych 57:1117

Why do genes matter?

A person's genetic makeup plays an important role in his or her addiction vulnerability. Based on research findings, it is estimated that close to 50 percent of the predisposition to addiction can be attributed to genetics. However, this influence is not a simple one—like many complex diseases, addiction is likely to show a multifactorial pattern of inheritance, meaning it emerges as the result of the contribution of many genetic determinants, each with a relatively small effect, often shaped by environmental factors. It is critical to gain a better understanding of these genetic influences to improve our prevention efforts. Indeed, ongoing developments in the field of high-throughput genomic screens herald a dramatic acceleration in our ability to identify specific gene variants that can contribute to (or guard against) addiction (see sidebar). The resulting knowledge could then be deployed preventively to identify individuals at risk, well before a substance use disorder emerges.

Epigenetics refers to the notion that exposure to drugs—and many other environmental factors—can lead to long-term changes in gene expression. Epigenetics represents an emerging area of research that NIDA will continue to support, looking at physical changes in the DNA structure that have functional implications. These changes are triggered not only by drug exposure, but

also by socio-economic factors, parenting style, and peer group influences, to name a few. Environmental influences during fetal development, including exposure to licit and illicit substances, can affect future vulnerabilities, including the propensity for developing an addiction. Understanding the causes and effects of epigenetic changes offer a real opportunity for developing interventions to counter, prevent, or take advantage of them.

What makes the developing brain more vulnerable to drug abuse and addiction?

Drug abuse is a developmental disease, meaning that it typically begins in adolescence and sometimes even earlier. We know that early drug exposure increases the risk of drug-related problems later in life but do not fully understand why. Current evidence suggests that adolescents may be particularly vulnerable because the brain regions involved in judgment, decision-making, and emotional control do not fully mature until early adulthood.

Childhood and adolescence: To increase our understanding of normal brain development throughout childhood to young adulthood, NIDA is participating in the NIH magnetic resonance imaging (MRI) Study of Normal Brain Development—a multi-center clinical trial designed to collect behavioral and brain MRI data from 500 children, ages 0-18 years, and to analyze relationships between brain structure and behavior at interim points. Once completed, results will provide baseline normative data in multiple domains; an invaluable resource for researchers trying to examine the age and gender specific effects of drugs of abuse on brain development.

Prenatal exposure: Prenatal (and possibly even postnatal) exposure to drugs can affect a variety of cognitive and mental health outcomes later in life, including problem solving, memory, learning, language, and reasoning—as well as the risk for addiction. For example, prenatal exposure to nicotine was recently shown to influence the risk for nicotine addiction 30 years later, an outcome that could reflect nicotine's ability to influence the expression of genes that affect fundamental processes in the developing brain. NIDA-supported longitudinal studies of prenatal exposure to several drugs of abuse will help us understand the drug-specific impact on developmental outcomes, including those affecting health, cognition and behavior, executive function, emotion, and attention regulation.

How does gender play a role in drug abuse and addiction?

Research has repeatedly shown that a broad spectrum of differences related to gender (e.g., social environment, physiological response to drugs, sexual dimorphisms in brain circuitry and hormones, etc.) can greatly influence not only drug abuse trajectories, but also the characteristics of prevention programs that work best for either girls or boys. The many differences already observed in preclinical and clinical studies highlight the need for research targeting the ways in which gender influences drug abuse and addiction risk.

What is the relationship between drug abuse and mental illness?

Many people who have a substance abuse disorder also have some other psychiatric disorder, and vice versa. For example, close to 90 percent of people with schizophrenia smoke, but we do not really know why. Other studies have shown that exposure to certain drugs may increase risk for mental illness in vulnerable individuals. Thus, a continuing NIDA priority will be to unravel the intimate connections between drug abuse and addiction and other mental disorders. Good

prevention hinges on a better understanding of whether these disorders have a shared origin, whether early drug abuse can trigger a mental illness, vice versa, or both.

Because comorbidity intersects with the missions of other NIH Institutes (NIMH, NIAAA), NIDA will continue to work with our colleagues to encourage research on the epidemiology and genetics of comorbidities, and their neurobiological underpinnings.

How does a person's environment affect his or her risk of drug abuse or addiction?

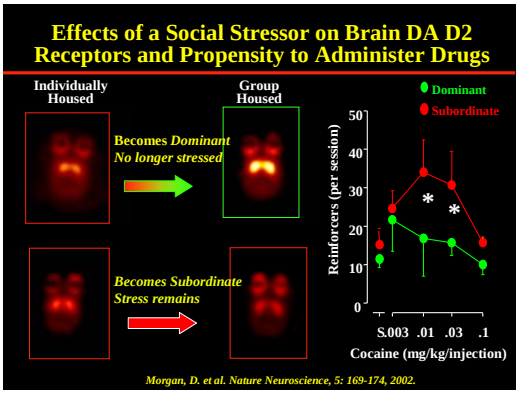
Working in concert with biological risk and protective factors are those that stem from our environment as we progress from fetal development to adulthood. For example, an individual genetic predisposition to drug abuse will never manifest itself in the absence of drug exposure. A variety of factors—from the makeup of an individual to the characteristics of his or her family, peers, neighborhood, and community—need to be taken into account and better characterized to fully understand what contributes to drug abuse and addiction, and which variables would be amenable to modification. Thus, NIDA is fully committed to developing standard measurements of environmental variables.

Neurobiological factors underlying social behaviors: While we know that environmental variables can positively and negatively modulate drug abuse risk, little is known about how they impact brain processes, particularly as a function of genetic makeup and age. Modern brain imaging technologies are increasingly being used as part of drug abuse and addiction research to illuminate how the brain is affected by social influences, such as peer pressure, in the context of drug abuse or decision-making (see sidebar). Gaining a better understanding of the mechanisms underlying peer influences, and whether or not and how they might be reversed, will be important in terms of prevention in adolescents, and will help us ascertain which messages are most salient for them.

NIDA is committed to better characterize social environments, for example, by mapping community risk factors for drug use, such as education level, socio-economic status, crime, and drug availability. A better understanding of the neurobiology of social behaviors is also relevant for the treatment of drug addiction, and for psychotherapeutic interventions for other mental illnesses, which also involve social aspects of human behavior.

Shedding light on the underlying connections between social stress and drug abuse behaviors

In this NIDA-supported study, monkeys that were transferred from isolation to group living and became dominant in the new social structure underwent biological changes that gave them stronger dopamine signaling and less interest in cocaine compared to animals that became submissive. These findings demonstrate that alterations in an organism's social environment can produce profound biological changes that have important behavioral consequences, including vulnerability to cocaine addiction.



Why It's Important: The emerging field of social neuroscience will examine how neurobiology and the social environment interact in abuse and addiction processes to influence initiation, maintenance, relapse, and treatment.

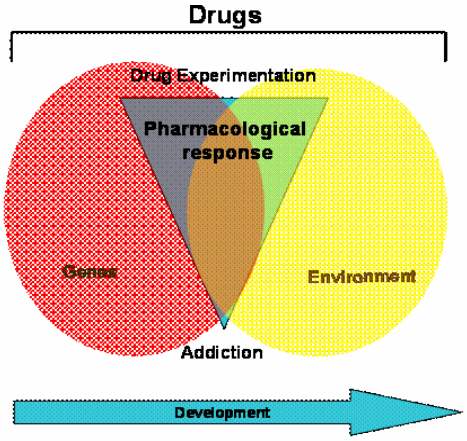
Morgan et al., 2002 – Nat Neurosci 5:169

How does stress facilitate drug abuse?

Stress and trauma, particularly if experienced early in life, can alter the brain and the response to stress throughout life. In humans, factors such as economic adversity, isolation, and parental abuse and neglect are all known to influence age of first drug use, level and duration of use, and psychiatric comorbidities. The reasons are complex—but many people who have experienced such trauma turn to alcohol or other drugs to help them deal with emotional pain, bad memories, poor sleep, guilt, shame, anxiety, or terror. Often, a vicious cycle ensues in which, abusing drugs to self-medicate, engenders additional stress, leading to even worse substance abuse, and so on. Animal research has begun to reveal some of the biological mechanisms responsible, and has suggested ways to reverse or mitigate these effects. Further research is needed to unravel the ways in which environmental factors like stress induce brain changes that interact with drugs of abuse and alter behavior—and to identify ways to counter or minimize stress effects.

How does drug abuse risk vary across the lifespan?

Because the risk factors associated with a person's biology and environment vary as a function of age, NIDA supports studies across all age groups, with a particular focus on life transitions. Significant developmental shifts include transitions to greater independence after high school (associated with increased substance use and progression from abuse to addiction), adult role transitions such as marriage, parenting, and full-time work (associated with decreased substance abuse), and older age transitions such as retirement and age-related medical comorbidities (associated with increased potential for substance abuse-related medical consequences).



Whether or not the exposure to drugs of abuse will lead to addiction is a function of the interaction between multiple domains, including genetic background, a person's response to the drug, and his/her environment and developmental stage.

It is clear that the course of drug addiction is related to both biological and cultural transitions (e.g., puberty, high school graduation, marriage). However, we need to further investigate the manner in which these developmental shifts interact with individual genetic and environmental backgrounds to influence the course of the disease (figure) in order to design and deploy developmentally appropriate interventions.

3. *Which parts of the brain are involved in drug abuse?*

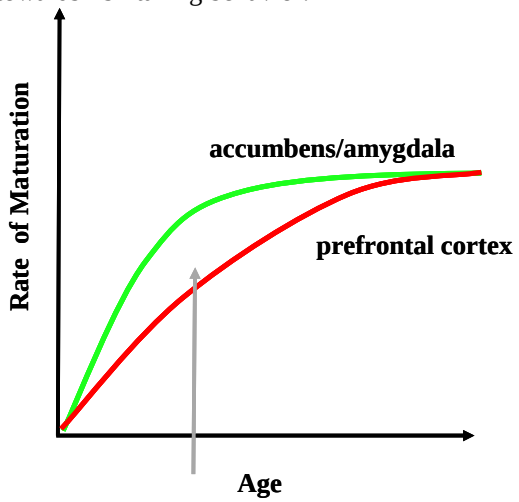
Understanding brain circuitry to improve prevention approaches

Research shows that the brain circuits affected by drugs of abuse are mainly those involved in reward, decision-making, risk-taking, emotional control, desires and motivation, and inhibition

of behaviors. The interactions among the densely interconnected circuits mentioned above determine the final course of action for an individual. So, for example, if the reward, motivation, and memory circuits overcome the inhibitory control circuit, a person may compulsively seek whatever the rewarding stimulus is, including drugs of abuse. Drugs of abuse tend to activate reward and motivational circuits more effectively than natural rewards, increasing their saliency and leaving behind robust memories (conditioned responses) of their effects. Again, some of these circuits are not fully mature until early adulthood, making them potentially more vulnerable to disruption by exposure to drugs of abuse (see sidebar).

Differential rates of brain maturation may account for teenager's risk-taking proclivity

This study reported that the nucleus accumbens, a part of the brain's reward circuitry, matured faster than the orbitofrontal cortex, involved in behavioral inhibition and control. This pattern of brain development was associated with a different valuing of rewards by adolescents as compared to adults and children, suggesting that the relative immaturity of the orbitofrontal cortex in adolescents might underlie their propensity towards risk-taking behavior.



Why it's important. These findings suggest that maturing subcortical systems become disproportionately activated relative to later maturing top-down control systems, biasing the adolescent's action toward immediate gratification over long-term gains.

Galvan, et al, 2006 – J Neurosci 26:6885

Our vision is broad and will apply the full power of research with human participants, neuropsychological testing, and functional neuroimaging so as to help us understand not just one molecule or one pathway at a time, but the addiction circuitry as an integral part of a wider network in which pathways influence one another in highly complex ways.

4. *How are research results used to improve practice?*

Applying research outcomes to develop and test promising prevention interventions.

A general set of science-based prevention principles has emerged from basic biological, psychological, and social science discoveries made over three decades of prevention research—knowledge that has been used to develop prevention programs with proven efficacy and effectiveness. However, much of the research on biological, psychological, and social processes and mechanisms has not been fully applied to develop and test innovative, potentially efficacious drug abuse prevention interventions.

To make the most of these findings, NIDA sponsors a Prevention Network of research centers nationwide, which integrate research from various disciplines to stimulate the translation of basic research to innovative prevention approaches and to inform basic science hypotheses that may help in developing new approaches or in refining existing programs. NIDA is also looking to expand research efforts on the factors that influence the adoption and long-term sustainability of evidence-based prevention initiatives in schools and other settings.

How can science help refine prevention messages?

NIDA recognizes that, along with addressing risk and protective factors, effective messages will also depend on incorporating imaginative communication strategies aimed at reaching different target audiences. Innovative research-based communication tools will help us decode and incorporate the preferences of young people, for example, so that our prevention messages are salient. Two highly successful NIDA-supported school-based programs that are designed specifically for male (ATLAS) and female (ATHENA) teenage athletes align with modern communication theory advocating that media messages flow from influential opinion leaders. ATLAS and ATHENA leverage the influence of coaches on their athletes, addressing steroid abuse and other unhealthy behaviors (e.g., drinking and driving) and highlighting positive alternatives to steroids. Closer attention to prevention science will be increasingly critical in a media environment where the landscape is constantly changing.

A smarter strategy to get the message across

Similar to ATLAS (Athletes Training and Learning to Avoid Steroids) for male athletes, ATHENA (Athletes Targeting Healthy Exercise and Nutrition Alternative), for female athletes, has the goal of increasing healthy behavioral choices and preventing drug abuse. 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.

ATHENA

ATLAS

Why it's important. Innovative prevention programs incorporated into the school setting present an effective way to reach young people, particularly when delivered by role models whom young people naturally admire and respect.

Elliot DL et al., 2004 – Arch Pediatr Adolesc Med 158:1043

The addition of new neuroimaging tools and methods of analysis will not only help refine research results, but will provide a means of testing how the brain reacts to prevention messages, the ultimate goal being to improve their effectiveness with the target audience. For example, neuroimaging technology could be applied to reveal how people process media messages in anti-drug advertising. This capability could provide keys to integrating popular culture and social influences to make prevention messages more salient. While we are not yet ready to design a prevention strategy on the basis of how adolescents might view a message relative to adults, the fundamental research that will form the basis for scientifically rational design is now under way. Indeed, these studies may spark a new generation of effective, tailored anti-drug messaging.

Our Vision for the Future of Prevention of Drug Abuse and Addiction:

We envision a future where new knowledge and leading-edge technologies produce selective, cost-efficient, and effective prevention products and initiatives. Our prevention toolkit will one day allow us to develop messages that flow from a dramatically better understanding of the many complex and interdependent phenomena that characterize drug abuse and addiction. Improved prevention efforts will incorporate what we have learned about genetic contributions to addiction vulnerability, about the human brain's inner workings and developmental processes under normal conditions or after drug exposure, and about specific brain and behavioral responses associated with an individual's age and social context. We work toward a future in which early recognition of significant risk for addiction is no different from early recognition of any other chronic disease, such as hypertension, diabetes, or asthma.

II TREATMENT

Overall Goal

To support research to develop successful treatments for drug abuse and addiction, and to improve their accessibility and implementation.

Objectives

1. To develop effective medications and behavioral interventions to treat drug abuse/addiction and to prevent relapse.
2. To support the design of treatments that target specific aspects of drug abuse and addiction, including an addicted person's changing needs over time.
3. To develop treatments for abuse/addiction in association with comorbid conditions.
4. To develop the knowledge that will lead to personalized or customized treatments.
5. To translate research-based treatments to the community.

Introduction––the Value of a Multi–Pronged and Integrated Approach to Addiction Treatment

Decades of research have led to today's improved understanding of addiction as a chronic, relapsing brain disease caused by the complex interaction of genetic, social, environmental, and developmental factors. Therefore, NIDA recognizes the need for a whole systems approach to treating drug abuse and addiction.

Drugs of abuse alter normal brain functioning in profound and long-lasting ways, so that the system may become reengineered to promote behaviors that seek the drug above all else. This occurs as a result of aberrant learning, whereby the addicted person is "conditioned" to need the drug and finds it difficult if not impossible to resist. This dysfunctional state also makes the addicted individual vulnerable to relapse triggers, even absent conscious awareness of them.

NIDA supports multidisciplinary research addressing the multiple factors that can influence drug abuse and addiction trajectories, and thus informs treatment strategies to facilitate abstinence and prevent relapse. New findings will continue to inspire **development of medications and behavioral interventions** to counteract drug-induced alterations in the circuits responsible for normal behavioral, cognitive, and emotional functions. Advances will result from the continued application of well-established approaches that tap into the potential benefits of:

- Expanding the range of drugs or populations that can be targeted with already approved addiction medications.
- Developing medications for targets (molecules and circuits) affected by specific drugs, as well as targets more generally affected by many drugs.
- Developing research-based treatments that **match an addicted person's changing needs**, attitudes, and motivation over time.
- Developing medications to restore cognitive functions disrupted by addiction. These impairments may present an obstacle to the success of behavioral therapies.
- Weakening the power of relapse triggers.
- Taking into account the possibility of **comorbid conditions** (e.g., mental illness, chronic pain, HIV/HCV) to achieve truly **customized treatments.**

NIDA recognizes that despite major strides in treatment research, only limited improvements have occurred in non-research settings. A scientific approach must be brought to bear on understanding how to most effectively **test and disseminate research-based treatments** and how health services systems and settings influence treatment implementation. Ultimately, it is our goal to make research-based treatments user friendly, cost effective, and available to a broad range of practitioners and their patients.

Strategic Approaches to Treatment

NIDA supports research that addresses the multiple and specific needs of a person trying to recover from drug abuse and addiction. The addition of new tools, particularly noninvasive neuroimaging technologies and those designed to generate detailed genetic information, will have major predictive and therapeutic value, allowing researchers to "see" and analyze the complex and individually specific cognitive and motivational processes that underlie compulsive drug-related behaviors.

1. How can NIDA research further the development of medications and behavioral therapies to reduce drug abuse and prevent relapse?

Strategies to develop effective anti-addiction medications and targeted behavioral interventions.

How does NIDA approach the development of medications for addiction?

NIDA supports a dual strategy—what we call (1) top-down and (2) bottom-up approaches—the former focusing on already approved medications with putative addiction applications, the latter on developing new compounds that can interact with novel potential targets for drug abuse/addiction, encouraging researchers to also work with commercial companies on both of these approaches. Advantages of already approved medications include the availability of safety profile information; lower development costs; and shorter times to obtain FDA approval (see sidebar).

New Approaches To Medication Development: Improving Behavioral Therapy Outcomes

Modafinil is currently approved for treating narcolepsy (a sleep disorder), and appears to also have *cognitive enhancing properties* in some populations. Addiction to drugs such as methamphetamine can disrupt cognitive functioning, and interfere with the efficacy of behavioral treatments.

Modafinil, a mild stimulant, with incompletely understood mechanisms of action, may be an important adjunctive medication to help people engage in behavioral therapies. Early results suggest modafinil's efficacy for cocaine treatment, with additional clinical trials under way in methamphetamine abusers.

Why It's Important: These findings represent a new approach to the treatment of stimulant abuse—improving cognitive function to improve the efficacy of behavioral treatment.

Dackis, C.A., Kampman, K.M., Lynch, K.G., Pettinati, H.M., & O'Brien, C.P. (2005). A double-blind, placebo-controlled trial of modafinil for cocaine dependence. *Neuropsychopharmacology: 30(1),* 205-211.

On the other hand, the bottom-up approach is more responsive to breakthrough discoveries that reveal new targets, such as several components of the cannabinoid system, or novel heterodimeric receptors (i.e., receptors that combine, or "dimerize," to create targets with novel biological properties that could be harnessed

to provide a broader array of medication options). Potent new pain medications without abuse liability are also being sought—specifically to help chronic pain sufferers get the relief they need while minimizing addiction risk (see sidebar).

Pain management: alternative approaches promise pain relief without abuse liability

GLIA. Research reveals that glia cells in the brain (historically regarded as supporting players) actually play key roles in regulating pain signals. Through the secretion of a host of molecules, glia cells influence pain and inflammatory processes. Targeting glia cells and their soluble products may provide a novel and effective therapy for controlling clinical pain syndromes.

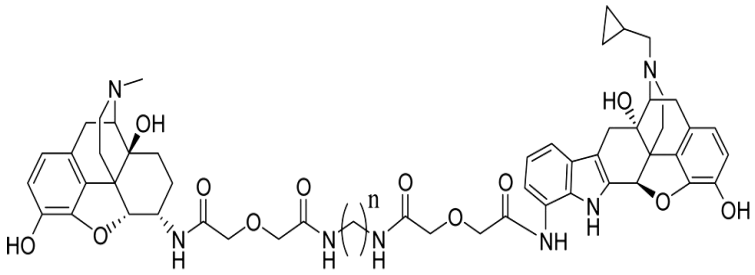
Watkins, L.R., Hutchinson, M.R., Ledeboer, A., et al. Glia as the "bad guys": Implications for improving clinical pain control and the clinical utility of opioids. Brain, Behavior, and Immunity 21:131–146, 2007.

CB2. Activation of cannabinoid type 2 (CB2) receptors inhibits acute, inflammatory, and neuropathic pain responses in animal models. . Since these receptors are located largely outside the brain, selective CB2 agonists are promising candidates for the treatment of acute and chronic pain without psychoactive effects.

Whiteside, G.T., Lee, G.P., and Valenzano, K.J. The role of the cannabinoid CB2 receptor in pain transmission and therapeutic potential of small molecule CB2 receptor agonists. Current Medicinal Chemistry 14:917–936, 2007.

Opioid receptor heterodimers. . Opioid receptors exist as dimers—protein molecules composed of two linked subunits—whose variable makeup affects resulting pharmacology. Strategies are being developed to identify compounds that will specifically bind and activate different opioid receptor combinations. Such compounds could represent the next generation of pain relievers with decreased side effects, including reduced drug abuse liability.

Daniels D.J., Lenard, N.R., Etienne, C.L., et al. Opioid-induced tolerance and dependence in mice is modulated by the distance between pharmacophores in a bivalent ligand series. PNAS 102(52):19208–19213, 2005.



3 - **8**, MDAN Series

Regardless of the approach used, NIDA takes advantage of the combination of validated animal models and translational human laboratory studies to develop and test medications (see sidebar).

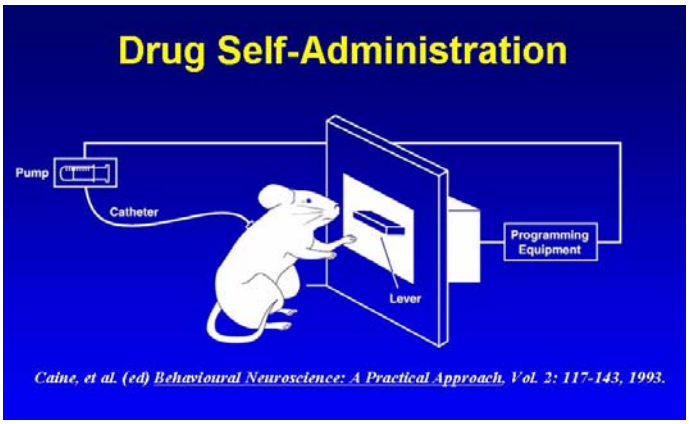
How do behavioral treatments help drug abusers?

Behavioral therapies have already been successfully developed to help individuals with addictions engage in the treatment process, modify their attitudes and behaviors related to drug abuse, and nurture those skills conducive to a healthy lifestyle. These treatments also have the potential to enhance the effectiveness of medications (and vice versa) and help people stay in treatment longer.

Some patients may require lengthy treatment protocols in the form of medications and therapeutic settings to help them develop the internal motivation and skills to succeed in treatment. In addition, follow–up support systems (e.g., recovery groups and job and health services) can be crucial to a person's achieving a drug-free lifestyle after treatment or in concert with it. NIDA will continue to support research to better understand how such therapies work and how to implement them in community settings.

Innovative and informative animal models of drug addiction

Animal models are crucial to basic research on drug abuse and have greatly contributed to our understanding of addiction's underlying substrates, the abuse liability of novel compounds, the role of candidate vulnerability genes and stress in relapse, and the persistence of drug taking. They allow scientists to rigorously control and analyze biological and environmental factors related to drug abuse, and test novel approaches to its prevention and treatment. The noteworthy development of buprenorphine as a treatment for opiate addiction began with studies using animal models, as is the case for most medications being tested in human clinical trials.



Self-administration, or the voluntary intake of abusable substances by animals, is now among the most widely used paradigms by pharmaceutical companies around the globe to evaluate the abuse liabilities of new medications. Because animals will self-administer nearly all drugs of abuse and continue to take them when available, they allow us to study the chronic effects of drugs on their brains and behavior.

2. What are effective treatments designed to do?

Applying evidence-based treatments or their proven components to target the different aspects of drug addiction and prevent relapse.

The strategic approaches described above are being employed to (1) counter relapse triggers; (2) strengthen self-control, and (3) reinstate the reward value of natural reinforcers.

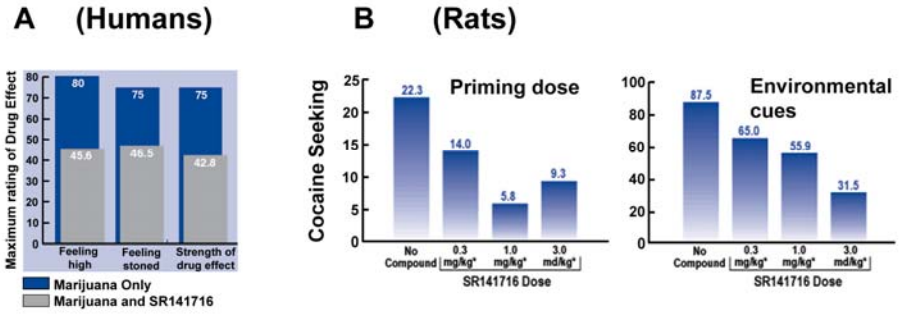
How does drug abuse treatment help to counter relapse triggers?

The most frequent triggers to relapse include stress, exposure to conditioned-cues, and priming (re-exposure to drugs of abuse). Medications that block reinstatement of drug-taking behaviors in animals by these three triggers are now being tested in humans.

Stress. Both clinical reports and preclincal studies have documented the important role that stress plays in relapse. Medications or behavioral treatments that can interfere with or mitigate the response to stress may thus offer promise for relapse prevention. Corticotropin-releasing factor (CRF) is known to be a key brain chemical involved in organizing the brain and body response to stress. Thus, medications that target CRF are of interest; this concept has been supported by studies in animals showing that compounds that block CRF signals attenuate the reinstatement of drug-taking following exposure to stressors. Since drug withdrawal syndromes and the often chaotic lifestyles of drug abusers are manifestly stressful states, strategies that improve coping mechanisms or reduce the stress response could be useful countermeasures to prevent stress-induced relapse.

Compound reduces marijuana's intoxicating effects and may help prevent relapse from drug exposure (priming) and environmental cues

Marijuana smokers given an experimental compound (SR141716—rimonabant) reported reduced highs (and smaller heart rate increases) than untreated smokers (A). Because SR141716 partially blocks the intoxicating effects of marijuana's active ingredient (THC), it may prove valuable in treating marijuana addiction and perhaps other addictions as well. Indeed, in a rat model of relapse to drug seeking, SR141716 was able to dramatically reduce resumption of cocaine-seeking triggered by two of the three most common relapse triggers: a priming dose of cocaine and conditioned cues associated with cocaine reward (B). The compound did not reduce cocaine-seeking triggered by stress.



Why It's Important: The cannabinoid system is a new player in our understanding of the rewarding effects of drugs, and compounds that target this system may have application for not only marijuana treatment, but also for other drugs, since they can block relapse triggers.

Huestis, M.A., et al. Blockade of effects of smoked marijuana by the CB1-selective cannabinoid receptor antagonist SR141716. Archives of General Psychiatry 58(4):322–328, 2001.

De Vries, T.J., Shahan, Y., et al. A cannabinoid mechanism in relapse to cocaine-seeking: A review. Pharmacological Reviews 54:1–42, 2002.

Conditioned cues. These are stimuli (e.g., people, place, moods, things) that become associated with the drug experience, and can serve as triggers to relapse. Conditioned cues can pose formidable obstacles to successful therapy for many individuals, especially because they can elicit craving, even without conscious recognition of their influence. Extinction is an active process whereby previously learned associations are weakened and new ones formed. Medications designed to blunt conditioned responses or to promote their extinction could enhance the efficacy of psychotherapeutic

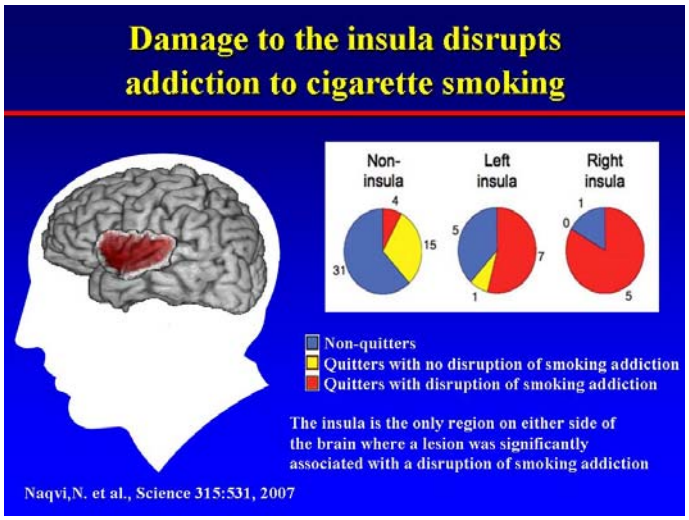
interventions. A proof of concept for this approach has already been shown with D-cycloserine (DCS), a partial agonist of the NMDA (glutamate) receptor. DCS may facilitate extinction and promote new learning and has been successfully used in conjunction with psychotherapy for treating acrophobia. There are also many medications currently available for other indications that are being tested for their ability to reduce cue-induced drug cravings.

Priming, or drug exposure. Priming is the response to a drug in a formerly addicted person, which propels them to further drug use and often to relapse. Data show that people in treatment who "slip" are at higher risk of relapse, or of returning to former levels of drug use. NIDA plans to continue supporting research on strategies designed to block the priming response.

Research in this area has already produced positive results. Cannabinoid and opioid antagonists, for example, have been shown to block the priming response in animals and suppress their self-administration of drugs in a relapse model of drug seeking (see sidebar, previous page). Another strategy being explored to block priming attempts to harness the immune response. The rationale behind this approach is to develop vaccines that induce the body to produce drug-specific antibodies. At high enough concentration, these antibodies would sequester drug molecules while they are still in the bloodstream, thereby preventing them from ever reaching the brain and exerting their psychoactive effects. Nicotine and cocaine vaccines have already been developed and are undergoing testing in animals and humans. A methamphetamine vaccine is currently in development.

How can drug abuse treatment help to strengthen people's self-control?

A complementary strategy supported by NIDA is to strengthen the function of brain regions involved with decision-making and inhibitory control (distributed throughout the frontal cortex) and interoception—one's perception of what is going on inside his or her body, linked to activity in the insula (see sidebar)—to help people better regulate their emotions and behaviors. The "thinking" and decision-making circuits of a human brain, which are not even fully developed until the mid-twenties, govern our ability to control impulses. Drug abuse and addiction can severely disrupt these processes, contributing to the compulsive features of addiction.



Despite being aware of negative consequences, many smokers have serious difficulty quitting, and even those who quit experience urges to smoke and often relapse. A recent study of patients who had suffered various brain injuries revealed a new role for the insula (shown in red) in regulating conscious urges, including drug craving. Researchers at the University of Iowa monitored the quit histories of approximately 70 smokers and found that those **with specific damage to the insula were much more likely to quit easily and immediately** and to remain abstinent than those with damage to other brain areas.

Why It's Important: This discovery could identify a new target to inhibiting craving.

Naqvi et al. Damage to the Insula Disrupts Addiction to Cigarette Smoking. Science, 315: 531-534, 2007.

Non-invasive brain stimulation and imaging may prove to be novel therapeutic tools in this context. Researchers are exploring the use of technologies such as rTMS (repetitive transcranial magnetic stimulation), and "neurofeedback," (see sidebar on pg. 12) to noninvasively influence brain activity in specific regions. Though not yet demonstrated for addiction, these techniques have shown promising results in managing depression and in influencing pain perception, respectively. Further validating research, could render these powerful psychotherapeutic interventions for rescuing the circuits and behaviors impaired by addiction.

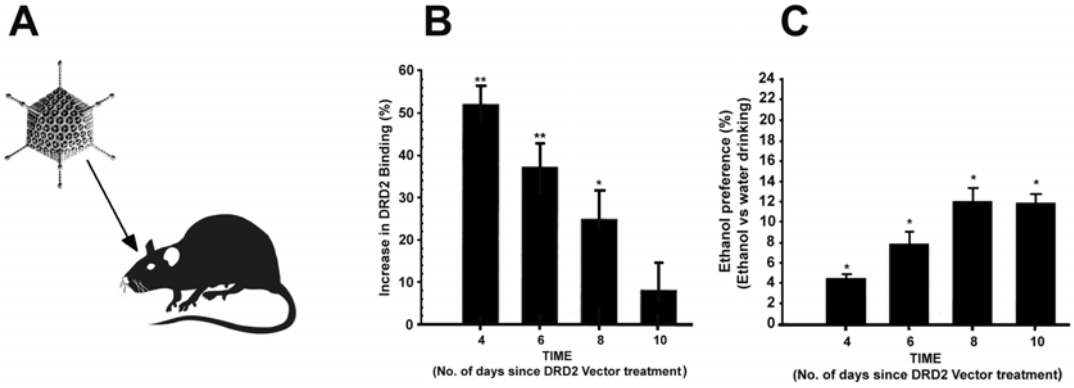
How can drug abuse treatment help addicted people to regain an appreciation for life's "natural" rewards?

Drug abuse and addiction impair the reward system, diminishing the value of formerly rewarding stimuli in a person's life. NIDA therefore seeks approaches to counter drugs' effects on brain systems affecting reward and motivation, and help restore the value of natural rewards.

Animal research has demonstrated the feasibility of modulating the dopamine reward system in ways that affect sensitivity to drug taking. For example, alcohol-preferring rats that were tricked into overexpressing dopamine receptors in the nucleus accumbens (a part of the reward circuitry) decreased their alcohol consumption (see sidebar). Further, in studies of non-human primates, social factors have been shown to influence the function of the dopamine system and vulnerability to drug taking (see sidebar Chapter 1, pg XX). These studies suggest a malleable reward system that may be capable of recovering from drug addiction. The goal would be to

Overexpression of dopamine D2 receptors reduces alcohol self-administration in rats.

Addiction is characterized by decreased sensitivity to natural rewards, likely related to diminished function in dopamine brain circuits. Human brain imaging studies have provided substantial evidence that individuals addicted to a variety of substances have low levels of dopamine type 2 (DRD2) receptors in the striatum (a part of the reward circuit). In this experiment, researchers sought to determine whether increasing levels of DRD2 in the brain could reduce alcohol consumption in animals trained to self-administer the drug. Brain levels of DRD2 in rats were increased by injecting a virus that expresses high levels of DRD2 protein in a key area of the brain's reward pathway (A). This manipulation led to an overexpression of DRD2 receptors that dissipated over time (B) and a corresponding decrease in alcohol consumption that resumed when the receptors returned to baseline (low) levels (C).



Thanos, P.K., Volkow, N.D., Freimuth, P. et al. Overexpression of dopamine D2 receptors reduces alcohol self-administration. J Neurochem. 78(5):1094–103, 2001.

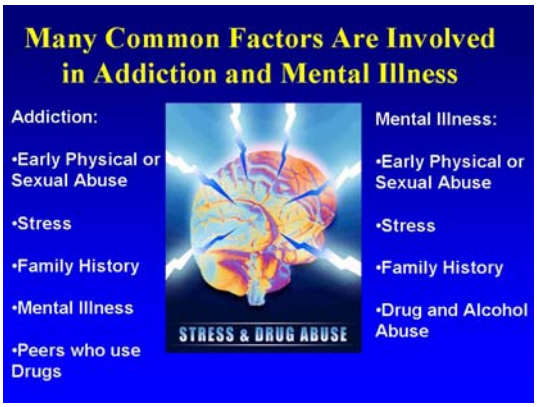
Why It's important: Although the use of viral–vector delivered genes is not practical for clinical use, these results provide a proof of concept that enhancement of dopamine D2 receptors may be a useful approach for treating drug abuse. Medications and behavioral strategies to reinstate dopamine receptor function in the reward circuitry may be beneficial in the treatment of addiction.

increase the sensitivity of the dopamine system in drug-addicted individuals in order to enhance the value of natural reinforcers (i.e., social interactions, eating good food, etc). NIDA would support research to discover new compounds that might compensate for this disruption of dopamine function by abused drugs.

3. What if people have another mental disorder—how does that affect treatment for addiction?

Treating addiction in association with co–occurring disorders

As many as 6 in 10 people who have an illicit drug use disorder also suffer from other mental illnesses. Having both can greatly increase the challenge of diagnosing and treating the disorders: ignorance of or failure to treat one disorder can jeopardize the chances of a successful intervention for the other. Patients with co-occurring disorders also often exhibit symptoms that are more persistent, severe, and refractory to treatment, compared to those with just one disorder. Healthcare providers and caregivers should therefore be aware that drug abuse and other mental illnesses often occur together, necessitating a comprehensive approach to treatment (see sidebar). Thus, NIDA will support research aimed at adapting and integrating treatments that tackle these overlapping conditions, which affect some of the same circuits in the brain.



Co-occurrence of addiction and other mental disorders is very frequent. Substance abuse sometimes begins as a way to alleviate symptoms of a mental illness. And, substance abuse may increase the vulnerability to other mental illnesses. Finally, some of the factors that contribute to other mental illnesses and to substance abuse overlap.

For some mental disorders, pharmacotherapies are already available to alleviate symptoms. Medications such as stimulants, antidepressants, mood stabilizers, and neuroleptics may be critical to treatment success for ADHD, depression, anxiety disorders, bipolar disorder, and schizophrenia. How these medications are affected by, or alter the effects of, abused substances is not well understood, and some may even prove efficacious for treating drug abuse and other mental illnesses. Effective medications also exist for opioid, alcohol, and nicotine addiction, though their use has not been well studied in comorbid populations, nor among those taking other psychoactive medications. In addition, various forms of behavioral treatment can be the cornerstone to achieving successful outcomes for many substance abuse and mental disorders—alone or in combination with medications. Their use in comorbid populations should also be evaluated.

Drug-abusing patients commonly report other co-occurring conditions, including pain, HIV, and HCV. These must also be treated in a comprehensive manner, as drug abuse can affect the clinical course of a variety of illnesses. In this vein, NIDA is interested in developing interventions that acknowledge mental and physical health outcomes.

4. How will treatments be tailored for optimal effectiveness?

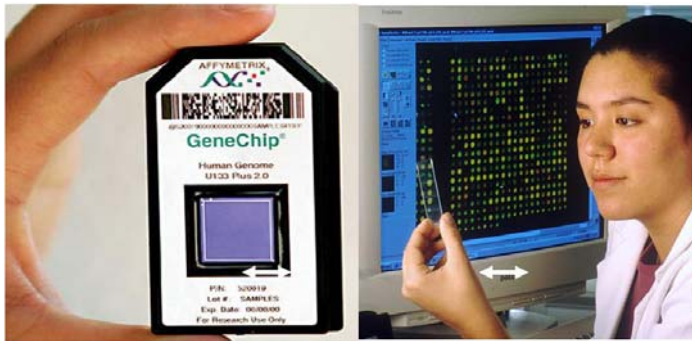
Exploiting new tools, data, and technologies to help customize drug treatments.

NIDA's research program is poised to play an important role in developing treatments that can take individual and group vulnerabilities into account and derive more personalized and thus more effective treatments for people with drug use disorders. To this end, NIDA is capitalizing on advances in genetics, epigenetics, and brain imaging technology, and on research revealing the influence of environment, and developmental factors.

Genetic expression profiles can influence substance abuse vulnerability and can change throughout development, either as a result of epigenetic modifications (e.g., genetic changes that occur in response to environmental factors such as quality of parenting, stress, exposure to drugs), or in response to individual variations in genetic programs that may affect neurodevelopmental trajectories. This knowledge lays the groundwork for analyzing the interacting factors that control substance abuse and related phenotypes (i.e., characteristics determined by both genetic makeup and environmental influences). Next-generation pharmaceuticals can take advantage of this knowledge to elucidate how a person's genetic makeup may affect his or her response to a therapeutic medication. Promising findings have already emerged in relation to the treatment of nicotine and alcohol addictions.

The social environment is also relevant to substance abuse, as studies continue to reveal how the interplay of biological (e.g., genes, developmental stage) and social influences (e.g., family, peers, culture) affect individual choices and decisions about drugs. Research to develop a comprehensive taxonomy of social and built environments (including family, peers, school, neighborhood, community, and culture) that can be monitored at various life stages will help characterize treatment needs for more targeted approaches.

NIDA will continue to support a large, multi-year initiative to integrate environmental (including the social environment) and developmental variables with genotypic information. Using existing longitudinal datasets as their foundation, new studies will employ systematic environmental and developmental measures to not only identify risk factors for substance abuse, but biomarkers of drug abuse as well.



New knowledge, combined with genetics technology, will allow researchers to use a single standardized platform to screen thousands of an individual's relevant gene variants at once. Potential applications of this technology include studies to understand how genetic differences contribute to brain development and to differential brain responses to drugs of abuse; prospective epidemiological studies to understand how genes and environment interact throughout the life span to modulate addiction risk; clinical trials to tailor treatments based on a patient's genetic make up (i.e., to enhance treatment effectiveness and minimize or even prevent adverse effects); and studies aimed at advancing understanding of disease vulnerability in relation to psychiatric co-morbidity (i.e., depression, ADHD, schizophrenia).

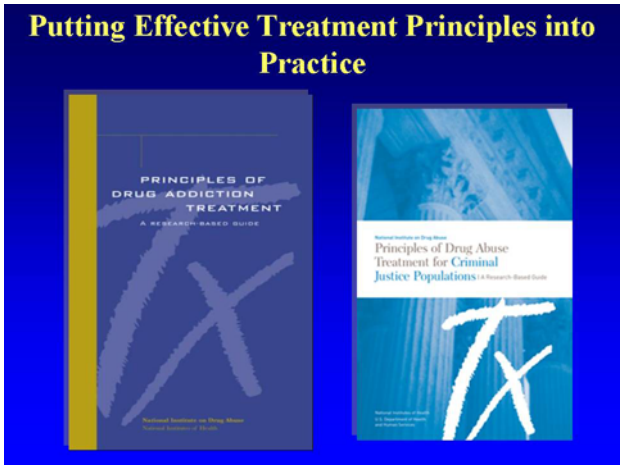
Another important goal in this research area is the development of better screening methods for health care providers to use so they can apply rational strategies to intervene early and more effectively. In this vein, NIDA will help support the development of a specialized substance abuse NeuroChip, which will allow researchers to rapidly screen thousands of an individual's relevant gene variants (see sidebar, previous page). In addition, new platforms for potential use in screening for the telltale signatures of chronic drug abuse in blood cells, serum, or saliva, such as messenger RNA (mRNA), epigenetic markers, and protein expression profiles (proteomics) could dramatically enhance our ability to diagnose chronic drug exposure in primary care and other settings.

5. How will drug abuse treatment reach the people who need it?

Testing Research–Based Treatments in Real-World Settings

NIDA's clinical trials are the cornerstone to test and evaluate promising treatments for drug abuse and addiction. We support research trials for all phases of medications and behavioral treatment development, and encourage collaboration with industry to optimize costs and resource allocation, and research to develop or adapt treatments.

As effective treatments emerge, NIDA tests them in real-world settings. These efforts are exemplified by our National Drug Abuse Treatment Clinical Trials Network (CTN) and our collaborative Criminal Justice Drug Abuse Treatment Studies (CJ-DATS) initiatives. They allow NIDA to exploit an open-channel communication approach with relevant stakeholders to collect information on how to generalize and further enhance treatments to make them more community/justice system friendly. Thanks to this process, NIDA can identify obstacles to the implementation of treatment protocols, thereby optimizing various treatment approaches.



Research has revealed a number of basic principles that underlie effective drug addiction treatment, as highlighted in NIDA's Principles of Drug Addiction Treatment Guides for the general population and for criminal justice offenders.

CTN studies will, for example, continue to reveal information to optimize the treatment of comorbid conditions, the translation of new medications to community settings and will assess novel interventions to reduce HIV risk among drug abusing populations. CJ-DATS will broaden the testing of proven drug abuse treatments in criminal justice settings, including with adolescents, and will continue to solicit the greater involvement of public health and public safety institutions across all system levels.

Overcoming Barriers to Implementing Research-Based Treatments––Health Services Research

Despite major strides in drug abuse treatment research, the adoption of science-based programs has been rather limited. This may be due in part to the fact that drug abuse treatment has several unique characteristics that differ from other diseases, including:

- service delivery outside of mainstream health care settings;
- involvement of non-medical personnel and practices;
- external pressure on individuals to seek care versus the stigma and non-reimbursed costs of seeking care;
- combined interventions as part of full-scale programs versus standalone approaches; and
- reliance on public sources for program funding.

Therefore, to have an impact, NIDA-supported drug abuse services research will continue to address the special organizational, workforce, funding, and policy issues known to influence the success of addiction–related treatment.

NIDA will support research to learn more about common practices, currently in widespread use, but which have not yet been formally researched. We continue to build and enhance our productive partnership with state agencies and to encourage them to team with research organizations to optimize their research infrastructure and improve the delivery of publicly supported drug abuse treatments. And, we will support research on strategies for practice improvement in community-based substance abuse care, evaluating technology enhancements to improve care for varied patient populations in diverse settings.

NIDA's overarching goal is to more quickly translate the results of drug addiction research into widespread clinical practice in a variety of settings. Accomplishing this goal will likely mean a culture and behavior change that will depend on improved communication within a distributed network of researchers, treatment providers, trainers, and mainstream public health and safety officials. Meaningful change will also depend on continuing to identify and overcome the barriers to implementation research (e.g., cost and feasibility) in different settings.

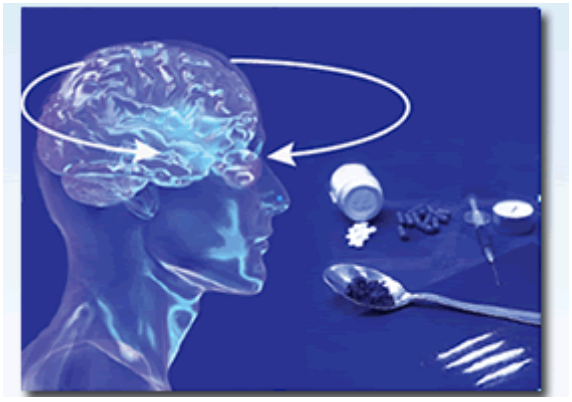
Our Vision for the Future of Treatment for Drug Abuse and Addiction:

NIDA's research program is entering an exciting new era in which treatments will be increasingly tailored to the individual—a more personalized approach that will translate into better and more cost-effective treatments for substance abuse disorders. This approach will be more effective than past approaches thanks to our new understanding that the plastic adaptations characterizing addiction erode the very same neural substrates that enable self- control, decisionmaking, accurate reward prediction, motivation, and memory, among other functions. We are committed to harnessing knowledge of how drugs affect circuits and behaviors and parlaying it into effective treatments to restore the addicted brain and allow people to regain their cognitive abilities and capacity to enjoy life.

Glimpses of this future can already be seen in various research areas. Indeed, next-generation screening and monitoring devices, therapeutic compounds, behavioral interventions and "neurofeedback" training (see sidebar) suggest a panoply of treatment options to efficiently reverse the drug-induced breakdown in brain neurochemistry. Addiction treatments will become increasingly adept at reducing the rewarding properties of drugs while enhancing those of healthier alternatives, inhibiting conditioned memories, and strengthening cognitive control.

In the future, we will seize upon new therapeutic opportunities stemming from deciphering an individual's genetic code to better prevent and cure disease. At the same time, however, we must recognize the responsibility that comes with such technological advances to ensure confidentiality and privacy. This stance also applies to rapidly evolving brain imaging technologies as they become part of a standardized toolset to prevent and treat drug addiction.
NIDA is constantly striving to transform scientific insight into effective and responsible public health interventions. This endeavor will continue to be shaped by promising discoveries and by the accompanying need to consider ethical concerns when treating illnesses like drug addiction.

The Exciting Potential of "Neurofeedback"



Researchers are exploring the use of "neurofeedback," where subjects are trained to modulate neural activity in specific regions of their brains by getting pictorial representations of the activity in those areas fed back to them in real-time. Though not yet demonstrated for addiction, this technique has shown promising results for altering the perception of pain in some healthy adults and chronic pain patients.

Why It's Important: This line of research could evolve into a powerful psychotherapeutic intervention capable of restoring function to the circuits and behaviors impaired by addiction.

DeCharms et al., (2006) Control over brain activation and pain learned by using real-time functional MRI. PNAS 102(51): 18626-18631

III HIV/AIDS

Overall Goal

To support research that seeks to diminish the spread of HIV among drug abusers and their partners, and minimize the associated health and social consequences of the disease.

Objectives

1. To support research to better understand the etiology, pathogenesis, and spread of HIV/AIDS among drug abusing populations.
2. To help prevent the acquisition (primary prevention) and transmission (secondary prevention) of HIV among drug abusers and their partners.
3. To decrease the health disparities associated with HIV/AIDS.
4. To support international research on the intertwined epidemics of drug abuse and HIV/AIDS.
5. To improve HIV treatment and outcomes in drug abusers through a better understanding of interactions with drugs of abuse, HIV/AIDS disease processes, and the medications used to treat both.

Introduction––The Need for Responsive Prevention and Treatment Strategies

HIV/AIDS remains one of the most serious medical consequences of drug abuse. Thus, NIDA will continue to support research to improve HIV prevention among drug abusers and enhance treatment access and use for HIV/AIDS and other co-occurring conditions, such as Hepatitis C Virus (HCV) infection (85-90% of HIV+ IDUs are also HCV+). This report details our strategic plan that relies on research across diverse areas, including epidemiology, prevention, health disparities, medical interactions, and disease consequences.

To effectively diminish the spread and consequences of HIV/AIDS, we must better understand how HIV is transmitted among different groups and communities. Studies that advance our knowledge of the changing behavioral and social **epidemiology** of drug abuse, HIV/AIDS, and co-morbid conditions will help in this regard, by revealing new information to guide our approach. We have already learned important lessons by focusing on a) the link between drug abuse and risky sexual behaviors and b) the distinct characteristics of the epidemic among special populations (women, youth, minorities, prisoners).

A key step in curtailing the spread of HIV will be the development of **primary prevention** strategies that target infection among high-risk groups. The Centers for Disease Control and Prevention (CDC) estimates that 25 percent of people living with HIV in the United States do not know they are infected, which heightens their risk of unknowingly transmitting the virus. Therefore, NIDA will also support research to develop effective **secondary prevention** strategies that promote testing and education among the undiagnosed to further reduce HIV transmission. NIDA is building on earlier research that helped prompt the CDC's decision to broaden its guidelines for providing HIV screening to populations at risk. An important aspect of encouraging testing and counseling is the need to make follow-up treatment more accessible to people with HIV and substance abuse problems.

A disproportionate number of affected people are ethnic minorities, whose access to and utilization of treatment options is often limited. Such **health disparities** particularly affect African Americans, who also to tend to be late testers, putting them at greater risk for disease transmission and accelerated disease progression. Gathering meaningful data on the various factors contributing to these disparities will be integral to efforts to resolve them through earlier diagnosis and treatment. Moreover, HIV/AIDS associated with drug use continues to expand globally. **International research** that systematically monitors changes and patterns in the transmission and manifestation of HIV disease will more effectively prevent and treat the AIDS pandemic.

Treatment with highly active antiretroviral therapy (HAART) can dramatically reduce HIV-related morbidity and mortality. HAART is enabling more people to live longer with HIV, helping to redefine HIV as a chronic illness. This circumstance brings about accompanying chronic **medical disease consequences**, particularly adverse consequences for the brain. Moreover, interactions between neurological complications, substance abuse, and other co-morbid psychiatric disorders may contribute to poor adherence and worse outcomes, requiring responsive counter interventions. Additionally, to optimize HAART for drug abusers, we must investigate interactions between HAART, drugs of abuse, and medications used to treat addiction. More research is needed to better understand and address these long-term clinical complications in drug-abusing populations.

Finally, because HIV/AIDS extends across many public health domains, NIDA is collaborating on projects with other NIH Institutes and Centers (ICs) focusing on complementary work in the areas of drug abuse, HIV/AIDS, and other sexually transmitted diseases (STDs).

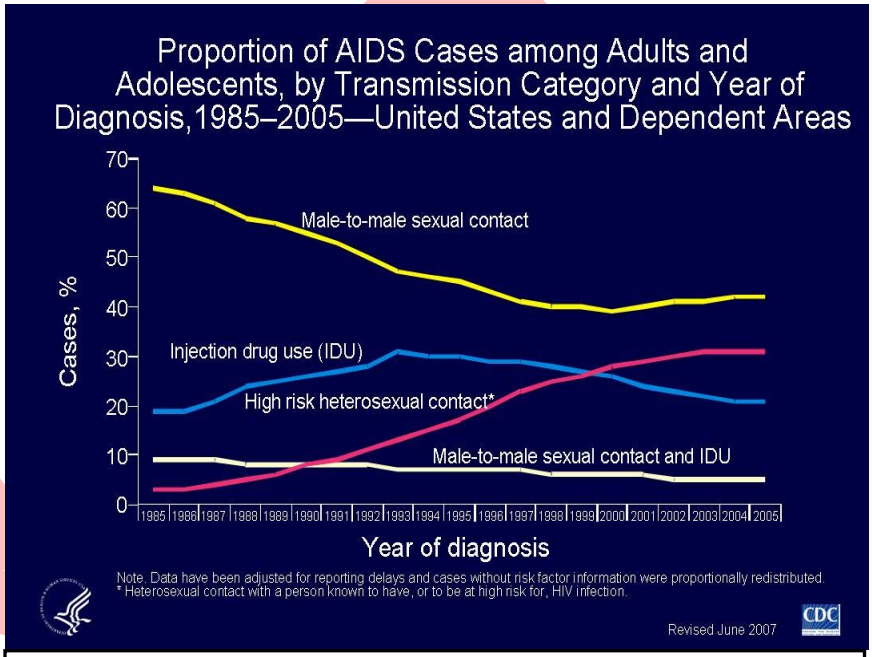
Strategic Approaches to HIV/AIDS Research

NIDA will continue to encourage basic, clinical, services, and natural history research that explores the underlying mechanisms of HIV-associated health outcomes in the context of drug abuse.

1. How has the HIV/AIDS epidemic changed over the past few decades in the U.S.?

Conducting epidemiological research to monitor trends and better understand the natural history of HIV/AIDS among drug abusing populations.

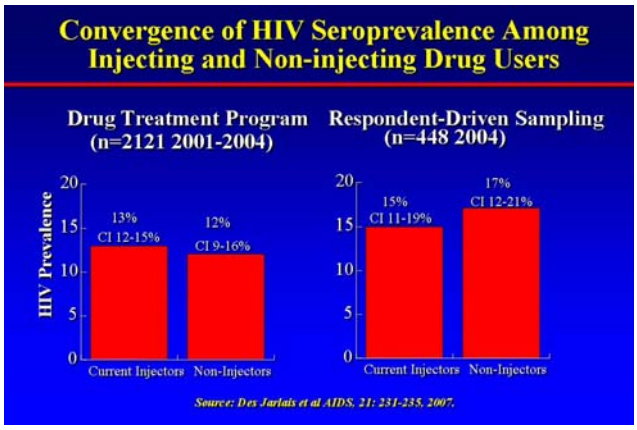
The patterns of HIV/AIDS relative to drug abuse are changing in this country. Formerly, injection drug use was a main vector through which HIV was spread. However, over the past three decades, a substantial reduction has occurred in the proportion of new HIV/AIDS cases attributable to injection drug use, while the proportion of cases attributable to high-risk heterosexual contact has increased steadily (see sidebar). NIDA research has contributed to this decline through support of research that has resulted in improved treatment for injection drug users (e.g., methadone and buprenorphine for heroin addiction).



CDC surveillance data show a notable shift in the HIV/AIDS epidemic in the United States. Over the past 30 years, the boundaries between groups at greater and lesser risk for contracting the virus have been dissolving, with heterosexual sex now a major transmission route for HIV and a leading cause of infection among women (especially within minority communities).

Recent findings illustrate the trend in HIV infection moving from injection drug use to non-injection drug abuse (see sidebar, next page). Drug use impairs people's judgment and lowers their inhibitions, which can lead to impulsive and unsafe behaviors; therefore effective drug abuse treatment is also HIV prevention. Indeed, the integration of HIV risk-reduction interventions into drug abuse treatment is imperative.

Additional epidemiological and natural history studies will help us to monitor epidemic trends, follow more closely the changing clinical manifestations of HIV disease and comorbid conditions, and measure the effects of HIV prevention efforts among drug abusers. They will also inform the development of effective primary and secondary prevention interventions. These studies should look at diverse settings and help characterize individual risk factors as well as the influence of social and sexual networks, environmental contexts, and their interactions. Such research will help elucidate HIV transmission dynamics, the disparate health effects of drug use and HIV/AIDS among different populations, and the best ways to reach them.



Rates of HIV infection are converging in drug abusers who inject drugs and those who do not inject. These results show that HIV is being spread among drug users by means other than needle sharing (i.e., risky sexual behaviors).

Why It's Important: We need to shift focus towards reducing risky sexual behaviors among drug abusers, regardless of the route of drug administration.

(De Jarlais et al. The transition from injection to non-injection drug use: long-term outcomes among heroin and cocaine users in New York City. Addiction 102(5):778–785, 2007).

NIDA will also focus more intently on criminal justice populations to learn how to best address the special risks presented by a group with high drug abuse and background infection rates compared to the general population; both while in prison/jail and when they return to the community.

2. How does NIDA plan to focus research efforts to prevent drug use and HIV/AIDS and to limit the spread of this infectious disease?

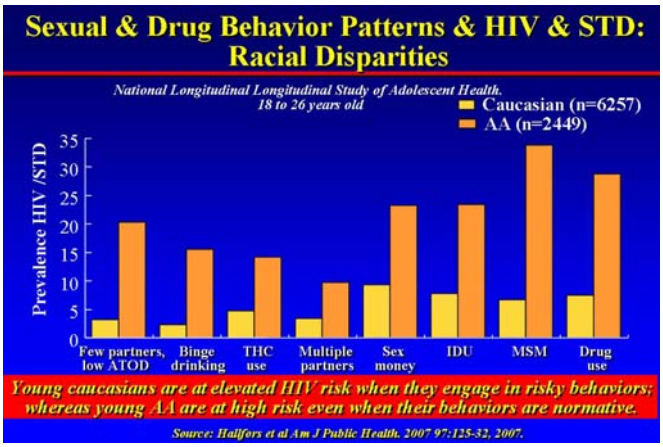
Preventing drug use and changing drug abuse–related behaviors associated with the acquisition and spread of HIV.

Primary Prevention. HIV prevention must be a component of early drug abuse prevention efforts. Therefore, NIDA-supported research will aim to develop and test new age-appropriate behavioral HIV risk-reduction interventions that will start early with the youngest age groups and "grow" along with them. NIDA is supporting initiatives aimed at developing youth/community-based HIV prevention programs designed specifically for urban youth, considered particularly vulnerable to drug abuse and HIV exposure. We will continue to support research to develop innovative means of delivering prevention programs to various high-risk populations.

Primary and Secondary Prevention. More attention needs to be given to strategies for how best to incorporate HIV education, testing, counseling, and referral to treatment into drug abuse treatment and outreach efforts. This direction requires that we identify and address barriers, including stigma and treatment access—both for HIV and drug abuse—that restrict the benefits associated with early HIV detection and linkage to care.

To assist in these efforts, NIDA is pursuing research on the best ways to integrate testing and counseling into drug abuse treatment settings in communities, among criminal justice populations, and in international regions hit especially hard by the epidemic. This includes efforts to advance the adoption of rapid-screen technologies. Screening for HIV in health care settings is as cost-effective as screening for other common diseases; thus it makes sense to incorporate screening among populations where HIV risk is higher than average. Individuals who learn they are HIV-positive significantly reduce their risk behaviors and, when linked to HAART, become less efficient transmitters because of the resulting reduction in viral load. Therefore, such screening would not only provide important health and survival benefits, but would help mitigate the likelihood of HIV transmission to non-infected people.

NIDA plans to test HIV rapid-screen technologies plus counseling about avoiding risky sexual behaviors in community treatment programs affiliated with NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN) and in the criminal justice system through our collaborative Criminal Justice–Drug Abuse Treatment Studies (CJ-DATS) initiative.



A study examining the relationship between race and sexually transmitted disease (STD)/HIV prevalence showed Caucasian young adults in the United States to be at elevated STD/HIV risk only when their behavior is high risk, whereas African American young adults are at high risk even when their behavior is normative.

Why it's important: This study suggests that factors other than individual risk behaviors appear to account for the racial disparities, arguing for population-level interventions.

Hallfors D, Iritani B, Miller W, Bauer D. Sexual and drug behavior patterns and HIV and STD racial disparities: the need for new directions. American Journal of Public Health 97(1):125–32, 2007.

3. What can be done to mitigate the health disparities associated with HIV/AIDS?

Developing strategies to improve treatment access and options among differentially affected populations, especially African Americans.

While all groups are affected by HIV/AIDS, not all are affected equally. Associated health disparities fall disproportionately on ethnic minorities, particularly African Americans, who are at especially high risk for developing AIDS. Even though they comprise only 13 percent of the U.S. population, African Americans accounted for approximately half of the total AIDS cases diagnosed in 2005.[1] Consequences have been particularly harsh on African American women, who accounted for 68 percent of the female HIV/AIDS diagnoses from 2001–2004[2]. Focused research is needed to understand the factors leading to such disparities and to develop targeted interventions to reduce HIV/AIDS and its consequences.

[1] http://www.cdc.gov/hiv/topics/surveillance/basic.htm#aidsrace

[2] 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

Studies are also needed to characterize the risk-modulating role of culture, family, and environmental factors. Indeed, recent research suggests that a strategy of targeting risk behaviors at the individual level may work for Caucasians but not for African Americans, who, in contrast to whites, appear to be at very high risk for STDs even if their behavior is normative[3] (see sidebar).

In addition, although the rates of testing are approximately equal across ethnic groups, minority members tend to be tested late in the course of infection and frequently experience delays in being linked to treatment, which contributes to meaningful health disparities in terms of disease consequences. We hope to improve this situation by increasing knowledge of the existence of HIV treatment, currently lower among African Americans and Hispanics than among Caucasians. NIDA is therefore encouraging studies investigating the relationship of disease progression to treatment and services availability and use by African Americans and other minority groups.

NIDA's multimedia "Learn the Link" campaign uses TV, print, and Web public service announcements to send the message to America's youth that using drugs and alcohol can have serious consequences, including HIV (http://hiv.drugabuse.gov/index.html) NIDA's new Spanish language public service announcement is designed to reach Hispanic youth with culturally sensitive messages about HIV prevention.

Finally, aggressive outreach must be part of our strategy, reflecting the need for media campaigns aimed at informing high-risk subgroups of the prevalence of HIV infection (sidebar); reducing stigma associated with testing; and providing testing, counseling, and treatment services through nontraditional venues.

4. How is NIDA's HIV research program contributing to global HIV prevention and treatment?

Taking a multifaceted approach to better integrate HIV/AIDS initiatives worldwide.

It is estimated that approximately 30 percent of the new HIV infections worldwide come from injection drug use. Drug intoxication contributes an additional burden of new infection by facilitating risky sexual behaviors that can result in HIV infection.

For example, in Russia, drug abuse is driving approximately 90 percent of the HIV epidemic, fueling a multi-drug resistant TB epidemic and higher rates of sexually transmitted diseases and HCV. In Asia, in the Golden Triangle area, molecular epidemiologic studies indicate the development of new recombinant HIV subtypes stemming from combined intravenous drug use

[3] Hallfors et al. Sexual and drug behavior patterns and HIV and STD racial disparities: the need for new directions. American Journal of Public Health 97(1):125–132, 2007.

and heterosexual epidemics. That is why our disease prevention strategies seek both to increase rates of HIV screening and to advance culturally relevant educational interventions that include information about drug abuse as a major vector for the spread of disease.

NIDA's multifaceted response works to better integrate international initiatives by region and to take advantage of the international research infrastructure funded by the National Institute of Allergy and Infectious Disease (NIAID). The latter aims to develop research that targets drug abuse treatment programs for their utility as HIV and HCV prevention approaches in different international settings (see sidebar). This involves behavioral as well as medication interventions, such as the development of a "heroin" vaccine to help decrease injection transmission of HIV.

5. What are we doing to improve HIV/AIDS treatment and outcomes in drug abusers?

Gaining a better understanding of drug interactions and how to enhance medication adherence.

The development of highly active antiretroviral therapy (HAART) has enabled many HIV-infected individuals to experience remarkable improvements in their general health and quality of life. However, since drug abuse can interfere with the efficacy of HAART, there is an urgent need to better understand drug interactions, both between drugs of abuse and HAART and between prescribed anti-addiction medications and HAART. These interactions have the potential to decrease the effectiveness of either or both treatments

Nonetheless, a primary reason that individuals fail to benefit from or may develop resistance to HAART is their non-adherence to antiretroviral therapy. Adherence can be particularly problematic for drug abusers with chaotic lifestyles, which can interfere with their ability to follow prescribed regimens. In addition, because HAART reduces viral load, some patients mistakenly believe that they do not need to adhere to the treatment regimen or that reduced viral load means elimination of the risk of transmitting HIV. This belief can, in turn, lead to complacency about risk behaviors and resumption of unsafe sex and injection practices. NIDA will support research to better assess the extent to which HIV-positive drug abusers adhere to their HAART medications and the impact that substance abuse may have on adherence.

Malaysia has lagged behind in the treatment of drug addiction and related disorders, even as it is coping with the second highest HIV prevalence rate among adult populations and the highest proportion of HIV cases from injection drug use. Historically, drug abusers were "rehabilitated" involuntarily in correctional facilities. This primarily criminal treatment approach had limited effectiveness, which led to widespread public dissatisfaction and the recent introduction of medications for addiction. These include naltrexone (1999), buprenorphine (2001), and methadone (2003).

Why it's important: These drug treatment programs, rapidly embraced by the country's medical community, have resulted in tens of thousands of opiate-dependent patients receiving medical treatment. A similar success story is starting to unfold in China as well.

Mazlan M, Schottenfeld R, Chawarski M. New challenges and opportunities in managing substance abuse in Malaysia. Drug Alcohol Review 25(5):473–8, 2006.

A promising strategic approach that urges the integration of treatment for HIV/HCV with drug abuse treatment services is one of NIDA's pivotal goals. This will require us to identify the organizational factors that limit the provision of coordinated drug abuse, HIV, HCV, and other treatment services; evaluate innovative approaches to achieve better treatment coordination; and determine the behavioral and social supports needed by drug abusers to engage in and adhere to HIV treatment regimens.

Supporting studies to examine HIV/AIDS comorbidities, including drug abuse and addiction and other brain disorders.

Because of HIV's ability to invade the brain, HIV/AIDS is often complicated by central nervous system dysfunction: approximately 10–15 percent of those living with HIV eventually develop HIV-associated dementia (HAD), which is characterized by a loss of mental functioning with notable motor deficits. Emerging evidence suggests a relationship between drug abuse (particularly stimulants) and accelerated or more severe nervous system complications of HIV. Moreover, in the era of HAART, the prevalence of such neurological complications may increase because more people are living longer with the disease.

Because HIV+ drug abusers can suffer greater neurological complications, it is critical to better understand how drug abuse affects disease progression and pathology. NIDA is therefore encouraging both animal and human studies examining the interactions between drugs of abuse and HIV with respect to neuropathological and neurobehavioral effects.

Animal models are valuable in understanding the basic mechanisms of HIV-associated disease progression and resulting brain dysfunction in the context of substance abuse. It is expected that a broad range of studies will increase collaboration among researchers in multiple areas, including drug abuse, virology, neurobiology, and immunology.

What is NIDA's Vision of the Future?

Our ultimate vision would be the eradication of HIV/AIDS throughout the world. This would of course require the development and worldwide distribution of effective prevention strategies (behavioral interventions and hopefully a vaccine), and therapeutic interventions. We will also ensure that drug abusers are represented in trials for all types of interventions, as we strengthen our national collaborative network to conduct clinical trials and related research on promising behavioral, microbicidal, prophylactic, therapeutic, and vaccine modalities in HIV-infected patients. Further, through pharmacogenomic studies, we expect to be able to tailor therapies to minimize adverse reactions and drug interactions. And given that drug abuse may play a unique role in exacerbating neurologic and psychiatric consequences, the future should see significant efforts applied to understanding their pathogenesis and to developing better therapies for addressing associated impairments. Finally, we envision adapting and translating interventions proven effective in this country to other areas of the world.

IV CROSS-CUTTING PRIORITIES

Several additional priority areas span NIDA's portfolio; these areas are highlighted below:

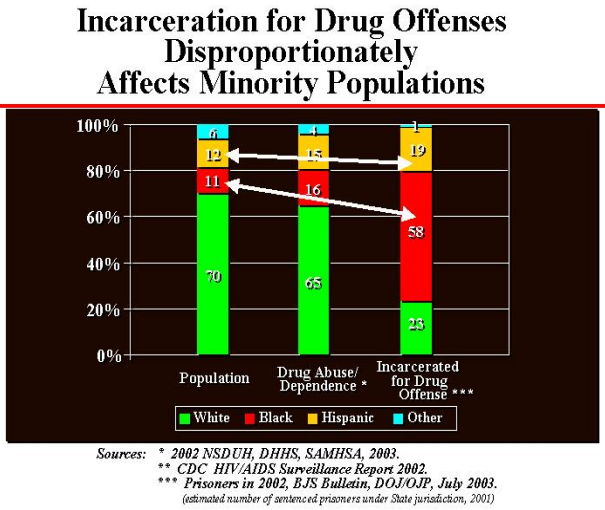
Major Goals

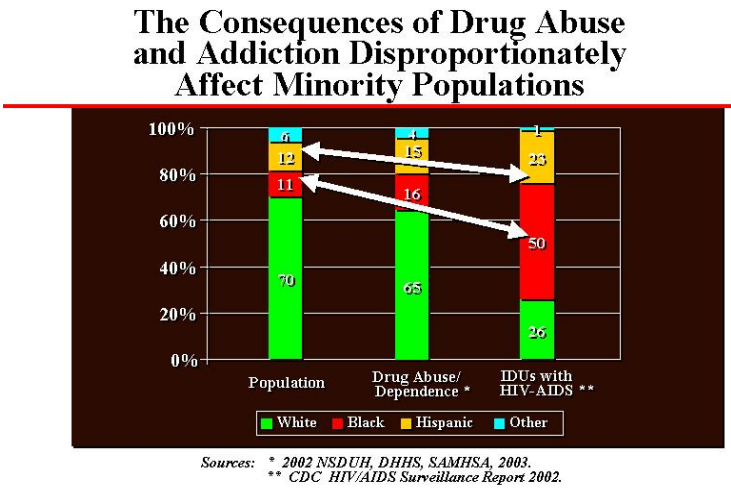
- To decrease **health disparities** related to drug addiction and its consequences.
- To ensure a **diverse and highly trained workforce** able to assume leadership roles in the research agenda on substance abuse and related disorders.
- To promote collaborative **international research** activities, including training and dissemination of science-based information on drug abuse.
- To promote a more **rapid translation of research findings** into clinical application and practice.
- To **educate a variety of audiences** (e.g., children, parents, teachers, media, legislators, and others) about the science underlying drug abuse.
- To **leverage NIDA resources across the entire NIH research community** to expand our knowledge base and increase awareness of the import of drug abuse on other health issues.

NIDA has built a solid foundation designed to achieve these goals by nurturing interactions with different agencies and other stakeholders and by supporting research and outreach in the following areas.

Health Disparities

The pattern of addictions and the burden of disease are not shared equally among members of our population. For example, the disproportionate abuse of methamphetamine among American Indians and Alaskan Natives—higher than in any other subgroup—prompts a need for targeted interventions that can effectively reach these groups. And, contrary to a common stereotype, overall rates of drug abuse among racial and ethnic minorities, particularly African Americans and Hispanics, are similar to rates in the general population. Nonetheless these groups incur greater *medical and social consequences* of their drug use than Whites (see sidebar, next page) including involvement with the criminal justice system and greater disease vulnerability (see Chapter III, HIV/AIDS).





How is NIDA addressing the need for research on health disparities related to drug abuse and addiction and their consequences?

NIDA has developed a separate Strategic Plan on Reducing Health Disparities that includes research, infrastructure and capacity building, and community outreach components (for more detail, see http://www.drugabuse.gov/StrategicPlan/HealthStratPlan.html). Highlights of our ongoing and planned activities include:

- Epidemiologic data clearly show that minority groups differ in patterns of drug use, preferences, accessibility, and risks. Thus, research is needed to look at factors that convey protection or risk across different ethnic and age categories, examining the role of culture, religion, ethnic identity, family, peer, and environmental/community level factors in drug initiation and drug abuse trajectories.

- There is also a need to better understand racial/ethnic implications of genetic variation that modifies the neurotoxicity of different drugs, and the neurobiological processes underlying tolerance, dependence, and relapse. Pharmacokinetic studies have revealed distinct differences in some ethnic populations' ability to metabolize different drugs, which affects sensitivity to the drugs' pharmacological effects.

Research Training, Infrastructure and Capacity Building

An important part of NIDA's mission is to help ensure a continuing supply of well-trained scientists equipped to conduct high-impact drug abuse research. Implicit is the need for trained clinicians and clinical research scientists from diverse backgrounds who can conduct research on various aspects of addiction, HIV/AIDS, health disparities, and other issues critical to drug abuse research. To meet this requirement, we must strengthen the training programs within our educational institutions, and the stability and reach of our research infrastructures.

How is NIDA sustaining its research infrastructure?

- **National Research Service Awards (NRSA**) to institutions and individuals, including the predoctoral diversity awards. NIDA currently funds more than 50 institutional training sites for both predoctoral and postdoctoral fellows nationwide.

- **Career development (mentored K) awards** for emerging scientists or those changing career trajectories to study drug abuse and its related consequences (e.g., HIV). These include the Mentored Clinical Scientist Development Award (K08) and Mentored Patient-Oriented Research Career Development Award (K23), designed to provide "protected time" for clinically trained individuals to participate in an intensive, supervised training program in biomedical or patient-oriented drug abuse research.

- **Pathway to Independence (PI) Award program (K99/R00)**, designed to augment existing programs that provide mentored research and career development experiences for new investigators. This program provides a unique opportunity for highly promising postdoctoral scientists to obtain support for both the initial 1-2 year mentored phase and the later independent phase preparatory to applying for an NIH R01 grant.

- **Dissertation awards (R36)** for specific drug abuse topic areas; **research education awards (R25)** for curriculum and program development; and **small grant programs (R03)** to allow researchers new to a field to obtain data to develop research programs in needed areas such as imaging, AIDS, behavioral research, and chemistry; **diversity supplements** and other training experiences for minority students, beginning in high school and continuing through their postdoctoral phase and beyond.

- **NIH Loan Repayment Programs**, a vital component of our nation's efforts to attract health professionals to careers in research and reflective of NIDA's commitment to developing clinical and pediatric researchers.

- **Minority Institutions' Drug Abuse Research Programs (MIDARP)** grants and cooperative agreements, aimed at building research capacity at institutions serving minority populations.

NIDA offers a strategic set of funding mechanisms to support the development of research scientists through various stages of their careers. These awards are designed to ensure that scientists of the very highest caliber will be available in adequate numbers and in the appropriate research areas and fields to meet the Nation's drug abuse and addiction needs.

International Research

NIDA's International Program fosters international cooperative research in drug abuse around the globe. An important focus for our efforts is the global HIV epidemic, which continues to expand in many parts of the world. Preventing HIV spread through better drug abuse prevention and treatment strategies is critical and depends on having local behavioral and social scientists to undertake the supporting research. To increase the capacity and capability of affected countries, NIDA plans to collaborate with other NIH ICs to encourage U.S. partnerships with skilled foreign investigators and thus help strengthen the research infrastructure of foreign research institutions. As part of this effort, NIDA's international program works closely with the Fogarty International Center, whose mission is to facilitate international cooperation throughout NIH.

How does NIDA expand opportunities for collaboration with colleagues in other countries?

NIDA's international program supports investigators at different stages of their careers working in diverse areas of study relevant to drug abuse and addiction. For example, NIDA's AIDS International Training and Research Program (AITRP) supports joint research training and infrastructure-building programs through partnerships with U.S.-based academic centers. Continued NIDA collaboration will support HIV/AIDS and drug abuse training efforts in Africa, Russia, and Asia. Another unique opportunity is provided through the INVEST Research Fellowship, which facilitates postdoctoral training with established scientists engaged in NIDA-supported research at U.S. institutions—and also with mentors affiliated with one of NIDA's CTN Regional Research and Training Centers. To further enhance international collaborative research on drug abuse and drug-related consequences, NIDA offers additional international fellowship and collaboration awards, which serve as vehicles to support professional exchange visits for drug abuse researchers from other countries and for NIDA-supported scientists working in the United States.

Research Translation

NIDA's overall mission is not just to develop knowledge about drug abuse but to disseminate that knowledge into practical use. We therefore engage in multiple activities—especially those designed to strengthen productive partnerships—that are aimed at closing the average 17-year lag between the discovery of an effective treatment intervention and its implementation into clinical practice in the community.[4]

How does NIDA promote more rapid translation of research findings?

NIDA's producitive alliances with researchers, community treatment practitioners, state directors of substance abuse agencies, and other Federal partners providing training and other supportive services will continue to further our goals of more rapidly translating drug abuse research into real-world use, as well as help identify barriers to implementation. Surmounting challenges and

[4] Institute of Medicine, Crossing the Quality Chasm: A New Health System for the 21st Century. March 2001, p. 5 (http://www.nap.edu/books/0309072808/html).

making our research practical and cost-effective will ensure that effective treatments reach the community-based populations that need them.

- Training community providers to deliver research-based treatments is essential to their implementation. Because such training is outside of NIDA's mission, our partnership with SAMHSA, known as the NIDA–SAMHSA Blending Initiative, uses blending teams composed of NIDA researchers, community treatment providers, and representatives from SAMHSA's nationwide network of Addiction Technology Transfer Centers (ATTCs) to develop research-based "products" and to train treatment providers in their use. The adoption of scientifically validated treatments for addiction (including medications) is garnering growing support from community treatment providers and state agencies, and is an example of real culture change issuing from NIDA's collaborative translation efforts.
- NIDA is also working to engage the medical community so that they can be the first line of defense in detecting potential drug abuse problems and in referring patients to treatment as needed. As part of our Physician Outreach Program—aimed at integrating substance abuse and addiction diagnosis, referral, and treatment into standard medical practice—NIDA has established four Centers of Excellence for Physician Information (CoEs) at several U.S. medical institutions. These CoEs are developing research-based educational materials for medical students and resident physicians about drug abuse and addiction.
- The NIDA Networking Project (NNP) provides opportunities for information sharing and research collaboration among NIDA's networks (e.g, CTN, CJDATS, Genetics Consortium) across the country. The NNP Web site provides a single source for the information emerging from NIDA's primary research and data collection networks, and includes multiple links to network websites, scientific protocols and papers, and procedural policies and manuals.

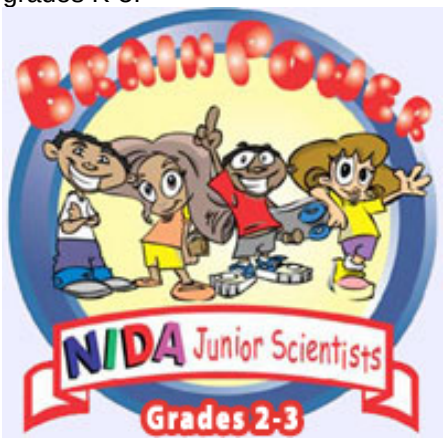
Outreach and Education

As the supporter of most of the world's research on the health aspects of drug abuse and addiction, NIDA is uniquely positioned to educate the public and displace long-held mistaken beliefs about drug abuse with scientific evidence about drugs and addiction

How does NIDA "get the word out" and educate various audiences about the multiple facets of drug abuse and addiction in order to prevent it?

Because most drug use begins during adolescence, it is vitally important that youth be made aware of the effects that drugs have on their developing brains and bodies so that they have the knowledge to help them choose not to use drugs.

Brain Power! The NIDA Junior Scientist Program is designed to take students through a step-by-step exploration of the scientific process and how to apply it to learn about the brain and the effects of drugs on the nervous system and body. Such materials have already been developed for elementary school grades K-5.

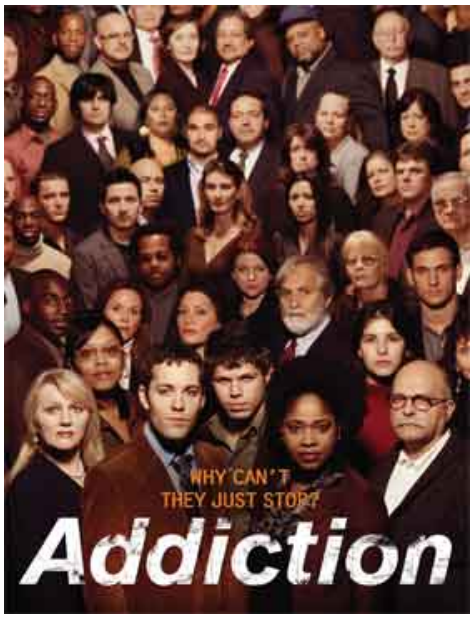


- NIDA will continue to develop and update science-based educational materials for grades K-12 (and beyond) and disseminate them free to schools (see sidebar). By exposing children of all ages to neurobiology and drug education in fun, age-appropriate, and relevant ways, we hope to prevent them from using drugs and spark their interest in scientific careers.

- NIDA plans to further develop our Teens website, aimed primarily at educating middle school adolescents ages 11–15 (as well as their parents and teachers) on the science behind drug abuse so that youth will be armed with better information to make healthy decisions. We have enlisted the help of teens in developing this site to ensure that the content addresses appropriate questions and timely concerns.

- NIDA will continue to design and develop public information and education campaigns, and materials on drug abuse and addiction for a variety of audiences, taking advantage of mainstream media vehicles such as Internet Chats and HBO broadcasts (see sidebar).

NIDA partnered with HBO, NIAAA and the Robert Wood Johnson Foundation on a groundbreaking and Emmy award winning documentary called ADDICTION. The feature-length film is part of a multimedia public health campaign that also includes a web site, book, and community outreach activities. The goal of this project, launched in 2007, is to help Americans understand addiction as a chronic yet treatable brain disease through spotlighting promising scientific advancements and personal testimonials. These materials have reached tens of millions.



Integration with Other Institutes and Centers

Active participation in NIH-wide initiatives is extremely important because drug addiction not only affects the probability of acquiring other diseases; it also affects the prognosis of other diseases. NIDA will continue to actively participate with other institutes to leverage our collective resources and optimally apply the knowledge that emerges from interacting around our common interests.

How is NIDA engaging in cross-institute activities to further its mission?

Several initiatives within the National Institutes of Health (NIH) have relevance to NIDA's mission and will continue to draw our active participation. The following is a select summary.

- The NIH Roadmap's purpose is to identify major opportunities and gaps in biomedical research that no single institute at NIH can tackle alone but that the agency as a whole must address to have the biggest impact on the progress of medical research.

- The NIH Blueprint for Neuroscience Research aims to develop new tools, pool resources, and train a new generation of cross-disciplinary neuroscientists to accelerate the pace of discovery in neuroscience research. By pooling resources and expertise from the 15 ICs that support research on the nervous system, the Blueprint provides a framework that serves the entire neuroscience community. The Blueprint is focusing on neurodegeneration in FY 2007, neurodevelopment in FY 2008, and neuroplasticity in FY 2009.