

Studies Identify Factors Surrounding Rise in Abuse of Prescription Drugs by College Students

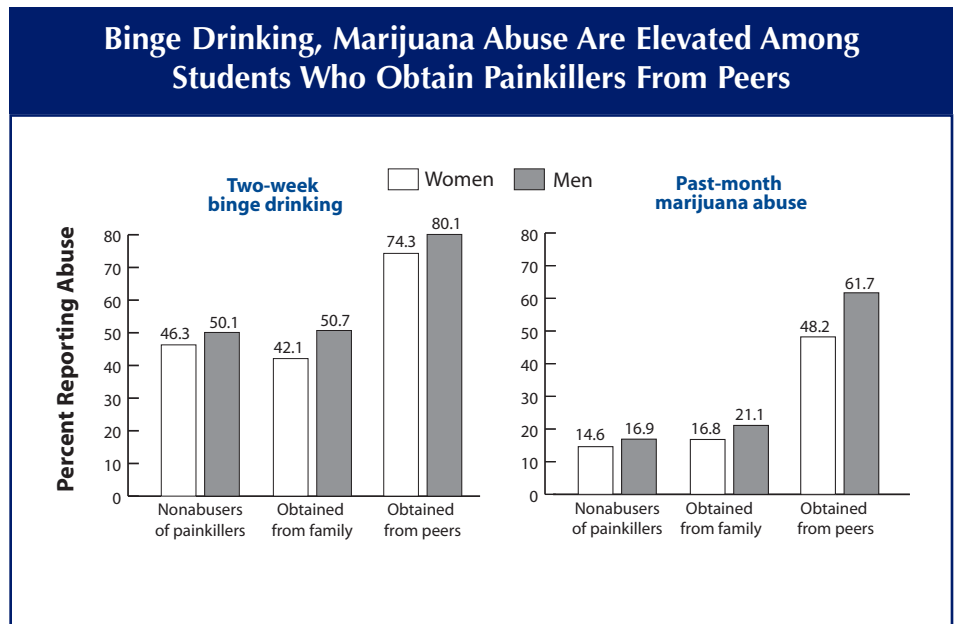
By Lori Whitten, NIDA NOTES Staff Writer

Prescription drug abuse among students in U.S. colleges and universities has been rising for several years. The 2004 Monitoring the Future (MTF) Survey of College Students and Adults—the most recent data available—estimated that 7.4 percent of college students used the painkiller hydrocodone (Vicodin) without a prescription in that year, up from 6.9 percent in 2002, with similar increases for other opioid medications, stimulants, and sedatives. Three new NIDA-funded studies reveal which students and campuses have the highest rates of abuse and connect such abuse to other unhealthy behaviors. According to the research, rates of collegiate prescription stimulant abuse are highest among men, Whites, fraternity/sorority members, and at schools in the Northeast.

Stimulant Abuse Nationwide

Dr. Sean Esteban McCabe and colleagues at the University of Michigan and Harvard University analyzed the

What's Inside	
HUMAN GENOME AND DRUG ABUSE RESEARCH in Director's Column	3
BEHAVIORAL THERAPY'S ROLE in Helping to Reduce Meth Abuse	4
COMBINED TREATMENT HELPS SMOKERS improve their likelihood of quitting	8



At one university, students who obtained prescription painkillers from peers reported higher levels of binge drinking and marijuana abuse than nonabusers or those who received painkillers from family.

answers from the Harvard School of Public Health College Alcohol Study, which in 2001 surveyed 10,904 randomly selected students enrolled at 119 colleges across the United States. Overall, 4 percent of the respondents reported having taken a stimulant medication without a prescription at least once during the previous year. Men were twice as likely as women (5.8 percent versus 2.9 percent) to have abused methylphenidate (Ritalin), dextroamphetamine (Dexedrine), and amphetamine/dextroamphetamine (Adderall). Stimulant medication abuse was also more prevalent among students who were:

- White (4.9 percent versus 1.6 percent for African-Americans and 1.3 percent for Asians);

continued on page 6



Do genes play a role in teens becoming regular smokers? p. 11

Research Findings

Studies Identify Factors Surrounding Rise in Abuse of Prescription Drugs by College Students. 1

Treatment Curbs Methamphetamine Abuse Among Gay and Bisexual Men. 4

Combination Treatment for One Year Doubles Smokers' Quit Rate 8

NIDA at Work: AIDS Research Program. 9

Genetic Predisposition and Depression Both Influence Teen Smoking. 11

Director's Column

Map of Human Genome Opens New Opportunities for Drug Abuse Research 3

Research in Brief

Highlights of recently published NIDA-supported studies 13

Bulletin Board

Dr. Bill Carlezon Receives the 2005 Jacob P. Waletzky Memorial Award 14

Psychological Association Honors Dr. Nora D. Volkow 14

Tearoff

NIDA and Scholastic Offer Teens and Teachers New *Heads Up* 15

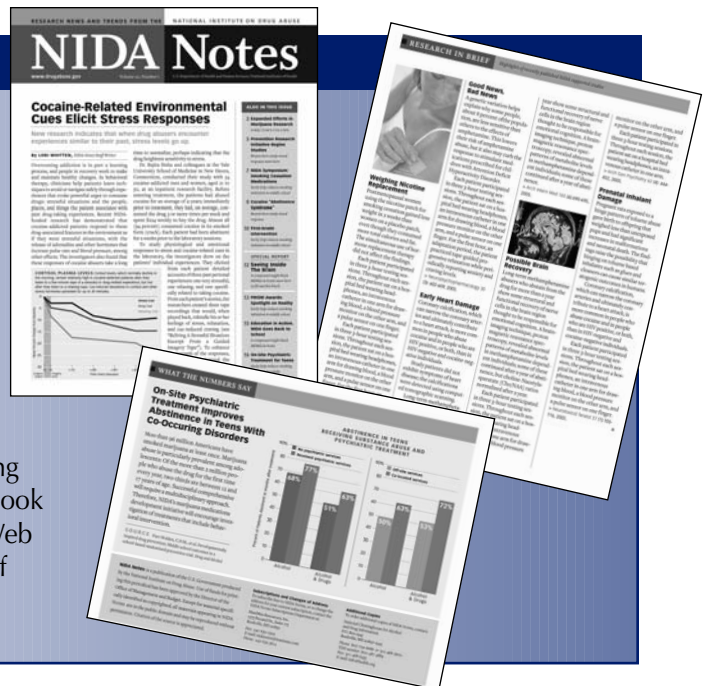


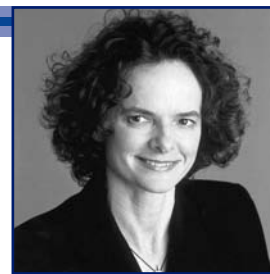
2005 Jacob P. Waletzky Memorial Award, p. 14

Coming Soon to NIDA NOTES

- Full-color design
- New content
 - Research in Brief
 - NIDA at Work
 - Reference Article: Animal Models in Research
 - Research Findings

NIDA NOTES, the publication you depend on for up-to-date information on drug abuse science, has been redesigned to bring you even more information in a colorful, easy-to-read format. Look for *NIDA NOTES*, Vol. 20, No. 5, coming to you soon on the Web and by mail. If you have not yet signed up for e-mail delivery of *NIDA NOTES*, please contact nidanotes@masimax.com.





Map of Human Genome Opens New Opportunities for Drug Abuse Research

By NIDA Director Nora D. Volkow, M.D.

Just under 3 years ago, scientists published the first complete maps of the human genome, the paired strands of deoxyribonucleic acid (DNA) that direct the development of every human cell. With these maps, scientists have already begun tightly focused investigations to pinpoint how each of the genome's 30,000 individual genes and its products—proteins or lipids—influence health and disease. NIDA is actively pursuing investigations in the emerging fields of genomics, proteomics, and lipidomics, which promise to reveal the molecular bases of drug responses and thereby open a new era of targeted, potentially individualized approaches to treating drug abuse and addiction.

Genomics

NIDA has initiated a public-private partnership through which drug abuse researchers will search the genome for gene variations that may affect vulnerability to nicotine addiction. The researchers will begin by studying associations between gene variations called single nucleotide polymorphisms (SNPs), smoking, and responses to nicotine. SNPs can be thought of as single-letter substitutions in the 3-billion-letter instructions of the human genome; for example, the sequence "CCAGTCA" may be changed to "TCAGTCA." More than 99 percent of such SNPs appear to make no significant biological difference, but others may alter cell functions in ways that influence a person's susceptibility to addictive drugs.

To begin, NIDA-supported researchers at Washington University in St. Louis will use a library of 1.5 million SNPs, developed by Perlegen Sciences, Inc., of Mountain View, California, to analyze genetic samples from 500 people with nicotine addiction and 500 who have smoked but have not become addicted. The researchers expect that their first sweep through Perlegen's library will yield 40,000 SNPs that appear in the genome of addicted smokers but not unaddicted smokers. Further screening will narrow the search to a few hundred, and, among these, the investigators hope to identify specific gene variations that contribute to nicotine addiction.

Proteomics

Identifying addiction-related sites on the genome is a daunting analytical task, but it is only a first step. The instructions encoded in a gene guide the assembly of amino acids that, in turn, combine in large complex molecules called proteins. While the genome remains unchanged throughout life, the proteome—the complete inventory of proteins in all

cells in the body—is dynamic, constantly changing as proteins are assembled or broken down in chemical interactions that are the molecular mechanisms of health and disease.

NIDA has initiated a research effort that will use proteomics, the exploration of the structure and function of proteins, to help reveal step-by-step molecular activities that enhance or inhibit the effects of addictive drugs. Under an initiative launched in 2004, investigators at Yale University and the University of Illinois will inventory and examine proteins in the brain. This effort will identify which proteins are present and active, but it will be far more than a mere catalog of neuroproteins: It will reveal how the proteins—such as those that act as receptors and transporters for chemical messengers like dopamine or serotonin—and their interactions change over time in healthy brains and in those affected by addictive drugs. This knowledge, in turn, will help us develop treatments that might prevent, reduce, or reverse the impacts of addictive drugs.

Lipidomics

More fully understanding the actions of proteins will require intensified study of still other biological compounds—the 1,000 or more chemical molecules called lipids, which include fatty acids that store energy, sterols such as testosterone and estrogen, and amides, which serve as chemical messengers. NIDA-supported researchers were among the first to study the role of lipids, in investigations that identified anandamide, a lipid that occurs naturally in the human body and plays a role in obesity, pain, and immune response. Increasing interest in these versatile molecules has led to the emergence of a research discipline called lipidomics.

NIDA has nurtured lipidomics with direct support for researchers and by convening symposia to summarize progress and generate goals and strategies for the next research phase. In 2004, NIDA sponsored the first international lipidomics conference (see "NIDA-Sponsored Conference Highlights Intensive Research Focus on Lipids," *NIDA NOTES*, Vol. 19, No. 5, p. 12). NIDA also organized lipidomics symposia at the meetings of the College on Problems of Drug Dependence and the International Cannabinoid Research Society. NIDA's direct contributions, including specific research support of lipidomics in its neuroproteomics research applications, will help elucidate the role of lipids in regulating the intricate biological processes that control the effects of addictive drugs. **NN**

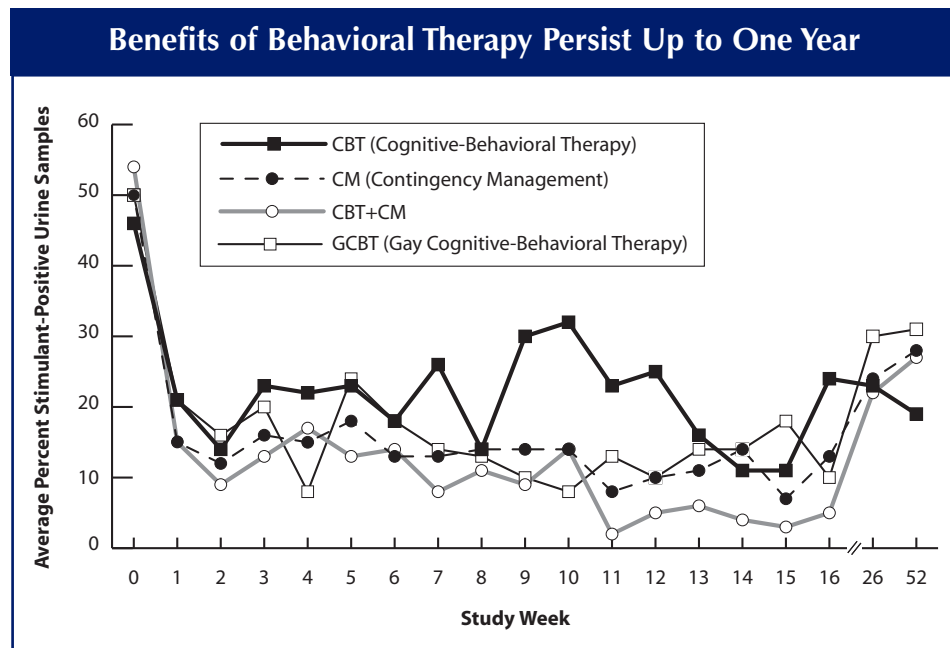
Treatment Curbs Methamphetamine Abuse Among Gay and Bisexual Men

By Lori Whitten, *NIDA NOTES* Staff Writer

Behavioral therapy can help gay and bisexual men (GBM) reduce methamphetamine abuse and risky sexual behaviors and sustain these gains for 1 year, NIDA-funded researchers report. By the end of a 16-week trial of four different behavioral therapies, study participants' stimulant-positive urine samples fell 31 percent, and their number of past-month sexual partners fell more than 50 percent—outcomes that regressed little at the followup visits. Symptoms of depression also improved.

Dr. Steven Shoptaw and colleagues at the University of California, Los Angeles and the Friends Research Institute recruited 263 methamphetamine-addicted GBM throughout Los Angeles County, particularly in Hollywood, where HIV prevalence is especially high. Of these, 162 completed the requirements for entering the treatment phase of the study, which were to attend six assessments and participate in at least two of four group sessions on abstinence skills during a 2-week “baseline period.” Men who met the requirements reported less severity and shorter duration of methamphetamine abuse than those who did not, despite having abused methamphetamine for 5 years and having spent \$293 on the drug in the past month, on average. Half had engaged in unprotected anal intercourse (UAI) with someone other than their primary partner in the past month, and 84 percent of these men linked the behavior to methamphetamine abuse. Most participants (73 percent) reported symptoms of depression, with about 30 percent describing these as moderate to severe.

The researchers randomly assigned each patient to one of four behavioral therapies: cognitive-



Although all interventions were effective, participants who received contingency management (CM), cognitive-behavioral therapy (CBT) and CM, or culturally tailored Gay CBT (GCBT) submitted fewer stimulant-positive urine samples during treatment, compared with those in standard CBT.

behavioral therapy (CBT), contingency management (CM), CBT+CM, or Gay CBT (GCBT). In CBT, participants analyzed situations and emotions linked with relapse, practiced ways to manage craving and thoughts about drug abuse, and discussed healthy behaviors in group sessions. In CM, participants received vouchers redeemable for groceries, transportation, and clothing if they submitted stimulant-negative urine samples. GCBT addressed standard CBT issues—including relapse, craving, and healthy behaviors—using specific examples from gay cultural events and environments. For example, they compared the experience of owning up to a drug problem with the experience of acknowledging sexual orientation by “coming out.” All four interventions were offered three times a week for 4 months.

Multiple, Lasting Benefits

Participants reduced methamphetamine abuse and risky sexual behaviors and experienced fewer depression symptoms in the last month of treatment compared with the month before therapy, regardless of the therapeutic approach. Overall, they decreased methamphetamine abuse from 9.6 to 2.4 days a month and reduced the number of past-month sexual partners from 9.8 to 4.3, on average. The percentage who reported unprotected insertive anal intercourse—a risk factor for HIV-infected individuals to transmit the virus to partners—fell from 36.9 percent to 16.7 percent by the end of treatment. Beck Depression Inventory (BDI) scores improved from 14.3 (in the “mild to moderate” range) at baseline to 5.4 (“minimal”) in the last week of treatment.

Although all therapies benefited participants, response to the treatments differed. During the treatment period, participants in GCBT and the combined treatments attended more weeks of therapy and submitted fewer stimulant-positive urine samples than those who received standard CBT during treatment. Participants receiving GCBT showed a faster decrease in unprotected receptive anal intercourse—a risk factor for acquiring the virus from a partner—compared with those in standard CBT. Most participants (80 percent) took part in the 1-year followup. Generally, they sustained the lower levels of methamphetamine abuse, risky sexual behaviors, and depression observed at the end of treatment (see page 4, “Benefits of Behavioral Therapy Persist Up to One Year”).

“It is encouraging that several types of behavioral treatment reduced both drug abuse and risky sexual behaviors among gay and bisexual men at high risk for contracting or transmitting HIV,” says Ms. Debra Grossman of NIDA’s Division of Neuroscience and Behavioral Research. However, more studies are needed to determine the components of treatment that affect risky sexual

behaviors and the link between methamphetamine abuse and such behaviors in other populations, she adds.

Methamphetamine Treatment as HIV Prevention

For about a decade in California, the drug most tightly linked with HIV infection in GBM has been methamphetamine. The drug conveys a sense of heightened sexuality in the short term and is associated with risky sexual behaviors and extremely high rates of HIV infection in those seeking treatment. Sixty percent of the participants in Dr. Shoptaw’s study reported HIV-positive status, a prevalence much higher than his group has observed among GBM seeking treatment for cocaine (30 percent), alcohol (15 percent), or heroin (5 percent) abuse.

“The reductions in risky sexual behavior in this study exceeded those observed in HIV prevention trials among GBM. We conclude that treatment for meth abuse fits into a comprehensive HIV prevention strategy,” says Dr. Shoptaw. The findings have already made an impact: These data helped policymakers at the California Office of AIDS decide to allocate

\$3 million for programs that address methamphetamine abuse among GBM.

Methamphetamine and the Blues

The researchers were not surprised by the high percentage of their study participants who reported depression symptoms at the beginning of the study. GBM are three times as likely as heterosexual men to have clinical depression.

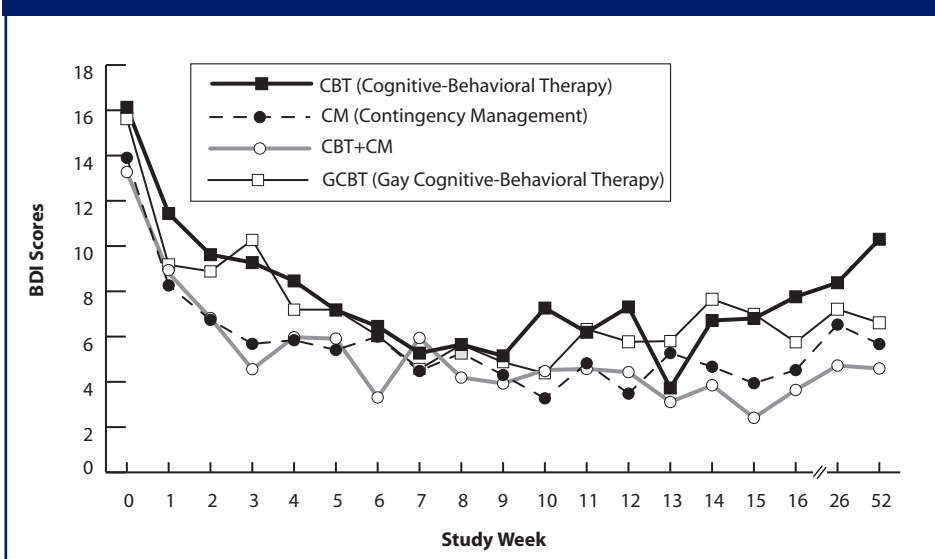
Methamphetamine abusers often say they take the drug to kick the blues, but results from the current study suggest that continuing abuse may serve to relieve low moods related to stimulant withdrawal rather than alleviate underlying chronic depression.

When they analyzed the temporal link between methamphetamine abuse and depression, Dr. Shoptaw and his colleagues found that a urine sample indicating abuse of the drug within the past 5 days strongly predicted high BDI scores and abstinence strongly predicted low scores. In contrast, BDI scores did not predict episodes of future methamphetamine abuse, which is what would be expected if the men were abusing the drug to alleviate depression. “Meth abusers probably remember feeling better after taking the drug, but this perception may not match the physiology of long-term stimulant abuse,” says Dr. James Peck, a member of the research team who led the analysis of the depression data.

Sources

- Shoptaw, S., et al. Behavioral treatment approaches for methamphetamine dependence and HIV-related sexual risk behaviors among urban gay and bisexual men. *Drug and Alcohol Dependence* 78(2):125-134, 2005.
- Peck, J.A., et al. Sustained reductions in drug use and depression symptoms from treatment for drug abuse in methamphetamine-dependent gay and bisexual men. *Journal of Urban Health* 82(1):i100-i108, 2005. **NN**

All Four Therapies Reduced Depression Symptoms



Participants demonstrated improvement in Beck Depression Inventory (BDI) scores, which dropped sharply the first week of treatment and leveled off at week 4.

Studies Identify Factors Surrounding Rise in Abuse of Prescription Drugs by College Students

continued from page 1

- Members of fraternities or sororities (8.6 percent versus 3.5 percent for nonmembers); and
- Earning lower grades (5.2 percent for grade point average of B or lower versus 3.3 percent for B+ or higher).

Students who abused prescription stimulants reported higher levels of cigarette smoking; heavy drinking; risky driving; and abuse of marijuana, MDMA (Ecstasy), and cocaine. Compared with other survey respondents, for example, they were 20 times as likely to report past-year cocaine abuse and 5 times as likely to report driving after heavy drinking.

The campus prevalence of past-year stimulant abuse ranged from 0 percent at 20 colleges—including the three historically African-American institutions included in the survey—to 25 percent. The prevalence was 10 percent or higher at 12 colleges. Students attending colleges in the Northeast, schools with more competitive admission standards, and noncommuter schools reported higher rates of abuse.

One University's Painkiller Picture

At a large Midwestern university, about 9 percent of 9,161 undergraduates surveyed had taken a prescription pain medication without a doctor's order at least once during the past year; 16 percent reported such abuse in their lifetime. Of the latter, 54 percent said they had obtained the drugs from peers, while 17 percent said their source was a family member. Dr. McCabe and colleagues at the University of Michigan Substance Abuse Research Center found that students who obtained medications from

Stimulant Abuse Varies by Campus Characteristics	
Selected Characteristics	Past-year Stimulant Abuse Rates, %
Admission criteria	
More competitive	5.9
Competitive	4.5
Less competitive	1.3
Geographical region	
Northeast	6.3
South	4.6
West	3.2
North Central	2.8
Commuter status	
Noncommuter school	4.6
Commuter school	1.2

Students enrolled in the most selective colleges reported relatively high levels of past-year stimulant abuse, as did those attending schools in the Northeast. Residential schools reported higher rates than commuter colleges.

peers were more likely to smoke and drink heavily and to have abused other substances—including marijuana, cocaine, and other illegal drugs—than those who obtained them from family members.

The researchers found that exposure to prescription pain medication early in life increased the likelihood of abuse in college. Women who had

received prescriptions for pain relievers in elementary school were more than four times as likely as those with no prescribed use to report abuse in the past year. Men with early prescribed use were twice as likely as those without to report such abuse.

In addition:

- Women students were more likely to be prescribed pain medication, while men were more likely to be approached to sell or give away prescribed medication.
- More men obtained the drugs from peers while more women obtained them from family members.
- Past-year prescription painkiller abuse was higher among fraternity members than nonmembers (17 percent versus 9 percent) and among sorority members compared with nonmembers (9.6 percent versus 8.6 percent).

“Students abuse prescription drugs to get high, to self-medicate for pain episodes, to help concentrate during exam time, and to try to relieve stress. Regardless of the motivation, people need to know the risks of abuse and the dangers of mixing drugs,” says Dr. Lynda Erinoff, formerly of NIDA's Division of Epidemiology, Services and Prevention Research. Most people assume that if a medication is available on the market, it must be safe—even if it has not been prescribed for them, says Dr. Erinoff, “but a drug or dose that a doctor orders for one person is not necessarily appropriate for another, and prescription abusers are potentially taking a serious risk.” NIDA continues to work with doctors and pharmacists and to link prevention specialists with researchers focusing on the problem. “Educating the public remains a critical challenge,” says Dr. Erinoff.

Membership Matters

Based on responses from more than 5,000 young people who participated in the MTF when they were

“... people need to know the risks of abuse and the dangers of mixing drugs.”

high school seniors in 1988 to 1997, and also when they were in college, Dr. McCabe and his Michigan colleagues found that active members of college fraternities or sororities engage in more heavy episodic, or “binge,” drinking, cigarette smoking, and marijuana abuse than nonmembers.

The students who joined fraternities or sororities in college were the same ones who reported the highest levels of substance abuse in high school. Moreover, cigarette smoking, binge drinking, and drug abuse increased for all survey participants as they progressed through college. Fraternity and sorority members showed greater elevations in binge drinking and marijuana abuse over

time compared with nonmembers. The picture that emerges is of students who are already heavy drinkers when they come to college selecting fraternities and sororities with a reputation for “partying” and then, as members, further increasing their drinking in an environment that supports the behavior.

“It’s important for each student to explore, perhaps with counseling, a possible mismatch between his or her college environment and individual needs. Some students benefit from settings that emphasize socialization outside of the party scene; these might include group living arrangements based on shared academic or extracurricular interests,” Dr. McCabe says.

Sources

- McCabe, S.E., et al. Non-medical use of prescription stimulants among US college students: Prevalence and correlates from a national survey. *Addiction* 100(1):96-106, 2005.
- McCabe, S.E., et al. Selection and socialization effects of fraternities and sororities on US college student substance use: A multi-cohort national longitudinal study. *Addiction* 100(4):512-524, 2005.
- McCabe, S.E.; Teter, C.J.; and Boyd, C.J. Illicit use of prescription pain medication among college students. *Drug and Alcohol Dependence* 77(1):37-47, 2005. **NN**

Science & Practice PERSPECTIVES

**Now Available
by E-mail**

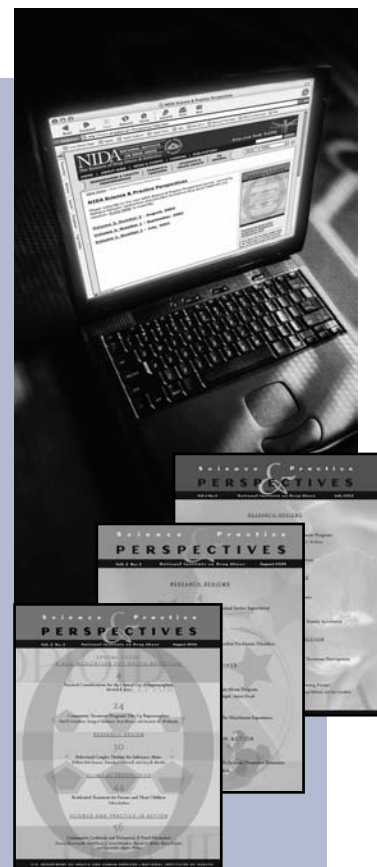
Sign up below to receive NIDA’s free innovative journal – a must-read for all drug abuse researchers and treatment providers – direct to your in-box!

The journal you rely on for

- Top researchers’ up-to-the-minute reviews of the most critical topics in the science of prevention and treatment
- Top service providers’ perspectives on what works and can work in diverse community treatment settings
- Roundtable discussions of each article
- Successful research-practice collaborations described by the partners involved
- Easy access to all the electronically available articles cited in our pages

is now even more accessible!

Sign up today for electronic delivery of *Science & Practice Perspectives*, and you will begin receiving the e-mail edition of the journal, complete with links to each article. Just fill out the subscription form at <http://www.drugabuse.gov/Perspectives>.



Combination Treatment for One Year Doubles Smokers' Quit Rate

By Patrick Zickler, NIDA NOTES Staff Writer

Most smokers understand the health risks associated with tobacco use and want to stop, but the addictive grip of nicotine makes quitting difficult; nearly 80 percent of smokers who try relapse within a year. Those poor odds can be improved, NIDA-supported investigators say, by extending the length of smoking cessation therapy to at least 1 year.

Among smokers who received medication and counseling for 12 months rather than the conventional 12 weeks, half were abstinent a year after quitting. This is more than double the success rate of other treatment programs, says Dr. Sharon Hall, who investigated the extended treatment approach at the University of California, San Francisco. "Smoking is not just a bad habit; it is a powerful and deadly addiction," Dr. Hall says. "It has to be treated with methods that are commensurate with its addictive properties, which are extensive and long term."

Dr. Hall and her colleagues assigned each of 160 trial participants who smoked 10 or more cigarettes daily to one of four regimens. All the participants received nicotine replacement therapy (transdermal patch) and took part in five group counseling sessions during the first 12 weeks of the study. These 90-minute sessions concentrated on understanding health issues associated with smoking and quitting, developing personalized quit strategies, and avoiding relapse. The investigators gave half the participants a placebo and half nortriptyline, an antidepressant that Dr. Hall's research group had previously found helps smokers to quit. The researchers adjusted participants' medication doses to maintain blood concentra-

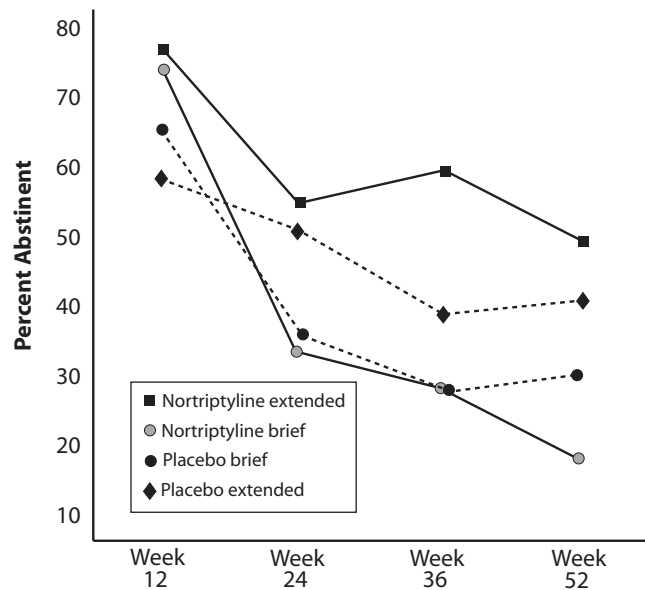
tions of 50 to 150 ng/L. At the end of 12 weeks, treatment ended for half of the participants. The rest continued their regimens of nortriptyline (40) or placebo (41) for 40 more weeks. During this time, they continued to participate in monthly 30-minute group counseling sessions and were contacted by phone 2 weeks after each session to reinforce counseling lessons.

At the end of weeks 24, 36, and 52, far fewer of the participants in extended treatment were smoking than were participants whose treatment ended after 12 weeks.

At the end of 1 year, 50 percent of patients who had received nortriptyline and counseling throughout were abstinent, compared with 18 percent who got this treatment for only 12 weeks. Forty-two percent of patients who received extended counseling and placebo were abstinent at 1 year, compared with 30 percent of those who got them for 12 weeks.

"The highest success rate was with nortriptyline and counseling for 52 weeks," Dr. Hall says. "Extended treatment with placebo and counseling came in a very close second, suggesting that prolonged psychological support and counseling are important

Smoking Cessation Rates Improve With Year-Long Treatment



After an initial 12-week therapy regimen, patients who received monthly counseling for 40 more weeks maintained higher abstinence rates than patients who did not. Concurrent nortriptyline therapy enhanced the advantage of extended counseling.

components in improved treatment outcomes." The mix of long-term combination treatment with both pharmacological and behavioral therapies reflects the complexity and power of smoking addiction, says Dr. Hall. "Smoking is more complex than just the physical addiction. There are psychological factors such as stress that can trigger a desire to smoke. There are social and environmental factors—a certain group of friends or a certain kind of meal or a certain type of gathering—that make a contribution, too," Dr. Hall says. "Simply treating the physical addiction doesn't address these psychological

continued on page 10

NIDA at Work: AIDS Research Program

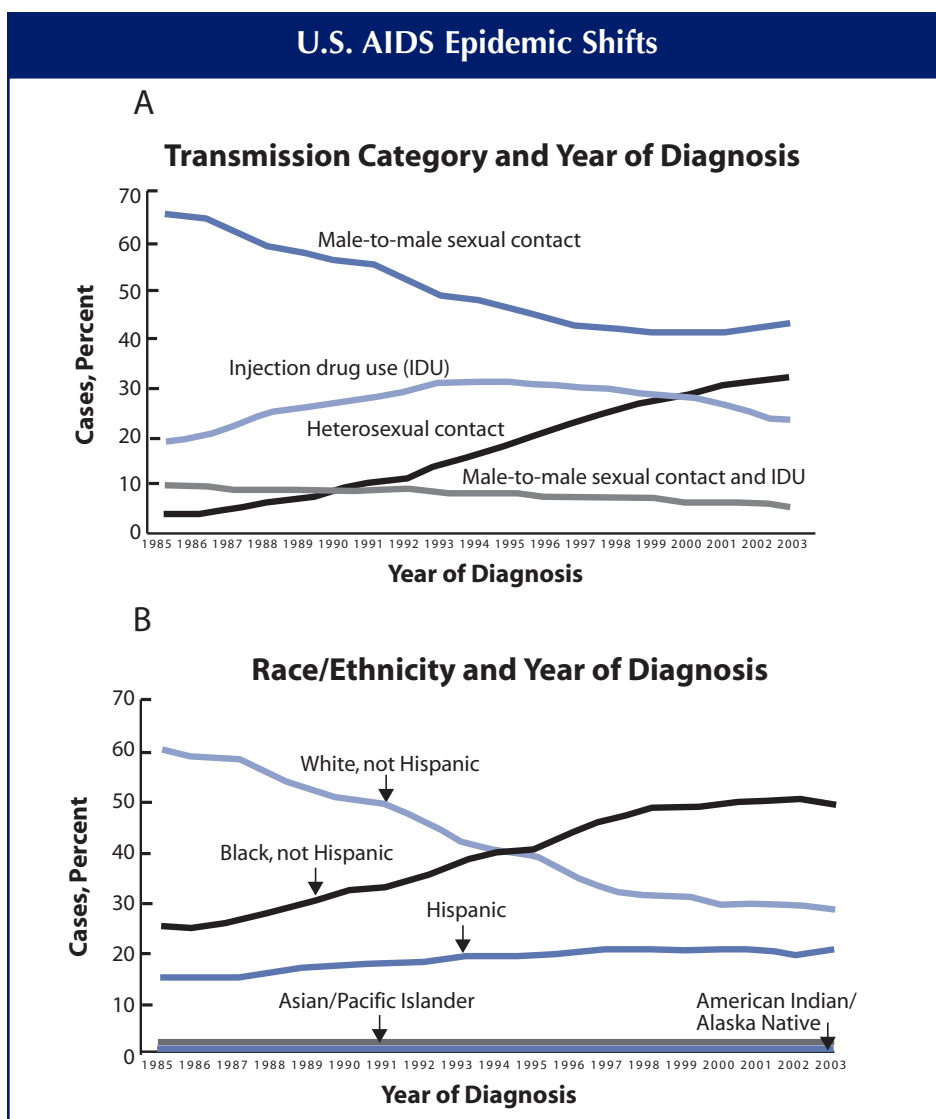
By Lori Whitten, NIDA NOTES Staff Writer

NIDA disburses more than \$275 million annually to support research on HIV and AIDS.

The mandate to ensure that this investment yields the greatest possible return in new knowledge leading to more effective treatment and prevention lies with NIDA's AIDS Research Program.

Under the direction of Dr. Jacques Normand, the AIDS Research Program oversees all the Institute's HIV-related grantmaking. Dr. Normand works with three associate directors: Dr. Lynda Erinoff is in charge of planning the basic science grant portfolio; Ms. Helen Cesari manages the social science programs; and Ms. Katherine Davenny coordinates collaborative projects with other NIH Institutes and external organizations engaged in HIV/AIDS research. Every other month, the AIDS Research Program staff convenes an AIDS workgroup consisting of 20 NIDA grantmaking staff with expertise in all science areas relevant to HIV, including representatives from four Program Divisions, three Offices, the Center for Clinical Trials Network, and the International Program. In the meetings, NIDA scientists exchange up-to-date information, identify research needs and opportunities, set priorities, and look for ways to coordinate ongoing research and new initiatives.

In pursuing its mandate, the AIDS Research Program builds upon NIDA's more than 20-year history of accomplishment in HIV research. In the early 1980s, when it became apparent that injection drug use was playing a critical role in the spread of the newly recognized deadly disease, Congress identified NIDA as a key component of the Nation's response. The Institute initiated a research program that has had significant impact on the epidemic.



(A) The proportion of newly diagnosed AIDS cases due to injection drug use has dropped since the 1980s, and the proportion due to heterosexual contact has increased. (B) Forty-seven percent of newly diagnosed AIDS cases in 2003 were in non-Hispanic Blacks.

Along with underwriting studies leading to crucial discoveries, such as the finding that providing methadone treatment slows the spread of the disease among injection opioid abusers, NIDA has supported the development and testing of effective science-based education, outreach, and preventive interventions for drug-abusing and other at-risk populations. Partly as a

result of these efforts, the number of newly diagnosed AIDS cases attributable to injection drug use in the United States dropped from 19,943 in 1995 to 6,938 in 2004.

Shifting With the Epidemic

Established in February 2005, the AIDS Research Program has come into being at a time when the character of

continued on page 10

NIDA at Work: AIDS Research Program

continued from page 9

the HIV epidemic is in transition. Since the mid-1980s, heterosexual contact—often with an injection drug user or while under the influence of drugs—has become an increasingly important route of transmission of the HIV virus. The proportion of newly diagnosed AIDS cases attributable to heterosexual contact has increased while that attributable to sexual contact among men who have sex with men and that directly attributable to injection drug use have dropped. The rise in heterosexual transmission has been especially pronounced among African Americans and women (see page 9, “U.S. AIDS Epidemic Shifts”).

A recent case highlights the AIDS Research Program’s role in generating efficient responses to developments in the epidemic. In February 2005, New York City public health officials reported that a new strain of HIV had been isolated from a methamphetamine-abusing man who engaged in high-risk sex with male partners. The patient responded poorly to initial treatment and progressed rapidly from

infection to AIDS. The officials, worried that such a highly virulent, treatment-resistant strain might become widespread, called for heightened monitoring of treatment-resistant HIV. The AIDS Research Program and the AIDS workgroup promptly developed a plan to promote collaborations between epidemiologists, social scientists, virologists, immunologists, and infectious disease experts. Their work aims to produce a comprehensive assessment of the potential for treatment-resistant viral strains among infected men who have sex with men and who also abuse methamphetamine.

As they realign research priorities to match the new dynamics of the epidemic, NIDA’s AIDS Research Program and the AIDS workgroup members will draw on the results of NIDA’s Sexual Acquisition and Transmission of HIV Cooperative Agreement Program (SATH-CAP). This program’s four interdisciplinary research teams are studying the patterns of viral spread from high-risk, drug-using groups to lower risk groups; for example, from drug injectors to noninjecting sexual partners, or from bisexual men to female sexual partners. Mapping these patterns will

enable prevention practitioners to focus their initiatives on the social networks and activities with the most potential for containing the spread of the epidemic. SATH-CAP investigative teams are working in geographical areas where HIV is in a rapid process of bridging from one population to another. For example, one team is studying the epidemic in St. Petersburg, Russia, where the primary route of transmission is in transition from injection drug use to sexual contact.

The treatment-resistant HIV and SATH-CAP initiatives exemplify how NIDA, through the AIDS Research Program, brings the power of interdisciplinary research to bear on the intertwined problems of drug abuse and HIV/AIDS. “Interdisciplinary research among investigators with different expertise typically does not happen without coordination,” says Dr. Normand. “The AIDS Research Program is the place where NIDA ensures that its research on epidemiological, biological, and behavioral aspects of the infection among drug abusers works in concert and that knowledge from the research is translated into clinical and community practice.” **NN**

Combination Treatment for One Year Doubles Smokers’ Quit Rate

continued from page 8

influences, which can trigger a relapse to smoking months or years after a person has quit.”

“These findings are significant because they show that a combination treatment provided over an extended period has great potential to improve smoking cessation rates,” says Ms. Debra Grossman of NIDA’s Division of Neuroscience and Behavioral Research. “Dr. Hall has shown that

providing smokers with a comprehensive extended treatment can achieve better abstinence rates than have ever previously been reported from a controlled trial.”

Dr. Hall and her colleagues are continuing to test long-term treatments in two other studies. One involves smokers older than 50, a group with markedly poorer outcomes than younger smokers. The second will evaluate bupropion, a prescription medication specifically approved for smoking cessation treatment, in combination with counseling.

For some smokers, the prospect of a year-long course of treatment is

daunting, Dr. Hall acknowledges. “But this may be what you need to do if you want to be successful. Smokers, as well as the practitioners who treat them, need to know that it is possible to achieve high rates of long-term abstinence. It is not a simple process because it’s not a simple addiction. But it is worth it to stop doing something that can kill you.”

Source

• Hall, S.M., et al. Extended nortriptyline and psychological treatment for cigarette smoking. *American Journal of Psychiatry* 161(11):2100-2107, 2004. **NN**

Genetic Predisposition and Depression Both Influence Teen Smoking

By Patrick Zickler, *NIDA NOTES* Staff Writer

NIDA-supported scientists have found that a gene, called *DRD2*, partly determines whether an adolescent who takes a first puff on a cigarette will progress to regular smoking. Adolescents who carry one of the two known forms of the gene (*A1*) are more likely than those with the other variant (*A2*) to become daily smokers. If the teen also suffers from depression, the genetic effect is amplified, further increasing the likelihood of smoking escalation, according to Dr. Janet Audrain-McGovern and colleagues at the University of Pennsylvania Transdisciplinary Tobacco Use Research Center (TTURC).

The new findings result from a large-scale study that Dr. Audrain-McGovern and her research group undertook to clarify outstanding issues surrounding *DRD2* and smoking. Scientists have suspected for some time that variations in *DRD2* might influence people's responses to tobacco, based on the gene's function: It helps guide construction of sites where the neurotransmitter dopamine—which plays a key role in producing the pleasurable effects of nicotine—attaches to brain cells. Some previous studies have found that, indeed, men and women who smoked or were nicotine-dependent were more likely to have the *A1* *DRD2* variant than the *A2*. However, other studies did not confirm the link.

DRD2 Variants and Smoking Progression

Dr. Audrain-McGovern's team recruited 615 adolescents (322 girls, 293 boys) to participate in their study. Because genetic diversity would

increase the difficulty of interpreting results, all the youths were of European ancestry. Analysis of DNA obtained from cheek swabs showed that the frequencies of the alternative *DRD2* forms, or alleles, were roughly the same among the participants as have been seen in general population samples of people of European stock:

Two-thirds (67 percent) had inherited the *A2* allele from both parents, 30 percent had one *A1* and one *A2*, and 3 percent had two copies of the *A1*.

The researchers interviewed the teens in ninth grade, asking questions used in the Youth Risk Behavior Survey, including, "Have you ever tried or experimented with cigarette smoking, even a few puffs?" "Have you smoked at least one whole cigarette?" "How many cigarettes have you smoked in the last 30 days?" and "How many cigarettes have you smoked in your lifetime?" Based on their responses, the teens were categorized as never smokers, puffers (a few puffs, but never a whole cigarette), experimenters (at least one but fewer than 100 lifetime cigarettes), and current smokers (smoked in the past 30 days and 100 or more lifetime cigarettes).

The teens answered the same questions again in the fall and spring



of their 10th-grade year and in the spring of their 11th-grade year. Analyzing the teens' sequential responses together with their genetic data, the researchers found no association between variation in *DRD2* alleles and the likelihood that participants who had never smoked would start, Dr. Audrain-McGovern says. "However, among adolescents who had taken at least a single puff, we found a clear association between the *A1* allele and progressing up the ladder of smoking frequency—for example, moving from puffer to experimenter, or experimenter to current smoker. Each additional copy of the *A1* allele nearly doubled the odds of progression," she says. Among teens who had at least puffed once, those with a single *A1* allele were 1.8 times as likely, and teens who had inherited *A1* alleles from both parents were 3.4 times as likely as those with two *A2* alleles to progress to heavier

continued on page 12

Genetic Predisposition and Depression Both Influence Teen Smoking

continued from page 11

smoking before they finished 11th grade.

“These results clearly illustrate the important interplay between a gene and the environment,” Dr. Audrain-McGovern says. “The *DRD2* variant appears to play no role in whether or not these teens took that first puff. Its effect isn’t seen until there is some biological exposure. Then, we see a markedly different response to nicotine, perhaps because the *A1* allele is associated with reduced density of dopamine receptors. If individuals with this allele have lower baseline levels of dopamine activity, they might experience greater reward when nicotine triggers an enhanced dopamine release.”

DRD2 and Depression

During the ninth-grade interviews, the researchers administered the Center for Epidemiological Studies Depression Scale (CES-D Scale) to the

study participants. Each teen rated how frequently he or she had experienced each of 20 depression symptoms during the past week. One hundred teens (16 percent) scored 23 or higher on this scale, which indicates clinically significant depression. Of the 100, 52 had at least one *A1* allele. Teens without an *A1* allele had an average CES-D score of 12.3; those with one *A1* and one *A2* had an average score of 15.1; and those with two copies of the *A1* allele averaged 16.7. There also was a significant association between the CES-D score and smoking status at the initial interview: The average score was 12.5 for never smokers, 14.6 for puffers, 13.7 for experimenters, and 20.8 for current smokers.

Teens with high depression scale scores and the *A1* allele were at the highest risk of smoking progression. Among teens with at least one *A1* allele, 33 percent of depressed teens, compared with 25 percent of nondepressed teens, reported smoking progression within 2 years.

The interaction of the *DRD2* allele and depression on smoking progression highlights the intricate

interplay of genetic, psychological, and social factors that influence adolescents’ smoking behavior, observes Dr. Allison Chausmer of NIDA’s Division of Basic Neurosciences and Behavior Research. “This research group has previously shown that adolescents who have depression are more receptive than nondepressed teens to the messages contained in tobacco advertising. This is not a trivial number of potential smokers. Roughly one in five high school students has symptoms that represent clinically significant depression. Those who succumb to the appeal of tobacco manufacturers’ advertising and have this particular genetic makeup may be more likely to progress to higher levels of smoking and ultimately experience consequences of reduced health and longevity.”

Source

• Audrain-McGovern, J., et al. Interacting effects of genetic predisposition and depression on adolescent smoking progression. *American Journal of Psychiatry* 161(7):1224-1230, 2004. **NN**

NIDA News and Information at Your Fingertips

Information about NIDA research, programs, and events is quickly and easily accessible through NIDA’s home page at www.drugabuse.gov.

NIDA’s home page includes:

- ➔ Information on Drugs of Abuse
- ➔ Publications (including *NIDA NOTES*)
- ➔ Calendar of Events
- ➔ Links to NIDA Organizational Units
- ➔ Funding Information
- ➔ International Activities
- ➔ Links to Related Web Sites

The screenshot shows the NIDA website homepage. At the top, it says "NIDA NATIONAL INSTITUTE ON DRUG ABUSE" and "The Science of Drug Abuse & Addiction". There is a search bar and a "keep your body healthy" slogan. Below the header is a navigation menu with categories: RESEARCHERS & HEALTH PROFESSIONALS, PARENTS & TEACHERS, STUDENTS & YOUNG ADULTS, and EN ESPAÑOL. There is also a "SELECT A TOPIC..." dropdown menu. The main content area is divided into several sections: "NEW! COMMUNITY DRUG ABUSE BULLETIN INHALANTS", "News & Events" with links to research reports and surveys, "Students & Young Adults" with education resources, "Parents & Teachers" with drug information and curriculum guides, "Researchers & Health Professionals" with grants and funding information, "En Español" with educational resources, "Publications Catalog" with a list of publications, and "NIDA Sites" with a list of related websites. On the right side, there is a "Drugs of Abuse" section listing various substances like Acid/LSD, Alcohol, Club Drugs, Cocaine, Ecstasy/MDMA, Heroin, Inhalants, Marijuana, Methamphetamine, PCP/Phencyclidine, Prescription Medications, Smoking/Nicotine, and Steroids (Anabolic). There is also a "Related Topics" section with links to Drug Testing, Prevention Research, Stress & Drug Abuse, Treatment Research, and Trends & Statistics.

Highlights of recently published NIDA-supported studies

Genes and Amphetamine

Individuals who inherit a particular variant of the *DAT1* gene from both parents may have a degree of innate protection against becoming chronic abusers of amphetamine or other stimulants, new research suggests. In a study by Dr. Harriet de Wit and colleagues at the University of Chicago, eight volunteers who carried two copies of the “9-repeat” variant of the gene reported feeling little different following oral administration of amphetamine than after placebo. In contrast, 88 individuals with either one or no “9-repeats” tended to experience the euphoric reaction that is a motivator for stimulant abuse, as well as elevated blood pressure and anxiety. The likely biological basis for the different reactions is that the *DAT1* gene affects expression of the dopamine transporter, one of the sites where stimulant drugs exert their pharmacological effects. The researchers note that along with its protective advantage against drug abuse, the 9/9 may have a downside: less benefit from stimulant medications, such as those prescribed for attention deficit hyperactivity disorder.

Neuropsychopharmacology 30(3):602-609, 2005.

Brain Recovery in Meth Abusers

Long-term methamphetamine abusers who abstain from the drug for more than a year show signs of structural and functional recovery of nerve cells in a brain region associated with emotion and cognition. Although some chemical signs

of cell damage continued after a year of abstinence, some metabolic indicators in the anterior cingulate cortex appeared to return to normal. Using a brain-imaging technique called proton magnetic resonance spectroscopy, Dr. Thomas Nordahl and colleagues at the University of California, Davis found that methamphetamine-addicted men and women showed abnormal metabolite ratios—chemical patterns that can indicate either healthy activity or injury of brain cells. Those who had initiated abstinence in the past 6 months showed some damage-related patterns that were absent in those who had not taken the drug for more than a year and in nonabusers. Patterns reflecting healthy brain activity increased with the duration of abstinence.

Archives of General Psychiatry 62(4):444-452, 2005.

New Tools for Studying Inhalant Abuse

Two teams of researchers have developed new tools for investigating the phases and effects of inhalant abuse. Dr. Edwin Zvartau and colleagues at the Pavlov Medical University in Russia, working with Dr. Robert Balster of Virginia Commonwealth University, devised a promising method for mice to self-administer solvents that are abused by humans via inhalation. The new procedure circumvents technical difficulties that have prevented researchers from performing with inhalants the same types of animal studies that have provided much basic information about the effects of other drugs. Another team, led by Dr. Jean Logan of

Brookhaven National Laboratory, successfully tested new chemicals that trace the levels of the inhalants acetone and butane in the brains of baboons. Such tracers allow researchers to monitor the effects of each inhalant on the brain: the time it takes to arrive, the regions affected, and how long it stays. These characteristics influence a substance’s potential for abuse in humans and its neurotoxic effects.

European Journal of Pharmacology 485(1-3):211-218, 2004; and *Nuclear Medicine and Biology* 32(2):201-208, 2005.



Weighing Nicotine Replacement

Postmenopausal women using the nicotine patch gained less weight during their first 2 weeks of abstinence from smoking than women on placebo, even though they consumed more total calories and fat and had the same level of physical activity. In one of the first studies to address the challenges older women face when they try to quit smoking, Dr. Sharon Allen and colleagues at the University of Minnesota also found that the simultaneous use of hormone

replacement therapy by participants did not affect the results. One-third of women over age 45 smoke, and researchers are looking for strategies to help them quit. Fear of weight gain can be a serious barrier to quitting, particularly during the menopausal period when women typically gain a few pounds.

Addictive Behaviors 30(7):1273-1280, 2005.

Teen Access to Cigarettes Declining, But Still High

Fewer underage teens bought cigarettes in 2002 than in 1997, but most still found the products easy to obtain, according to the Monitoring the Future (MTF) Survey of 8th-, 10th-, and 12th-graders. Half the teens who said they were current smokers reported personally buying cigarettes from a retail store, down about 5 percent from 1997; only one-third said they were asked to provide proof of age during their last purchase. They most often bought cigarettes at gas stations or convenience stores, which have the highest rates of pro-tobacco advertising and self-service access to tobacco products. Dr. Lloyd Johnston and colleagues at the University of Michigan say the findings suggest that some policies to limit access to cigarettes by minors—for example, requiring clerk-assisted purchases—may be having an impact, but also point to considerable retailer noncompliance with underage sales regulations.

American Journal of Preventive Medicine 27(4):267-276, 2004.



Dr. Bill Carlezon Receives the 2005 Jacob P. Waletzky Memorial Award

Dr. Bill Carlezon, associate professor of psychiatry and neuroscience and director of the Behavioral Genetics Laboratory at Harvard Medical School, received the 2005 Jacob P. Waletzky Memorial Award for Innovative Research in Drug Addiction and Alcoholism. Dr. Carlezon received the award and gave the keynote lecture at NIDA's "Frontiers in Addiction Research" miniconvention in Washington, D.C. on November 11.

Dr. Carlezon's work has focused on the neuromechanisms and neural adaptations in brain reward systems that underlie addictions. "Ten years ago, he began using simple but elegant molecular manipulations to dissect out how molecular adaptations in reward systems lead to long-lasting behavioral modifications," said Dr. Robert Malenka, the chairman of the Society for Neuroscience 2005 Waletzky Award Selection Committee. Dr. Malenka noted that Dr. Carlezon has since been proven prescient in realizing the power of applying molecular techniques to behavioral analyses.

Dr. Carlezon's keynote lecture described his recent work examining the comorbidity of addictive and depressive disorders, focusing primarily on the role that elevated levels of the transcription factor CREB play in regulating moods. Dr. Carlezon's studies of rodents have shown that increased levels of CREB and dynorphin in the nucleus accumbens, which can be caused by stress and repeated drug use, inhibit the brain reward circuit and lead to depressive-like behaviors. His group is now working to determine whether a kappa opioid antagonist can be used to block overexpression of dynorphin. Results thus far have been positive, as kappa antagonists have been shown to have antidepressant effects.

The \$25,000 Waletzky Memorial Award is presented to a young scientist within 15 years of obtaining his or her doctoral degree and is intended to reward and encourage innovative research into the neurobiology of drug addiction and alcoholism. The



Selection Committee Chairman Dr. Robert Malenka (right) congratulates Dr. Bill Carlezon, 2005 Jacob P. Waletzky Memorial Award recipient.

award was established in 2003 by Jacob P. Waletzky's parents in memory of their son, who died at the age of 29 of cocaine-induced cardiac arrhythmia. The award does more than honor an individual investigator, said Dr. Malenka in thanking the Waletzky family; it also brings positive attention to drug abuse research and establishes an incentive for young scientists to join the field. **NN**

Psychological Association Honors Dr. Nora D. Volkow

Dr. Nora D. Volkow, Director of NIDA, received a Presidential Citation from the American Psychological Association in appreciation for her leadership at the Institute. The award, which recognizes distinguished service in the field of addiction research, was presented at the organization's annual conference, August 19, 2005, in Washington, D.C. Members of the association's Division on Addiction and Division on Pharmacology and Substance Abuse honored Dr. Volkow during a reception at the Renaissance Hotel. **NN**

NIDA Director Dr. Nora D. Volkow accepts the Presidential Citation award from APA President Dr. Gerald P. Koocher.



NIDA and Scholastic Offer Teens and Teachers New *Heads Up*

NIDA and Scholastic, Inc., have joined forces to produce a third installment of the series *Heads Up: Real News About Drugs and Your Body*. The new science-based articles and vivid, informative graphics will be distributed to nearly 2 million middle and high school students via the pages of Scholastic's publications *Junior Scholastic*, *Science World*, and *Up Front*. This year's materials, which include a teacher's guide, once again strike the theme of the unique dangers drugs pose to teens.

"Research indicates that adolescence, a time when many changes are occurring in the brain, may be a period of significantly increased vulnerability to drugs' effects," says NIDA Director Dr. Nora D. Volkow. By presenting NIDA's research in an accessible format, *Heads Up* speaks directly to its youthful audience about issues including HIV and drug abuse, the link between food cravings and drug cravings, the health dangers of inhalants, and the misuse of prescription drugs.

Adolescents, AIDS, and Abuse: A Deadly Connection

Between 1998 and 2000, one of every six persons with a newly diagnosed HIV infection was between the ages of 13 and 25. Along with injecting drugs, which 1 in 50 U.S. high school students report having done at least once, drug-influenced bad judgments can lead to infection, and drugs can reduce the body's ability to fight off infection. "Teens, Drug Abuse, and AIDS: The Deadly Connection" provides young people with the statistics and scientific information they need to understand the potential health consequences of their decisions concerning drugs and sexual relationships.

Linking Addictions to Food and Drugs

"Two Teen Health Dangers: Obesity & Drug Addiction" tells readers how NIDA scientists discovered that cravings for food and cravings for drugs have a common biological basis in the brain. Both drug abusers and obese people tend to have lower than average numbers of the brain proteins called dopamine receptors, a deficit that could limit the amount of pleasure they gain from ordinary activities and achievements. Overeating and drug abuse may be attempts to compensate; both stimulate the dopamine system to higher activity levels.

The article leads readers through the specific experiments researchers conducted to find these connections and teaches how to design a scientific experiment and calculate their own body mass index. It points out that people can enhance the brain's dopamine activity without overeating or taking drugs by exercising and spending time with friends and family.

Bucking the Trend: Increase in Inhalant and Prescription Drug Abuse

The 2005 University of Michigan Monitoring the Future (MTF) Survey found that the number of U.S. 8th-, 10th-, and 12th-grade students who reported abusing drugs in the past month dropped 19 percent from 2001 to 2005. However, past-year inhalant abuse among eighth-graders increased, and abuse of the prescription drugs oxycodone (OxyContin) and hydrocodone (Vicodin) remained high. "Abuse of Inhalants and Prescription Drugs: Real Dangers for



Teens" paints a vivid, realistic picture of these substances' ill effects. Even in an otherwise healthy person, a single session of abusing highly concentrated amounts of certain inhalants can lower oxygen levels enough to cause asphyxiation or disrupt heart rhythms and cause death from cardiac arrest.

Prescription medication abuse can cause both short-term and long-term health problems, from potentially fatal overdose to addiction and long-term brain changes. In addition to exposing the dangers of these substances, the *Heads Up* article explains how the MTF Survey data were collected and why these data are important in understanding and fighting drug abuse.

All *Heads Up* materials can be found at either www.drugabuse.gov/scholastic.html, or at Scholastic's Web site, www.scholastic.com/headsup.

NN

NIDA NOTES

Editor: David Anderson, *Public Health Advisor, Public Information and Liaison Branch, Office of Science Policy and Communications*

Managing Editor: Johanna Weekley, *MasiMax Resources, Inc.*

Associate Managing Editor: Simon Weavers, *MasiMax Resources, Inc.*

Editorial Board: David Anderson, *Cochair; Public Health Advisor, Public Information and Liaison Branch, Office of Science Policy and Communications*

Jan Lipkin, *Cochair; Acting Chief, Public Information and Liaison Branch, Office of Science Policy and Communications*

Jessica J. Campbell, Ph.D., *Health Science Administrator, Division of Epidemiology, Services and Prevention Research*

J.C. Comolli, *Public Health Advisor, Division of Pharmacotherapies and Medical Consequences of Drug Abuse*

Paul Coulis, Ph.D., *Scientific Review Administrator, Office of Extramural Affairs*

Lee Cummings, *Special Assistant to the Director, Division of Pharmacotherapies and Medical Consequences of Drug Abuse*

Gaya Dowling, Ph.D., *Deputy Branch Chief, Science Policy Branch, Office of Science Policy and Communications*

Bennett Fletcher, Ph.D., *Research Psychologist, Division of Epidemiology, Services and Prevention Research*

Stephen J. Heishman, Ph.D., *Associate Director for Education and Training, Intramural Research Program*

Mary Ellen Michel, Ph.D., *Deputy Director, Center for the Clinical Trials Network*

Joni Rutter, Ph.D., *Program Director, Genetics and Molecular Neurobiology Research Branch, Division of Basic Neurosciences and Behavior Research*

Vincent Smeriglio, Ph.D., *Research Psychologist, Division of Clinical Neuroscience, Development and Behavioral Treatment*

Jack Stein, Ph.D., *Chief, Services Research Branch, Division of Epidemiology, Services and Prevention Research*

Frank Vocci, Ph.D., *Director, Division of Pharmacotherapies and Medical Consequences of Drug Abuse*

Cora Lee Wetherington, Ph.D., *Psychologist, Behavioral and Cognitive Science Research Branch, Division of Basic Neurosciences and Behavior Research*

Staff Writers: Lori Whitten, Ph.D., and Patrick Zickler, *MasiMax Resources, Inc.*

Copyeditor: Debra Davis, *MasiMax Resources, Inc.*

Design/Layout: Maggie Bray, *MasiMax Resources, Inc.*

This publication was produced and printed by MasiMax Resources, Inc., under Contract No. N01DA-4-1117 from the National Institute on Drug Abuse.



NIDA NOTES covers drug abuse research in the areas of treatment and prevention, epidemiology, neuroscience, behavioral science, health services, and AIDS. The publication reports on research; identifies resources; and promotes communication among clinicians, researchers, administrators, policymakers, and the public. Readers are encouraged to identify subject areas they would like to see highlighted.

NIDA NOTES is a publication of the U.S. Government produced by the National Institute on Drug Abuse. Use of funds for printing this periodical has been approved by the Director of the Office of Management and Budget. Except for material specifically identified as copyrighted, all materials appearing in **NIDA NOTES** are in the public domain and may be reproduced without permission. Citation of the source is appreciated.

Subscriptions and Changes of Address

To subscribe free to **NIDA NOTES**, or to change the address for your current subscription, contact the **NIDA NOTES**

Subscriptions Department at:

MasiMax Resources, Inc.

1375 Piccard Dr., Suite 175

Rockville, MD 20850

Fax: 240-632-0519 **E-mail:** nidanotes@masimax.com

Phone: 240-632-5614

Additional Copies

To order additional copies of **NIDA NOTES**, contact:

National Clearinghouse for Alcohol and Drug Information
P.O. Box 2345

Rockville, MD 20847-2345

Phone: 800-729-6686 or 301-468-2600

TDD number: 800-487-4889

Fax: 301-468-6433 **E-mail:** info@health.org



**DEPARTMENT OF
HEALTH & HUMAN SERVICES**

National Institutes of Health
National Institute on Drug Abuse
6001 Executive Boulevard
Room 5213
Bethesda, MD 20892-9561

ADDRESS SERVICE REQUESTED

Official Business
Penalty for Private Use \$300

**NIH Publication No. 05-3478
Printed March 2006**

PRSR STD
POSTAGE AND FEES
PAID
DHHS/NIH
PERMIT NO. G-827