NIDA
NATIONAL INSTITUTE
ON DRUG ABUSE

March 5, 2007

# NewsScan
## NIDA ADDICTION RESEARCH NEWS

NEWS UPDATE

## PAIN, OPIOIDS, AND ADDICTION

### Physician Concerns Regarding Prescribing Opiates for Chronic Pain

Opiate medications are highly effective in the control of pain. However, physician comfort level in prescribing opiate drugs for the treatment of chronic pain varies with patient characteristics, according to a recently published survey.

Researchers at the University of Wisconsin and the Medical College of Wisconsin analyzed questionnaire responses from 248 primary care physicians. Results showed that the most common concerns about prescribing opioids for chronic pain were prescription drug abuse and addiction. Other concerns included: adverse effects, tolerance, interaction with other medications, not knowing enough about which narcotic to prescribe, not knowing enough about dosage requirements, and having partners who prefer not to use opioids for treating chronic pain. The majority of the physicians were comfortable in prescribing narcotics to someone with terminal cancer, but were less confident in prescribing for patients with back pain. They were even less comfortable with prescribing narcotics to patients with a past history of drug or alcohol abuse.

The survey also noted that only a small percentage of physicians are conducting urine toxicology screens on their patients either before or during opioid therapy, and that this was dependent on whether or not they had a system to track patients on opioids.

- **WHAT IT MEANS:** Although opioids are effective in treating chronic pain, many physicians have concerns about prescribing them. There is a need for management guidelines that are straightforward and effective in addressing the issues faced by primary care physicians. Research is needed to assess the use of clinical guidelines and other clinic-based approaches to address physician concerns about abuse of opioids.

The study, led by Dr. Bhushan Bhamb, was published in the September 2006 issue of *Current Medical Opinion and Research*.

### Researchers Assess Adolescents' Motivations To Abuse Prescription Medications

The nonmedical use of prescription drugs is a serious health problem among U.S. youth. University of Michigan scientists surveyed almost 1,100 middle and high school students in one southeastern Michigan school district to determine why students engage in the nonmedical use of four classes of prescription medications (sleep aids, sedatives/anxiolytics, stimulants, and opioid analgesics) and to examine if such motivations were associated with a higher risk of substance abuse problems.

The researchers found that 12 percent of the respondents had engaged in the nonmedical use of opioid pain medications during the previous 12 months. In addition, three percent had nonmedically used sleeping medications, two percent had nonmedically used sedatives/tranquilizers, and two percent had nonmedically used stimulants.

Motivations varied by drug classification. Although 69 percent of respondents who used pain medications used them solely for pain control and 79 percent endorsed pain relief as at least one motivation for their use, 11 percent said they used the drugs to get high. For the nonmedical use of stimulant medications, 29 percent gave only one motive to use stimulants (i.e., to help with concentration or alertness) and 21 percent endorsed several motivations, the most frequently mentioned of which were to "get high," "help with concentration," or "increase my alertness." The most frequently cited reasons for the use of sedatives and tranquilizers were to help with sleep, to decrease anxiety, and to get high.

The researchers also found evidence that the nonmedical use of prescription medications is associated with an increase in general substance abuse problems, particularly with opioid analgesics. When the students noted multiple motivations for the nonmedical use of prescription opioid medications, the scientists observed that each additional motivation carried a greater

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# Drug Abuse and Risky Behaviors: The Evolving Dynamics of HIV/AIDS

**In collaboration with:**

National Institute on Alcohol Abuse and Alcoholism
National Institute of Allergy and Infectious Diseases
National Institute of Child Health & Human Development
National Institute of Mental Health

## Save the Date!

## May 8–9, 2007

**Natcher Conference Center**
**National Institutes of Health**
9000 Rockville Pike
Bethesda, MD 20892

Drug abuse and addiction continue to fuel the spread of HIV/AIDS. This meeting will provide a broad understanding of the multiple ways that drug abuse and addiction affect HIV/AIDS and how research can inform public health policy. Presentations will focus on the successes, research challenges, and opportunities for addressing the evolving HIV/AIDS pandemic. Attendees will be drawn from the research community, public health organizations, Federal agencies, and drug abuse and HIV/AIDS organizations.

**To register or for more information, go to:**
http://conferences.masimax.com/riskybehaviors

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likelihood of scoring higher on the Drug Abuse Screening Test (DAST-10). However, the authors suggest that there may be two distinct groups of non-medical users of prescription drugs?those who self-medicate and those who use for other reasons, including to experiment and get high. The latter seem to be at greater risk for other forms of substance abuse.

- **WHAT IT MEANS:** This study further emphasizes the problem of prescription drug abuse among the Nation's youth, highlighting the motivations for abuse of these medications and their link to future substance abuse problems. These findings suggest that future research is necessary to better understand the reasons for the nonmedical use of prescription medications and to evaluate which nonmedical prescription drug abusers are at greatest risk for developing further substance abuse problems.

Dr. Carol Boyd and her colleagues published their findings in the December 2006 issue of *Pediatrics*.

## Study Reveals a New Cellular Adaptation that Contributes to Opiate Tolerance

Opiate drugs, such as morphine, are considered the gold standard for treating severe pain. They bind to specific receptors in the brain and spinal cord to inhibit the transmission of pain signals. However, prolonged or repeated use of these drugs can produce a tolerance to their effects, requiring more of the drug to achieve the desired effect. Now, NIDA-supported research reveals a new mechanism that may account for important features of opiate tolerance in rats.

Dr. Gregory Terman, of the University of Washington School of Medicine, and his colleagues induced opiate tolerance by injecting increasing amounts of morphine into two-week old rat pups, for six days. They then investigated the electrophysiological properties of neurons in their spinal cords and compared them to those in the spinal cords of control pups that had not been exposed to the drug. They found that spinal cord cells from the tolerant pups were much more excitable than cells from control pups.

Further examination showed that these over-excitable cells were surrounded by more fibers containing larger than normal numbers of NMDA receptors, a subtype of glutamate receptor. The authors suggest that these enhanced levels of NMDA receptors are involved in the transmission of pain signals, and that this adaptive change makes those neurons much more likely to convey pain signals.

Importantly, these new NMDA receptors in the spinal cord of opiate tolerant animals were located upstream of the cells being recorded (i.e., on the cell before the synapse—the junction between nerve cells). The distinct properties of these receptors make them potentially interesting targets for the development of medications to reverse opiate tolerance. Indeed, a preliminary experiment showed that blocking NMDA receptors with a specific NMDA antagonist inhibited the expression of morphine analgesic tolerance without disrupting pain responses.

- **WHAT IT MEANS:** Previous studies have shown that NMDA receptors play a role in the development of tolerance to opiate pain relievers. This new research suggests that an increase in anatomically and functionally distinct NMDA receptors, produced by repeated exposure to opiate drugs, can enhance excitatory signaling in the spinal cord. These new receptors represent novel potential targets for agents capable of reversing opiate tolerance. Studies seeking to more fully define the biochemical and physiological characteristics of these NMDA receptors in the spinal cord are ongoing.

The scientists published their findings in the November 15, 2006 issue of the *Journal of Neuroscience*.

## URB597 Relieves Pain in Rats Without Cannabinoid-Associated Side Effects

Findings in rats suggest that a compound called URB597, a fatty acid amide hydrolase (FAAH) inhibitor, relieves pain by blocking the breakdown of endocannabinoids, naturally occurring molecules that act on cannabinoid receptors. Cannabinoid receptors are a class of receptors in the brain that recognize THC, the active ingredient in marijuana.

Dr. Christopher Vaughan and his colleagues at the University of Sydney and the University of California at Irvine compared the effects of URB597 and HU210, which directly activates cannabinoid receptors in the brain.

The scientists found that in rats, both compounds reduced inflammatory pain. However, HU210 also reduced motor performance, measured by the time the animals were able to stay on a rotating bar after being given the drug. In contrast, HU210, but not URB597, was effective in reducing neuropathic pain. The scientists say the findings suggest that URB597 produces cannabinoid receptor-mediated pain relief, specifically with respect to inflammatory pain, without causing the undesirable motor effects associated with cannabinoid receptor activation.

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- **WHAT IT MEANS:** This rat study shows that the FAAH inhibitor URB597, like the cannabinoid-receptor activator HU210, was able to provide analgesia in a model of inflammatory pain. Unlike HU210, though, URB597 did not produce side effects generally associated with cannabinoid drugs. The findings suggest that FAAH inhibitors may be a promising class of compounds for pain relief, with fewer side effects than those produced by globally acting cannabinoid agonists.

The study was published in the February 2006 issue of the *British Journal of Pharmacology*.

### Managing the Impact of Pain: Antidepressants May Be Useful Part of Pain Therapy

Scientists from the University of Kansas Medical Center have found that nonsteroidal anti-inflammatory drugs (NSAIDs) and certain types of antidepressants both affect gene expression within the spinal cord, and that antidepressants also affect brain regions involved in the emotional and cognitive aspects of pain.

Dr. Vanja Duric and Dr. Kenneth McCarson pretreated rats with the NSAID indomethacin or the tricyclic antidepressant imipramine. They then injected a substance into the animals to cause inflammatory pain or immobilized them to cause stress. When the researchers examined cells from the rats' spinal cords and brains they observed that NSAID treatment reduced spinal cord pain transmission, as well as reversing pain-evoked upregulation (switching on of a particular gene leading to increased production of a certain protein) of NK-1 receptors and BDNF gene expression in the spinal cord to levels similar to those seen in control animals. However, indomethacin was unable to prevent the impact of pain on the hippocampus (a part of the brain involved in learning, emotion, and the formation of memories). Conversely, imipramine did not provide significant pain relief whereas it significantly blocked both pain- and stress-evoked alterations in hippocampal and spinal NK-1 and BDNF gene expression.

- **WHAT IT MEANS:** These results show that neither the NSAID nor the antidepressant alone fully protect against pain processing in the brain and spinal cord. Whereas indomethacin may reduce the sensory experience of pain at the level of the spinal cord, it may have little effect on the negative emotional and cognitive impact of pain. In contrast, imipramine appears to block the expression of long-term changes in both the spinal cord and certain brain regions. The findings suggest that early antidepressant drug administration as part of therapy for persistent pain may prevent predisposition toward development of pain-related depression.

The study was published in the December 2006 issue of the *Journal of Pharmacology and Experimental Therapeutics*.

## FUNDING NEWS

### Prescription Drug Abuse (PA-07-123)

Data from the 2005 National Survey on Drug Use and Health reported that 6.4 million Americans age 12 and older were current (past-month) users of prescription drugs—pain relievers, tranquilizers, stimulants, and sedatives—for nonmedical purposes. Information from NIDA's Monitoring the Future survey of 8th-, 10th- and 12th- graders indicates that although their past-month use of illicit drugs has dropped 23.2 percent since 2001 (from 19.4 percent in 2001 to 14.9 percent in 2006), their abuse of prescription opioids remains at high levels. Concerns also have been raised about increasing substance abuse, particularly prescription drugs, among older adults and the potential impact of aging on baby boomers' needs for substance abuse treatment.

A range of research is needed to combat the problem of prescription drug abuse—from specifying the extent and nature of the problem to developing, evaluating, and disseminating effective prevention and treatment approaches. Areas of research that may be considered under this program announcement (PA) include, but are not limited to:

- Studies on the role of the Internet as a source of prescription drugs and as a source of information about these drugs;
- Research to determine how the misuse and abuse of prescription drugs—particularly by pregnant women, children, and adolescents—might increase the lifetime risk of substance abuse and addiction;
- Using animal models to probe the effects of prescription drugs on neurobiological, neurochemical, and neurobehavioral processes;

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- Determining the health consequences of prescription drug abuse and the underlying pathophysiology in diverse populations (for example, people with HIV/AIDS and other infectious diseases, adolescents, the elderly, and women);
- Studies that develop and evaluate treatment approaches that maintain abstinence from prescription drug abuse and prevent relapse; and
- Research that adapts existing treatments for other drugs of abuse, and research that develops new and innovative therapies to treat prescription drug abuse.

For more information on this PA, go to http://grants.nih.gov/grants/guide/pa-files/PA-07-123.html.

## MEETINGS OF INTEREST

### Drug Abuse and Risky Behaviors: The Evolving Dynamics of HIV/AIDS

*NIDA meeting to bring together clinicians, researchers, and policymakers*

Drug abuse and addiction continue to fuel the spread of HIV/AIDS in the United States and abroad. To address this significant public health threat, research is examining every aspect of HIV/AIDS, drug abuse, and addiction, including risk behaviors associated with both injection and non-injection drug abuse, how drugs of abuse alter brain function and impair decision making, and HIV prevention and treatment strategies for diverse groups.

This meeting, scheduled to take place May 8–9, 2007 in the Natcher Conference Center at the National Institutes of Health, Bethesda, Maryland, will provide a broad understanding of the multiple ways that drug abuse and addiction affect HIV/AIDS and how research can inform public health policy. Presentations will focus on the successes, research challenges, and opportunities for addressing the evolving HIV/AIDS pandemic. Attendees will be drawn from the research community, public health organizations, Federal agencies, and drug abuse and HIV/AIDS organizations. The meeting is sponsored by the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health, in collaboration with the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute on Child Health and Human Development (NICHD), and the National Institute of Mental Health (NIMH).

Topics that will be covered include, but are not limited to, the following:

- How drugs of abuse alter brain function, leading to impaired decision making and risky behaviors, which in turn can facilitate the acquisition and transmission of HIV;
- How and to what extent substance abuse influences sexual risk behaviors;
- How substance abuse affects HIV/AIDS risk in diverse populations (e.g., adolescents, minorities, those involved with the criminal justice system); and
- How testing and counseling can be incorporated as a key component of HIV prevention strategies for drug-abusing populations.

Featured speakers include NIDA Director Dr. Nora D. Volkow and NIAID Director Dr. Anthony Fauci. A full agenda and speaker list is available at: http://conferences.masimax.com/riskybehaviors/agenda.cfm

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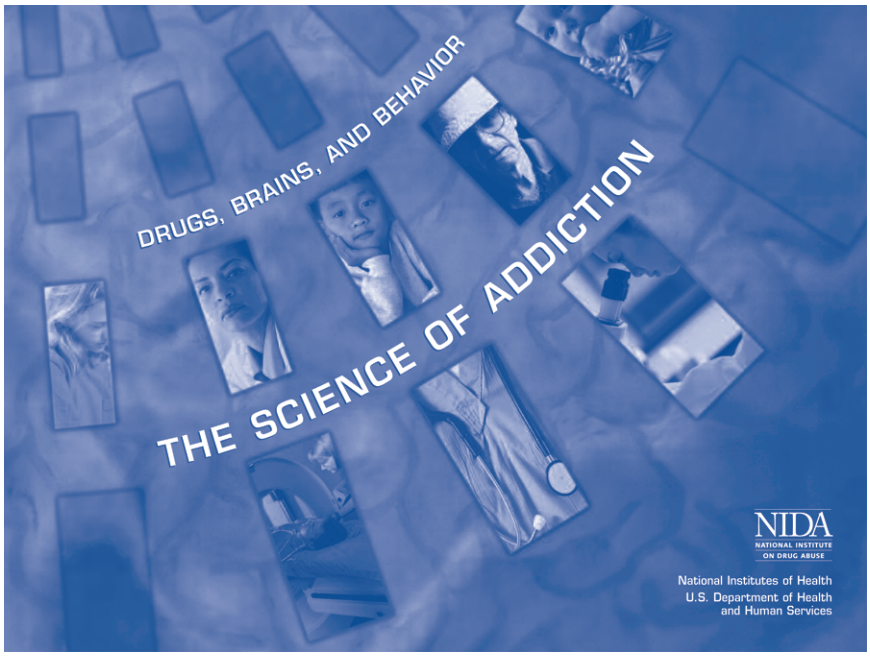
## Other News

### NIDA Unveils Its First Consumer Publication To Explain the Science of Addiction

*Booklet's release complements collaborative documentary on addiction to air on HBO*




In February, NIDA unveiled "Drugs, Brains, and Behavior: The Science of Addiction," a 30-page full-color booklet that explains in layman's terms how science has revolutionized the understanding of drug addiction as a brain disease that affects behavior. NIDA hopes this new publication will help reduce stigma against addictive disorders.

"Thanks to science, our views and our responses to drug abuse have changed dramatically, but many people today still do not understand why people become addicted to drugs or how drugs change the brain to foster compulsive drug abuse," said NIDA Director Dr. Nora D. Volkow. "This booklet aims to fill that knowledge gap by providing scientific information about the disease of drug addiction in language that is easily understandable to the public."

The "Science of Addiction" booklet discusses the reasons people take drugs, why some people become addicted while others do not, how drugs work in the brain, and how addiction can be prevented and treated. Like diabetes, asthma, or heart disease, drug addiction is a chronic disease that can be managed successfully. Treatment helps to counteract addiction's powerful disruptive effects and helps people regain control of their lives. The new booklet points out that just as with other chronic diseases, relapses can happen. The publication further explains that relapse is not a signal of treatment failure—rather, it indicates that treatment should be reinstated or adjusted to help the addict fully recover.

The new publication was unveiled at a press briefing for the upcoming HBO documentary called Addiction, to air Thursday, March 15, from 9:00 to 10:30 p.m. ET/PT. The 90-minute program, produced in partnership with the Robert Wood Johnson Foundation, NIDA, and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), is aimed at helping Americans understand addiction as a treatable brain disease, as well as spotlighting new medical advancements.

The documentary will explore many elements of drug and alcohol addiction through the eyes of those who are addicted and those of the scientific experts working to better understand and treat this devastating disease.

Abuse and addiction to alcohol, nicotine, and illegal substances cost Americans upwards of half a trillion dollars a year, considering their combined medical, economic, criminal, and social impact. In addition, abuse of illicit drugs and alcohol contributes to the deaths of more than 100,000 Americans every year, while tobacco is linked to an estimated 440,000 deaths per year. People of all ages suffer the harmful consequences of drug abuse and addiction.

Drug addiction is considered a brain disease because drugs change the brain in structure and in function. For most people, the initial decision to take drugs is voluntary, but over time drug abuse can cause changes to the brain that impair a person's self-control and ability to make sound decisions, while sending intense impulses to take drugs.

"The Science of Addiction" can be viewed and downloaded as a PDF file at the NIDA Web site: **http://www.drugabuse.gov/scienceofaddiction/**.

## Notes

## Notes

**For more information about any item in this *NewsScan*:**

- **Reporters**, call **Sara Rosario Wilson** at 301-443-6245.
- **Congressional staffers**, call **Geoffrey Laredo** at 301-594-6852.

The National Institute on Drug Abuse (NIDA) is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports most of the world's research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to ensure the rapid dissemination of research information and its implementation in policy and practice. Fact sheets on the health effects of drugs of abuse and other topics are available in English and Spanish. These fact sheets and further information on NIDA research and other activities can be found on the NIDA home page at **www.drugabuse.gov**.

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