NIDA
NATIONAL INSTITUTE
ON DRUG ABUSE

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NewsScan
NIDA ADDICTION RESEARCH NEWS

NEWS UPDATE

Research News

Graphic Warnings Change Viewers' Perception of Tobacco Advertisements

Advertisements for potentially reduced-exposure tobacco products (PREPs), such as chewing tobacco and reduced-carcinogen cigarettes, often make claims of the products' safety in comparison to regular tobacco products. A study conducted by the Minnesota Trandisciplinary Tobacco Use Research Center and funded by NIDA and the National Cancer Institute found that including a graphic warning label on PREPs' advertising affects both consumer appeal for the product and perception of the safety claims included in the advertisements. Researchers recruited 92 college students for the study, 24 of whom had smoked in the last 30 days, and asked them to view advertisements for three different types of PREPs: chewing tobacco, nicotine lozenge, and reduced-carcinogen cigarettes. Half of the participants viewed advertisements with standard Surgeon General's tobacco warning labels, and half viewed advertisements where the warnings included a picture of a diseased heart or mouth. Participants who viewed advertisements containing the graphic warning label were less interested in trying the products, found the products less appealing, and rated the safety claims of the advertisements as less trustworthy. Compared to the other PREPs in the study, inclusion of the graphic warning did not significantly alter perceptions of the nicotine lozenge, perhaps because nicotine lozenges are an accepted aid for smoking cessation. "As more and more products enter the market with diverse claims about reduced harm, health policymakers may wish to consider incorporating the use of graphic pictures with warnings to ensure balanced information about these products for the consumer," state the authors. Future studies testing such warnings in heavy smokers will be useful to determine to what extent this population is influenced by graphic warnings.

Stark E, Kim A, Miller C, Borgida E. Effects of including a graphic warning label in advertisements for reduced-exposure products: Implications for persuasion and policy. *J Appl Soc Psychol*. 2008;38(2):281–293.

Disulfiram and Naltrexone May Help Adherent Patients Abstain from Cocaine and Alcohol

Addiction to a single substance is the exception rather than the rule. Because alcoholism is also seen in a large percentage of treatment-seeking cocaine users, the development of pharmacotherapeutic agents that help users to maintain abstinence from both drugs is of the utmost importance. In a randomized clinical trial funded by NIDA, investigators tested the combination of disulfiram and naltrexone, medications used to treat alcohol and cocaine addiction, respectively, in people attempting to quit use of both drugs. The investigators randomly assigned 208 treatment-seeking individuals into groups receiving disulfiram alone, naltrexone alone, a combination of the two medications, or placebo pills, given over an 11-week treatment period. All participants also received twice-weekly cognitive-behavioral therapy (CBT) and underwent urine screenings three times per week. On average, participant medication regimen adherence was generally poor—only about 46 percent of the study participants took at least 80 percent of their assigned pills, even though side effects were not reported as being severe enough to discontinue the medications. Furthermore, participants attended only 44 percent of the assigned CBT sessions. Overall, while patients taking the combination of disulfiram and naltrexone (compared to either drug alone or placebo) were more likely to achieve 3 weeks of consecutive abstinence during the treatment period, there was no significant difference in discontinuation rates across the four treatment groups. Authors conclude that "this study provides modest evidence that treating

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co-occurring cocaine and alcohol dependence with a combination of disulfiram and naltrexone may be beneficial for some patients…[but] we would need to identify the patients whom we think will adhere to taking [the] medications."

Pettinati HM, Kampman KM, Lynch KG, Xie H, Dackis C, Rabinowitz AR, O'Brien CP. A double blind, placebo-controlled trial that combines disulfiram and naltrexone for treating co-occurring cocaine and alcohol dependence. *Addict Behav*. 2008;33(5):651–667.

Smokers' Brains Ignore Error Messages

Individuals that are addicted to drugs, including nicotine, pursue and consume those drugs even in the face of negative consequences or the knowledge of positive outcomes that might come from forgoing the drugs. A study funded in part by NIDA has identified specific neural (brain) responses to potential rewards that correlate with behavioral response in nonsmokers but not chronic smokers. Investigators used a simple stock market investment game to assess the response to fictive prediction errors—mental measurements of the maximum reward that could be gained in a particular situation versus the amount that is actually gained—in heavy smokers and nonsmokers. Fictive prediction error-related learning, which is commonly used in everyday life, allows us to update or make changes in our behavior based on our expectations and experience. For example, stock market investors regularly compare actual profits from their investments versus profits that they could have made if they had made different investment decisions. Using functional magnetic resonance imaging (fMRI), researchers scanned the brains of 31 heavy smokers (once after smoking and once in a state of withdrawal) and 31 nonsmokers to correlate neural and behavioral responses to fictive prediction errors. While fMRI scans showed that the brains of both smokers and nonsmokers produced a neural response to fictive errors, only the nonsmokers used the fictive error signal to change their game-playing behavior. This finding suggests a kind of "decoupling" in smokers' brains between the neural signals encoding "what might have happened" and their actual behavioral output. This decoupling between fictive and experiential error signals could at least partially explain why smokers continue to smoke even though they may be knowledgeable of the severe health ramifications associated with smoking. The investigators are currently performing studies to determine whether such a decoupling is a cause or an effect of being addicted to nicotine.

Chiu PH, Lohrenz TM, Montague PR. Smokers' brains compute, but ignore, a fictive error signal in a sequential investment task. *Nat Neurosci*. 2008;11(4):514–520.

Nicotine Receptor Subunit Alters Postsynaptic Signaling

Neurons communicate by sending electrical impulses down their axons, causing the cell to release brain chemicals (neurotransmitters) in the space between cells (synapse), which then generates an electrical signal (action potential) in the receiving neuron. Neurons can release neurotransmitters without the electrical impulse, but in a random fashion that generates small currents, called "minis," that are insufficient to activate the receiving cell (postsynaptic neuron). Until recently, minis were thought to be "leaks" of no biological consequence. Investigators funded in part by NIDA have now shown that activation of a nicotine acetylcholine receptor (nAChR) in the brain that contains a subunit called the α7 subunit can cause changes in these minis, leading to activation of the postsynaptic cells. Investigators recorded signals from brain slices taken from the hippocampus of rat brains that were exposed to low concentrations of nicotine, similar to those found in smokers. They found that these levels of nicotine could increase the size and frequency of these minis by releasing calcium stored within the terminal itself. This modulation by nicotine is sufficient to drive the postsynaptic neuron to fire action potentials. These results demonstrate a novel way of communication mediated by nicotine, one which bypasses information coming down to the presynaptic terminal and uses these "leaks" to generate signals. This finding also indicates that nicotine can usurp signaling across synapses, thus altering the strength of connections that were not normally meant to be altered. The authors suggest that such alterations could make the stability of these synapses become dependent on the presence of the drug, thus promoting its continued usage to prevent instability.

Sharma G, Grybko M, Vijayaraghavan S. Action potential-independent and nicotinic receptor-mediated concerted release of multiple quanta at hippocampal CA3-mossy fiber synapses. *J Neurosci*. 2008;28(10):2563–2575.

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Computerized Cognitive-Behavioral Therapy Plus Standard Therapy Helps Reduce Drug Use

Cognitive-behavioral therapy (CBT), a type of behavioral therapy that teaches people how to unlearn unhealthy behaviors and incorporate more effective behaviors and change strategies, has been shown to be effective in the treatment of substance use disorders. CBT, however, is rarely used in clinical practice due to limited resources in most treatment clinics. A new study funded by NIDA indicates that a computer-assisted version of CBT, known as CBT4CBT, can improve treatment outcomes in drug abusers receiving standard counseling. The researchers randomly assigned 77 adults who were currently undergoing treatment for a substance dependence disorder at an outpatient community setting to receive either standard counseling or counseling plus biweekly CBT4CBT sessions. The CBT4CBT lessons consisted of six positive skill-building modules whose content is based on the NIDA-published CBT manual. Participant self-reports on drug use were collected weekly and confirmed using breathalyzer and urine sample screenings. Participants were also assigned weekly "homework" or practice assignments derived from the most recently completed CBT module. Overall, participants using the computerized training reported their program as being more engaging. They had significantly fewer positive urine tests (for any type of drug), had longer continuous periods of abstinence during treatment, and completed more homework assignments than the control group. "These data suggest that computer assisted CBT can be an effective adjunct to standard outpatient treatment for substance dependence," state the authors, "and may provide an important means of making CBT more broadly available".

Carroll KM, Ball SA, Martino S, Nich C, Babuscio TA, Nuro KF, Gordon MA, Portnoy GA, Rounsaville BJ. Computer-assisted delivery of cognitive-behavioral therapy for addiction: A randomized trial of CBT4CBT. *Am J Psychiatry*. 2008;165(7):881–888.

Computerized Therapy for Opioid Addiction Effective at Promoting Abstinence

In a randomized clinical trial testing community reinforcement approach (CRA) therapy for opioid dependence, people receiving a computerized version of the therapy program achieved the same number of weeks of continuous abstinence from opioid and cocaine use as patients who received the CRA intervention from a therapist. CRA therapy seeks to improve patients' satisfaction with aspects of their life outside of drug abuse, including family relationships, social networks, and work, in order to reduce the probability of relapse. Investigators funded by NIDA recruited 135 opioid-dependent adults, who then received 23 weeks of treatment. Subjects were randomly assigned to one of three groups: therapist-delivered CRA, computer-delivered CRA, or standard counseling. All participants were treated with the opioid dependence medication buprenorphine/naloxone before and during therapy. Approximately equal percentages of all participants completed all treatment sessions; however, participants in both CRA groups achieved almost 8 weeks of continuous abstinence, as measured by urine drug tests, compared to approximately 5 weeks for the counseling-only group. "Participants in the computer-assisted treatment condition achieved a similar number of weeks of continuous opioid and cocaine abstinence as those in the therapist-delivered treatment condition, but with markedly reduced contact time with their counselor during the trial," state the authors. Computerizing some aspects of addiction treatment can enable more widespread delivery of treatment services and allow counselors to focus on other areas of treatment or on patients that have the greatest need for personal attention.

Bickel WK, Marsch LA, Buchhalter AR, Badger GJ. Computerized behavior therapy for opioid-dependent outpatients: A randomized controlled trial. *Exp Clin Psychopharmacol*. 2008;16(2):132–143.

Nonmedical Use of Prescription Stimulants Among First-Year College Students

In a large study of first-year college students at a mid-Atlantic university, NIDA-funded researchers found that 13.5 percent of students they interviewed had used prescription stimulants for nonmedical reasons at least once in their lifetime. The investigators selected 1,253 first-year students, ranging in age from 17 to 19, from a college orientation session—the demographic characteristics of this sample were similar to those of the general university population. Out of 45 students taking prescription stimulants for attention-deficit hyperactivity disorder (ADHD), 33 percent had either overused their own prescription, used someone else's medication in addition to their own, or both. Out of the remaining 1,208 students without a diagnosis of ADHD, 18 percent had used prescription stimulants for nonmedical reasons at least once. Some of the reasons given for nonmedical use were to improve concentration for studying or schoolwork, partying, or to get high. Most students obtained the drugs from friends with a prescription, and most received the drugs for free. Students who had used

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prescription stimulants nonmedically at least once in their life were significantly more likely to have past-year use of other illicit or prescription drugs (nonmedical). These results were independent of a diagnosis of ADHD or sociodemographic background. Determining the extent of overuse of prescription drugs and the reasons as to why it occurs will be helpful in developing prevention strategies to curb their use on college campuses. Authors plan to follow their sample of students to better understand the later consequences of nonmedical use of prescription stimulants.

Arria AM, Caldeira KM, O'Grady KE, Vincent KB, Johnson EP, Wish ED. Nonmedical use of prescription stimulants among college students: Associations with attention-deficit-hyperactivity disorder and polydrug use. *Pharmacotherapy*. 2008;28(2):156–169.

Parental Monitoring Reduces High School Drinking, Leading to Reduced College Drinking

Drinking among college students, especially those that are underage, is a major public health concern. A recent study of more than 1,200 first-year college students revealed that parental monitoring in the last year of high school significantly impacts alcohol consumption. Interviewers asked students about their living situation in college; alcohol consumption in high school and college; and their perceptions of parental monitoring during the last year of high school, such as being required to tell parents of their evening plans and having consequences for breaking curfew. Higher levels of parental monitoring and supervision were associated with less alcohol consumption in high school, regardless of students' sex or race or the importance of religion in their lives. Moreover, the amount that students drank in high school was a significant predictor for drinking in college. "While parental monitoring did not directly influence college alcohol consumption, evidence for mediation was observed whereby parental monitoring indirectly reduced college drinking through reductions in high school drinking," explain the authors. Although the study was limited to a single university and did not explore the mechanism by which parental monitoring reduces high school alcohol consumption, the results "extend support for parental monitoring and supervision during the high school years as a strategy to reduce adolescent drinking," conclude the authors.

Arria AM, Kuhn V, Caldeira KM, O'Grady KE, Vincent KB, Wish ED. High school drinking mediates the relationship between parental monitoring and college drinking: A longitudinal analysis. *Subst Abuse Treat Prev Policy*. 2008;7:3–6.

"Good Behavior Game" Improves Early Classroom Behavior and Leads to Impact in Young Adulthood

First tested in 1969, the Good Behavior Game (GBG) helps teachers manage disruptive classroom behavior by dividing students into teams and rewarding the groups as a whole for good behavior. A review of the earlier history of the GBG showed the game to be promising in reducing early disruptive classroom behavior. Observational studies conducted between 1969 and 2000 identified the most effective components of the game and focused on regular elementary and middle school classrooms, with later trials expanding to a wider range of ages, grades, and educational settings. "The GBG seemed to hold promise based on these studies, but the fairly small samples without randomization and short follow-up periods pointed towards the need for more rigorous tests with larger, defined populations and longer follow-up," explain the authors. Beginning in the mid-1980s, investigators in Baltimore performed the first of three generations of population-based randomized, controlled field trials designed to reduce aggressive, disruptive behavior in the first and second grade classrooms in 19 schools. By young adulthood, the results revealed significant reduction, mostly among higher risk males, in drug and alcohol dependence disorders, rates of regular smoking, antisocial personality disorder, delinquency and incarceration for violent offenses, suicide ideation and attempts, and use of school-based services. These results are reported in detail in the June 2008 supplemental issue of *Drug and Alcohol Dependence*. "Independent replications in different cultures and social contexts using population-based randomized designs strengthen the promise of GBG as an effective preventive intervention," conclude the authors.

Mackenzie AC, Lurye I, Kellam SG. History and evolution of the Good Behavior Game. Supplemental material in: Kellam SG, Brown CH, Poduska JM, Ialongo NS, Wang W, Toyinbo P, Petras H, Ford C, Windham A, Wilcox HC. Effects of a universal classroom behavior management program in first and second grades on young adult behavioral, psychiatric, and social outcomes. *Drug Alcohol Depend.* 2008;95(Suppl 1):S5–S28.

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Experts Encourage More Research into Drugged Driving: New Study Guidelines Released

Driving under the influence of drugs, also known as drugged driving, is a growing problem in many countries. In the United States alone, the National Highway Traffic Safety Administration reports that more than 17,000 people were killed in alcohol-related crashes in 2006. Studies also have found that drugs were used by 10 to 22 percent of drivers involved in crashes, often in combination with alcohol. Yet research into drugged driving and its effects on traffic safety has been hampered by a lack of standard techniques for studies in the field. There simply is no proven on-the-spot way to test drivers—in other words, there is no drug "breathalyzer" technology and no standard measurements to evaluate drugged driving.

Researchers studying drugged driving use a wide range of different measurements and test for a variety of drugs that differ among studies, making comparisons between studies that could advance the science difficult. To overcome these barriers, the International Council on Alcohol, Drugs and Traffic Safety (ICADTS) convened a 4-day meeting in 2006 to develop formal guidelines for research on drugged driving, which was supported by international organizations including the National Institute on Drug Abuse. Three groups, focusing on behavioral research, epidemiology, and toxicology, discussed issues including ethical and legal issues in the field, the most important drug classes on which to focus research, and the best methods for detecting drug use in impaired drivers. Draft guidelines were posted on the Web sites of the ICADTS and the International Association of Forensic Toxicologists for a 45-day comment period to collect and ultimately incorporate feedback from experts around the world. The final guidelines, including 32 recommendations for behavioral research, 40 recommendations for epidemiology, and 64 recommendations for toxicology, were published in the August 2008 issue of the journal *Addiction*. "It is anticipated that these guidelines will improve significantly the overall quality of drugged driving research and facilitate future cross-study comparisons nationally and globally," conclude the authors.

Walsh, JM, Verstraete AG, Huestis MA, Mørland J. Guidelines for research on drugged driving. *Addiction*. 2008;103(8):1258–1268. Supplemental information in: Voas, R. Commentary: Guidelines for research on drugged driving: A good first step. *Addiction*. 2008;103(8):1269–1270. Available in: http://www3.interscience.wiley.com/cgi-bin/fulltext/120776314/PDFSTART

Dialing Up or Down: The Surprising Versatility of Dopamine Receptors

Neurotransmitters, or brain chemicals, play a key role in the long-term changes that allow a brain to continuously adapt in response to experience. This hinges on the ability of neurotransmitters to change the efficiency with which neurons "talk" with one another. In the striatum, a brain region critically involved in certain types of learning, dopamine is the main chemical responsible for tuning the efficiency of this communication up and down. Two types of dopamine receptors (D1 and D2) were previously thought to have completely opposite functions in this process, whereby D1- and D2-expressing neurons could only tune the strength of the connections up or down, respectively. The present study dispels that notion, demonstrating that conditions in the local brain environment can make it possible for both cell types to carry out either function, thereby resolving a long-standing scientific puzzle posed by conflicting experimental evidence.

These findings were reported in an article in the August 8, 2008 issue of *Science* by NIH-funded investigators Paul Greengard, Ph.D., of Rockefeller University and James Surmeier of Northwestern University and their colleagues.

Drugs of abuse can elevate dopamine to abnormally high levels and disrupt the carefully balanced actions of dopamine and other neurotransmitters in the striatum. This study reveals a mechanism by which exposure to drugs can corrupt the adaptive training of neural circuits and lead to the deleterious learned behaviors that characterize addiction. A better understanding of the molecular processes that regulate this type of learning may bring to light novel strategies to weaken these behaviors and provide new targets for treatment development.

For more information about this study, or to speak with an expert, please contact the National Institute on Drug Abuse press office at *media@nida.nih.gov* or call 301-443-6245.

Shen W, Flajolet M, Greengard P, Surmeier DJ. Dichotomous dopaminergic control of striatal synaptic plasticity. *Science*. 2008;321(5890):848–851.

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Meetings of Interest

Frontiers in Addiction Research

NIDA to Hold Mini-Convention at Society for Neuroscience Annual Meeting

The National Institute on Drug Abuse (NIDA), National Institutes of Health, will convene a one-day mini-convention at the Society for Neuroscience Annual Meeting in the Nation's capital, Washington, DC, bringing together scientists to explore novel approaches to addiction and treatment. NIDA scientists will present recent findings and discuss future directions in the neurobiology of drug abuse and addiction.

WHAT: Frontiers in Addiction Research
NIDA 2008 Mini-Convention

HIGHLIGHTS:

- **Jacob P. Waletzky Memorial Award Lecture** — award given in recognition of innovative research in drug addiction and alcoholism.
- **Epigenetics and Brain Function** — an exploration of diverse mechanisms that govern the brain and behavior, learning and relapse to drug seeking, other drug seeking behaviors.
- **Multimodal Imaging of Neuropathways** — research updates in groundbreaking optogenetic technology which offer unprecedented opportunities for biomedical research.
- **Willpower: What Really Governs Our Choices?** — new perspectives on freewill and its significance in the human brain and behavior.
- **Cortical Development and Substance Abuse** — an exploration of recent discoveries in cortical development and research in substance abuse.

WHEN: Friday, November 14, 2008
8:00 a.m. – 6:10 p.m.

WHERE: Society for Neuroscience Annual Meeting
Renaissance Washington DC Hotel
Grand Ballroom North and Central
999 Ninth Street, NW
Washington, DC 20001

For more information or to arrange an interview with NIDA staff, call NIDA press officers Dorie Hightower or Stephanie Older at 301-443-6245 or e-mail your request to *media@nida.nih.gov*

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Other NIDA News

NIDA Announces *DrugPubs*—A New Research Dissemination Center

1-877-NIDA-NIH

Anyone interested in receiving the latest scientific information about drug abuse and addiction has a new number to call: *1-877-NIDA-NIH.* NIDA, part of the National Institutes of Health (NIH), today launches **DrugPubs**, its new research dissemination center, designed to distribute materials and information on drug abuse and addiction to virtually all audiences: drug abuse researchers, health professionals, teachers, advocacy groups, and teenagers and other members of the general public. Callers to *1-877-NIDA-NIH* can receive scientific information on drug abuse in a timely and effective manner. Requests for information also can be emailed to: *drugpubs@nida.nih.gov*. NIDA supports most of the world's research on the health aspects of drug abuse and addiction, and views information dissemination as a key part of its public mission.

DrugPubs distributes a wide range of free or low-cost materials including fact sheets, brochures, pamphlets, posters, and video tapes, on a variety of drug abuse topics. For example, *DrugPubs* houses NIDA's most popular publications, including:

- *Drugs, Brains and Behavior: The Science of Addiction*, a landmark, plain-language publication on the disease of drug addiction;
- *Marijuana: Facts for Teens*, which provides teens with answers to frequently asked questions about marijuana;
- *Marijuana: Facts Parents Need to Know*, which provides parents with the latest scientific information on marijuana;
- *Brain Power! The NIDA Junior Scientist Program*, a series of science education materials on the brain and the effects of drugs for children of all ages; and
- *Mind Over Matter*, a series of eight booklets for middle-school aged children in English and Spanish, that discuss drug abuse topics, such as inhalants, methamphetamine, nicotine and steroids.

NIDA's new DrugPubs number can serve as a resource to the public in two ways:

- **Get Information on NIDA Publications.** NIDA information specialists answering requests for publications are familiar with NIDA's materials and can suggest publications that are appropriate for the requester's situation, event, or reading level.
- **Place Publication Orders.** The public can view and download NIDA publications at *www.drugabuse.gov*. To order publications in English or Spanish, call the NIDA *DrugPubs* center toll-free at *1-877-NIDA-NIH* (1-877-643-2644), or 240-645-0228 (TDD). Order requests can also be sent via fax to 240-645-0227 or emailed to: *drugpubs@nida.nih.gov*.

Notes

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

- All studies described can be obtained through PubMed (www.pubmed.gov).
- Reporters, call Dorie Hightower 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 http://www.drugabuse.gov. To order publications in English or Spanish, call NIDA's new DrugPubs research dissemination center at 1-877-NIDA-NIH (1-877-643-2644) or 240-645-0228 (TDD) or fax or e-mail requests to 240-645-0227 or drugpubs@nida.nih.gov.

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