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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

NewsScan

NIDA ADDICTION RESEARCH NEWS

RESEARCH NEWS

Study Finds That Methamphetamine Use Can Increase Stroke-Related Brain Damage

Researchers from the National Institute on Drug Abuse (NIDA) found that methamphetamine use prior to stroke increases damage to the brain. Methamphetamine appears to inhibit factors that occur naturally within the brain and that help protect it from neuronal damage following trauma such as stroke or other injury.

NIDA researchers, joined by scientists from the Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, used mice to ascertain the effects of methamphetamine on the brain following stroke. The researchers pretreated mice with either methamphetamine or a saline solution, temporarily blocked the blood flow through the animals' right middle cerebral artery and bilateral carotid arteries (mimicking an ischemic stroke), and observed the effects.

The researchers found more extensive brain damage in the mice pretreated with methamphetamine than in those treated with the saline solution.

Dr. Yun Wang, head of the research team, says that their experiments found at least one possible mechanism to explain this effect. They observed that methamphetamine pretreatment decreased glial-cell-line-derived neurotrophic factor (GDNF) in the mice brain; when GDNF was administered into the brains of the mice before their arteries were blocked, the effects of methamphetamine-facilitated stroke were reduced.

This result, Dr. Wang says, indicates that methamphetamine may act to exacerbate brain damage following stroke by inhibiting GDNF pathways.

- WHAT IT MEANS: Scientists knew that methamphetamine, an addictive stimulant drug, increases heart rate and blood pressure and can cause irreversible damage to blood vessels in the brain, resulting in strokes. This evidence that methamphetamine can increase stroke-related damage to the brain further illustrates the danger of this drug.

The study, led by Dr. Yun Wang, appears in the March issue of *Stroke*. The paper is posted on the journal's Web site at http://stroke.ahajournals.org/.

Study Examines Link Between Dopamine Receptor and Curtailing Cue-induced Craving for Cocaine

Cue-induced craving—seeing, hearing, or smelling something that triggers desire—often prompts a former addict to resume drug use even after long periods of abstinence. Recently, researchers at the Scripps Research Institute in La Jolla, California, used rats to demonstrate that it may be possible to reduce cue-induced craving for cocaine by blocking the dopamine receptor D1. Dopamine is a neurotransmitter that regulates feelings of pleasure, and cocaine use increases the concentration of dopamine in the brain, resulting in the "rush" cocaine users feel when using the drug.

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"Better understanding of the biological basis of cue-induced craving and relapse has substantial potential clinical benefit, including providing leads to the development of more effective medications and behavioral interventions to treat addiction," says NIDA Director Dr. Alan I. Leshner.

The researchers trained 34 rats to self-administer cocaine by pressing a lever, accompanied by the sound of a tone. Once the rats established stable levels of daily cocaine intake, investigators withheld the drug. When the lever/tone cue no longer administered cocaine, the rats lost the learned behavior.

Four months later, the rats were again given access to cocaine using the lever/tone cue at intervals immediately following behavior-extinction training. Once the lever/tone cue again signaled cocaine availability, the rats quickly resumed pressing the lever in an attempt to take the drug.

During this study, scientists pinpointed the regions of the rat brain that may be involved in the motivating effects of drug cues. The D1 antagonist treatment not only reversed drug-seeking behavior induced by the cocaine cues, but concurrently reversed the neural activation.

- WHAT IT MEANS: These observations support the hypothesis that learned responses to drug-related behavior are important in long-lasting vulnerability to relapse to drug use and help explain the neurobiological basis for this vulnerability.

This study, led by Dr. Friedbert Weiss, appeared in the February 13, 2001, issue of *PNAS: Proceedings of the National Academy of Sciences.* An abstract and other information about the article is available at www.pnas.org.

Nicotine Causes Degeneration in Brain's "Weak Link" for Addictive Drugs

Researchers at the University of California, Los Angeles (UCLA), have found that, in rats, continuous doses of nicotine cause degeneration of brain cells in the fasciculus retroflexus (FR), a bundle of nerve cells that acts as a pathway between limbic forebrain regions and the midbrain. Previous research established that one half of FR's two parts is damaged by amphetamine, cocaine, methamphetamine, and other addictive stimulants. It now appears that nicotine is selectively neurotoxic to the other half of the FR tract.

The UCLA researchers exposed rats for 5 days to continuous doses of nicotine, including doses that produced plasma concentrations of nicotine equivalent to those experienced by humans who smoke a pack and a half of cigarettes each day. Analysis of the animals' brains revealed highly selective degeneration in the axons projecting from FR nerve cells. The half of the FR tract damaged by dopaminergic drugs showed nearly no nicotine-induced degeneration.

- WHAT IT MEANS: The fasciculus retroflexus may represent a "weak link" in the brain for the chronic drug effects, including addiction and relapse, as a result of use of nicotinic as well as dopaminergic drugs.

The study, led by Dr. Gaylord Ellison, appears in the December 2000 issue of the journal *Neuropharmacology*.

Brain Hormone That Helps Regulate Food Intake May Dampen Drug Craving: Finding Exploits Possible Relationship Between Addiction and Eating Disorders

Food restriction or deprivation is associated with increased drug use in humans and with increased self-administration of heroin and cocaine in laboratory animals. Acute food deprivation also potently reinstates heroin and cocaine seeking in a rat model of relapse to drugs. The neuronal mechanisms underlying this effect, however, are not known. In experiments using rats, NIDA scientists now report that fasting-induced heroin seeking is suppressed by leptin, a hormone involved in the regulation of energy balance and food intake.

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Rats were trained to self-administer intravenous heroin by pressing a lever. This was followed by a 10-to-13 day period during which lever presses did not yield heroin. When they no longer received heroin, the rats greatly reduced the number of times they pressed on the lever. Rats were then subjected to one of several situations, previously shown to induce heroin seeking—1 day of food deprivation, re-exposure to heroin, or mild intermittent footshock stress—and then tested to see if they would resume their drug seeking. Drug seeking in the food-deprived rats was greatly reduced following administration of leptin. Conversely, leptin did not dampen drug seeking in rats that had received either intermittent footshock stress or heroin injections.

- WHAT IT MEANS: Many people suffering from eating disorders also have drug addiction problems. This study suggests that medications that target brain systems involved in energy balance and food consumption may be useful in treating these individuals.

The researchers, Drs. Uri Shalev, Jasmine Yap, and Yavin Shaham of the NIDA Intramural Research Program, published their findings in the February 15, 2001, issue of *The Journal of Neuroscience,* Rapid Communications Section. The paper is posted online at www.jneurosci.org.

SPECIAL EVENTS

NIDA Joins in Recognizing National Inhalants and Poisons Awareness Week in March

Nearly one in five students in eighth grade has abused an inhalant sometime during their lifetime, according to results from the 2000 Monitoring the Future survey, which was funded by NIDA. While this represents a slight drop from 1999 (19.7 to 17.9 percent), too many children continue to abuse these potentially fatal substances.

To combat this abuse, NIDA is recognizing National Inhalants and Poisons Awareness Week during the third week in March by publicizing the availability of science-based informational materials on inhalant abuse.

Inhalants are substances whose vapors can be inhaled to produce a mind-altering effect. Inhalants can be categorized as follows:

- Volatile solvents, such as paint thinners, degreasers, and glues;
- Aerosols, such as hair sprays and vegetable oil sprays for cooking;
- Gases, including ether, nitrous oxide, and propane; and
- Nitrates, including cyclohexyl nitrate, amyl nitrite, and butyl nitrite.

Inhalants often are among the first drugs that young children use. About 6 percent of children in the United States have tried inhalants by the time they reach fourth grade. Early recognition of inhalant abuse is important for parents and physicians. Signs include chemical odors on the breath or clothes, paint or other stains on skin or clothes, slurred speech, drunk or disoriented appearance, nausea or lack of appetite, and inattentiveness and lack of coordination.

The most serious hazard for inhalant abusers is a syndrome called “sudden sniffing death.” A single, prolonged session of inhalant use can produce rapid and irregular heart rhythms, heart failure, and death. “Sudden sniffing death” can happen within minutes and can strike an otherwise healthy young person. But inhalant abuse can cause death in other ways, too, through asphyxiation, suffocation, or choking.

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Chronic exposure to inhalants causes widespread and long-lasting damage to the nervous system and other vital organs. The toxic chemicals damage parts of the brain that control learning, movement, vision, and hearing. Damage to the heart, lungs, liver, and kidneys may be permanent.

More information on inhalant abuse can be found on the NIDA Web site at www.drugabuse.gov. Free copies of NIDA's *Research Report on Inhalant Abuse* and a color poster on inhalants, appropriate for middle-school children and part of the Institute's award-winning "Mind over Matter" series, may be ordered from the National Clearinghouse for Alcohol and Drug Information at 1-800-729-6686 or 1-800-487-4889 for the deaf. A fact sheet entitled "Inhalants" can be ordered from NIDA's *Infofax* service by calling 1-888-644-6432 or 1-888-889-6432 for the deaf.

UPCOMING EVENTS

- April 4, 2001: Fifth Annual PRISM Awards, Los Angeles, CA
- April 10, 2001: Prescription Drugs: Misuse, Abuse and Addiction, National Press Club, Washington, DC
- July 19-20, 2001: Advances in MDMA (Ecstasy) Research, William H. Natcher Conference Center, NIH Campus, Bethesda, MD
- August 9-10, 2001: 2nd National Conference on Drug Abuse Prevention Research: A Progress Update, Omni Shoreham Hotel, Washington, DC
- September 24-26, 2001: National Conference on Health Disparities Among Racial and Ethnic Groups, Wyndham Franklin Plaza Hotel, Philadelphia, PA

Watch upcoming issues of *NewsScan* for more information on these events, or call NIDA at 301-443-6245.

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

- Reporters, call Michelle Muth at 301-443-6245 in the NIDA Press Office.
- Congressional staffers, call Mary Mayhew or Keith Van Wagner, NIDA Congressional Affairs Office, at 301-443-6071.

The National Institute on Drug Abuse is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports more than 85 percent 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 can be ordered free of charge in English and Spanish by calling *NIDA Infofax* at 1-888-NIH-NIDA (644-6432) or 1-888-TTY-NIDA (889-6432) for the deaf. 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.