

Research News

Medication May Reduce Inhalant-Seeking Behavior in Rats

Scientists at the U.S. Department of Energy's Brookhaven National Laboratory have found that the anticonvulsant drug vigabatrin (also known as gamma vinyl-GABA or GVG) may block the addictive effects of toluene, a substance found in many household products that are abused as inhalants.

In the study, rats learned that one of three chambers contained toluene vapors, and they would spend more of their time in that chamber than the others. On the final day of the study, the rats received either saline or vigabatrin one hour prior to testing. When the rats were given access to the three chambers, those that had been previously treated with vigabatrin spent only 80 seconds in the toluene-containing chamber. The rats pretreated with saline spent 349 seconds in that chamber.

Human abuse of inhalants remains a health concern in the United States, where many young people attempt to get high by inhaling vapors from common household products that contain volatile solvents or aerosols. National surveys indicate that more than 22.9 million Americans have abused inhalants at least once in their lives. Results from the annual Monitoring the Future (MTF) survey of 8th-, 10th-, and 12th-grade students in U.S. schools show that lifetime inhalant use for 8th-graders increased significantly during 2004.

- **WHAT IT MEANS:** Vigabatrin appears to block toluene-seeking behavior in rats. Further research that explores the value of this drug as a treatment for inhalant abuse in humans may prove useful.

Dr. Stephen Dewey and his colleagues published this study, which was funded in part by NIDA, in the December 1, 2004 issue of the journal *Synapse*.

Study Examines Rates of Injection Drug Use in Metropolitan Areas

A study that estimates the prevalence of injection drug use in 96 U.S. metropolitan areas places the lowest rate of this practice in Ann Arbor, Michigan, and the highest in Fresno, California.

Dr. Samuel Friedman and his colleagues at the National Development and Research Institutes in New York City analyzed data from 96 U.S. metropolitan statistical areas (which include the central urban area and the surrounding suburbs) that had populations greater than 500,000 in 1996. They found that the number of injection drug users per 10,000 persons in each metropolitan area varied from 19 to 173.

- **WHAT IT MEANS:** Knowing the approximate number of injection drug users within a specific geographic area can help policymakers and health officials assess the adequacy of existing services and policies and make more informed decisions about allocating funds for services.

This NIDA-funded study was published in the September 2004 issue of the *Journal of Urban Health*.

Formula Can Help Determine Number of Urban Men at Risk for Diseases Associated with Injection Drug Use, Sexual Practices

Researchers have developed a mathematical formula to determine the approximate number of urban men at risk for HIV infection by estimating populations of injection drug users and men who have sex with men.

Spencer Lieb of the Florida Department of Health and his colleagues developed a model to estimate the populations of these two groups at high risk for infection with HIV and other diseases. When applied to the Miami, Florida population, the model suggests that 1.4 percent of the total adult population are injection drug users, and almost 10 percent of males aged 18 years or older are having sex with men.

- **WHAT IT MEANS:** Knowing the approximate number of injection drug users, as well as how many males are engaging in sex with other men, is useful for assessing current and future capabilities of services designed to reduce the burden of infectious diseases in these at-risk populations.

This NIDA-funded study was published in the September 2004 issue of the *Journal of Urban Health*.

Vouchers Help Methadone Patients Kick Cocaine Abuse

People who continue to abuse cocaine while undergoing methadone therapy for opiate addiction may benefit from long-term abstinence reinforcement that incorporates the use of vouchers, new research reports.

A total of 78 methadone patients who used cocaine during their methadone treatment were randomly assigned to either an abstinence reinforcement group that included take-home doses of methadone, an abstinence reinforcement group that included take-home doses of methadone and monetary vouchers, or a usual care control group that included daily methadone in a clinic setting. All participants also received individual and group counseling.

When the scientists analyzed the results of the 52-week intervention, they found that the take-home plus voucher group had significantly longer durations of sustained abstinence from cocaine and opiates than either of the other groups. Members of this group sustained about 19 weeks of continuous abstinence compared to 6.3 weeks for the take-home only group and 2.3 weeks for the usual care group.

- **WHAT IT MEANS:** Persistent cocaine use has been a serious problem in individuals receiving methadone treatment for opiate addiction. However, no drug treatment and few psychosocial therapies have proven effective in reducing cocaine use. These results point to the potential efficacy of long-term, voucher-based reinforcement to achieve and maintain drug abstinence in this population, and suggest the need to develop practical vehicles to deliver such interventions on a wide scale.

Dr. Kenneth Silverman, of the Johns Hopkins University School of Medicine, and his colleagues published the study in the October 2004 issue of the *Journal of Consulting and Clinical Psychology*.

Sex, Drug Use Increase Risk of Teen Depression, Suicide

Teens who engage in sexual intercourse and/or drug abuse (including abuse of alcohol and tobacco) are significantly more likely than youth who abstain from such activities to become depressed, have suicidal thoughts, and attempt suicide.

NIDA-funded scientists at the Pacific Institute for Research and Evaluation and the University of North Carolina at Chapel Hill analyzed sex and drug behavior patterns among 18,924 teens from 132 U.S. schools. The data were gathered from September 1994 to December 1995 as part of the National Longitudinal Study of Adolescent Health.

The researchers found that teens who had not initiated sex or drug abuse had the lowest levels of depression, suicidal thoughts, and suicide attempts. The highest levels were seen in youth with patterns that included illegal drug abuse and risky sexual behavior. The scientists also observed that although girls were less likely than boys to pursue high-risk behaviors, girls who did were more vulnerable to depression and suicidal behaviors.

- **WHAT IT MEANS:** Healthcare professionals should consider screening youth for depression and suicidal tendencies if they suspect the youth are engaging in risky behaviors. Further research is warranted to understand whether causal links exist between such behaviors and mental health status.

Dr. Denise Hallfors and her colleagues published this study in the October 2004 issue of the *American Journal of Preventive Medicine*.

Men, Women Use Different Brain Regions in Making Decisions

Researchers have shown that men and women use different brain regions and cognitive strategies when faced with decisionmaking tasks.

Dr. Karen Bolla, of The Johns Hopkins University School of Medicine, and her colleagues at the National Institute on Drug Abuse Intramural Research Program recruited 20 healthy men and women to participate in a brain imaging study using the Iowa Gambling Test to identify decisionmaking differences. The Iowa Gambling Test measures the ability to choose between high gains with high risk and low gains with low risk by selecting cards from decks with different potential cash payouts and penalties. Using positron emission tomography (PET), the researchers were able to see and record which brain regions were used during participation in the tasks.

The 10 men and 10 women who participated in the study had no past history of drug abuse and did not currently abuse drugs. They consumed fewer than 10 alcoholic drinks per week.

Upon analyzing the PET scans, the scientists found that in men, these tasks primarily activated the region on the right side of the brain that is sensitive to punishment and can override a person's behavior if the stimulus has proved rewarding. In women, the tasks primarily activated the region on the left side of the brain that is involved in reward and guessing situations when the rewards are undetermined. The researchers also found that men appeared to be more successful than women in achieving monetary gain on the task.

Among healthy individuals, right side brain activation may offer benefits in achieving greater rewards in similar decisionmaking tasks. However, previous research has shown that decisionmaking in real-life situations becomes impaired after damage to areas of the right side of the brain, while damage to the left side has little effect on decisionmaking.

- **WHAT IT MEANS:** The results suggest that men and women employ different neural pathways and cognitive strategies when making decisions, and supports the concept of sexual dimorphism of the brain. More research is needed to understand sex-related differences in cognitive processing, and how damage to the areas of the brain most related to decisionmaking may affect men's and women's decisions to engage in unhealthy behaviors.

This NIDA-supported study was published in the November 2004 issue of *Cerebral Cortex*.

Computer Program May Detect Substance Abuse in Older Adults

Scientists have developed a new computerized screening tool that allows primary care practitioners to detect older substance-abusing adults.

Results of a study that tested the diagnostic capabilities of the Drug Abuse Problem Assessment for Primary Care (DAPA-PC) showed that older adults and younger adults had similar rates of alcohol and drug abuse. The study, which involved 266 adults aged 18–54 and 61 adults aged 55–86, also showed that older adults were less likely than younger adults to view their drug use as problematic. Older adults were less likely to report that they felt their use of alcohol and/or drugs was excessive. When compared with younger respondents, older adults also were less likely to report that they had tried to quit, control, or reduce their drinking and/or other drug abuse during the past 6 months.

The scientists at Danya International, Inc. who developed the DAPA-PC, predict that the number of older adults who abuse alcohol and other drugs will greatly increase over the next several decades. Because virtually all of today's alcohol and drug screening devices have been developed and validated with younger adults, they say there is a need for tools to help identify older substance abusers.

Users of the DAPA-PC, which was developed via a Small Business Innovation Research Grant from NIDA, first answer a brief series of questions about trauma, and then progress to a brief questionnaire about alcohol and drug use. Asking about trauma, the researchers say, is a predictive yet nonthreatening way to determine a person's level of drug and alcohol use or abuse.

- **WHAT IT MEANS:** Computerized screening instruments for drug and alcohol abuse can help identify substance abuse in older adult patients who may not report substance-related problems and appear to be less likely than younger adults to seek help for them.

Dr. Susanna Nemes and her colleagues published the study in the October 12, 2004 issue of *The American Journal of Drug and Alcohol Abuse*.

Dopamine Connection Seen in HIV Dementia

A study by NIDA Director Dr. Nora D. Volkow, Dr. Gene-Jack Wang, Dr. Linda Chang, and others at NIDA and Brookhaven National Laboratory is the first to show that people with HIV dementia experience dopamine decreases in their brains. Dopamine is a brain chemical associated with pleasure/reward and motivation.

The scientists used the brain scanning technology known as positron emission tomography (PET) to examine the brain chemistry of 15 HIV patients (some of whom had dementia) and 13 HIV-negative volunteers. The researchers found that HIV patients with dementia showed impairment in the brain's system for delivering dopamine to brain cells when compared with control subjects.

Previous research has also shown low dopamine levels in patients with conditions such as Parkinson's disease. HIV dementia is a type of cognitive decline that is more common in the later stages of HIV infection. Symptoms include slowed thinking and expression, difficulty concentrating, and apathy. Movements are slow, and muscle weakness and lack of coordination may be present.

- **WHAT IT MEANS:** The findings suggest that HIV patients with dementia may benefit from dopamine-enhancing treatments.

The study was published in the September 2004 issue of the journal *Brain*.

Receptors May Be Key to Nerve Damage from Drug Abuse

NIDA scientists hypothesize that the use of compounds that promote the production of myelin—the protective sheath that surrounds the axons of nerve cells—may prevent nerve damage from cocaine or methamphetamine abuse.

Some studies have suggested that cocaine and methamphetamine can damage the myelin sheath. This sheath, an insulating layer of protein and fatty substances, allows impulses to travel rapidly and efficiently between cells. If the myelin is damaged through drug abuse or a disease process such as multiple sclerosis, the impulses are disrupted.

Through a series of experiments on rat nerve cells, NIDA scientists have determined that proteins called sigma-1 receptors are involved in promoting the development of myelin.

Because myelination continues in humans until about the age of 20, using very selective, pure sigma-1 receptor agonists to stimulate the process may protect against nerve damage in young substance abusers.

- **WHAT IT MEANS:** Compounds that promote the production of sigma-1 receptors may act as shields against myelin degeneration processes related to cocaine and methamphetamine abuse. Future research will help clarify the mechanisms involved in these processes.

Dr. Tsung-Ping Su and Dr. Teruo Hayashi published their findings in the October 12, 2004 issue of the *Proceedings of the National Academy of Sciences*.

FUNDING NEWS

Request for Applications

Supplemental Support for Existing Research in African-Americans

NIDA's Health Disparities Initiative supports research to help understand why some populations suffer disproportionately from the consequences of drug abuse. Projects funded under this initiative may improve our understanding of the incidence and causes of drug abuse and addiction in racial and ethnic populations; strengthen and expand the community and institutional infrastructure for conducting research within these populations; and provide the scientific foundation for improved prevention and treatment for racial and ethnic groups at highest risk for addiction and drug abuse.

Under this initiative, NIDA is offering supplemental research support to NIDA-funded scientists investigating the relationships between criminal justice involvement and drug abuse and addiction among African-Americans.

Statistics indicate that the greatest increase in the number of people incarcerated for various drug offenses has occurred among African-Americans. Although African-Americans comprise approximately 12 percent of the U.S. population, they represent about 42 percent of male inmates and 45 percent of female inmates imprisoned for drug-related offenses. According to one study, nearly 75 percent of the increase in the prison population is related to drug abuse and addiction.

Research that would qualify for additional support includes but is not limited to projects that seek to increase our knowledge of:

- variables within African-American society that affect involvement in or protection against drug abuse and criminal activity;
- the impact of imprisonment and criminal justice supervision on drug use, continued criminal behavior, and HIV risk behavior;
- factors that account for the differential pattern of HIV status between African-American female and male offenders (females are twice as likely to be HIV-positive than males);
- outcomes of drug abuse treatments and services provided to African-Americans in the criminal justice system; and
- effective design of drug abuse and HIV prevention programs for African-Americans within the criminal justice system.

Approximately \$500,000 will be available in FY 2005 to fund these administrative supplements. Applications may be submitted through May 1, 2005. For more information, contact Dr. Lula Beatty, Chief of the Special Populations Office, at 301-443-0441.

Consequences of Drug Abuse and Alcohol Exposure on Brain and Behavioral Development (RFA-DA-05-007)

Adolescence is a unique period of development marked by changes in the brain, behavior, and social functioning. It also is a time when people may begin to abuse drugs and may start exhibiting symptoms of a number of psychiatric disorders.

Animal studies have begun to improve our understanding of how drug exposure affects the developing nervous system. Clinical studies have added to our knowledge of the behavioral consequences of early exposure to drugs of abuse, and imaging studies have shown how drugs of abuse affect adult human brains. But little research is available that directly explains how drugs of abuse affect adolescent human brains.

This request for applications (RFA) encourages researchers in diverse fields to design and conduct investigations that define and characterize the consequences of drug exposure on the developing human brain and how these changes relate to behaviors.

Examples of appropriate research projects include, but are not limited to:

- studying the effects of drugs of abuse on the neural circuits that mediate motivation, reward, and decisionmaking, and differences in these effects as they relate to developmental staging;
- understanding how drug abuse might precipitate or intensify psychiatric symptoms for youth at risk for mental disorders (such as those with a family history of mental disease), as well as defining pathways that render adolescents with specific psychiatric disorders more susceptible to drug abuse, dependence, and addiction; and
- investigating the relationship between drug abuse and the development of high-risk sexual behaviors, including those associated with HIV/AIDS.

The receipt date for letters of intent is March 18, 2005. For more information about this RFA, go to <http://grants.nih.gov/grants/guide/rfa-files/RFA-DA-05-007.html>.

HIV and Psychiatric Comorbidity Research Project (RFA-MH-05-010)

The National Institute on Drug Abuse (NIDA) is one of two NIH components seeking applications for research projects addressing the cellular, molecular, and genetic factors underlying high comorbidity between HIV-1 infections and psychiatric disorders.

Many HIV-1 infected people are expected to experience some form of psychiatric illness during the course of their infection. The presence of such disorders may interfere with the ability to adhere to medication regimens. Additionally, such problems also may promote abuse of alcohol or drugs.

This request for application (RFA) involves studies of the physiologic mechanisms by which HIV-1 infection acts on the brain to alter behavior and affect disease progression. Examples of appropriate research projects include, but are not limited to:

- examining the contributions of certain genes to variability in HIV disease progression with an emphasis on identifying novel candidates that may influence HIV-1 and co-occurring psychiatric disorders and potential interaction with drugs of abuse;
- identifying markers of co-occurring illness relating to immunologic, virologic, and neurobiologic processes; and
- characterizing HIV viral strains associated with psychiatric comorbidity, with and without a history of drug abuse.

The receipt date for letters of intent is March 29, 2005. For more information about this RFA, go to <http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-05-010.html>.

Program Announcements

MDMA: Research Areas Needing More Emphasis (PA-04-152)

MDMA is a synthetic, psychoactive drug chemically similar to the stimulant methamphetamine and the hallucinogen mescaline. Known popularly as ecstasy, this drug primarily affects neurons in the brain that use the chemical serotonin to communicate with each other.

Because MDMA is a prominent drug of abuse among youth, scientists need to identify epidemiologic patterns surrounding the decision to begin or continue using it, as well as population-appropriate interventions to prevent initiation or repeated MDMA use.

Examples of research topics that may be considered for funding under this program announcement (PA) include:

- identifying risk and protective factors for MDMA use in different populations;
- examining the roles of social networks for youth and the Internet in the dissemination of information and misinformation about MDMA use, alone and in combination with other drugs;
- conducting studies to understand HIV transmission and progression in MDMA users;
- designing and conducting case-control studies to compare the health and behavioral outcomes of infants and children of MDMA users;
- identifying the behavioral, cognitive, psychological, or biological risk factors that contribute to MDMA abuse and addiction; and
- characterizing the acute and chronic cardiovascular and cerebrovascular effects of MDMA.

For more information about this PA, go to <http://grants1.nih.gov/grants/guide/pa-files/PA-04-152.html>.

Supplements to Promote Re-entry into Biomedical and Behavioral Research Careers (PA-04-126)

NIDA and other components of the National Institutes of Health (NIH) have developed a new program for people who have temporarily left the scientific workforce but now wish to resume their research careers. The program provides administrative supplements to existing NIH research grants to support full- or part-time research for such individuals to enhance and update their research skills.

NIH recognizes that various populations may be underrepresented in the scientific and research community. For example, the low number of women in research endeavors may reflect the societal emphasis on female responsibilities in child and family care.

Candidates must have a doctoral degree, as well as sufficient prior research experience to have qualified them for a doctoral-level research or faculty position when they left active research. The duration of the career interruption should be between 1 and 8 years. Examples of career interruptions that meet the requirements of this program include:

- raising children;
- personal incapacitating injury or illness;
- incapacitating injury or illness to spouse, partner, or immediate family member;
- pursuit of nonresearch endeavors to retire debt incurred obtaining a doctoral degree; and
- military service.

A candidate should not be engaged in full-time paid research activities at the time of application.

For more information about this program announcement (PA), go to <http://grants2.nih.gov/grants/guide/pa-files/PA-04-126.html>.

Cross-Disciplinary Translational Research at NIH (PA-04-109)

Part of NIDA's mission is to translate knowledge gained from basic scientific investigations into tools and resources that aid in the development of effective prevention and treatment strategies for addiction and drug abuse. To this end, NIDA is one of two components of the National Institutes of Health (NIH) encouraging research projects that extend the transfer of information from the laboratory into clinical and behavioral practices.

Collaborations between basic and applied researchers with diverse areas of interest may be helpful in developing innovative approaches to drug abuse prevention or treatment. Projects that unite the efforts of clinical scientists and healthcare service researchers may result in advances in the delivery of such services.

Goals of such projects may include, but are not limited to:

- designing clinical studies that seek to discover whether neurochemical or related mechanisms previously observed in the laboratory or in animal models can serve as important targets for drug addiction;
- implementing Phase I clinical studies that use human subjects to evaluate drugs currently used to treat nonaddiction disorders that may be useful in treating drug abuse;
- developing models of longitudinal care that include medications, behavioral therapies, social services, and education for defined populations; and
- producing new paradigms for studying adolescent decisionmaking related to drug use and sexual risk behaviors.

For more information about this program announcement (PA), go to <http://grants1.nih.gov/grants/guide/pa-files/PA-04-109.html>.

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

- Reporters, call Michelle Person 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 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 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>.

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