

Research News

Abstaining From Marijuana Associated With Better Quality of Life

Results of a study suggest that people who abstain from smoking marijuana appear to have a better quality of life and higher levels of educational achievement than marijuana users. Also, early use of marijuana was associated with lowered income and reduced health later in life.

Dr. Phyllis Ellickson, of the Rand Corporation's Drug Policy Research Center, and her colleagues analyzed survey data from 5,833 California and Oregon middle school students. The participants completed the surveys six times over a 10-year period between the ages of 13 and 23. About 44 percent of them also responded to survey questions at age 29.

A total of 3,185 participants identified themselves as marijuana users, while 2,648 reported they did not use the drug. The scientists categorized the marijuana users into four groups, based on the age at which they began using marijuana and their subsequent level of use.

The researchers then compared responses from the marijuana users at age 29 with data from age-matched abstainers. They found that abstainers had an overall higher level of educational attainment, better health, greater life satisfaction, and a lower rate of other drug use. In contrast, those who had reported a relatively high level of marijuana use at age 13 fared significantly worse than all other groups on overall health and yearly earnings.

- **WHAT IT MEANS:** People underestimate the harm marijuana can cause on many aspects of their lives.

The scientists published this NIDA-funded study in the May 2004 issue of *Health Psychology*.

Sight, Smell of Favorite Foods Are Related to Drug Craving

A team of researchers that included NIDA Director Dr. Nora Volkow indicates that peoples' brains "light up" when they see and smell their favorite foods, a response similar to that observed in cocaine addicts when they think about using the drug.

Led by Dr. Gene-Jack Wang of the Brookhaven National Laboratory, the scientists used positron emission tomography (PET) to examine metabolic changes in the brains of 12 healthy, food-deprived adults who had been asked to provide information about their favorite foods. Between 17 and 19 hours after the participants' last meals, the scientists presented them with samples of these foods to taste and smell while their brains were being scanned. In a second phase of the study, the scientists presented the participants with neutral, nonfood items while initiating PET scans.

The researchers found that food presentation significantly increased metabolism in the whole brain by 24 percent. Changes were most noticeable in areas of the brain that have been implicated in addiction—the anterior insula and the orbitofrontal cortices.

- **WHAT IT MEANS:** This research suggests that the same brain regions play roles in the desire and motivation for such natural stimuli as food, as well as drug craving in drug-addicted people.

The scientists published this study in the April 2004 issue of *NeuroImage*.

Earning a Reward Elicits Greater Brain Activity Than Merely Receiving One

Results of a NIDA-funded study show that a part of the brain associated with reward processing and pleasure becomes more active when someone “earns” money compared with just receiving a prize.

Scientists at the Emory University School of Medicine used functional magnetic resonance imaging (fMRI)—which measures the quick, tiny metabolic changes that take place in an active part of the brain—to assess brain activity in response to monetary reward.

In their study, 16 healthy adults played a simple computer game in which a representation of paper money occasionally appeared on the video screen and automatically dropped into a bag. The participant received the amount of money that collected in the bag. In another version of the game, the participant had to push a button to make the bill drop into the bag. In this case, receiving the collected money was contingent on the person’s performance. In yet another version of the game, an ill-defined shape (described by the researchers as a “blob”) either passively dropped into the collecting bag, or the participant directed it into the bag.

The researchers observed that the striatum, a brain structure associated with reward processing and pleasure, became active only when the participant pushed the button that resulted in money dropping into the bag—essentially earning the money.

They also measured general arousal via skin conductance responses, which technicians use in lie detector tests. Active participation in receiving the reward was the only condition that elicited a higher measure of skin conductance, indicating greater arousal.

- **WHAT IT MEANS:** This study suggests that the striatum’s role in reward processing depends on the context in which the reward—identified in this study as money—is obtained, rather than the reward’s value or pleasurable feelings.

Dr. Gregory Berns and his colleagues published their findings in the May 13, 2004 issue of the journal *Neuron*.

Novel Compounds Reduce Cocaine Toxicity in Mice

There are no effective medications for the treatment of cocaine abuse, despite its detrimental health and societal consequences. Higher doses of cocaine produce toxic symptoms, including psychotic behavior, seizures, and sudden cardiac arrest and death. In a study, Dr. Rae Matsumoto and colleagues at the University of Oklahoma Health Sciences Center have demonstrated that three new compounds show promise as possible medications for reducing cocaine toxicity.

Dr. Matsumoto, currently at the University of Mississippi, and his team built on previous research demonstrating that sigma receptors located in the brain and heart are promising biological targets to counter cocaine toxicity. The team’s earlier investigations found that the compound BD1008 and related compounds block these receptors and reduce some behavioral effects of cocaine.

After producing six new BD1008 compounds, Dr. Matsumoto and colleagues tested the chemicals at various doses to determine if they would bind to the brain receptors and reduce two important measures of cocaine-induced toxicity in mice—convulsions and death. The researchers pretreated different groups of mice with saline or one of the six compounds, each at a different dose. Fifteen minutes later, the mice received an injection of cocaine at a dose known to produce convulsions. Within 30 minutes, all mice given saline experienced convulsions. However, pretreatment with certain doses of three of the new compounds—UMB 100, 101, and 103—significantly reduced this percentage to at least half, and to about 25 percent at the best doses. The investigators next pretreated mice 15 minutes before a lethal dose of cocaine. All mice given saline died, but pretreatment with UMB 100, 101, and 103 significantly reduced this percentage to about 25 percent.

- **WHAT IT MEANS:** The results suggest that three novel compounds are possible medication leads for treatment of cocaine toxicity. These compounds bind strongly to sigma receptors in the brain and significantly reduce cocaine-induced convulsions and death in mice. Researchers may find the chemicals useful for studying the effects of cocaine at these sites.

Dr. Matsumoto and colleagues published this NIDA-funded study in the May 2004 issue of the *European Journal of Pharmacology*.

Studies Suggest Common Factors Responsible for Marijuana and Co-Occurring Drug Abuse

Marijuana and other drugs of abuse often are used concurrently, and one model of explanation claims that marijuana use leads to the use of other substances. However, research by Arpana Agrawal and her colleagues at the Medical College of Virginia, Richmond, suggests that the propensity to use multiple drugs depends not on an introduction to drug use through marijuana, but on common genetic and environmental factors that influence the decision to use a variety of substances.

The researchers analyzed survey data from 1,191 male and 934 female same-sex twin pairs to test 13 different models to understand the co-occurrence of marijuana use with other substances of abuse.

The scientists found that one model—the correlated liabilities model, which proposes that use of marijuana and other illicit drugs are influenced by genetic and environmental factors that are common to these substances—provided the best fit for explaining co-occurring drug use in men and women. Genetic factors would include genes that influence common neurobiological pathways for addiction, while environmental factors might include influences on behaviors that impact novelty-taking or risk-seeking, such as social pressure or the availability of multiple drugs.

In another published study, these researchers used the same twin data to further examine the association between early use of marijuana and subsequent use of other drugs. These findings also suggest that the relationship between early use of marijuana and subsequent use of other illicit drugs seems to depend mainly on correlated genetic and environmental factors. In addition, the scientists report that early use of marijuana in one twin strongly influences other illicit drug use and abuse or addiction in the other twin.

- **WHAT IT MEANS:** Although marijuana use may precede use of other drugs of abuse, prevention programs may not be successful if they do not take into account the underlying biology that predisposes people to use multiple drugs. Successful programs should focus on minimizing or eliminating risk factors that may be common to different drugs of abuse.

These studies, which received funding from NIDA, were published in the May 2004 issue of *Behavior Genetics* and the June 2004 issue of *Psychological Medicine*.

Activity, Involvement Key to Adolescents Not Smoking

Adolescents who are involved with school activities, academic pursuits, and physical activities (including participation in team sports) are less likely to begin smoking cigarettes or progress to regular smoking.

Dr. Janet Audrain-McGovern, of the University of Pennsylvania, and her colleagues followed 983 adolescents in five public high schools in Northern Virginia. They collected survey data four times during 9th, 10th, and 11th grades.

The researchers found that involvement in activities or schoolwork was associated with a twofold reduced likelihood of smoking progression. Similarly, there was a significant association between progressing to regular smoking and nonparticipation.

The survey data also showed an upward trend in student smoking from 9th grade to 11th grade.

In a second study, Dr. Audrain-McGovern and Dr. Daniel Rodriguez, also of the University of Pennsylvania, assessed smoking likelihood among 1,098 Northern Virginia adolescents in grades 9 to 11 with different patterns of team sports participation.

They found that adolescents whose participation in team sports was erratic or decreased steadily were more likely to smoke than adolescents with either low or high participation in team sports.

- **WHAT IT MEANS:** Encouraging students to actively participate in academic achievement activities or extracurricular activities like team sports may help protect them against smoking. People who work with youth sports programs should focus on ways to improve accessibility and retention.

Dr. Audrain-McGovern and her colleagues published the first study in the March 2004 issue of *Psychology of Addictive Behaviors*. She and Dr. Rodriguez published the second study in the June 2004 issue of the *Journal of Pediatric Psychology*. Both studies were partly funded by NIDA.

Experimental Compound May Lead to New Anti-Addiction Medications

In the not-too-distant future, people struggling with drug addiction may benefit from new drugs based on a synthetic chemical that targets the brain's "bliss" system.

Dr. Daniele Piomelli and his colleagues at the University of California at Irvine College of Medicine, in collaboration with Dr. Alex Makriyannis at the University of Connecticut, have created a molecule, AM1172, that regulates the way the brain chemical anandamide is processed. Derived from an ancient Indian-language word meaning "bliss," anandamide is a natural cannabinoid, or marijuana-like compound, that acts on certain brain receptors involved in pain, mood, and appetite. For example, when the body senses pain, anandamide binds to CB-1 cannabinoid receptors and nullifies the sensation by blocking the ability of the nerves to transmit the signal. However, this effect is short-lived because anandamide is quickly broken down.

In the current study, tests on mice showed that AM1172 keeps anandamide from degrading and prevents its transport from the intercellular spaces between neurons into the cells.

- **WHAT IT MEANS:** By blocking anandamide degradation, and boosting its actions without activating the brain's cannabinoid receptors, AM1172 can selectively target specific receptors involved with specific behaviors.

This NIDA-funded study was published in the June 8, 2004 issue of the *Proceedings of the National Academy of Sciences*.

Death Risk Rises for New Injection Drug User

People who recently began injecting heroin or cocaine face a risk of death more than three times higher than similarly aged people who do not inject drugs, researchers report. This study is one of the first using new onset injection drug users to suggest that mortality risk rises significantly soon after a person starts injecting and continues to escalate.

In the study, scientists recruited 256 new onset injection drug users in Baltimore in 1988–89, and followed them for 12 years.

After only 3 years of injecting, drug users faced a death risk that was 3.1 times higher than what would be expected among the general population of their peers in the same age, gender, and race groups. The risk of death after 8 years was 8-fold higher than their peers. Causes of death included HIV/AIDS, drug overdose, cardiovascular disease, gunshot, and medical complications of drug abuse, such as liver disease.

- **WHAT IT MEANS:** Data from this study suggest that the danger of death associated with injection drug use starts early, and the risk increases with continued injections.

Dr. David Vlahov and his colleagues at the New York Academy of Medicine and the Johns Hopkins Bloomberg School of Public Health published this NIDA-funded study in the August 2004 issue of the journal *Addiction*.

Short-Term Treatments Benefit Women With Coexisting Substance Abuse and Post-Traumatic Stress Disorder

Results of a NIDA-funded study suggest that two short-term treatment programs can effectively reduce substance abuse and symptoms of post-traumatic stress disorder (PTSD) in women.

Up to 80 percent of women seeking substance abuse treatment report lifetime histories of sexual and/or physical assault, and a substantial subset have symptoms of PTSD, the researchers report.

One-hundred seven urban, low-income women between 18 and 55 years of age diagnosed with comorbid substance abuse and PTSD participated in the study. Seventy-five were randomly assigned to receive one of two

cognitive-behavioral treatments (“Seeking Safety” or “Relapse Prevention Treatment”), and 32 were assigned to a community care group that received other therapies. All treatments were administered during a 3-month period. The women were assessed at the end of treatment, and at 6 months and 9 months post-treatment.

In the Seeking Safety model, the clinician simultaneously addresses substance abuse and trauma issues. Relapse Prevention Treatment, considered to be the “gold standard” for addiction treatment, focuses on identifying triggers for substance cravings and relapse and coping strategies for managing them. Women in the community care group received such local care as outpatient psychological treatment that did not conform to Seeking Safety or Relapse Prevention protocols, but may have included psychiatric medication, inpatient psychiatric treatment, other drug or alcohol treatment, or attended self-help meetings.

At the end of 3 months of treatment, participants who received both forms of cognitive-behavioral treatment had significant reductions in substance abuse and PTSD symptom severity compared to women in the community care group. In addition, women who received either of these treatments showed sustained improvement in both areas at 6 and 9 months post-treatment. Women in the comparison group showed no significant changes and their PTSD symptoms worsened over time.

- **WHAT IT MEANS:** These findings illustrate that carefully conducted cognitive-behavioral treatments can substantially decrease symptoms of substance abuse and concurrent PTSD in a relatively brief period in a hard-to-reach and often underserved population. The study also generated strong support for the Seeking Safety model by showing it to be as effective as Relapse Prevention.

Dr. Denise Hien and her colleagues at the Women’s Health Project Treatment and Research Center at St. Luke’s/Roosevelt Hospital Center in New York City published the study in the August 2004 issue of the *American Journal of Psychiatry*.

Research Examines Patient Placement Criteria in Addiction Treatment

A series of reports published in 2004 as a special issue of the *Journal of Addictive Diseases* examined the American Society of Addiction Medicine (ASAM) addiction treatment criteria to assess patient outcomes and service utilization. The reports suggest that ASAM’s Patient Placement Criteria are associated with less morbidity, better post-treatment outcomes, and less overall service utilization.

Because no single treatment model or level of care is appropriate for all people with substance abuse disorders, it became essential to develop ways to match such individuals to a variety of modalities and levels of care. But standardized placement matching for substance abuse and addictive disorders poses challenges due to variability in settings, services, syndromes, and other factors. Despite these obstacles, guidelines for placement, continued stay, and discharge have been developed by ASAM with input from NIDA and others. And, with these strategies in place, it has become possible to initiate controlled research with placement criteria in a continuing effort to refine treatment plans and policies.

The NIDA-funded research topics included in the publication include:

- Determining Service Variations Between and Within ASAM Levels of Care;
- Impact of Patient Placement Criteria on Substance Abuse Treatment Under the Oregon Health Plan;
- Reliability of Multidimensional Substance Abuse Treatment Matching: Implementing the ASAM Patient Placement Criteria;
- Development of Service Intensity Criteria and Program Categories for Individuals with Co-Occurring Disorders;
- Feasibility of Multidimensional Substance Abuse Treatment Matching: Automating the ASAM Patient Placement Criteria; and
- Predictive Validity of the ASAM Patient Placement Criteria for Naturalistically Matched vs. Mismatched Alcoholism Patients.

Dr. David Gastfriend, editor of these published reports titled "Addiction Treatment Matching: Research Foundations of the American Society of Addiction Medicine (ASAM) Criteria," notes that this first volume of papers on the ASAM Criteria establishes a knowledge foundation to support a new architecture for the information technology of substance disorder treatment.

Funding News

Request for Applications

The NIH Roadmap is a series of initiatives designed to pursue major opportunities in biomedical research and address gaps in current knowledge that must be addressed by NIH as a whole, rather than through any one institute or agency.

Here are new requests for applications (RFAs) under the NIH Roadmap:

Interdisciplinary Training: Behavior, Environment, and Biology (RFA-RM-05-010)

Many of today's pressing health problems involve disease processes that are influenced by biological, behavioral, and social environment factors. The purpose of this National Research Service Award is to help train scientists with diverse skills and knowledge that can be used to integrate multiple interdisciplinary approaches to solve complex health problems.

Eligible organizations include domestic, nonprofit, public and private entities with strong, well-established research and training programs.

Examples of research areas that might benefit from an interdisciplinary approach may include:

- Clarifying the biological mechanisms by which racial, ethnic, socioeconomic, and gender inequality affect physiology;
- Treatment of drug addiction based on translating basic behavioral science, and on cognitive, affective, and social neuroscience research into novel behavioral therapies;
- Understanding the roles of biological, social, and environmental factors in the manifestation of conditions in which pain is the primary symptom.

It is anticipated that programs will provide formal coursework and research training for individuals already holding advanced degrees (e.g., training an epidemiologist in cognitive neuroscience, or an economist in behavior genetics).

Letters of intent must be received by January 14, 2005. For more information, go to <http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-05-010.html>.

Pilot-Scale Libraries for High-Throughput Screening (RFA-RM-05-014)

High-throughput screening techniques have revolutionized the ability to quickly and efficiently screen high numbers of small molecules to identify those that have therapeutic potential. However, members of the academic community often have limited access to automated screening facilities and libraries of structurally diverse compounds.

Thus, the purpose of this project is to solicit applications for chemical library generation to increase the diversity and utility of the NIH Molecular Libraries Small-Molecule Repository.

Eligible organizations include for-profit or nonprofit organizations; public or private institutions, such as colleges, universities, hospitals, and laboratories; units of state and local governments; eligible Federal agencies; and domestic institutions or organizations.

Letters of intent must be received by January 14, 2005. For more information, go to <http://grants1.nih.gov/grants/guide/rfa-files/RFA-RM-05-014>.

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Assay Development for High-Throughput Molecular Screening (RFA-RM-05-011)

For several years, scientists have been able to identify and catalog genes and associated proteins, including those that promote or inhibit disease. What they lacked was a way of doing a mass study of possible chemical agents. High-throughput molecular screening is the automated, simultaneous testing of thousands of distinct chemical compounds in models of biological mechanisms or diseases.

The goal of this request for application (RFA) is to initiate a continuously evolving stream of scientifically and technologically outstanding assays that can be automated and used for screening at the molecular libraries screening centers. It is open to all areas of biological and biomedical research, with the goal of providing new ways to explore the functions of major components of the cell.

This RFA will support the development of innovative assays for use in both basic research and therapeutics development programs, with an emphasis on novelty of approach to biology or disease. Appropriate assays might include but are not limited to:

- biochemical or cell-based assays of activity or interaction involving proteins and/or other biological molecules;
- assays of cellular or molecular phenotypes;
- assays using model organisms such as yeast or *C. elegans*;
- assays involving mutant proteins associated with disease; and
- modulation of expression of genes of interest, including effects on transcription, translation, or RNA splicing.

Letters of intent must be received by January 31, 2005. For more information about this RFA, go to <http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-05-011.html>.

Exploratory Centers for Cheminformatics Research (RFA-RM-05-012)

A key facet of any drug discovery effort is the library-screening step in which researchers test millions of chemical compounds for a desired property. Scientists must try to determine what the results have in common chemically, and then they must scour chemical libraries for other candidate compounds containing those features. This, fundamentally, is the challenge of cheminformatics, which may be defined as the application of techniques and technology associated with managing chemical structures databases, especially small, drug-like structures.

The purpose of this request for application (RFA) is to invite applications to establish Exploratory Centers for Cheminformatics Research. Support provided under this RFA will stimulate the creation of multi-investigator research centers that will develop state-of-the-art methodologies for computational exploration of chemical diversity space and the relationship to biological activities.

Examples of topics that would be appropriate for investigation under this RFA include:

- the design, operation, and dissemination of virtual chemical library enumeration and screening algorithms;
- tools for user-defined multidimensional analysis of high-throughput screening data; and
- analysis of the dimensionality of chemical diversity space critical for designing an optimal compound collection for screening of biological targets.

Letters of intent must be received by February 17, 2005. For more information about this RFA, go to <http://grants1.nih.gov/grants/guide/rfa-files/RFA-RM-05-012>.

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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The National Institute on Drug Abuse
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