

NATIONAL INSTITUTES OF HEALTH



NIDA NEWS  



HOME
ABOUT NIDA
NEWS
MEETINGS & EVENTS
FUNDING
PUBLICATIONS
SEARCH

MEDICAL & HEALTH PROFESSIONALS
RESEARCHERS
PARENTS & TEACHERS
STUDENTS & YOUNG ADULTS
EN ESPAÑOL

[NIDA Home](#) > [Publications](#) > [NIDA Notes](#) > [Vol. 21, No. 1](#) > [Research Findings](#)

Research Findings
Vol. 21, No. 1 (October 2006)

Low-Cost Incentives Improve Outcomes in Stimulant Abuse Treatment

In community-based treatment programs, the intervention added \$2.42 per patient per day to counseling costs.

BY LORI WHITTEN, *NIDA Notes* Staff Writer

The opportunity to win rewards worth as little as \$1 for abstinence can help motivate outpatients to stay in behavioral therapy and remain drug-free, according to a NIDA Clinical Trials Network (CTN) study. At eight community-based addiction treatment programs across the United States, stimulant abusers who could earn a chance to win a prize by providing drug-free urine samples were four times as likely as peers who were not offered this incentive to attain 12 weeks of continuous abstinence. Prizes for the incentive intervention cost the programs about \$200, or \$2.42 a day per participant.

Many addiction treatment clinics face the challenge of high patient dropout rates. Reinforcing abstinence helps keep patients interested in attending treatment for longer periods, which can facilitate behavioral changes to keep them off drugs for the long haul," says Dr. Nancy Petry of the University of Connecticut School of Medicine, coleader of the study. Prior research has found that, no matter how it is achieved, duration of abstinence during treatment is one of the best predictors of abstinence 1 year later. "More patients achieve this therapeutic milestone with a boost from incentive programs," says the study's other coleader, Dr. Maxine Stitzer of The Johns Hopkins University School of Medicine.

The CTN investigators randomly assigned 415 treatment-seeking stimulant abusers ([see chart](#)) to one of two conditions: usual care or usual care plus abstinence-based incentives for 12 weeks. Usual care typically consisted of group counseling, although some patients received individual and family therapy. Patients gave urine and breath samples twice weekly. Research assistants tested the urine samples for stimulants, opiates, and marijuana, and tested the breath samples for alcohol.

CHARACTERISTICS OF STUDY PARTICIPANTS	
Patients at eight community-based clinics across the country were ethnically diverse and generally reflected the national population of treatment-seeking stimulant abusers.	
Characteristic	%
Ethnicity	
White	42
African-American	35
Hispanic	12
Other	9
Male	44

Unemployed	65
On parole or probation	35
Abuse of other drugs	
Alcohol	42
Marijuana	20
Opioids	9

Each participant in the incentive condition received immediate feedback on his or her samples. After submitting stimulant- and alcohol-negative samples, the patient could draw from an opaque container with 500 chips, each with words of encouragement or an assigned value: Half of the chips simply said, "good job;" 209 could be traded for \$1 prizes, 40 for \$20 prizes, and 1 for a \$100 prize. Prizes were conferred immediately and included many options, ranging from toiletries, snacks, and bus tokens to kitchen items, telephones, and retail store certificates for televisions, music players, and DVD players. The number of draws earned increased by one each week in which all the patient's samples were stimulant- and alcohol-negative, but fell back to one following a positive sample or an unexcused absence. When a participant first achieved two consecutive weeks of abstinence, he or she received a \$20 prize. Participants who submitted stimulant- and alcohol-negative samples could earn two bonus draws a week if their urine samples were also opioid- and marijuana-negative.

More patients in the incentive program (49 percent) than in usual care (35 percent) completed 12 weeks of counseling. Patients in the incentive group achieved an average duration of sustained abstinence of 4.4 consecutive weeks, compared with only 2.6 weeks among counseling-only patients. Nineteen percent of patients receiving the incentive intervention attained 12 weeks of continuous abstinence compared with 5 percent of those in usual care. Intervention patients also attended more counseling sessions (19 versus 16) and submitted more stimulant-negative urine samples during treatment than patients in usual care (48 versus 36 percent).

Blending Initiative Disseminates Information on Low-Cost Incentives

Clinicians and administrators who wish to learn more about using low-cost incentives to motivate patients to stay off drugs can get information through the Blending Initiative, a program established by NIDA and the Substance Abuse and Mental Health Services Administration to speed the adoption of scientific findings into drug abuse treatment. The Blending Initiative has developed an awareness program that disseminates practical information on low-cost incentive programs and a summary of research evidence that supports their use as an adjunct to addiction treatment.

A DVD/CD-ROM describes the principles underlying incentive programs, the range of behaviors that clinics can target, and findings from studies of the intervention with a variety of patient populations. In the video component, clinicians, patients, and managers describe their experiences with the use of low-cost incentives in Manhattan and Connecticut outpatient methadone treatment programs. Viewers observe a group of Connecticut clients participating in a prize draw and a panel of directors and clinical managers discussing implementation challenges, ways to overcome problems, and the reasons they think the low-cost incentive program is effective. The CD-ROM component includes a flexible PowerPoint presentation suited for executive briefings or a 3-hour workshop. The Blending Initiative expects to release the information package in fall 2006, and it will be posted on NIDA's Web site, www.drugabuse.gov and on the Addiction Technology

Transfer Center (ATTC) Web site, www.nattc.org.

"We anticipate that the awareness campaign will leave the addiction treatment community wanting more, for example, Web-based training and workshops on how to implement low-cost incentive programs," says Ms. Lonnetta Albright, director of the Great Lakes ATTC and leader of the Promoting Awareness of Motivational Incentives Blending Team. The 2006 Blending Initiative program, "Bridges to the Future," was held October 16 and 17, 2006 in Seattle, Washington (see www.sei2003.com/blendingseattle/topics.htm).

INCENTIVES ACCENTUATE THE POSITIVE

"Incentive programs, including low-cost ones, add excitement and additional reasons to attend substance abuse treatment. Many substance abusers are ambivalent about treatment, and rewards may help them stay involved in counseling," says Dr. Petry. Extending retention in treatment may prolong abstinence, in part, because it gives counselors more time to help patients re-engage in a drug-free lifestyle, says Dr. Stitzer. Helping patients sustain abstinence once they leave therapy is a challenge for all treatments, including incentive programs.

Some previous clinical trials of voucher-based incentive programs showed benefits of the treatment persisting for 1 to 2 years, but others found no added value over the long term compared with usual care. Further research will focus on followup with patients to determine the conditions under which incentive interventions, particularly as applied by community-based treatment programs, support extended abstinence.

Other relatively small, often single-site NIDA-funded clinical trials over the past 15 years have demonstrated that motivational incentives are an effective adjunct to standard therapy for opiate-, marijuana-, alcohol-, and cocaine-addicted patients. Patients in most of those early studies always received vouchers exchangeable for goods or services, rather than chances to win prizes, for positive behaviors; costs typically ran to about \$1,000 per patient over 3 months, with the result that few community programs adopted the motivational incentive approach. Dr. Petry developed her prize-drawing system to make incentives affordable for community programs. She has tested it successfully in several Connecticut treatment programs, and now its effectiveness is confirmed by the CTN trial. NIDA is collaborating with the Substance Abuse and Mental Health Services Administration's Addiction Technology Transfer Center to promote awareness of the low-cost motivational incentive technique ([see textbox](#)).

The CTN researchers note that some community-based treatment providers resist the idea of motivational incentives based on a belief that clinicians should not reward patients for behaviors "that they are supposed to do anyway." In response, the researchers point out that groups and individuals often use external incentives to motivate others—from employees' bonuses to children's allowances for household chores. Dr. Stitzer advocates a shift in perspective from punishing lapses to celebrating successes. She observes that counselors have often changed their views when they have seen incentives help revolving-door patients stay in therapy. "Incentive programs—the idea of catching people being good and rewarding the behavior—can infuse addiction treatment with a positive outlook and reinvigorate patients and counselors," says Dr. Stitzer.

SOURCE

Petry, N.M., et al. Effect of prize-based incentives on outcomes in stimulant abusers in outpatient psychosocial treatment programs: A National Drug Abuse

Treatment Clinical Trials Network Study. *Archives of General Psychiatry*
62(10):1148-1156, 2005. [[Abstract](#)]

Volume 21, Number 1 (October 2006)

[NIDA Home](#) | [Site Map](#) | [Search](#) | [FAQs](#) | [Accessibility](#) | [Privacy](#) | [FOIA \(NIH\)](#) | [Employment](#) | [Archives](#)



The National Institute on Drug Abuse (NIDA) is part of the [National Institutes of Health \(NIH\)](#), a component of the [U.S. Department of Health and Human Services](#). Questions? See our [Contact Information](#).





[NIDA Home](#) > [Publications](#) > [NIDA Notes](#) > [Vol. 20, No. 6](#) > [Research Findings](#)

Methamphetamine Evokes and Subverts Brain Protective Responses

Research Findings
Vol. 20, No. 6 (July 2006)

Two new studies appear to highlight the role of glial cells—the nervous system's equivalents to the body's immune cells—in methamphetamine abuse.

By Patick Zickler, NIDA NOTES Contributing Writer

NIDA-supported researchers have produced brain images demonstrating that structures in an area called the striatum expand in volume during early methamphetamine abuse, then regress toward normal. The investigators believe their findings likely are attributable to neuroprotective cells in the brain mounting an initial attempt to counteract the drug's toxic effects, which continued exposure subsequently overwhelms. In a related result, scientists working with mice have produced evidence that methamphetamine may prompt cells that normally serve neuroprotective functions to instead attack healthy brain cells.

STRUCTURAL FLUCTUATION SUGGESTS GLIAL ACTIVATION

Dr. Linda Chang (now at the University of Hawaii) and colleagues at the University of California, Los Angeles, used magnetic resonance imaging to measure the volumes of striatal brain structures, including the putamen and globus pallidus, in a group of methamphetamine abusers. The studied individuals, 26 women and 24 men (average age 31 years), had abused methamphetamine (average 1.6 g/day on 6.3 days/week) for periods ranging from 4 to 15 years. All had been abstinent for periods ranging from 1 week to 4 years at the time of the study; 44 also took tests of verbal memory and intelligence, gross and fine motor function, mood, executive function, and other capacities likely to be affected by striatal damage.

The researchers expected to find that the methamphetamine abusers' striatal regions were smaller than those of a comparison group of age- and gender-matched individuals with no history of methamphetamine abuse. Such a finding would be consistent with previous research showing that methamphetamine reduces the density of striatal dopamine terminals. Instead, says Dr. Chang, "Contrary to our hypothesis, striatal volumes were larger in the methamphetamine abusers as a group." The size difference was greatest among individuals with less cumulative exposure to the drug, and smaller among those with more. Those with the most exposure also performed slightly worse on neuropsychological tests of verbal fluency and visual-motor coordination.

Dr. Chang believes the surprising increase in striatal volumes of methamphetamine abusers may reflect the activity of glia—cells that provide protective and reparative functions for the brain's main functional cells, the neurons. When molecules potentially harmful to neurons penetrate the brain, glia mount a response resembling the inflammation and scar tissue formation associated with immune responses in other parts of the body. Possibly, Dr. Chang suggests, methamphetamine provokes glia to react in this way, leading to an increase in regional volume analogous to the swelling seen in bodily immune responses. Subsequently, she speculates, the glial response may taper off as cumulative exposure to the drug—and neuron damage—mount. Continued abuse results in damage that is manifested in decreased cognitive performance.

"This work is consistent with an increasing body of research that shows a relationship between methamphetamine exposure and structural changes in the brain," says Dr. Steven Grant of NIDA's Division of Clinical Neuroscience and Behavioral Research. "It

links methamphetamine abuse, structural change, and functional deficits and suggests that the magnitude of these effects is related to the degree of abuse. We don't understand what is happening at deeper levels, but the observations made in this study suggest that the volume changes are related to methamphetamine's direct or indirect effect on glial cells. We still need to understand how structural changes result in functional deficits; how much, if any, of this damage can be reversed; and how methamphetamine acts at the cellular level."

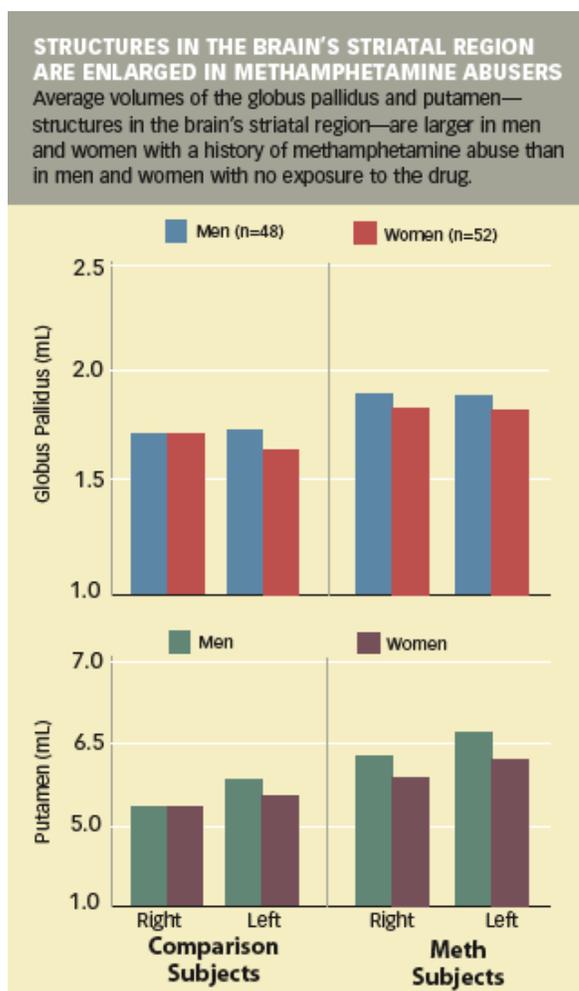
IN MICE, METHAMPHETAMINE MISDIRECTS GLIA TO ATTACK BRAIN CELLS

A study by Drs. Donald Kuhn and David Thomas and colleagues at Wayne State University School of Medicine indicates that methamphetamine's toxic effects may include subverting some glial cells to attack rather than preserve neurons. Specifically, their results indicate that the drug incites a subset of glia called microglia to mount an immune response against dopamine neurons.

Normally, microglia protect neurons against toxic injury by several mechanisms. They detect and bind to invading molecules, including viruses or bacteria, making them easily accessible to destructive immune system cells such as lymphocytes. As well, they produce compounds, some toxic, to help contain or eliminate the danger. Methamphetamine, the new study suggests, causes dopamine neurons to release a signal that decoys the microglia into turning these normally protective responses against the neurons themselves. When that happens, Dr. Kuhn says, "The microglia aren't reacting to methamphetamine's neural damage. Instead, they are active participants in the drug's neurotoxicity."

To begin their experiments, the researchers reasoned that if microglia contribute to methamphetamine toxicity to dopamine terminals, compounds that protect against such toxicity might do so, at least in part, by inhibiting microglial activation. Their first hypothesis, accordingly, was that the compound MK-801, which is known to be protective, blunts microglial activation. The team showed this to be the case by exposing cell cultures of mouse microglia to two proteins known to precipitate damaging microglial responses: lipopolysaccharide (LPS) and HIV Tat, a derivative of the human immunodeficiency virus. Compared with LPS and HIV Tat exposure without pretreatment, exposure following pretreatment with MK-801 significantly reduced the amount of two protein products of microglial activation, called cyclooxygenase-2 (Cox-2) and tumor necrosis factor- α (TNF- α). Dextromethorphan (DXM), a compound biochemically similar to MK-801, had the same effect.

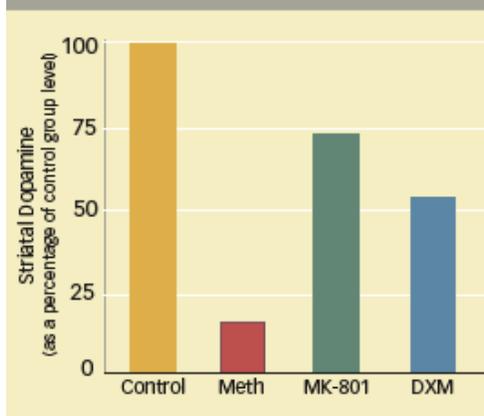
"These results suggested that both MK-801 and dextromethorphan exert direct action on the microglial cells in culture to block the activation process," Dr. Kuhn says. Having determined that the two compounds block microglial activation *in vitro*, the researchers next hypothesized that they would also do so in living animals.



Drs. Kuhn and Thomas injected mice with either MK-801 or DXM and then methamphetamine (5 mg/kg of body weight) 15 minutes later, repeating this sequence four times at 2-hour intervals. A control group of mice received the same regimen, but with saline substituted for methamphetamine. Forty-eight hours after the last injection, the researchers assayed the brains of the mice for Cox-2 and TNF- α , the indicators of microglia activation, and for striatal dopamine levels, a widely used index of damage to dopamine neurons. Dr. Kuhn says, "We found that both DXM and MK-801 significantly reduced the markers of striatal microglial activation associated with methamphetamine exposure and protected against dopamine nerve terminal damage in the striatum. The close association between the ability of MK-801 and DXM to significantly lower both microglial activation and neuronal damage suggests a causal link between the two. It looks as though the damage associated with methamphetamine abuse is the result of microglial action."

COMPOUNDS THAT BLOCK THE ACTION OF MICROGLIA COUNTER A TOXIC EFFECT OF METHAMPHETAMINE

Striatal regions of mice exposed to methamphetamine contain decreased dopamine content, compared with those of unexposed controls. Treatment with MK-801 or dextromethorphan (DXM) prior to methamphetamine injection reduced the extent of depletion, suggesting that microglia play a role in methamphetamine's toxic effect on the brain's dopamine system.



The apparent association of microglia and damage to dopamine neurons has implications beyond what it may reveal about methamphetamine abuse, says Dr. Jerry Frankenheim of NIDA's Division of Basic Neuroscience and Behavioral Research. "Microglia are the primary immune defense cells in the brain. They safeguard neural functions, yet excessive activation can cause microglia to harm neurons. Other research implicates microglial involvement in a wide range of neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, and stroke. Understanding how methamphetamine is able to decoy microglia into a destructive rather than reparative role could also help explain the processes involved in these other disorders."

SOURCES

Chang, L., et al. Enlarged striatum in abstinent methamphetamine abusers: A possible compensatory response. *Biological Psychiatry* 57(9):967-974, 2005. [[Abstract](#)]

Thomas, D.M., and Kuhn, D.M. MK-801 and dextromethorphan block microglial activation and protect against methamphetamine-induced neurotoxicity. *Brain Research* 1050(1-2):190-198, 2005. [[Abstract](#)]

Volume 20, Number 6 (July 2006)

[Archive Home](#) | [Accessibility](#) | [Privacy](#) | [FOIA \(NIH\)](#) | [Current NIDA Home Page](#)



The National Institute on Drug Abuse (NIDA) is part of the [National Institutes of Health \(NIH\)](#), a component of the [U.S. Department of Health and Human Services](#). Questions? See our [Contact Information](#).

