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## Brain Activity Patterns Signal Risk of Relapse to Methamphetamine

Research Findings  
 Vol. 20, No. 5 (April 2006)

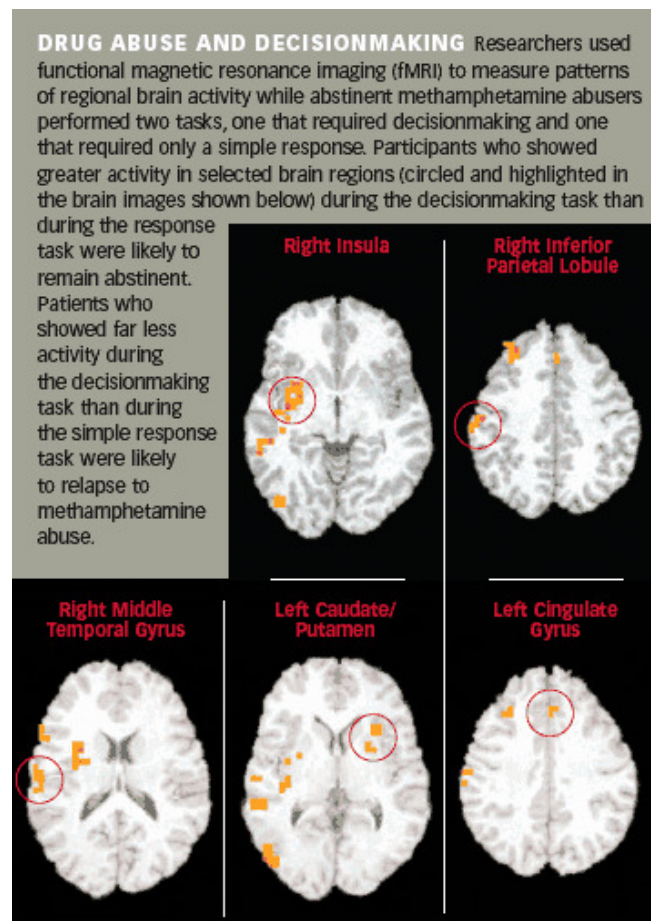
**Methamphetamine abusers who relapse after treatment appear to make decisions using different brain regions than do those who remain abstinent.**

**By Patrick Zickler, NIDA NOTES Contributing Writer**

NIDA-supported investigators have found that functional magnetic resonance imaging (fMRI) of the brain, performed during a psychological test, can predict with high accuracy whether an individual will relapse following treatment for methamphetamine abuse. Their study revealed a characteristic pattern of brain activity in methamphetamine-abusing men who relapsed within 1 to 3 years after completing treatment and a different pattern in men who did not.

Dr. Martin Paulus and colleagues at the University of California, San Diego, took the point of departure for their work from previous research that showed methamphetamine abusers and nonabusers activating different brain areas during psychological tests of decisionmaking. These earlier studies showed that poor choices made by drug abusers correlate to distinctive patterns of activity in some areas of the brain. Dr. Paulus's team hypothesized that activity patterns in those regions might also be associated with relapse to drug abuse, which involves similarly destructive decisions.

To test their hypothesis, the researchers recruited 46 men who had voluntarily entered and completed a 28-day inpatient drug treatment program after abusing methamphetamine for periods ranging from 3 to 34 years. When each man had been abstinent for about 4 weeks, he participated in two psychological tests. During one, he was asked to watch a computer screen and press



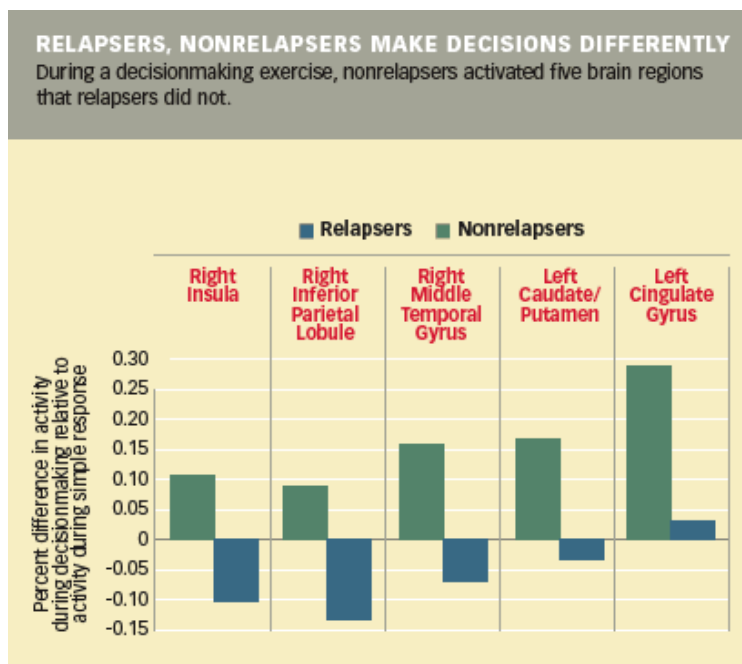
a button every time a symbol appeared. In the other, he was asked to try to predict whether a flashing symbol would next occur on the left side or right side of the computer screen. The difference between the two tasks was that, in the first, the test-taker needed only to react upon seeing the symbol, while in the second, he needed to decide which side to choose. The researchers recorded the men's brain activity with fMRI throughout the tests.

A year or more (360 to 967 days) after the imaging sessions, Dr. Paulus's team was able to locate and contact 40 of the 46 patients. Of these, 18 had relapsed to methamphetamine abuse (median time to relapse, 279 days; range, 36 to 820 days). Comparing their fMRI results with those of the 22 nonrelapsers, the researchers noted nine regions where the groups' brain activity had differed during decisionmaking. The relapse group showed less activation of the dorsolateral, prefrontal, parietal, and temporal cortices and the insula—regions associated with evaluation and choice among actions that may lead to either beneficial or harmful outcomes. The patterns of brain activation predicted relapse in 17 of the 18 men who had resumed methamphetamine abuse and predicted successful abstinence in 20 of the 22 patients who had not relapsed, Dr. Paulus says.

"The most striking aspect of this result is that the fMRI pattern has 90 percent accuracy in predicting outcome," Dr. Paulus says. "The differences in brain activity are pronounced, with little overlap." Differences in the right insula, right posterior cingulate, and right middle temporal gyrus differentiated relapsers from nonrelapsers. Other brain regions predicted the timing of relapse.

**"The most striking aspect of this result is that the fMRI pattern has 90 percent accuracy in predicting outcome. The differences in brain activity are pronounced, with little overlap."**

"Some of these predictive areas have not previously been strongly associated with drug abuse," observes Dr. Steven Grant of NIDA's Division of Clinical Neurosciences and Behavioral Research. "For example, while other investigators have reported alterations in the parietal lobe related to drug abuse, this is the first study to show the parietal cortex playing an important role. However, because so many brain regions were related to relapse, we still do not have a full understanding of what specific process might be dysfunctional in the relapse group."



The potential clinical implications of the new finding are promising, but uncertain. For example, no women were included among the participants, who were enrolled from treatment programs. "It's important to confirm the findings in women, for whom

social, demographic, and other factors associated with relapse may differ," Dr. Paulus points out. Nonetheless, he says that, in principle, programs treating methamphetamine abuse might use the fMRI protocol to assess patients, then assign those likelier to relapse to higher levels of care. Dr. Paulus believes such an approach might prove cost-effective, even with typical fMRI charges of up to \$700 per hour in academic imaging centers. "The human and social costs of relapse are high," Dr. Paulus says. "Using this imaging technique to precisely allocate care to the patients who need it most might well produce enough savings elsewhere to more than offset its expense. An alternative, more practical course of action might be to use these fMRI results as a benchmark for development of other assessments that are less costly, but have the same predictive strength."

#### Source

Paulus, M.P.; Tapert, S.F.; and Schuckit, M.A. Neural activation patterns of methamphetamine-dependent subjects during decision making predict relapse. *Archives of General Psychiatry* 62(7):761-768, 2005. [[Abstract](#)]

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## Community-Based Treatment Benefits Methamphetamine Abusers

Research Findings  
Vol. 20, No. 5 (April 2006)

**A large California study finds favorable effects for inpatients and outpatients; women's gains are larger.**

**By Lori Whitten, NIDA NOTES Staff Writer**

Methamphetamine abusers can achieve long-term abstinence with the help of standard community-based drug abuse treatment. Nine months after beginning therapy, 87 percent of patients treated for heavy or long-term methamphetamine abuse in California outpatient and residential programs were abstinent from all drugs, according to a NIDA-supported analysis. "In the public dialogue, and even among professionals in the field, one sometimes hears that meth abuse is 'not treatable.' But that view is not borne out by recent clinical trials or our study, which shows that community-based treatment reduces drug abuse and other problems," says lead investigator Dr. Yih-Ing Hser.

Dr. Hser and colleagues at the University of California, Los Angeles analyzed data from the California Treatment Outcome Project (CaTOP), an ongoing study that has followed the progress of adult substance abusers treated at 43 outpatient and residential programs throughout the State since April 2000. The researchers focused on 1,073 patients who reported that methamphetamine abuse was their primary drug problem (572) or that they had abused the stimulant regularly for at least 1 year before beginning treatment (501). Most were in their 30s or younger, White or Latino, unemployed, and on public assistance; most had an arrest history. They had abused methamphetamine for about 9 years, on average, and nearly one-quarter (22 percent) reported injecting drugs at least once. Although 64 percent had children aged 18 or younger, one-third of parents did not live with their children in the month before beginning treatment. One parent in five reported that a child protection court had ordered that his or her children live with someone else, and 6.3 percent had their parental rights terminated by the State.

The patients received the addiction treatment services routinely provided by each program. These usually included group therapy, with an average of 69 drug-related and 51 alcohol-related sessions during the first 3 months of treatment. On average, the patients also received 22 sessions on dealing with mental health symptoms and 13 addressing psychosocial problems, including family, parenting, and employment.

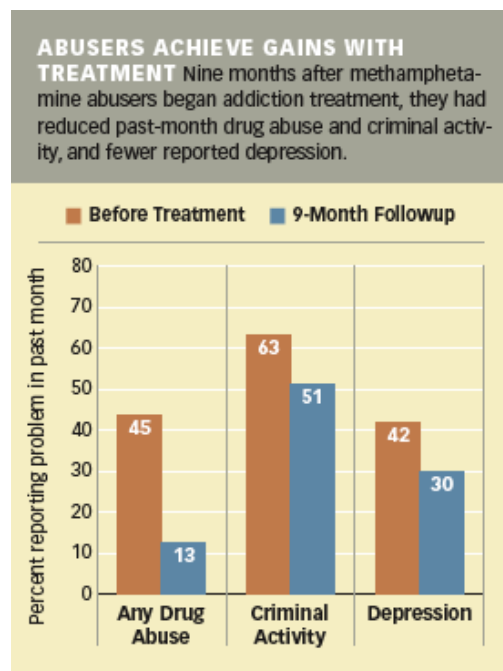
More than 60 percent of the patients completed 3 months of treatment. Among all the patients in the study—those who finished 3 months and those who did not—the average reported frequency of methamphetamine abuse fell from 2.7 to 0.5 days per month from the start of treatment to 9 months later. The portion who were abstinent from all drugs rose from 55 percent to 87 percent in the same interval, and 68 percent were abstinent and also not incarcerated. Patients improved in all areas—drug and alcohol abuse; mental health symptoms; and employment, family, and legal problems—except one: men's medical problems.

**"Because methamphetamine abusers respond to treatment, getting them into therapy is a top priority. For women, there is added urgency to help them avoid exposing the children they may bear to the consequences of prenatal drug exposure."**

Dr. Thomas Hilton of NIDA's Division of Epidemiology, Services and Prevention Research says these findings should reassure professionals working in the addiction, social services, and criminal justice fields that current therapies work for these troubled patients. "Dr. Hser's findings suggest that treatments available in the community help meth abusers reduce drug abuse and start to get their lives back on track, echoing prior research," he says.

**WOMEN'S EXPERIENCES**

Dr. Hser's findings confirm gender differences seen in other studies: Women began treatment with more severe psychosocial problems than men (see [chart](#)) and benefited more. Although treatment retention levels were similar for the two sexes, the women made greater gains in the areas of family relationships and medical problems, while achieving similar improvements in all other areas at the 9-month followup. The women's better outcomes may have resulted in part from more intensive services (see [chart](#)); as well, Dr. Hser says that many women in the study had a powerful motivator—family. "Many were trying to maintain or regain custody of their children by demonstrating improvement during treatment. Others had 'hit bottom,' saw how drug abuse was hurting their families, and decided to make a change," she says.



**WOMEN RECEIVE MORE SERVICES IN SOME AREAS** For some problems, women received more services than men during the first 3 months of treatment.

Services	Women (No. of interventions†)	Men (No. of interventions†)
Employment*	4.6	2.3
Family‡	6.5	4.6
Mental Health‡	23.6	19.9
Parenting*	4.2	1.7

†Includes counseling sessions, medical appointments, and prescriptions.  
\*Outpatients. ‡Outpatient and residential.

"Because methamphetamine abusers respond to treatment, getting them into therapy is a top priority. For women, there is added urgency to help them avoid exposing the children they may bear to the consequences of prenatal drug exposure," says Dr. Hser.

**MEN, WOMEN EXPERIENCE DIFFERENT PROBLEMS** Women beginning treatment for methamphetamine abuse reported more psychosocial problems, while men reported more crime and criminal justice involvement.

Family and Social Circumstances	Women, % (n=567)	Men, % (n=506)	Total, % (N=1073)
Children living with someone else by court order	29.3	9.9	20.1
Parental rights terminated	10.1	2.2	6.3
Family abused substances	21.7	10.5	16.4
Physically abused (past month)	5.5	1.8	3.7
Sexually abused (past month)	2.5	0.6	1.6

Employed	23.8	43.9	33.3
On public assistance	63.1	37.0	50.8
<b>Criminal Justice System Involvement</b>			
On parole	4.4	12.7	8.3
On probation	32.3	37.6	34.8
Ever arrested	76.7	88.3	82.2
Arrest in past year	36.7	45.1	40.6
Criminal activity (past month)	55.2	71.7	63.0
<b>Psychiatric Symptoms (Past Month)</b>			
Serious depression	38.8	29.8	34.6
Difficulties with understanding, concentrating, remembering	36.2	26.5	31.6
Suicidal thoughts	11.3	6.3	9.0
Prescribed psychiatric medicine	21.3	15.4	18.6

Dr. Hser and her colleagues continue to analyze CaTOP data, aiming to determine the longer-term impact of therapy and identify ways programs can improve outcomes. "Enhancing psychiatric, parenting, and employment services would better match patients' needs, and my team plans to study the relationship between help for these problems and longer-term outcomes," says Dr. Hser. They also plan to investigate whether women-only treatment is more effective for pregnant methamphetamine abusers than mixed-gender programs.

"The field needs more research following meth abusers over time to get a picture of the long-term outcomes of treatment, relapse episodes, and whether these patients require additional support to sustain gains made during therapy," says Dr. Hilton. "Because the availability of community health and social services varies across States, we cannot generalize the findings from one State, such as California. We need data from across the country," he adds.

#### Source

Hser, Y.-I.; Evans, E.; and Huang, Y.-C. Treatment outcomes among women and men methamphetamine abusers in California. *Journal of Substance Abuse Treatment* 28(1):77-85, 2005. [[Abstract](#)]

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## Mood Disorders in Methamphetamine Abusers Linked to Changes in Brain Metabolism

Research Findings  
Vol. 19, No. 4 (December 2004)

Impaired metabolism in one part of the brain, the striatum, may be the culprit in methamphetamine-linked mood disturbances. In a study similar to the one reported in the accompanying article (see "[Long-Term Abstinence Brings Partial Recovery From Methamphetamine Damage](#)"), 17 chronic abusers of methamphetamine underwent positron emission tomography (PET) brain scans in the first week of rehabilitative treatment, a time when many patients report high levels of depression and anxiety. The scans revealed that metabolic activity in the striatum varied with the severity of the patients' affective symptoms.

The patients in the study (11 men and 6 women, with an average age of 34.5 years) had used methamphetamine, on average, for about 10 years. PET studies also were conducted on a comparison group of 18 volunteers who had never taken the drug but had comparable histories of marijuana and alcohol abuse. The lead investigator on the NIDA-funded study was Dr. Edythe London of the University of California, Los Angeles.

All participants completed research questionnaires designed to assess levels of depression and of generalized (trait) and transitory (state) anxiety. For methamphetamine abusers, the average depression inventory score was 9.8 (scores between 9 and 15 are considered minimal to mild depression) compared with an average score of 1.1 for the comparison group. On a 1-to-4 scale of anxiety, abusers scored an average 1.9 for state anxiety and 2.2 for trait anxiety (compared with 1.4 and 1.5, respectively, for the comparison group). The higher measures of mood disturbances among methamphetamine abusers corresponded to differences, relative to the comparison group, in regional brain metabolism.

"It appears that, at least in early abstinence, methamphetamine abusers who report negative mood states have dysfunctions in these brain regions," says Dr. London. "The abnormalities in metabolism that we see involve brain regions that other investigations have implicated in mood regulation."

There is no pharmacological treatment for methamphetamine abuse, and negative moods can hinder behavioral therapy, which relies on patients' voluntary participation. "Early abstinence is the toughest stage of treatment for methamphetamine abuse," says Dr. Joseph Frascella of NIDA's Division of Clinical Neuroscience, Development, and Behavioral Treatments. "It's in the early stage that mood disturbances may derail or complicate the most effective treatment, cognitive behavioral therapy. Methamphetamine abuse and addiction do not exist in isolation, and this study suggests that associated depression and anxiety also must be addressed in treatment."

### Source

London, E.D., et al. Mood disturbances and regional cerebral metabolic abnormalities in recently abstinent methamphetamine abusers. *Archives of General Psychiatry* 61(1):73-84, 2004.  
[\[Abstract\]](#)

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