News Release

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Addicts' Brains Work Harder to Control Behavior

Overloaded circuits may explain tendency to binge, relapse

UPTON, NY - A brain-imaging study conducted at the U.S. Department of Energy's Brookhaven National Laboratory reveals that recently abstinent methamphetamine abusers who reported they avoided harmful situations had higher resting metabolic rates in a part of the brain responsible for making decisions and modifying behaviors than those with low harm-avoidance scores. In non-addicted, comparison subjects, there was no significant association between harm avoidance and metabolism in this brain region.

The findings, reported in the December 3, 2002, issue of *NeuroReport*, suggest that this higher-level brain center -- the orbitofrontal cortex -- is involved in drug addiction, and might be working extra hard in addicts trying to stay off drugs. Furthermore, the correlation between orbitofrontal cortex metabolism and harm-avoidance scores may indicate a greater vulnerability among addicts whose behavior-control centers are "maxed out" to have occasional episodes of lost control, or drug-taking binges.

"Drug addiction, by nature, is a relapsing disorder that is very hard to control," explains Brookhaven's Rita Goldstein, the lead author on the paper. "If addicts' behavior-control centers are already overworked, and you expose them to cues or environments that have previously been associated with drug use, or some kind of stress that increases their probability of relapse, they may no longer be able to resist the urge to use drugs."

Rita Goldstein

The study was conducted in 14 methamphetamine abusers who had not used methamphetamine or any other drug for at least two weeks and 22

comparison subjects. All subjects were asked to complete a personality questionnaire about their tendencies to approach or avoid physically dangerous activities and situations, which was used to derive each subject's "harm-avoidance" score. High-scoring people reported restricting themselves to relatively safe situations and avoiding danger.

Each subject also underwent a brain scan using positron emission tomography (PET) to measure resting baseline glucose metabolism in the orbitofrontal cortex. In this technique, each subject was given a radioactively labeled substitute for glucose, the brain¹s metabolic fuel. The PET camera picks up the signal from the radiotracer to indicate how much is present as an indicator of metabolic activity in various parts of the brain. The stronger the signal, the higher the metabolic activity.

Among the methamphetamine abusers, the higher the harm-avoidance score, the higher the relative metabolic activity in the orbitofrontal cortex compared to the rest of the brain. Non-addicted comparison subjects showed no significant association between harm avoidance and metabolism in this brain region. If anything, the control data showed a tendency toward the reverse: lower orbitofrontal resting metabolism in those most likely to avoid harm.

"The results indicate that, in the methamphetamine abusers, something may have gone awry in the orbitofrontal cortex," Goldstein says. Non-addicted subjects, she explains, maintain a steady state of metabolic activity, which allows the orbitofrontal cortex to exert control over behaviors. But in drug addicts, where the metabolic rate is variable and highest in those most interested in avoiding harm, the orbitofrontal cortex may fail to properly inhibit excessive drug consumption and may also fail to trigger aversive reactions to other potentially dangerous situations.

"This dysfunction may help explain why addicts often relapse to drug use shortly after being in drug rehabilitation, when they are no longer under the monitoring of a structured program," Goldstein says.

On a more hopeful note, Goldstein suggests that if addicts remain in treatment, and if treatment is not discontinued due to relapse but rather is intensified, their brain function might normalize over time to a point where they'd no longer have to work as hard to maintain control and where they'd no longer need as much external monitoring and guidance. She is planning a follow-up study to see how brain activity changes with prolonged abstinence, and whether differences in orbitofrontal cortex activity can predict either tendency to relapse or recovery success.

This research was funded by the National Institute on Drug Abuse, the National Institute on Alcohol Abuse and Alcoholism, and the U.S. Department of Energy, which supports basic research in a variety of scientific fields.

Related material: other news releases on addiction research at Brookhaven.

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