
FOR IMMEDIATE RELEASE
July 31, 2008

Contacts: Dorie Hightower or
Stephanie Older
(301) 443-6245
media@nida.nih.gov

A Long Lasting Impression: New Study Finds Persistent Brain Changes in Response to Cocaine Depend on the Expectation of Reward

NIDA Study Sheds Light on why Addiction is a Chronic Disease

Drug addiction dramatically shifts a person's attention, priorities, and behaviors towards a focus almost entirely on seeking out and taking drugs. Now, an animal study funded by the National Institute on Drug Abuse, part of the National Institutes of Health, has identified some of the specific long-term adaptations in the brain's reward system that may contribute to this shift. These long-lasting brain changes may underlie the maladaptive learning that contributes to addiction and to the propensity for relapse, even after years of abstinence from the drug. The study was published in *Neuron* on July 30, 2008.

Investigators from the University of California, San Francisco (UCSF) using an animal model of addiction, were able to distinguish brain changes in rats trained to self-administer cocaine, versus those animals that were trained to self-administer natural rewards such as food, or sucrose for several weeks. The investigators also were able to look at how much the "expectation" of receiving the drug influenced those brain changes by comparing rats trained to self-administer the drug versus animals who received the same amount of cocaine, but received it passively, i.e. they could not control their own drug taking by self-administration.

It has been hypothesized that persistent drug seeking alters the brain's natural reward and motivational system. The current study focuses on how drug seeking alters the communication between brain cells in this critical circuitry. In the normal processes of learning and memory formation there is a well documented strengthening of communication between brain cells, this process is known as "long-term potentiation" (LTP). The new study reports that LTP was similar in the rats that had learned to self-administer cocaine, food or sucrose, but with a critical distinction. The increase in LTP due to cocaine persisted for up to three months of abstinence, but the increase in response to natural rewards dissipated after only three weeks. Importantly, the nature of the

cocaine experience had a strong effect on the outcome, since rats exposed to cocaine when they did not expect it (passive infusions) displayed no LTP, neither transient nor long lasting. Finally, the study showed that LTP in rats that self-administered cocaine persisted after they were trained to stop drug self-administration behaviors. This indicates that, once established, it is very difficult to reverse the “memory trace” associated with drug reward.

“This research provides a better characterization of the variables, at the cellular, circuit, and behavioral level that contribute to the persistent nature of addictive disorders,” said Dr. Elias A. Zerhouni, NIH director.

“The researchers were able to illuminate why drug related memories are so stable,” said NIDA Director Dr. Nora Volkow. “Their persistence is highly refractory to new learning, which makes our jobs that much tougher, and reminds us that treatment must recognize and address the high propensity for relapse almost anywhere down the road.”

“These results indicate that the LTP induced by self administered cocaine is more persistent than that produced by natural rewards, such as food; and that the LTP is not just a result of exposure to cocaine, but also is linked to the drug’s effects and the animal’s learning to obtain the drug,” said Dr. Billy Chen, postdoctoral fellow at UCSF’s Ernest Gallo Clinic and Research Center and lead author of the study. “These are important distinctions that will help us better understand how addiction develops, and why drugs can overshadow other natural rewards and become the mainstay of an addicted person’s life.”

In 2006, six million Americans age 12 and older had abused cocaine in any form. There are currently no medications for cocaine addiction, therefore standard treatments typically rely on behavioral interventions. However, relapse after treatment for cocaine addiction is common.

###

The National Institute on Drug Abuse is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports most of the world’s research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to inform policy and improve practice. Fact sheets on the health effects of drugs of abuse and information on NIDA research and other activities can be found on the NIDA home page at www.drugabuse.gov.

The National Institutes of Health (NIH) - The Nation's Medical Research Agency - includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary Federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.