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Halting retrieval of drug-associated memories may prevent addiction relapse

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Disrupting the brain's retrieval of drug-associated memories may prevent relapse in drug addiction, according to new research in the August 13 issue of *The Journal of Neuroscience*. Researchers reduced drug-seeking behaviors in rats by blocking specific receptors in the brain during the recall of drug-associated memories. The NMDA-type glutamate receptor blocked in the study is important in learning and memory. The findings suggest potential new strategies to treat drug addiction in people.

The findings build on earlier research about learning and memory: researchers have known that during memory recall, even long-held memories can be altered. When they are retrieved, memories become unstable and can be reinforced, weakened, or altered in a process now called reconsolidation.

In drug abusers, researchers have known that recalling memories associated with past drug use, such as environmental cues, can cause them to relapse. The new study's authors, Amy Milton, PhD, Barry Everitt, ScD, and colleagues at the University of Cambridge showed that disrupting memories of drug-associated cues during reconsolidation reduced drug-seeking behavior, even in animals with extensive drug taking experience.

The researchers trained rats to associate the switching on of a light with an infusion of cocaine. Then the researchers "reactivated" the memory of the association by exposing the rats to the light without the cocaine infusion. Later, the rats continued to perform behaviors that turned on

the light — or learned to perform new behaviors — in an effort to get more cocaine.

However, when the researchers treated the rats with a chemical that interfered with the action of the NMDA-type glutamate receptor prior to the "reactivation" session, the rats showed reduced cocaine-seeking behaviors. Whether injected into a brain region activated by drug-associated cues, or given systemically, this single treatment reduced or even stopped drug-seeking behavior for up to a month.

In contrast, blocking NMDA-type glutamate receptors after or without the reactivation session had no effect on subsequent drug-seeking behaviors. These findings suggest that drug-associated memories and the drive to abuse drugs may be disrupted by blocking NMDA receptors during, but not after reconsolidation.

"This paper and the work that this group has done on reconsolidation and drug taking behaviors represent some of the most promising avenues of research for treating addiction," said Karim Nader, PhD, at McGill University, an expert unaffiliated with the study. "I don't know of any other study in the field of drug addiction where an acute treatment causes long-term cessation of drug taking behavior in rodent models," Nader said.

Previous efforts to expose human addicts to drug-associated cues in the absence of drug reward have been ineffective at preventing relapse. The current findings suggest that the combination of this existing therapy with properly timed use of NMDA receptor inhibitors may help addicts abstain from drugs. Several NMDA receptor inhibitors are already approved by the U.S. Food and Drug Administration, including the cough suppressant dextramethorphan and the Alzheimer's disease drug memantine.

"This is an example of hypothesis-driven basic research that can be readily translated to the treatment of cocaine addiction in humans," said Yavin Shaham, PhD, at the National Institute on Drug Abuse, an expert also uninvolved in the study.

Source: Society for Neuroscience