Study using animal model provides clues to why cocaine is so addictive

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A pile of cocaine hydrochloride. Credit: DEA Drug Enforcement Agency, public domain

Scientists at Wake Forest Baptist Medical Center are one step closer to understanding what causes cocaine to be so addictive. The research findings are published in the current issue of the *Journal of*

Neuroscience.

Cocaine addiction is a debilitating neurological disorder that affects more than 700,000 people in the United States alone, according to the Substance Abuse and Mental Health Services Administration. With repeated use, tolerance may develop, meaning more of the drug is required to achieve the same euphoric effect. Cocaine addiction can be characterized by repeated attempts at abstinence that often end in relapse.

"Scientists have known for years that cocaine affects the dopamine system and dopamine transporters, so we designed our study to gain a better understanding of how tolerance to cocaine develops via the dopamine transporters," said Sara R. Jones, Ph.D., professor of physiology and pharmacology at Wake Forest Baptist and lead author of the study.

"Currently there isn't any effective treatment available for cocaine addiction so understanding the underlying mechanism is essential for targeting potential new treatments."

Using an animal model, the research team replicated cocaine addiction by allowing rats to self-administer as much cocaine as they wanted (up to 40 doses) during a six-hour period. Six-hour-a-day access is long enough to cause escalation of intake and tip animals over from having controlled intake to more uncontrolled, binge-like behavior, Jones said.

Following the five-day experiment, the animals were not allowed cocaine for 14 or 60 days. After the periods of abstinence, the researchers looked at the animals' dopamine transporters and they appeared normal, just like those in the control animals that had only received saline.

However, a single self-administered infusion of cocaine at the end of

abstinence, even after 60 days, fully reinstated tolerance to cocaine's effects in the animals that had binged. In the control animals that had never received cocaine, a single dose did not have the same effect.

These data demonstrate that cocaine leaves a long-lasting imprint on the dopamine system that is activated by re-exposure to cocaine, Jones said. This 'priming effect,' which may be permanent, may contribute to the severity of relapse episodes in cocaine addicts.

"Even after 60 days of abstinence, which is roughly equivalent to four years in humans, it only took a single dose of cocaine to put the rats back to square one with regard to its' dopamine system and tolerance levels, and increased the likelihood of binging again," Jones said. "It's that terrible cycle of addiction."

Jones added that hope is on the horizon through preclinical trials that are testing several amphetamine-like drugs for effectiveness in treating cocaine addiction.

Provided by Wake Forest University Baptist Medical Center

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