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# Rat study reveals long-term effects of adolescent amphetamine abuse on the brain

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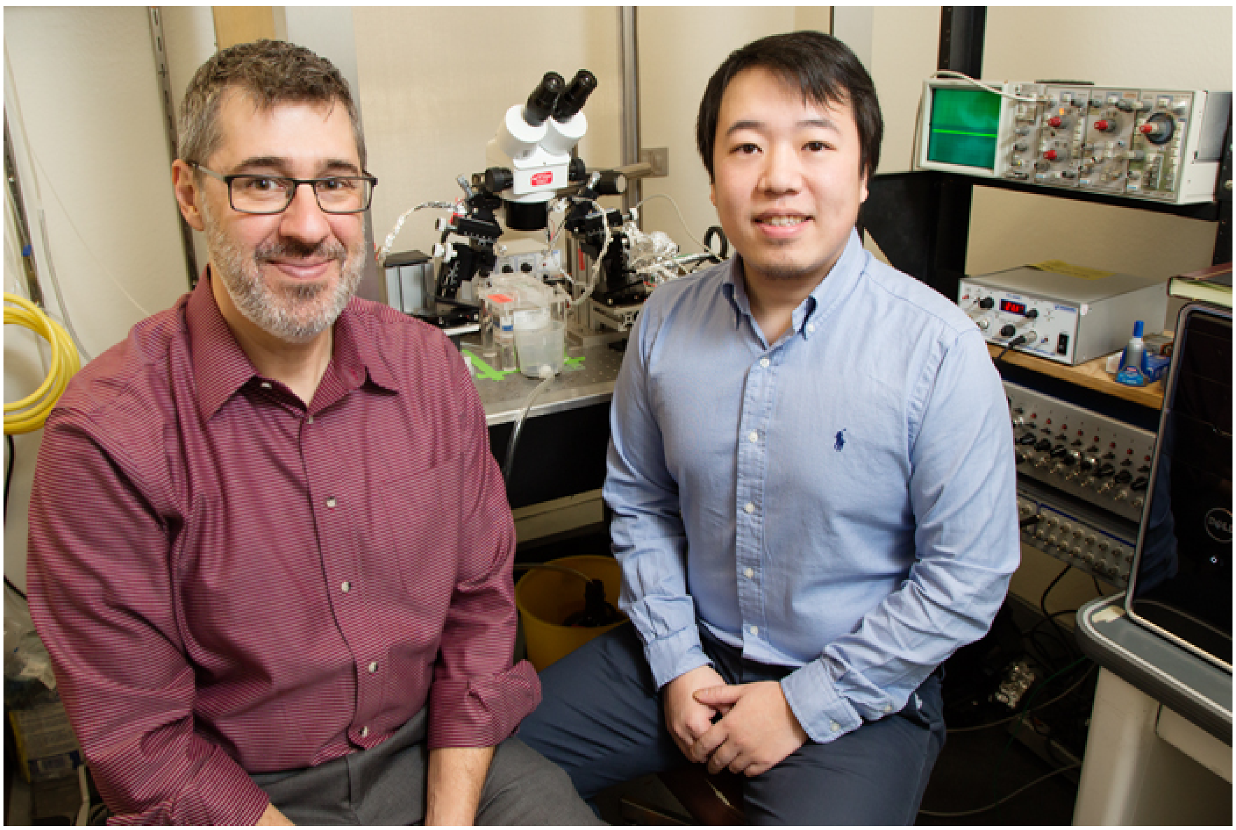

Psychology professor Joshua Gulley, left, graduate student Shuo Kang and their colleagues found that amphetamine abuse in young rats led to changes in dopamine signaling in the brain that persisted into adulthood. Credit: L. Brian Stauffer

A study of rats given regular, high doses of amphetamine finds that those exposed to the drug at an age corresponding to human adolescence experience long-term changes in brain function that persist into adulthood.

The study, reported in the journal *Neuroscience*, found that amphetamine leads to changes in dopamine signaling. Dopamine is a neurotransmitter that plays a role in memory, attention, learning and feelings of pleasure.

"The dopamine system, which continues to develop throughout adolescence and young adulthood, is a primary target of psychostimulant drugs like amphetamine," said University of Illinois psychology professor Joshua Gulley, who led the new research. "Changes in dopamine function in response to repeated drug exposure are likely to contribute to the behavioral consequences - addiction and relapse, for example - that abusers experience."

Parallels between rat and human development make rats a worthy model for the study of human drug addiction, which often begins in adolescence, Gulley said.

"Rats exhibit many of the characteristics that human adolescents do. They tend to be more impulsive than adult rats; they tend to make more risky decisions," he said. They also can engage in "addiction-like behaviors," he said.

"They show increased drug use in response to stress," Gulley said. "And, just as in humans, there is evidence that animals that start using drugs in adolescence are more likely to relapse than animals that start in adulthood."

A limitation of the new study was that, unlike humans, who generally choose whether or not to partake in drug use, "the rats had no say in whether they got amphetamine," Gulley said.

A previous study from Gulley and his colleagues looked at the effects of amphetamine abuse on working memory - the ability to retain information just long enough to use it - in young and adult rats.

"In that study, we found that animals that were exposed to the drug during adolescence had much more significant deficits in working memory than those exposed during adulthood," Gulley said.

The researchers hypothesized that drug exposure during adolescence, a time of vast changes in the brain, "somehow influences the normal developmental trajectory," Gulley said. "But how?"

To get at this question, the team focused on the prefrontal cortex, a brain region behind the forehead that is among the last to fully develop during adolescence. The researchers found that repeated exposure to amphetamine - beginning in adulthood or in adolescence - reduced the ability of key cells in the rats' prefrontal cortex to respond to dopamine. In this part of the brain, dopamine influences "inhibitory tone," telling cells to stop responding to a stimulus, Gulley said.

"Inhibition in the nervous system is just as important as activation," he said. "You need cells that are firing and communicating with one another, but you also need cells to stop communicating with one another at certain times and become quiet.

"Our research suggests that a subtype of dopamine receptor, the D1 receptor, is altered following amphetamine exposure," Gulley said. "It's either not responding to dopamine or there are not as many of these receptors after exposure as there used to be."

This change in dopamine signaling persisted for 14 weeks after exposure to amphetamine in the adolescent-exposed rats, he said.

"That's akin to a change in humans that persists from adolescence until sometime in their 30s, long after drug use stopped," he said.

"Along with other studies, this shows pretty clear evidence that drug use during adolescence, a time when the brain is still developing, has extremely long-lasting consequences that go far beyond the last drug exposure," Gulley said.

**More information:** S. Kang et al. D1 receptor-mediated inhibition of medial prefrontal cortex neurons is disrupted in adult rats exposed to amphetamine in adolescence, *Neuroscience* (2016). DOI: 10.1016/j.neuroscience.2016.02.064

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