A rat's brain, on and off methamphetamine

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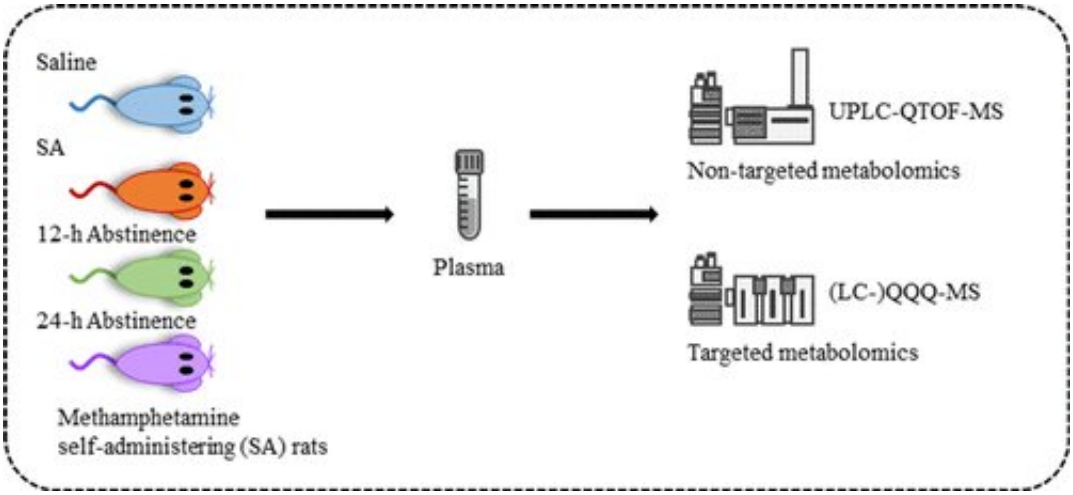

Credit: American Chemical Society

Drug addiction is a vicious cycle of reward and withdrawal. Chronic users often relapse because of the unpleasant physical and psychological symptoms they experience when they stop taking the drug. Now, researchers report in the *Journal of Proteome Research* metabolic changes in the brains of rats during methamphetamine self-administration and withdrawal that could help identify biomarkers and treatments for addiction.

Methamphetamine is a highly addictive stimulant that increases the activity of neurotransmitters, particularly dopamine, in the brain. Scientists lack a detailed understanding of the neurochemical changes that occur during methamphetamine use and withdrawal, which could

help them develop new treatments or diagnostic tests for addiction. So, Chul-Ho Jeong, Sooyeun Lee and colleagues wanted to investigate metabolic alterations in the early withdrawal period following methamphetamine self-administration in rats.

The researchers trained rats to give themselves infusions of methamphetamine or saline (as a control) upon pressing a lever. After 16 days, the team removed rats' access to the drug and collected blood samples at 0, 12 and 24 hours after withdrawal. The researchers found substantial changes in metabolic pathways related to energy metabolism, the nervous system and cell membrane lipid metabolism. For example, the amino acids phenylalanine, tyrosine and tryptophan—which are precursors of several neurotransmitters—were depleted in methamphetamine-using rats compared with controls, but during withdrawal, the levels recovered. These and other potential biomarkers could help identify early warning signs of methamphetamine dependence, the researchers say.

More information: Suji Kim et al. Integrated Non-targeted and Targeted Metabolomics Uncovers Dynamic Metabolic Effects during Short-Term Abstinence in Methamphetamine Self-Administering Rats, *Journal of Proteome Research* (2019). DOI: 10.1021/acs.jproteome.9b00363

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