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Cocaine addiction traced to increase in number of orexin neurons

A study in Biological Psychiatry identifies a critical role of the orexin system in the expression of an addicted state in rats

Philadelphia, September 12, 2018 – A [study](#) in cocaine-addicted rats reports long-lasting increases in the number of neurons that produce orexin—a chemical messenger important for sleep and appetite—that may be at the root of the addiction. The study, performed by researchers at Rutgers University, New Jersey, was published in [Biological Psychiatry](#). Restoring the number of orexin neurons to normal, or blocking orexin signaling in the brain, made the rats no longer addicted, suggesting the increased orexin neurons to be essential brain changes that cause the addicted state.

The findings identify a promising avenue for treating addiction with orexin-based therapies. Drugs targeting orexin signaling are already being developed for sleep disorders and eating disorders. “The development of a growing array of drugs targeting orexin signaling creates new opportunities to test new medications for the treatment of addiction,” said John Krystal, MD, Editor of *Biological Psychiatry*.

In the process of studying the role of orexin signaling, first author Morgan James, PhD, and colleagues also found that mimicking the typical binge-like pattern of drug use—with access to cocaine on-and-off throughout the day—produced a model that reflected addiction in humans better than the “gold standard” of continuous access. Rats given intermittent cocaine demonstrated behaviors observed in human users, including increased motivation for cocaine, even when they received a painful shock to acquire the drug, depression- and anxiety-like behaviors, and ‘relapse’ after several months of abstinence.

“Remarkably, these ‘addicted’ rats had a greater number of brain cells that produce the neuropeptide orexin,” said Dr. James. The increased number of neurons was persistent, lasting for at least six months after cocaine use, which might explain why addicts often relapse following long periods of abstinence, said Dr. James.

“The addicted brain appears to become more dependent upon this increased number of orexin neurons,” noted Dr. Gary Aston-Jones, the study’s senior author. “Lower doses of an orexin blocker were effective at decreasing addiction behaviors in these rats than in those with shorter access to cocaine and that were less addicted.”

When people think of addiction, they tend to focus on a single chemical messenger, dopamine, and the reward center of the brain. But this greatly oversimplifies the addiction process—a complex pattern of brain circuits and multiple brain chemicals contribute to the anticipation, experience, and seeking of reward. “Viewing addiction as mediated by a single neurotransmitter in a single brain region is not only inaccurate, but it prevents us from harnessing the complexity of brain signaling mechanisms in the process of developing treatments for addiction,” said Dr. Krystal.

Notes for editors

The article is "Increased number and activity of a lateral subpopulation of hypothalamic orexin/hypocretin neurons underlies the expression of an addicted state in rats," by Morgan H James, Colin M Stopper, Benjamin A Zimmer, Nikki E Koll, Hannah E Bowrey, and Gary Aston-Jones (<https://doi.org/10.1016/j.biopsych.2018.07.022>). It appears in *Biological Psychiatry*, published by Elsevier.

Copies of this paper are available to credentialed journalists upon request; please contact Rhiannon Bugno at Biol.Psych@UTSouthwestern.edu or +1 214 648 0880. Journalists wishing to interview the authors may contact Morgan James at morgan.james@rutgers.edu or +1 843 557 9289.

The authors' affiliations and disclosures of financial and conflicts of interests are available in the article.

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