Team uncovers the disconnect between the brain's dopamine system and cocaine addiction

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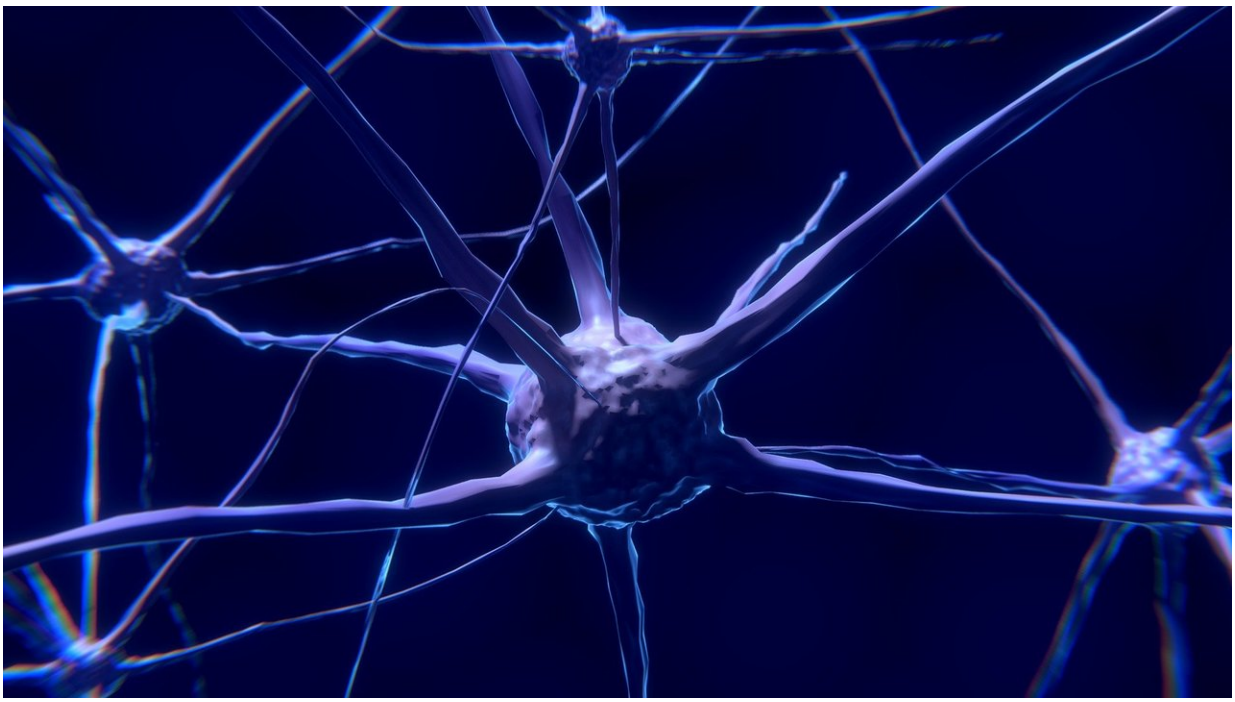

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Researchers at The University of Texas at San Antonio have revealed significant insight into cocaine addiction, a phenomenon which has grown significantly in the United States since 2015.

Now new data by UTSA shows how the release of the neurotransmitter dopamine changes when working for cocaine. Our brains naturally release dopamine to reward us for working hard for something gratifying, for example, enjoying a sweet piece of chocolate. Yet when it comes to illicit substances such as cocaine, the harder the effort put into getting cocaine, the less likely there will be a large jolt of dopamine.

With the new understanding that there is a difference between how the brain responds to additional effort in relation to a specific object of desire, either food vs. illicit drugs, the UTSA data suggests that this new finding into the dopamine production complex could help guide future solutions for drug addiction.

"By identifying these differences, you can come up with pharmacological or behavior strategies so you can maintain normal responses for natural rewards but at the same time manage the responses for drugs," says Matthew Wanat, assistant professor in the Department of Biology at UTSA.

Dopamine is a neurotransmitter that plays key roles in the brain and body. The chemical messenger is involved in regulating physical movement. It's a catalyst for a person to be able to engage in motivated behaviors and also facilitates learning. Scientific studies show that a disruption in dopamine production can lead to neurological disorders such as Parkinson's but also drug addiction.

Wanat's previous research showed that there is a larger dopamine response when we delay gratification for food. Now his work on cocaine adds another dimension which can aid to solve the complex puzzle of the impact of illicit drug use on brain chemistry. The latest UTSA research will be published in an upcoming issue of the *Journal of Neuroscience*.

Professor Wanat and post-doctoral fellow Idaira Oliva, the lead

researcher on the project, used rats that were trained to work for infusions of cocaine. The rodents in order to obtain the desired stimulant, had to engage in a progressive series of nose pokes before getting another dose of cocaine. Later, voltammetry measurements of the dopamine levels in the rats' brain were taken while they worked to obtain cocaine.

As to why there is an opposite effect of dopamine surge in cocaine usage with added effort is still not fully understood. However, UTSA scientists don't necessarily think it's related to the actual drug.

"We think there might be a change in the subjective value. It's just perceived as less valuable. It fits in with the idea that you don't like the drug as much," says Wanat. "They (drug users) want it but they don't like it as much as they would."

Although much of the recent drug crisis which impacts the country has centered on opioids, cocaine usage in the United States has surged since 2015. The latest Centers for Disease Control data suggests that after marijuana, cocaine is the second most abused illicit drug, and deaths have grown by 37%. Moreover, the DEA shows that another factor for increased cocaine usage is the boom in global cultivation and coca production of the psychostimulant.

The independent effects of illicit drugs are difficult to tease out. Many drug users tend to rely on several abused substances and the interplay between them and the combined impact on the body is not understood. For now, researchers at UTSA will still continue future investigations on what beyond dopamine causes addiction.

"This effect is not due to cocaine levels in the brain, it's something upstream to what's getting the dopamine neurons to fire," says Wanat.

More information: Idaira Oliva et al, Operant costs modulate dopamine release to self-administered cocaine, *The Journal of Neuroscience* (2018). DOI: 10.1523/JNEUROSCI.1721-18.2018