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Unlocking the Secrets of Our Compulsions

Researchers have shed new light on dopamine's role in the brain's reward system, which could provide insight into impulse control problems associated with addiction and a number of psychiatric disorders.

A joint study by the University of Michigan and University of Washington found that, contrary to the prevailing conception, differences in individuals' styles of response to environmental cues can fundamentally influence chemical reward patterns in the brain.

Deeper understanding of these differences between individuals may lead to new preventive tools or treatments for compulsive behavior.

"We were able to answer the longstanding question, 'What role does dopamine play in reward learning?'," says the study's Co-lead Author Shelly B. Flagel, Ph.D., a Research Investigator at the U-M Medical School's Molecular and Behavioral Neuroscience Institute.

The findings were published online December 8 in the journal Nature ahead of print publication.

To understand what the research uncovered, picture the classic experiment in which a rat learns to associate a lever with a getting a food reward. (In this case, the rats didn't actually have to press the lever to get the food; the researchers were testing its power as a signal of the food's appearance.)

What scientists hadn't yet figured out was the extent to which the dopamine released by the rat's brain was related to the lever's ability to accurately predict the appearance of food, or whether it made the lever desirable in its own right.

The answer, the researchers found, is that it depends on what kind of rat you are?

Think of it this way, Flagel says: Some people will see a sign for an ice cream shop and for them it's simply that, an indicator that ice cream is available nearby. But other people will have a stronger reaction to the sign -- the tantalizing association between the sign and ice cream is so powerful, they can already taste the treat and often hurry to buy some.

The researchers studied rats that had been selectively bred for certain behavioral traits, including different proclivities for addictive drugs. Rats in the drug-prone group tended to focus their attention on the lever. The other group cared a lot more about the place where the food actually appeared.

Still, if the rats' brains saw the lever merely as a signal that accurately predicted the arrival of the food, the dopamine reward for both groups should be the same.

However, if the dopamine reward was tied to the strength of the rats' desire for lever itself, one would expect a different pattern for each of the two groups.

And that's exactly what happened.

U-M's collaborators at the University of Washington used a technique called fast-scan cyclic voltammetry to measure the dopamine responses in the rats' brains as they shifted over mere fractions of a second. Their analysis showed that the drug-prone rats got a jolt of happiness just from the lever, while the food-oriented rats did not.

And their desire for the lever continued, even when the food reward was removed.

The study additionally measured the rats' ability to learn when dopamine was blocked and repeated the experiments with rats that had not been selectively bred.

Flagel, co-lead author Jeremy J. Clark, Ph.D., of UW, and their colleagues hope the animal model will help scientists figure out why some people are more strongly motivated by environmental cues and therefore at increased risk for compulsive behavior -- or, among addicts, relapse.

"We have been interested in understanding how differences in temperament control our day-to-day behavior, how they determine the types of pathologies we express," says Huda Akil, Ph.D., co-director of MBNI, a Professor of Neuroscience at U-M and co-senior author of the study. "This study helps us understand how, in some situations, dopamine amplifies messages in the world around us, playing a role in controlling behaviors."

Meanwhile, Paul E.M. Phillips, Ph.D., Akil's counterpart at UW, emphasized the collaboration, "Collectively the contributions of our groups amounted to something much more important than the sum of the components."

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Shelly B. Flagel, Jeremy J. Clark, Terry E. Robinson, Leah Mayo, Alayna Czuj, Ingo Willuhn, Christina A. Akers, Sarah M. Clinton, Paul E. M. Phillips, Huda Akil. A selective role for dopamine in stimulusreward learning. Nature, 2010; DOI: 10.1038/nature09588