Research shows rat neurons increase dopamine immediately after setbacks

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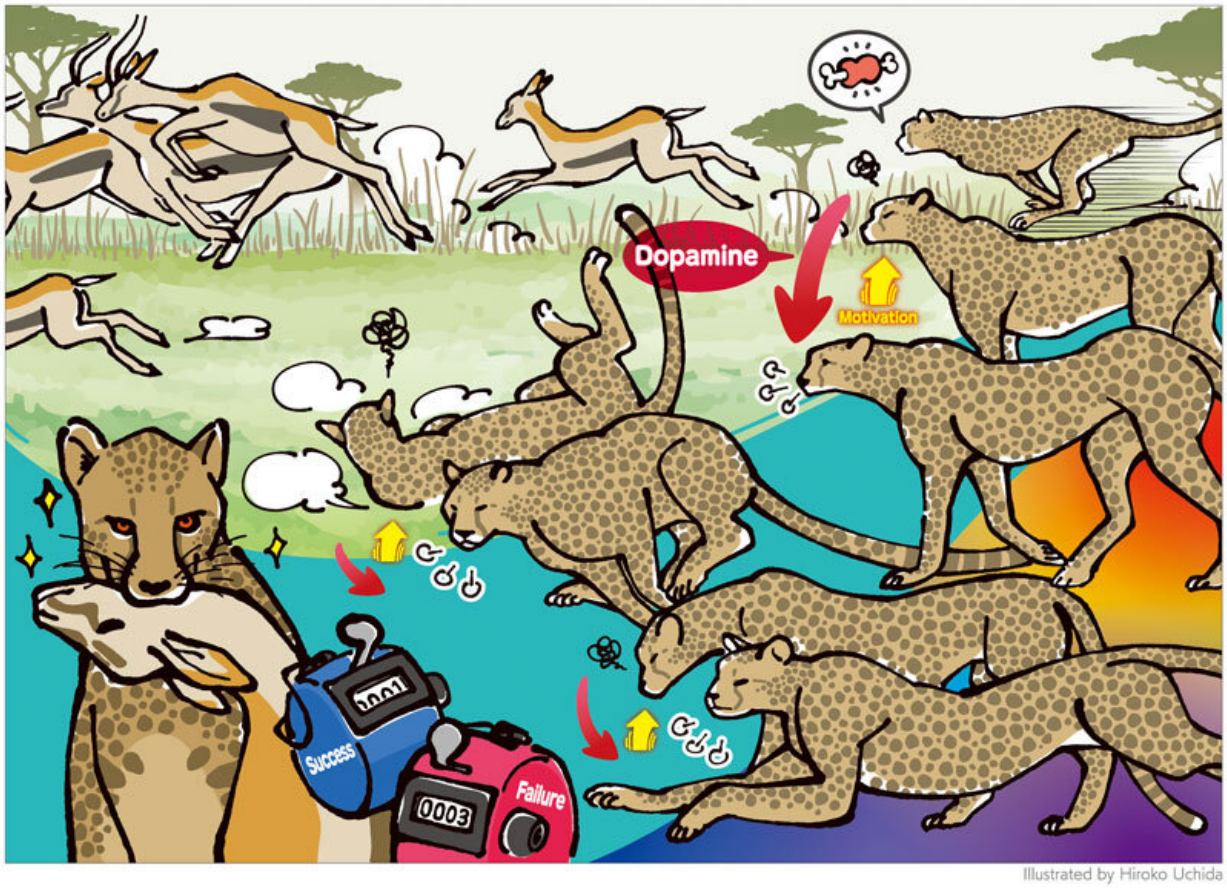

Caption: Brain chemical dopamine enables adaptive reward pursuit to overcome lack of reward and ultimately obtain more rewards. Credit: KyotoU/Hiroko Uchida

Dopamine has been known to increase when results are promising and decrease when expectations are not met. However, this role does not explain the ability to overcome disappointment.

Now, researchers at Kyoto University's Graduate School of Medicine have discovered neurons in rats that increase dopamine immediately after a disappointment as a coping mechanism. The research is published in the journal *Science Advances*.

"Every day, we strive to achieve goals but are often met with failure and disappointment. Fortunately, thanks to dopamine, our brain can cope with such setbacks," says corresponding author Masaaki Ogawa at Kyoto University. "Conventionally, we associate dopamine with self-reward, but our results suggest that its other function is self-motivation."

This neural mechanism that supports dealing with disappointment may lead to new treatments for psychiatric and neurological disorders, including depression, addiction, and Parkinson's disease.

"It will also give insights into activities aimed at higher goals, such as independent learning and self-development."

In animals besides humans, on the other hand, failure and disappointment are intertwined with their survival, particularly in foraging and mating.

Ogawa's team trained rats to continue seeking sweet water. Then, even when the rats failed to attain their reward, they could switch their behavior to the subsequent reward acquisition afterward.

The neuronal activity in the rats during that behavior—measured with millisecond–to–second temporal precision using opto-electrophysiology and calcium imaging—confirmed that the observed cells were indeed

dopamine neurons.

The researchers manipulated the rats' behavior by artificially stimulating the neural circuit at the moment of perceived disappointment resulting from not acquiring their expected rewards.

"It was surprising that activity of the dopamine neurons that showed increased activity after a disappointment decreased after the rats received unexpected rewards," explains Ogawa.

Midbrain dopamine neurons may affect learning and motivation, benchmarks in studying psychiatric disorders. In addition, these neurons give a signal for rewards, termed reward prediction error—or RPE—which represents the difference between received rewards minus expected rewards. RPE-type neurons—critical for learning based on reward value—do not directly support the behavioral switching to pursue a reward after the moment of an unexpected non-reward but instead support negative learning.

However, Ogawa's team suggests a new type of dopamine neuron—an anti-RPE type—that show an increased response to the lack of reward and a decreased response to unexpected rewards.

"This bidirectional response fundamentally changes our understanding of how dopamine works in motivational behavior," Ogawa says.

More information: Seiya Ishino et al, Dopamine error signal to actively cope with lack of expected reward, *Science Advances* (2023). DOI: 10.1126/sciadv.ade5420

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