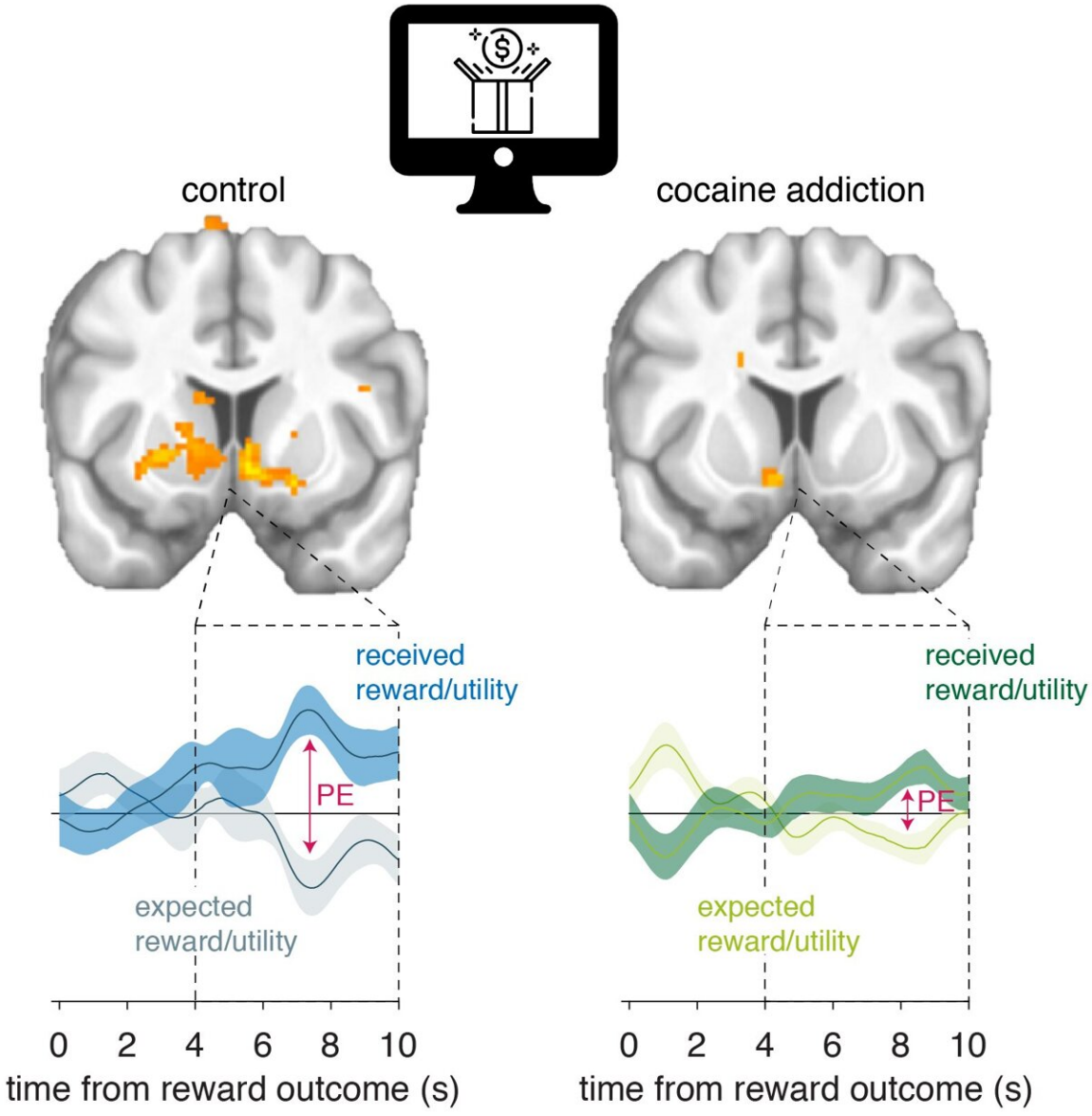
Perception—but not expectation—of reward is altered in people with cocaine addiction

October 25 2023



The authors measured a subjective reward signal linked to dopamine utility prediction error. Credit: Konova et al.

Researchers report October 25 in the journal *Neuron* that cocaine addiction disrupts the dopamine neurons that govern how we perceive and learn from rewards. Though people with cocaine addiction have similar expectations of rewards compared to controls, their dopamine neurons send out much weaker signals when these rewards are actually received. This dysregulation could make it more difficult for people with cocaine addiction to learn from their experiences and change addictive behavior.

"Our results support the medical model of addiction as a disorder of the brain that deserves treatment," says senior author Rita Goldstein, a neuroscientist and addiction expert at the Icahn School of Medicine at Mount Sinai. "Addiction is a disorder and not a choice or a moral weakness."

"If you're not tracking the reward signal appropriately, it makes it much harder to disengage from something that's no longer rewarding," says first author Anna Konova, a neuroscientist at Rutgers University.

It's well documented from both animal and human studies that cocaine addiction impacts multiple aspects of dopamine signaling in the brain. However, it's unclear whether certain parts of the dopamine signaling pathway are more important than others.

Rather than general errors with dopamine signaling, addictive behavior is thought to be due to disruptions to the reward prediction error, a system that calibrates future expectations based on past experiences by comparing expected rewards to actual rewards as encoded by dopamine

neurons in the midbrain. However, few studies have directly demonstrated the impact of cocaine use on reward prediction error in humans.

To examine the role of prediction error in cocaine addiction, the research team used fMRI scanning to examine neural activity in people with cocaine addiction compared to healthy controls while they were performing a simple decision-making task: choosing between a "safe" monetary reward and a "risky" reward that carried a chance of being either much higher or lower in value than the safe option.

The researchers compared brain activity during the two phases of the prediction error calculation: first during the expectation phase (while participants were making their decision and anticipating the resulting reward), and then during the actual reward phase (when participants were presented with the outcome).

They found that people with cocaine addiction had reduced prediction error responses, consistent with animal studies. When they broke the prediction error response down into its component parts, they found that signals of reward expectation were similar for both groups, but the signal for received reward was weaker for people with cocaine addiction.

This weakened reward signal was visible in the ventral striatum, the brain region where prediction error is processed, and there was also reduced activity in the orbitofrontal cortex, a brain region involved in integrating the prediction error signal to inform future behavior.

"We found evidence that people with chronic cocaine addiction have reduced prediction error responses, and this difference seems to be caused by differences in the subjective perception of received reward," says Konova. "The reduced reward signal seems to propagate to other regions of the brain that would receive this information to then update

your expectations for the next time you encounter this same situation."

The team also showed that people with cocaine addiction were more likely to choose risky options compared with controls, and this risk tolerance was more apparent in people who had begun using cocaine at an earlier age, pointing to potential predisposing factors for developing addiction.

Understanding the mechanisms behind addictive behavior could inform treatment strategies for addiction, the researchers say. "Our findings suggest that interventions that boost the perception of received rewards might be a valuable component of addiction treatment," says Goldstein. "Understanding the brain mechanisms behind addiction is also extremely valuable for the public and for the person experiencing addiction."

Next, the team wants to understand how this dysregulation of reward signaling changes during different stages of addiction and recovery and whether reward perception is involved in other types of substance disorder, for example in addiction to opioids such as heroin.

"We want to understand how this signal changes through the progression of recovery, or as a function of different stages of addiction to understand whether it's really driven by chronic cocaine exposure or something that comes on earlier, maybe even before you start substance use," says Goldstein.

More information: Anna Konova et al, Reduced neural encoding of utility prediction errors in cocaine addiction, *Neuron* (2023). DOI: 10.1016/j.neuron.2023.09.015.
www.cell.com/neuron/fulltext/S0896-6273(23)00700-6

Provided by Cell Press