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Cocaine users have impaired ability to predict loss

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Cocaine addicted individuals may continue their habit despite unfavorable consequences like imprisonment or loss of relationships because their brain circuits responsible for predicting emotional loss are impaired, according to a study conducted at the Icahn School of Medicine at Mount Sinai and published today in *The Journal of Neuroscience*.

The study focuses on the difference between a likely reward (or loss) related to a given behavior and a person's ability to predict that outcome, a measurement known as Reward Prediction Error, or RPE. Such RPE signaling is believed to drive learning in humans, which guides future behavior. After learning from an experience, we can, in the best case, change our behavior without having to go through it again, and thus maximize rewards and avert expected losses. Past research has determined that prediction of actual reward or loss is managed by shifting levels of the nerve signaling chemical dopamine produced by nerve cells in the midbrain, where changes in dopamine levels accompany unexpected gains and losses.

The Mount Sinai study recorded the brain activity of 75 subjects (50 cocaine users and 25 healthy controls) using EEG, a test that detects electrical activity in the brain, while subjects played a gambling game. Each person had to predict whether or not they would win or lose money on each trial.

Results showed that the group of the 50 cocaine users had impaired loss

prediction signaling, meaning they failed to trigger RPE signals in response to worse-than-expected outcomes compared to the 25 healthy people comprising the control group. The results offer insights into the compromised ability of addicted individuals to learn from unfavorable outcomes, potentially resulting in continued drug use and relapse, even after encountering numerous losses.

"We found that people who were addicted to cocaine have impaired loss prediction signaling in the brain," said Muhammad Parvaz, PhD, Assistant Professor of Psychiatry at the Icahn School of Medicine at Mount Sinai and the lead author of the study. "This study shows that individuals with substance use disorder have difficulty computing the difference between expected versus unexpected outcomes, which is critical for learning and future decision making. This impairment might underlie disadvantageous decision making in these individuals."

Next, the study looked at individual differences among the 50 cocaine users. Half of the subjects had used cocaine within 72 hours of the study and the other half had abstained for at least 72 hours. The cocaine addicted individuals with the more recent use had higher electrical activity associated with the brain's reward circuit when they had an unpredicted compared to a predicted win, a pattern that was similar to the 25 healthy controls. The cocaine users who had abstained for at least 72 hours did not show this higher activity in response to an unpredicted win. These findings are consistent with the hypothesis that in addiction the drug is taken to normalize a certain brain function, which in this case is RPE signaling of better-than-expected outcomes.

"This is the first time a study has targeted the prediction of both gains and losses in drug addiction, showing that deficits in prediction error signaling in cocaine addicted individuals are modulated by recent cocaine use," said principal investigator Rita Goldstein, PhD, Chief of Neuropsychoimaging of Addiction and Related Conditions, Chief of the

Brain Imaging Center, and Professor of Psychiatry and Neuroscience at the Icahn School of Medicine. "Direction of results supports the self-medication hypothesis in drug addiction whereby drug self-administration improves response to reward in drug addicted individuals. The reductions in prediction of loss across all cocaine addicted individuals included in this study are also of great interest; they could become important markers that can be used to predict susceptibility for addiction or relapse or to develop targeted interventions to improve outcome in this devastating, chronically relapsing disorder."

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