

Cocaine decreases activity of a protein necessary for normal functioning of the brain's reward system

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New research from Mount Sinai Medical Center in New York reveals that repeated exposure to cocaine decreases the activity of a protein necessary for normal functioning of the brain's reward system, thus enhancing the reward for cocaine use, which leads to addiction. Investigators were also able to block the ability of repeated cocaine exposure, to induce addiction. The findings, published online April 22 in the journal *Nature Neuroscience*, provide the first evidence of how cocaine changes the shape and size of neuron rewards in a mouse model.

Repeated exposure to cocaine decreases the expression of a protein necessary for normal functioning of the brain's reward system, thus enhancing the reward for [cocaine use](#) and stimulating addiction. Using the protein's light-activated form in real time, in a technique known as optogenetics, investigators were also able to block repeated [cocaine exposure](#) from enhancing the brain's reward center from cocaine. Even though the results are very early and many steps will be important in moving from mice to humans, the researchers say that the finding opens the door to a new direction for treatment for [cocaine addiction](#).

"There are virtually no medication regimens for cocaine addiction, only psychotherapy, and some early work with vaccines," said the study's senior investigator, Eric Nestler, MD, PhD, Nash Family Professor of Neuroscience, Chairman of the Neuroscience and Director of the

Friedman Brain Institute at Mount Sinai School of Medicine. The protein, Rac1, is found in many cells in mice, rats, monkeys, and humans, and it is known to be involved in controlling the growth of nerve cells.

Investigators "knocked out," or deleted, the gene responsible for Rac1 production, or injected a virus to enhance expression of Rac1.

"The research gives us new information on how cocaine affects the brain's [reward center](#) and how it could potentially be repaired," said Dr. Nestler. "This is the first case in the brain in vivo where it's been possible to control the activity of a protein, inside [nerve cells](#) in real time. Our findings reveal new pathways and target -- a proof of principle study really -- for treatment of cocaine addiction."

Provided by The Mount Sinai Hospital / Mount Sinai School of Medicine

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