

# Addiction silences synapses in reward circuits

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In addiction, cues in the environment can form strong associations with the drug of abuse. A new study in *Biological Psychiatry* suggests that alterations in silent synapses, inactive connections between neurons, could be the neural mechanism underlying the formation of these drug-related memories. The alterations were found in the nucleus accumbens, a brain region involved in reward-related learning.

"The persistence and inflexibility of addiction-related associations are factors that trigger craving and relapse," said Dr. John Krystal, Editor of *Biological Psychiatry*. "This study suggests that one factor that may contribute to this inflexibility is that synapses in reward circuits that might promote recovery are silenced," he said, adding that with better understanding of this phenomenon, engaging these silent synapses during treatment may be an important component of recovery.

Long-term memories likely form when selective alterations in synaptic connections occur within patterns of neurons called neuronal ensembles. In the study, Bruce Hope, from the National Institutes of Health National Institute on Drug Abuse Intramural Research Program in Baltimore, Maryland, and colleagues used animal models to investigate if the brain forms drug-related memories in a similar way.

The researchers administered cocaine injections to mice, always in the same environment. After repeated injections, the mice developed an association between the drug and the environment, which produced a learned behavior when the mice were returned to the same location.

To determine how the brain encodes this drug-related behavior, the researchers need to know exactly which neurons are involved. This seemingly impossible task led most previous studies to examine randomly selected neurons or focus on a specific type of cell. In this study, the researchers used a marker that caused neurons to fluoresce when activated, allowing them to pinpoint specific neuronal ensembles involved in the behavior.

The researchers measured electrical activity of the neurons within the ensemble and compared it with nearby neurons that were not activated by the environmental cue. They found an increase in silent synapses on only the activated neurons, indicating the synaptic alterations were specific to the neuronal ensemble that encoded the drug-related memory. According to Hope, "These ensemble-specific silent synapses may be one of the mechanisms by which neuronal ensembles are modified to store memories."

Identification of the alterations responsible for drug-related memories could open the door to treatment options for people with addiction. "Therapeutic targeting of such alterations on only this small percentage of drug memory-specific [neurons](#) could be a highly specific method for disrupting drug-related memories that mediate human addiction," said Hope.

**More information:** Leslie R. Whitaker et al. Associative Learning Drives the Formation of Silent Synapses in Neuronal Ensembles of the Nucleus Accumbens, *Biological Psychiatry* (2016). [DOI: 10.1016/j.biopsych.2015.08.006](#)

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