

Low doses of psychedelic drug erases conditioned fear in mice

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Psilocybin, which exerts psychoactive effects, has been isolated from certain mushrooms.

(Medical Xpress)—Low doses of a psychedelic drug erased the conditioned fear response in mice, suggesting that the agent may be a treatment for post-traumatic stress disorder and related conditions, a new study by University of South Florida researchers found.

The unexpected finding was made by a USF team studying the effects of the compound [psilocybin](#) on the birth of new neurons in the brain and on learning and short-term [memory formation](#). Their study appeared online June 2 in the journal *Experimental Brain Research*, in advance of print publication.

Psilocybin belongs to a class of compounds that stimulate select serotonin receptors in the brain. It occurs naturally in certain mushrooms that have been used for thousands of years by non-Western cultures in their religious ceremonies.

While past studies indicate psilocybin may alter perception and thinking and elevate mood, the psychoactive substance rarely causes hallucinations in the sense of seeing or hearing things that are not there, particularly in lower to moderate doses.

There has been recent renewed interest in medicine to explore the potential clinical benefit of psilocybin, MDMA and some other [psychedelic drugs](#) through carefully monitored, evidence-based research.

"Researchers want to find out if, at lower doses, these drugs could be safe and effective additions to psychotherapy for treatment-resistant psychiatric disorders or adjunct treatments for certain neurological conditions," said Juan Sanchez-Ramos, MD, PhD, professor of neurology and Helen Ellis Endowed Chair for Parkinson's Disease Research at the USF Health Morsani College of Medicine.

Dr. Sanchez-Ramos and his colleagues wondered about psilocybin's role in the formation of short-term memories, since the agent binds to a serotonin receptor in the hippocampus, a region of the brain that gives rise to new neurons. Lead author for this study was neuroscientist Briony Catlow, a former PhD student in Dr. Sanchez-Ramos' USF laboratory who has since joined the Lieber Institute for Brain Development, a

translational neuroscience research center located in the Johns Hopkins Bioscience Park.

The USF researchers investigated how psilocybin affected the formation of memories in [mice](#) using a classical conditioning experiment. They expected that psilocybin might help the mice learn more quickly to associate a neutral stimulus with an unpleasant environmental cue.

To test the hypothesis, they played an auditory tone, followed by a silent pause before delivering a brief shock similar to static electricity. The mice eventually learned to link the tone with the shock and would freeze, a fear response, whenever they heard the sound.

Later in the study, the researchers played the sound without shocking the mice after each silent pause. They assessed how many times it took for the mice to resume their normal movements, without freezing in anticipation of the shock.

Regardless of the doses administered, neither psilocybin nor ketanserin, a serotonin inhibitor, made a difference in how quickly the mice learned the conditioned fear response. However, mice receiving low doses of psilocybin lost their fearful response to the sound associated with the unpleasant shock significantly more quickly than mice getting either ketanserin or saline (control group). In addition, only low doses of psilocybin tended to increase the growth of neurons in the hippocampus.

"Psilocybin enhanced forgetting of the unpleasant memory associated with the tone," Dr. Sanchez-Ramos said. "The mice more quickly dissociated the shock from the stimulus that triggered the [fear response](#) and resumed their normal behavior."

The result suggests that psilocybin or similar compounds may be useful in treating [post-traumatic stress disorder](#) or related conditions in which

environmental cues trigger debilitating behavior like anxiety or addiction, Dr. Sanchez-Ramos said.

More information: "Effects of psilocybin on hippocampal neurogenesis and extinction of trace fear conditioning," Briony J. Catlow, Shijie Song, Daniel A. Paredes, Cheryl L. Kirstein and Juan Sanchez-Ramos; *Experimental Brain Research*, published online June 2, 2013; [DOI 10.1007/s00221-013-3579-0](https://doi.org/10.1007/s00221-013-3579-0)

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