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Study suggests path to prolonging treatment effectiveness for phobias or post-traumatic stress disorder

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MIT scientists have identified a way to enhance the long-term benefit of exposure therapy in rats, offering a way to improve the therapy in people suffering from phobias and more complicated conditions such as post-traumatic stress disorder (PTSD). Credit: Christine Daniloff/MIT

People who are too frightened of flying to board an airplane, or too scared of spiders to venture into the basement, can seek a kind of treatment called exposure therapy. In a safe environment, they repeatedly face cues such as photos of planes or black widows, as a way to stamp out their fearful response—a process known as extinction.

Unfortunately, the effects of exposure therapy are not permanent, and many people experience a relapse. MIT scientists have now identified a way to enhance the long-term benefit of extinction in rats, offering a way to improve the therapy in people suffering from phobias and more complicated conditions such as post-traumatic stress disorder (PTSD).

Work conducted in the laboratory of Ki Goosens, an assistant professor in MIT's Department of Brain and Cognitive Sciences and a member of the McGovern Institute for Brain Research, has pinpointed a neural circuit that becomes active during exposure therapy in the rats. In a study published Sept. 27 in eLife, the researchers showed that they could stretch the therapy's benefits for at least two months by boosting the circuit's activity during treatment.

"When you give extinction training to humans or rats, and you wait long enough, you observe a phenomenon called spontaneous recovery, in which the fear that was originally learned comes back," Goosens explains. "It's one of the barriers to this type of therapy. You spend all this time going through it, but then it's not a permanent fix for your problem."

According to statistics from the National Institute of Mental Health, 18 percent of U.S. adults are diagnosed with a fear or anxiety disorder each year, with 22 percent of those patients experiencing severe symptoms.

How to quench a fear

The neural circuit identified by the scientists connects a part of the brain involved in fear memory, called the basolateral amygdala (BLA), with another region called the nucleus accumbens (NAc), that helps the brain process rewarding events. Goosens and her colleagues call it the BLA-NAc circuit.

Researchers have been considering a link between fear and reward for some time, Goosens says. "The amygdala is a part of the brain that is tightly linked with fear memory but it's also been linked to positive reward learning as well, and the accumbens is a key reward area in the brain," she explains. "What we've been thinking about is whether extinction is rewarding. When you're expecting something bad and you don't get it, does your brain treat that like it's a good thing?"

To find out if there was a specific brain circuit involved, the researchers first trained rats to fear a certain noise by pairing it with foot shock. They later gave the rats extinction training, during which the noise was presented in the absence of foot shock, and they looked at markers of neural activity in the brain. The results revealed the BLA-NAc reward circuit was recruited by the brain during exposure therapy, as the rats gave up their fear of the bad noise.

Once Goosens and her colleagues had identified the circuit, they looked for ways to boost its activity. First, they paired a sugary drink with the fear-related sound during extinction training, hoping to associate the sound with a reward. This type of training, called counterconditioning, associates fear-eliciting cues with rewarding events or memories, instead of with neutral events as in most extinction training.

Rats that received the counterconditioning were significantly less likely to spontaneously revert to their fearful states, compared to those that received regular extinction training for up to 55 days later, the scientists found.

They also found that the benefits of extinction could be prolonged with optogenetic stimulation, in which the circuit was genetically modified so that it could be stimulated directly with tiny bursts of light from an optical fiber.

The ongoing benefit that came from stimulating the circuit was one of the most surprising—and welcome—findings from the study, Goosens says. "The effect that we saw was one that really emerged months later, and we want to know what's happening over those two months. What is the circuit doing to suppress the recovery of fear over that period of time? We still don't understand what that is."

Another interesting finding from the study was that the circuit was active during both fear learning and fear extinction, says lead author Susana Correia, a research scientist in the Goosens lab. "Understanding if these are molecularly different subcircuits within this projection could allow the development of a pharmaceutical approach to target the fear extinction pathway and to improve cognitive therapy," Correia says.

Immediate and future impacts on therapy

Some therapists are already using counterconditioning in treating PTSD, and Goosens suggests that the rat study might encourage further exploration of this technique in human therapy.

And while it isn't likely that humans will receive direct optogenetic therapy any time soon, Goosens says there is a benefit to knowing exactly which circuits are involved in extinction.

In neurofeedback studies, for instance, brain scan technologies such as fMRI or EEG could be used to help a patient learn to activate specific parts of their brain, including the BLA-NAc reward circuit, during exposure therapy.

Studies like this one, Goosens says, offer a "target for a personalized medicine approach where feedback is used during therapy to enhance the effectiveness of that therapy."

More information: Susana S Correia et al. Amygdala-ventral striatum circuit activation decreases long-term fear, *eLife* (2016). DOI: 10.7554/eLife.12669

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