

Neuroscientists determine how treatment for anxiety disorders silences fear neurons

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(Medical Xpress)—Excessive fear can develop after a traumatic experience, leading to anxiety disorders such as post-traumatic stress disorder and phobias. During exposure therapy, an effective and common treatment for anxiety disorders, the patient confronts a fear or memory of a traumatic event in a safe environment, which leads to a gradual loss of fear. A new study in mice, published online today in *Neuron*, reports that exposure therapy remodels an inhibitory junction in the amygdala, a brain region important for fear in mice and humans. The findings improve our understanding of how exposure therapy suppresses fear responses and may aid in developing more effective treatments. The study, led by researchers at Tufts University School of Medicine and the Sackler School of Graduate Biomedical Sciences at Tufts, was partially funded by a New Innovator Award from the Office of the Director at the National Institutes of Health.

A fear-inducing situation activates a small group of neurons in the amygdala. Exposure therapy silences these fear neurons, causing them to be less active. As a result of this reduced activity, fear responses are alleviated. The research team sought to understand how exactly exposure therapy silences fear neurons.

The researchers found that exposure therapy not only silences fear neurons but also induces remodeling of a specific type of inhibitory junction, called the perisomatic synapse. Perisomatic [inhibitory synapses](#) are connections between neurons that enable one group of neurons to silence another group of neurons. Exposure therapy increases the

number of perisomatic inhibitory synapses around fear neurons in the amygdala. This increase provides an explanation for how exposure therapy silences fear neurons.

"The increase in number of perisomatic inhibitory synapses is a form of remodeling in the brain. Interestingly, this form of remodeling does not seem to erase the memory of the fear-inducing event, but suppresses it," said senior author, Leon Reijmers, Ph.D., assistant professor of neuroscience at Tufts University School of Medicine and member of the neuroscience program faculty at the Sackler School of Graduate Biomedical Sciences at Tufts.

Reijmers and his team discovered the increase in perisomatic inhibitory synapses by imaging neurons activated by fear in genetically manipulated mice. Connections in the human brain responsible for suppressing fear and storing fear memories are similar to those found in the mouse brain, making the mouse an appropriate model organism for studying fear circuits.

Mice were placed in a box and experienced a fear-inducing situation to create a fear response to the box. One group of mice, the control group, did not receive exposure therapy. Another group of mice, the comparison group, received exposure therapy to alleviate the fear response. For exposure therapy, the comparison group was repeatedly placed in the box without experiencing the fear-inducing situation, which led to a decreased fear response in these mice. This is also referred to as fear extinction.

The researchers found that mice subjected to exposure therapy had more perisomatic inhibitory synapses in the amygdala than mice who did not receive exposure therapy. Interestingly, this increase was found around fear neurons that became silent after exposure therapy.

"We showed that the remodeling of perisomatic inhibitory synapses is closely linked to the activity state of fear [neurons](#). Our findings shed new light on the precise location where mechanisms of fear regulation might act. We hope that this will lead to new drug targets for improving exposure therapy," said first author, Stéphanie Trouche, Ph.D., a former postdoctoral fellow in Reijmers' lab at Tufts and now a medical research council investigator scientist at the University of Oxford in the United Kingdom.

"Exposure therapy in humans does not work for every patient, and in patients that do respond to the treatment, it rarely leads to a complete and permanent suppression of [fear](#). For this reason, there is a need for treatments that can make [exposure therapy](#) more effective," Reijmers added.

More information: Trouche, S., Sasaki, J.M., Tu, T., Reijmers, L.G. (Online October 31, 2013; print edition November 20, 2013). Fear extinction causes target-specific remodeling of perisomatic inhibitory synapses, *Neuron*, 80 (4). [DOI: 10.1016/j.neuron.2013.07.047](https://doi.org/10.1016/j.neuron.2013.07.047)

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