

Do antidepressants impair the ability to extinguish fear?

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An interesting new report of animal research published in *Biological Psychiatry* suggests that common antidepressant medications may impair a form of learning that is important clinically.

[Selective serotonin reuptake inhibitors](#), commonly called SSRIs, are a class of antidepressant widely used to treat depression, as well as a range of anxiety disorders, but the effects of these drugs on [learning and memory](#) are poorly understood.

In a previous study, Nesha Burghardt, then a graduate student at New York University, and her colleagues demonstrated that long-term SSRI treatment impairs fear conditioning in rats. As a follow-up, they have now tested the effects of antidepressant treatment on extinction learning in rats using auditory fear conditioning, a model of fear learning that involves the amygdala. The amygdala is a region of the brain vitally important for processing memory and emotion.

They found that long-term, but not short-term, SSRI treatment impairs extinction learning, which is the ability to learn that a conditioned stimulus no longer predicts an aversive event.

"This impairment may have important consequences clinically, since extinction-based exposure therapy is often used to treat anxiety disorders and antidepressants are often administered simultaneously," said Dr. Burghardt. "Based on our work, medication-induced impairments in extinction learning may actually disrupt the beneficial effects of exposure-therapy."

This finding is consistent with the results of several clinical studies showing that combined treatment can impede the benefits of [exposure therapy](#) or even natural resilience to the impact of traumatic stress at long-term follow-up.

The authors also suggest a mechanism for this effect on fear learning. They reported that the

antidepressants decreased the levels of one of the subunits of the [NMDA receptor](#) (NR2B) in the amygdala. The NMDA receptor is critically involved in fear-related learning, so these reductions are believed to contribute to the observed effects.

Dr. John Krystal, Editor of [Biological Psychiatry](#), commented, "We know that antidepressants play important roles in the treatment of depression and [anxiety disorders](#). However, it is important to understand the limitations of these medications so that we can improve the effectiveness of the treatment for these disorders."

More information: The article is "Chronic Antidepressant Treatment Impairs the Acquisition of Fear Extinction" by Nesha S. Burghardt, Torfi Sigurdsson, Jack M. Gorman, Bruce S. McEwen, and Joseph E. LeDoux ([doi: 10.1016/j.biopsych.2012.10.012](#)). The article appears in *Biological Psychiatry*, Volume 73, Issue 11 (June 1, 2013), published by Elsevier.

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