

# Study finds natural chemical helps brain adapt to stress

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Credit: Human Brain Project

A natural signaling molecule that activates cannabinoid receptors in the brain plays a critical role in stress-resilience—the ability to adapt to repeated and acute exposures to traumatic stress, according to researchers at Vanderbilt University Medical Center.

The findings in a mouse model could have broad implications for the potential treatment and prevention of mood and anxiety disorders, including major depression and post-[traumatic stress](#) disorder (PTSD), they reported in the journal *Nature Communications*.

"The study suggests that deficiencies in natural cannabinoids could result in a predisposition to developing PTSD and depression," said Sachin Patel, M.D., Ph.D., director of the Division of Addiction Psychiatry at Vanderbilt University School of Medicine and the paper's corresponding author.

"Boosting this signaling system could represent a new treatment approach for these stress-linked disorders," he said.

Patel, the James G. Blakemore Professor of Psychiatry, received a Presidential Early Career Award for Scientists and Engineers last year for his pioneering studies of the endocannabinoid family of signaling molecules that activate the CB1 and CB2 [cannabinoid receptors](#) in the brain.

Tetrahydrocannabinol (THC), the active compound in marijuana, binds the CB1 receptor, which may explain why relief of tension and anxiety is the most common reason cited by people who use marijuana chronically.

Patel and his colleagues previously have found CB1 receptors in the amygdala, a key emotional hub in the brain involved in regulating anxiety and the fight-or-flight response. They also showed in animal models that anxiety increases when the CB1 receptor is blocked by a drug or its gene is deleted.

More recently they reported anxiety-like and depressive behaviors in genetically modified mice that had an impaired ability to produce 2-arachidonoylglycerol (2-AG), the most abundant endocannabinoid.

When the supply of 2-AG was increased by blocking an enzyme that normally breaks it down, the behaviors were reversed.

In the current study, the researchers tested the effects of increasing or depleting the supply of 2-AG in the amygdala in two populations of mice: one previously determined to be susceptible to the adverse consequences of acute stress, and the other which exhibited stress-resilience.

Augmenting the 2-AG supply increased the proportion of stress-resilient mice overall and promoted resilience in mice that were previously susceptible to stress, whereas depleting 2-AG rendered previously stress-resilient mice susceptible to developing anxiety-like behaviors after exposure to acute stress.

Taken together, these results suggest that 2-AG signaling through the CB1 receptor in the amygdala promotes resilience to the adverse effects of acute traumatic stress exposure, and support previous findings in animal models and humans suggesting that 2-AG deficiency could contribute to development of stress-related psychiatric disorders.

Marijuana use is highly cited by patients with PTSD as a way to control symptoms. Similarly, the Vanderbilt researchers found that THC promoted stress-resilience in previously susceptible mice.

However, marijuana use in psychiatric disorders has obvious drawbacks including possible addiction and cognitive side effects, among others. The Vanderbilt study suggests that increasing production of natural cannabinoids may be an alternative strategy to harness the therapeutic potential of this signaling system.

If further research finds that some people with stress-related mood and [anxiety disorders](#) have low levels of 2-AG, replenishing the supply of

this endocannabinoid could represent a novel treatment approach and might enable some of them to stop using marijuana, the researchers concluded.

**More information:** Rebecca J. Bluett et al, Endocannabinoid signalling modulates susceptibility to traumatic stress exposure, *Nature Communications* (2017). [DOI: 10.1038/ncomms14782](https://doi.org/10.1038/ncomms14782)

Provided by Vanderbilt University Medical Center

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