Cannabinoid Science Sheds New Light on the Darkness of PTSD

MARTIN LEE

Martin Lee

A recent article in the journal *Neuroendocrinology* highlights the crucial role of the endocannabinoid system in protecting against posttraumatic stress disorder (PTSD), a debilitating chronic condition involving horrific memories that cannot be erased.

In an effort to understand the neurobiological mechanisms that underlie the onset and development of PTSD, a team of U.S. and Canadian scientists analyzed 46 subjects who were near the World Trade Center in New York City during the September 11 terrorist attacks. Twenty-four of these subjects suffered from PTSD following the attacks; 22 did not.

The researchers found that people with PTSD had lower serum levels of anandamide, an endogenous cannabinoid compound, compared to those who did not show signs of PTSD after 9/11. Innate to all mammals, anandamide (our inner cannabis, so to speak) triggers the same brain receptors that are activated by THC (tetrahydrocannabinol: The High Causer) and other components of the marijuana plant.

Concentrated in the brain and central nervous system, the cannabinoid receptor known as CB-1 mediates a broad range of physiological functions, including emotional learning, stress adaption, and fear extinction. Scientists have determined that normal CB-1 receptor signaling deactivates traumatic memories and endows us with the gift of forgetting.

But skewed CB-1 signaling, due to endocannabinoid deficits (low serum levels of anandamide), results in impaired fear extinction, aversive memory consolidation, and chronic anxiety, the hallmarks of PTSD.

PTSD is one of many enigmatic conditions that may arise because of a dysfunctional endocannabinoid system. A 2009 report by Virginia Commonwealth University scientists discerned a link between the dysregulation of the endocannabinoid system and the development of epilepsy. Researchers at the University of Rome in Italy have documented low levels of anandamide in the cerebrospinal fluid in patients with untreated newly diagnosed temporal lobe epilepsy.

Dr. Ethan Russo postulates that clinical endocannabinoid deficiency underlies migraines, fibromyalgia, irritable bowel disease, and a cluster of related degenerative conditions—which may respond favorably to cannabinoid therapies.

Individuals have different congenital endocannabinoid levels and sensitivities that factor into how one responds to stress and trauma. Alcoholism induces endocannabinoid deficits. So does lack of exercise and a diet laden with corn syrup and artificial sweeteners.

Additional research has established that clinical depression is an endocannabinoid deficiency disease. Canadian scientist and Rockefeller University post-doc Matthew Hill analyzed the serum endocannabinoid content in depressed women and found that it was "significantly reduced" compared with controls.

Animal studies show that chronic stress is associated with decreased endocannabinoid levels. Cannabinoid receptor signaling has been identified as a key modulator of adaptation to stress.

In healthy individuals, acute stress triggers a spike in endocannabinoid levels. Scientists view this as a protective response—the fleeting uptick of anandamide eases stress and facilitates homeostasis (a return to baseline) by dialing down the production of stress hormones through a process known as "pre-synaptic inhibition."

PTSD is one of many enigmatic conditions that may arise because of a dysfunctional endocannabinoid system.

But chronic stress has a different effect than acute stress. Chronic stress depletes endocannabinoid tone and sets the stage for all manner of illness. Chronically elevated stress levels boost anxiety and significantly hasten the progression of Alzheimer's dementia. Emotional stress has been shown to accelerate the spread of cancer. Stress also alters how we assimilate fats.

In 2012, a team of Brazilian scientists found that chronic stress decreases CB-1 receptor binding and expression in the hippocampus, an area of the brain that plays a major role in short and long-term memory consolidation. This has major implications for treating PTSD.

Chronic stress impairs endocannabinoid signaling and impedes fear extinction, according to NYU Medical Center professor Alexander Neumeister. In a recent scientific paper Neumeister argued for PTSD treatments that target the endocannabinoid system.

Neumeister notes that "chronic stress produces an upregulation" of a crucial metabolic enzyme—fatty acid amide hydrolase, otherwise known as FAAH—which decisively influences endocannabinoid signaling.

Various enzymes are involved in the biosynthesis and creation of anandamide; other enzymes break down endogenous cannabinoid compounds. The FAAH enzyme figures prominently in the metabolic breakdown of anandamide and several other fatty acid messenger molecules. FAAH degrades these endogenous compounds; this is part of the normal, fleeting life cycle of anandamide and its fatty acid cousins.

Polymorphisms or unusual amino acid sequence repeats in the genes that encode FAAH are associated with a propensity for drug addiction and predisposition toward various afflictions. But it is the aberrant upregulation and/or down-regulation of genes—more so than the genes themselves—that drives disease vectors. Stress messes with gene expression.

Chronic stress upregulates FAAH, and more FAAH results in lower endocannabinoid levels. Conversely, less FAAH means more anandamide, and more anandamide means elevated cannabinoid receptor signaling.

Cannabidiol—CBD—is a nonpsychoactive component of marijuana and hemp that enhances endocannabinoid tone by inhibiting the FAAH enzyme. And this is just one of the ways that CBD shows promise as a treatment for PTSD.

Brazilian scientists report that CBD reduces anxiety in animal models by binding directly to the 5HT1A serotonin receptor; activating this receptor confers an anxiolytic and anti-depressant effect. Preclinical research in Brazil indicates that "CBD has beneficial potential for PTSD treatment and the 5-HT1A

receptors could be a therapeutic target in this disorder."

CBD and other therapeutic interventions that enhance cannabinoid receptor signaling could become breakthrough treatments for PTSD. CB-1 receptor transmission, in particular, has emerged as a target of novel cannabinoid-based remedies for anxiety and other mood disorders tied to stressful life events.

Smoking marijuana is one method of augmenting CB-1 receptor transmission. Numerous combat veterans and other PTSD patients claim that nothing can calm the storm that rages in their heads like a few puffs of pot. A 2011 observational study by Israeli scientists found that smoked cannabis, which directly activates the CB-1 receptor, improved symptoms of PTSD.

The National Institute on Drug Abuse continues to block FDA-approved research proposed by MAPS, which seeks to study the effects of smoked and vaporized cannabis—including a CBD-rich variety—on military veterans with PTSD.

CBD and other therapeutic interventions that enhance cannabinoid receptor signaling could become breakthrough treatments for PTSD.

Some scientists aren't high on marijuana as a PTSD treatment option. NYU's Neumeister contends that despite "their potential therapeutic value, direct-acting cannabinoid receptor compounds [such as THC] have very limited medical applications, mainly because of their undesirable psychotropic side effects and ability to cause addiction."

This assertion reflects politically correct assumptions rather than scientific fact. The operative premise—that the marijuana high is an adverse side effect—doesn't pass the unbiased smell test. Cannabis doesn't cause addiction any more than food causes a person to become a compulsive eater.

Dismissing smoked cannabis as "an appealing short-term 'solution' that will more likely create longer term problems," Neumeister favors "blocking endocannabinoid deactivation" by inhibiting FAAH, which "may lead to a more circumscribed and beneficial spectrum of biological responses than those produced by direct CB-1 receptor activation."

That is (some of) what CBD does: it inhibits FAAH. Big Pharma, meanwhile, has its sights set on developing and patenting synthetic FAAH-inhibitors to treat PTSD, depression, and other pathological conditions—the very same conditions for which whole plant cannabis provides politically incorrect relief.

Cannabis is often the remedy of choice for people coping with PTSD and other stress-induced maladies. Some are already using CBD-rich extracts and flowers. Many others self-medicate with THC-dominant strains to ease posttraumatic stress. PTSD sufferers can't afford to wait for whatever benefits synthetic FAAH-inhibitors may offer in the years ahead. They need help now.

REFERENCES

Campos AC, *et al.,* "Cannabidiol blocks long-lasting behavioral consequences of predator threat stress: possible involvement of 5HT1A receptors," *Journal of Psychiatric Research,* 2012 Nov4; 46(11):12501-10

Campos, *et al.,* "Predator threat stress promotes long-lasting anxiety-like behaviors and modulates synaptophysin and CB1 receptors expression in brain areas associated with PTSD symptoms," *Neuroscience Letters* (2012) http://dx.doi.org/10.10.16/j.neulet 2012.11.016

Ganon-Elazar E, Akirav I, "Cannabinoids and traumatic stress modulation of contextual fear extinction and GR expression in the amygdala-hippocampal, prefrontal circuit," *Psychoneuroendocrinology,* 2013 Feb 20.

Gorzalka BB, *et al.,* "Regulation of endocannabinoid signaling by stress: implications for stress-related affective disorders," *Neuroscience Biobehavioral Review,* 2008 Aug.

Hill, MN, *et al.,* "Reductions in circulating endocannabinoid levels in individuals with post-traumatic stress disorder following exposure to the world trade center attacks," *Psychoneuroendocrinology,* 2013 Sept 10.

Hill, MN, *et al.,* "Endogenous cannabinoid signaling is essential for stress adaptation," *Proceedings of the National Academy of Science USA,* 2010 May 18.

Hill, MN, *et al.,* "Downregulation of endocannabinoid signaling in the hippocampus following chronic unpredictable stress," *Neuropsychopharmacology,* 2005 March

Mikuriya, Tod, MD, "Cannabis Eases Post-Traumatic Stress," O'Shaughnessy's, Spring 2006.

Neumeister, Alexander, "The endocannabinoid system provides an avenue for evidence-based treatment development for PTSD," *Depression and Anxiety,* 30:93-96 (2013).

Van Rijn *et al.,* "Endocannabinoid System Protects Against Cryptogenic Seizures," *Pharmacology Reports* 63[1][2011]: 165–68).

Martin A. Lee *is the author of several books including* Acid Dreams *and most recently* Smoke Signals: A Social History of Marijuana: Medical, Recreational, and Scientific. *He is a co-founder of the media watch group Fairness and Accuracy in Reporting (FAIR) and director of Project CBD, an educational service focusing on cannabis science and therapeutics. For more information, visit* ***projectCBD.org*** *or to make a tax-deductible contribution to support Project CBD's efforts, visit* ***maps.org/projectCBD****. Martin can be reached at aciddreamer@gmail.com.*