Cannabis for Posttraumatic Stress Disorder

Psychological Health Center of Excellence Psych Health Evidence Briefs

December 2020

What is cannabis?

Cannabis, a derivative of the *Cannabis sativa* plant, is a commonly used psychoactive drug. Cannabinoids, the active ingredients of cannabis, include Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD). The psychoactive properties of cannabis are largely attributed to THC. Referred to as medical marijuana when used for therapeutic purposes, cannabis has been proposed as a therapeutic intervention for a wide range of medical and psychological conditions, including cancer, HIV/AIDS, multiple sclerosis, posttraumatic stress disorder (PTSD), anxiety disorders, mood disorders, and chronic pain (Turna, Patterson, & Van Ameringen, 2017). Researchers face significant barriers to examining the potential therapeutic value of cannabis as a consequence of its classification as a Schedule 1 Drug (Krumm, 2016). Despite federal legal restrictions, many states have approved cannabis for the treatment of medical and psychological conditions. PTSD is among the approved conditions for medical marijuana in some states (Steenkamp, Blessing, Galatzer-Levy, Hollahan, & Anderson, 2017).

What are the potential mechanisms of action underlying cannabis for the treatment of PTSD?

Cannabinoids that occur naturally in the body (endocannabinoids), plant-produced phytocannabinoids (such as THC and CBD), and synthetically derived cannabinoids target the CB₁ and CB₂ receptors of the endocannabinoid system. Cannabis has wide-ranging acute neuropsychological and subjective effects with limited data on long-term effects (Hunault et al., 2014; Volkow et al., 2016). CB₁ receptors are widespread throughout the prefrontal-limbic system, including brain regions implicated in PTSD, and are involved in modulation of a variety of behaviors, including mood, stress, anxiety, learning, memory, and fear extinction (Bailey, Cordell, Sobin, & Neumeister, 2013). It is hypothesized that treatment with cannabinoid drugs could result in modulation of cognitive processes (memory, anxiety, depression) involved in the development or maintenance of PTSD symptoms, leading to a reduction in those symptoms. However, to date there is little human data available to support this hypothesis (Berardi, Schelling, & Campolongo, 2016). Recent research indicates that the CBD constituents of cannabis may have anxiolytic properties (Steenkamp et al., 2017). Research has also found differences in endocannabinoid receptor sensitivity between people with and without PTSD, and animal studies have shown that the endocannabinoid system appears to be involved in the extinction of fear memories (Yehuda et al., 2015), a likely deficit in PTSD.

Is cannabis recommended as a treatment for PTSD in the Military Health System (MHS)?

No. The 2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder recommends against the use of cannabis for treating PTSD, due to lack of evidence of its efficacy, known adverse effects, and associated risks, with a "Strong Against" strength of recommendation.

The MHS relies on the Department of Veterans Affairs (VA)/Department of Defense (DoD) clinical practice guidelines (CPGs) to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

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Do other authoritative reviews recommend cannabis as a treatment for PTSD?

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No. Other authoritative reviews have not substantiated the use of cannabis for PTSD.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) and Cochrane.

- · AHRQ: No reviews were found on cannabis as treatment for PTSD.
- · Cochrane: No reviews were found on cannabis as treatment for PTSD.

What conclusions can be drawn about the use of cannabis as a treatment for PTSD in the MHS?

The lack of an evidence base along with the known adverse effects and associated risks of cannabis use have led to a strong recommendation against the use of cannabis as an evidence-based treatment for PTSD in the MHS (VA/DoD, 2017). There is currently little to no evidence of the efficacy of cannabis as a treatment for PTSD (Sarris, Sinclair, Karamacoska, Davidson, & Firth, 2020). Furthermore, there is a concern about the potential negative effects of cannabis use, which may include impairments in learning, memory, and attention with acute cannabis use, worsened respiratory symptoms and more frequent chronic bronchitis episodes with long-term cannabis smoking, increased risk of motor vehicle crashes, increased risk of developing schizophrenia and other psychoses, and increased risk for developing social anxiety disorder, among others (National Academies of Sciences, Engineering, and Medicine, 2017). However, ongoing research is examining the use of marijuana as a treatment for PTSD in veterans, along with several trials examining civilian populations.

There are additional legal barriers for veterans and active-duty service members in regard to medical marijuana. Veterans Health Administration (VHA) Directive 2011-004 (Department of Veterans Affairs, 2011) stipulates that the VA must comply with the Controlled Substances Act, under which marijuana is classified as a Schedule I drug. Veterans participating in state marijuana programs must not be denied VHA services, but VA providers are prohibited from completing forms that seek recommendations or opinions regarding a veteran's participation in a state marijuana program. The VA will not provide or pay for medical marijuana approved by a state program. Within DoD, Article 112a of the Uniform Code of Military Justice (2010) specifically prohibits active-duty service members from using marijuana.

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