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What About Medical Marijuana Use for Veterans With PTSD?

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Editor's Note: *Post-traumatic stress disorder (PTSD) is increasingly acknowledged as a serious health concern. People suffering from PTSD are at a higher risk of substance abuse, suicide, and other comorbidities.*

PTSD Common Among Veterans and Complicated by Pharmaceuticals

An estimated one in 15 Americans will experience PTSD at some time in their lives, producing high levels of stress and anger. (Mark Thompson, *Post-traumatic Marijuana*, 188(8) *Time Mag.* 34-37 (2016).) For veterans, the rates are even higher. The Veterans Administration (VA) has diagnosed over 100,000 veterans with PTSD (approximately 30% of veterans it has treated). (Jaimie L. Gradus, *Epidemiology of PTSD*, Dep't of Veterans Affairs (last updated Mar. 30, 2017), available at www.PTSD.VA.gov/professional/PTSD-Overview/Epidemiological-Facts-PTSD.asp.) According to annual estimates from the VA, nearly one in five veterans who served in Afghanistan and Iraq have experienced PTSD; 30% of Vietnam veterans have suffered from the disorder; and many have been arrested for drug- or alcohol-related charges. (Rand Corp., *One In Five Iraq and Afghanistan Veterans Suffer From PTSD or Major Depression*, press release, Apr. 17, 2008; *Invisible Wounds of War: Psychological and Cognitive Injuries, Their Consequences, and Services to Assist Recovery* (Terri Tanielian & Lisa H. Jaycox, eds. Rand Corp. 2008); J. Sundin et al., *PTSD After Deployment to Iraq: Conflicting Rates, Conflicting Claims*, 40 *Psychological Med.* 367-82 (2010).)

There is also a correlation between PTSD, substance use disorders (SUD), and suicide rates among veterans. Nearly one of every three veterans seeking treatment for SUD also has PTSD. (*Veterans Statistics: PTSD, Depression, TBI, Suicide*, Feb. 14, 2015, available at www.VeteransAndPTSD.com/PTSD-Statistics.html.) A research paper published by JAMA found that VA doctors prescribed significantly more opiates to patients with PTSD and depression than to other veterans. (K.H. Seal et al., *Association of Mental Health Disorders With Prescription Opioids and High-Risk Opioid Use in U.S. Veterans of Iraq and Afghanistan*, 307(9) *JAMA*, 940-47 (2012).) Additionally, it is reported that off-label use of opioids is widespread among veterans who have been diagnosed with PTSD. (Aaron Glantz, *VA's Opiate Overload Feeds*

Veterans' Addictions, Overdose Deaths, The Center for Investigative Reporting, Sept. 28, 2013, available at <http://CIROnline.org/Reports/VAs-Opiate-Overload-Feeds-Veterans-Addictions-Overdose-Deaths-5261>.)

The veteran population is especially prone to PTSD and related health problems, which makes this population paradoxically vulnerable to suicidal ideation with the fortitude to carry it out. Moreover, the two most prevalent antidepressants prescribed for PTSD, Zoloft® and Paxil®, have been found, ironically, to double the risk of suicidal thinking and suicidal attempts in people under the age of 24, the same cohort as returning veterans. (See *J.R. Minkel*, *Risks and Benefits Collide in Expanded Suicide Warning for Antidepressants*, *Sci. Am.* (May 3, 2007), available at www.ScientificAmerican.com/article/Risks-and-Benefits-Collide-in-Expanded-Suicide-Warning-for-Antidepressants. See generally *Medical Cannabis Resource Center*, *Information on PTSD (2015)*, available at http://MercyCenters.org/libry/i_PTSD.html.) With all these influences eroding their mental health, it should not be surprising that veterans “are not only more predisposed to have suicidal thoughts, often associated with PTSD and depression, they are more likely to act on it.” (*L. Sher et al.* *Posttraumatic Stress Disorder, Depression, and Suicide in Veterans*, 79(2) *Cleveland Clinic J. Med.* 92-97 (2012). See also *Center for a New American Security*, *Losing the Battle: The Challenge of Military Suicide (Oct. 2011)*; *Amy S.B. Bohnert et al.*, *Accidental Poisoning Mortality Among Patients in the Department of Veterans Affairs Health System*, 49 *Med. Care* 393-96 (2011).) The federal government has classified marijuana as a dangerous drug and has ignored its possible medical value. The 29 states with medical marijuana (MMJ) laws are about evenly divided on categorizing PTSD as a debilitating disease or illness for the purpose of MMJ use. While scientists, lawmakers, the general public, and the veterans themselves have mixed opinions on the topic, MMJ use for veterans with PTSD is gaining traction. Many veterans’ organizations and associations are involved in the push for laws and policies that permit veterans to use MMJ without legal consequences. VA policy changes permit veterans to use MMJ in states that permit it under their MMJ programs. The federal Veterans Equal Access Amendment has been resurrected in Congress, which would lift the “gag order” that currently prevents VA doctors from discussing the benefits of MMJ therapy with their veteran patients. Also, the DEA has approved a study that specifically addresses MMJ for PTSD in veterans. This article will define PTSD; explain how and why marijuana may medically assist with PTSD; discuss the brain science and the efficacy of MMJ use for PTSD; set forth the status of state MMJ laws related to PTSD as a debilitating medical condition; and set forth VA policies and federal legislation related to the topic.

Definition of PTSD

PTSD is an anxiety disorder that presents an array of symptoms ranging from flashbacks, nightmares, and sleep disorders to depression. Typically, PTSD is triggered by experiencing or witnessing a traumatic event, such as an event that involves a life threat, serious injury, or death, which is the primary reason the disorder is prevalent among veterans. Recurring symptoms may be triggered by later unrelated events.

Despite its prevalence, PTSD was not considered a psychological disorder until the 1980s.

Diagnostic criteria for PTSD contemplates a history of exposure to a traumatic event that meets specific stipulations and symptoms from each of the following four symptom clusters:

1. Intrusion;
2. Avoidance;
3. Negative alterations in cognitions and mood; and
4. Alterations in arousal and reactivity.

Other criteria include the duration of symptoms, the level of functioning of the patient, and the determination that the symptoms are not attributable to a substance or co-occurring medical condition. (Am. Psychiatric Ass'n, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V)*.)

Marijuana and the Brain

The interplay between marijuana and the brain occurs in the endocannabinoid system. Unlike the opiate system and opiate receptors that were identified in the early 1970s, scientists did not learn about the endocannabinoid system and cannabinoid receptors until the late 1980s and early 1990s, respectively. Endocannabinoids—chemical cannabinoids—are naturally produced by the body and brain. There are primarily two chemical endocannabinoids: anandamide (the so-called "bliss molecule"), identified in 1992, and sn-2 arachidonoylglycerol (2AG), identified in 1995. Anandamide is involved in regulating mood, memory, appetite, pain, cognition, and emotions. (See L.O. Hanus, *Pharmacological and Therapeutic Secrets of Plant and Brain (Endo)cannabinoids*, 29(2) *Med. Res. Rev.* 213-71 (Mar. 2009); Alexandros Makriyannis et al., *Therapeutic Opportunities Through Modulation of the Endocannabinoid System*, 48(8) *Neuropharmacol.* 1068-71 (June 2005).)

Phytocannabinoids. The marijuana plant contains plant cannabinoids—phytocannabinoids—that mimic the body's naturally produced endocannabinoids like anandamide. These plant cannabinoids bind to human endocannabinoid receptors. The marijuana plant contains between 60 and 85 cannabinoids, some of which are psychoactive and some of which are not. The "premier" marijuana plant psychoactive cannabinoid is delta 9-tetrahydrocannabinol, more commonly referred to as THC. Cannabidiol (CBD) is another cannabinoid with little psychoactive effect that is gaining much attention for its potential medicinal qualities. Not unlike the poppy plant, which produces opium that is refined into heroin, which mimics the body's naturally produced dopamine, the marijuana plant produces cannabinoids that mimic the body's naturally produced anandamide and 2AG. (See P. Anand et al., *Targeting CB2 Receptors and the Endocannabinoid System for the Treatment of Pain*, 60(1) *Brain Res. Rev.* 255-66 (2009). See also M.O. Bonn-Miller et al., *Cannabis Use Among Military Veterans After Residential Treatment for Posttraumatic Stress Disorder*, 25(3) *Psychol. Addict. Behav.* 485-91 (Sept. 2011).)

Cannabinoid Receptors. Cannabinoid receptors (CB1 and CB2 receptors) are situated throughout the body and the brain. In fact, it is the largest receptor system in the human body and affects all areas of the brain, and as such, the system regulates everything humans feel, think, and do. It includes, most importantly to PTSD, the hippocampus region that affects memory.

Research has demonstrated that the human endocannabinoid system plays a significant role in PTSD. People with PTSD have greater availability of CB1 receptors than trauma-exposed or healthy controls. As a result, marijuana use by individuals with PTSD may result in short-term reduction of PTSD symptoms. Cannabis plays an important role in the extinction learning of aversive memories. (See Nora D. Volkow, *The Biology and Potential Therapeutic Effects of Cannabidiol*, NIDA, June 24, 2015, available at www.DrugAbuse.gov/About-NIDA/Legislative-Activities/Testimony-to-Congress/2016/Biology-Potential-Therapeutic-Effects-Cannabidiol; K. Maresz et al., *Direct Suppression of CNS Autoimmune Inflammation via the Cannabinoid Receptor CB1 on Neurons and CB2 on Autoreactive T Cells*, 13 *Nat. Med.* 492-97 (2007); A. Neumeister et al., *Elevated Brain Cannabinoid CB1 Receptor Availability in Post-traumatic Stress Disorder: A Positron Emission Tomography Study*, 18(9) *Molecular Psychiatry* 1034-1040 (2013). See also E.S. Onaivi, *Cannabinoid Receptors in Brain: Pharmacogenetics, Neuropharmacology, Neurotoxicology, and Potential Therapeutic Applications*, Ch. 12, 88 *Int'l Rev. of Neurobiology* 335-69 (2009).)

Benefits of MMJ May Be More Pronounced Among Veterans

Given the way that the brain operates and the “scars” that are common among veterans, MMJ may help this population more than other (non-traumatized) populations. Other differences in the groups tested may account for other disparities in the study outcomes, discussed further below.

Extinction Therapy. One team of brain scientists has shown that giving a single dose of THC may be helpful to people during the process known as extinction therapy, which is designed to train the brain to stop reacting to triggers that produce fear and anxiety. (C.A. Rabinak et al., *Cannabinoid Facilitation of Fear Extinction Memory Recall in Humans*, 64 *Neuropharmacology* 396-402 (Jan. 2013). See also P. Roitman et al., *Preliminary, Open-Label, Pilot Study of Add-On Oral Δ 9-Tetrahydrocannabinol in Chronic Post-traumatic Stress Disorder*, 34(8) *Clinical Drug Investigation* 587-91 (2014); A.R. Gutman et al., *Functional Interactions Between Endocannabinoid and CCK Neurotransmitter Systems May Be Critical for Extinction Learning*, 34(2) *Neuropsychopharmacol.* 509-21 (2009); Giovanni Marsicano et al., *The Endogenous Cannabinoid System Controls Extinction of Aversive Memories*, 418(6897) *Nature* 530-34 (2002).) The study found that THC in addition to the therapy produced long-term reductions in anxiety. So, THC may be most useful when used for a short time in combination with other therapy.

However, THC has been shown to have long-term negative effects on the brain. It has been found to be a predictor of stress cardiomyopathy in younger men. Heavy cannabis use is associated with reduced dopamine release in the brain, affecting learning behavior. It affects the corpus callosum, affects bipolarity, causes psychosis, places male adolescents at high risk for schizophrenia, shrinks and rewires the brain, and

causes a reduction in IQ for those under 21. (See R.J. Hilt, *Cannabis and the Adolescent Brain*, 43(3) *Pediatric Annals* 89-90 (2014).)

Preventing PTSD. Some studies suggest that, not only is MMJ capable of treating the symptoms associated with PTSD, it may be able to prevent the development of this debilitating condition. A University of Haifa study concluded that marijuana use prevents the negative behavioral and physiological effects of a traumatic event and its reminders and thus aids with the symptoms of PTSD. (Compassionate Care New York, *The New York Medical Marijuana Program: Medical Cannabis for PTSD*, press release, Oct. 15, 2015, available at www.CompassionateCareNY.org/wp-content/uploads/mmj_ptsd_Fact-Sheet.pdf.) In 2016, the Drug Enforcement Administration approved a Colorado MMJ and PTSD study, sponsored by the nonprofit group Multidisciplinary Association for Psychedelic Studies (MAPS) with a \$2.16 million grant from the Colorado Department of Public Health and Environment. The DEA's approval allows researchers, using marijuana from the National Institute of Drug Abuse, to set up protocols to measure the efficacy of various potencies of smoked or vaporized marijuana among military veterans with chronic, treatment-resistant PTSD against a placebo treatment. (Bryan Bender, *American Legion to Trump: Allow Marijuana Research for Vets*, Politico.com, May 20, 2017, available at www.Politico.com/story/2017/05/20/Veterans-Marijuana-Trump-American-Legion-238626.)

Pain Management. There is also research indicating that MMJ can help with pain. Studies have found that MMJ can be substituted for prescription opioids. "Used in combination with or instead of opioids, the addition of cannabis often allows the patient to decrease the dosage of opioid medication required to relieve pain," which in turn may decrease opioid overdoses. (P. Lucas, *Cannabis as an Adjunct to or Substitute for Opiates in the Treatment of Chronic Pain*, 44(2) *J. Psychoactive Drugs* 125-33 (Apr.-June 2012); D.I. Abrams et al., *Cannabinoid-Opioid Interaction in Chronic Pain*, 90(6) *Clinical Pharmacology & Therapeutics* 844-51 (2011); B.E. Perron et al., *Use of Prescription Pain Medications Among Medical Cannabis Patients: Comparisons of Pain Levels, Functioning, and Patterns of Alcohol and Other Drug Use*, 76(3) *J. Studies on Alcohol & Drugs* 406-13 (2015); NY State Office of Mental Health, *Post-traumatic Stress Disorder Booklet*, 2014, available at www.OMH.ny.gov/omhweb/booklets/PTSD.pdf.)

Medication Use Reduced. According to a recent study published in Health Affairs, researchers found that in nine states with MMJ, Medicaid prescriptions for painkillers, antidepressants, and anti-anxiety medications dropped significantly. (Brian Heuberger, *Medical Marijuana: Can It Help Combat the Opioid Addiction Epidemic?*, Colorado Politics, May 24, 2017, available at www.ColoradoStatesman.com/Medical-Marijuana-Help-Combat-Opioid-Addiction-Epidemic.) One study found that deaths related to opiate abuse in 13 states fell roughly one-third in the six years after the states' MMJ laws took effect. (M.A. Bachhuber et al., *Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010*, 174(10) *JAMA Internal Med.* 1668-73 (2014).) Other studies have shown similar reductions in deaths caused by opiates in states that have passed medical marijuana laws, as well as a decrease in prescriptions for painkillers. (See, e.g., B. Gordon, *Advocates Concerned*

New York Medical Marijuana Rules Omit Approval for PTSD Treatment, Watertown Daily Times, Apr. 8, 2015, available at www.WatertownDailyTimes.com/news03/Advocates-Concerned-New-York-Medical-MarijuanaRules-Omit-Approval-for-PTSD-Treatment-20150408.)

Some Studies Question Effectiveness of MMJ

Uncertainty in Efficacy. There are mixed findings regarding the effectiveness of MMJ as a treatment option for ailments and illnesses. (P. Whiting et al., *Cannabinoids for Medical Use: A Systematic Review and Meta-analysis*, 313 JAMA 2456-73 (2015); K. Hill, *Medical Marijuana for Treatment of Chronic Pain and Other Medical and Psychiatric Problems: A Clinical Review*, 313 JAMA 2474-83 (2015).)

With respect to the efficacy of MMJ for PTSD in particular, there are conflicting studies. For example, a 2015 report published in *Addiction Science & Clinical Practice* found that there is insufficient scientific evidence for MMJ use at this time, including for the treatment of PTSD. (Katherine A. Belendiuk et al., *Narrative Review of the Safety and Efficacy of Marijuana for the Treatment of Commonly State-Approved Medical and Psychiatric Disorders*, 10(10) *Addiction Sci. & Clin. Practice* (2015). See also Marcel O. Bonn-Miller & Glenna S. Rousseau, *Marijuana Use and PTSD Among Veterans*, Nat'l Ctr. for PTSD (n.d.) (cautioning that "there is no evidence at this time that marijuana is an effective treatment for PTSD. In fact, research suggests that marijuana can be harmful to individuals with PTSD.") See generally P. Roitman et al., *Preliminary, Open-Label, Pilot Study of Add-On Oral Δ 9-Tetrahydrocannabinol in Chronic Post-traumatic Stress Disorder*, 34(8) *Clinical Drug Investigation* 587-91 (2014).) One meta-study on the efficacies of medical marijuana found only limited evidence that medical marijuana assists with PTSD. (Nat'l Academies of Sciences, Engineering, & Medicine, *The Health Effects of Cannabis and Cannabinoids: Committee's Conclusions*, Jan. 2017, available at <http://NationalAcademies.org/hmd/~media/Files/Report%20Files/2017/Cannabis-Health-Effects/Cannabis-Conclusions.pdf>.)

Possible Tolerance, Addiction. Some studies have suggested that MMJ may be harmful. Data suggest that continued use of marijuana among individuals with PTSD may lead to a number of negative consequences, including marijuana tolerance and addiction. (See Sidebar: *NAS Report Evaluates Evidence on Medical Marijuana*.) Beyond being physically dependent on a drug and experiencing physiological effects if the drug is stopped suddenly, "addiction" refers to behaviors that are compulsive, partially out of control or worse, and often escalating in severity and intensity. (See J.E. Joy et al., *Marijuana and Medicine: Assessing the Science Base* (1999). See also Barret Michalec et al., *Assessing Physicians' Perspectives and Knowledge of Medical Marijuana and the Delaware Medical Marijuana Act*, 9(3) *J. Global Drug Policy & Practice* 1 (Fall 2015). Cf. R.J. Hilt, *Cannabis and the Adolescent Brain*, 43(3) *Pediatric Annals* 89-90t (2014).)

There are reports, however, indicating that marijuana is no more addictive than anti-anxiety medication and far less addictive than alcohol and tobacco. Some research indicates that there is a strong *psychological* addiction to marijuana, but there is not a consensus on *physiological* addiction. Most people can use marijuana without

becoming addicted, but for users with vulnerabilities like stress, mental illness, or genetic predisposition, the risk of dependence is serious.

In fact, addiction to marijuana, also known as "cannabis use disorder," is already prevalent in the veteran population suffering from PTSD. There has been an increase from 13% in FY 2002 to 22.7% in FY 2014. As of FY 2014, there were more than 40,000 veterans with PTSD and SUD seen in VA diagnosed with cannabis use disorder. (Bonn-Miller & Rousseau, *supra*.) Cannabis use disorder is classified and coded in the *DSM-V*.

Medical Marijuana Law and Policies

VA Policies. While marijuana use by veterans is still prohibited under the military's zero tolerance drug policy, beginning in 2010, the U.S. Department of Veterans Affairs formally allowed patients treated at its hospitals and clinics to use MMJ in states where it is legal. The VA itself will not actually prescribe medical marijuana, but veterans who are using it will not have their benefits or their pain medications ended. A congressional committee circulated a petition seeking to allow veterans to discuss MMJ as an option for treatment with their VA doctors. "The Veterans Equal Access Amendment would lift the 'gag order' that currently prevents V.A. doctors from discussing the benefits of MMJ therapy with their veteran patients." (*See* www.SafeAccessNow.org/veteran_2017_Daines.)

The American Legion, in September 2016, passed a resolution and asked Congress "to recognize the potential medical value of marijuana on behalf of the millions of U.S. military veterans who could benefit by seeing cannabis reclassified by the federal government." (Andrew Blake, *American Legion Asks Congress for New Marijuana Laws*, *The Wash. Times*, Sept. 9, 2016, available at www.WashingtonTimes.com/news/2016/sep/9/American-Legion-Veterans-Group-Asks-Congress-New-m.)

Federal Regulations. Marijuana use still remains illegal under federal law. According to the Federal Controlled Substances Act, marijuana is a Schedule I drug, along with heroin, LSD, PCP, and crack cocaine, meaning a drug with a high risk of abuse and no safe and accepted medical use. There have been two major legal challenges to this classification, both unsuccessful, even with support from the American College of Physicians and other professional health-oriented societies, and as recently as August 2016, the DEA decided not to change marijuana from its Schedule I status. However, the DEA has approved further growing facilities for research in addition to the sole grower and researcher, the University of Mississippi. In May 2017, the House and Senate passed an omnibus spending bill that included a provision to prevent federal entities, such as the DOJ and DEA, from prosecuting individuals and businesses acting in compliance with state MMJ laws. For now, MMJ laws are safe.

Congress revived an old bill (HR 1538) in June 2017 (now HR 2924), the Compassionate Access, Research Expansion, and Respect States Act of 2017 (CARERS Act), to "extend the principle of federalism to State drug policy, provide access to medical marijuana, and enable research into the medicinal properties of marijuana."

(*Id.*, available at www.GovTrack.us/congress/bills/115/HR2920.) The 2015 version of the CARERS Act was the first bill in the U.S. Senate to seek to legalize MMJ for veterans receiving care in VA facilities.

However, the 114th congressional legislative term also saw the death of the Marijuana Effective Drug Studies Act of 2016 (the MEDS Act), bipartisan legislation that would have made it easier for researchers to study the medical effectiveness and safety of marijuana.

In May 2016, both the Senate and the House approved the Veterans Equal Access Amendment, which would have given veterans the right to access medical marijuana programs in those states with MMJ laws on the books without recrimination against the veteran or the doctor. (See www.Congress.gov/bill/114th-congress/house-bill/667.) This bill has been reintroduced in the 2017-2018 session.

One successful bill was the bipartisan Comprehensive Addiction and Recovery Act (CARA), which seeks to improve opioid safety measures at the Department of Veterans Affairs medical centers and expand research and education on complementary and integrative health to veterans. (S. 524, 114th Cong. (2016).)

Veterans Deserve Any Possible Assistance

Twenty-nine states, the District of Columbia, and two territories have MMJ laws on the books; eight states allow recreational marijuana. Approximately 50% of the MMJ state programs list PTSD as qualifying condition. Several states are contemplating bills to add PTSD to the list of qualifying conditions for MMJ use, including New York, Illinois, and Iowa. States such as Utah, Michigan, and New Jersey, have had recent proposals to include PTSD as a debilitating condition under existing MMJ laws. Many of these battles are led by veterans' organizations. In Michigan, veterans led the fight and were successful. In Utah, the Utah Veterans for Medical Cannabis remains actively pursuing changes to state law, and in New Jersey, the Coalition for Medical Marijuana New Jersey, a veterans' group, fought for the laws to change.

All of these developments seem to be softening the access to MMJ for veterans with PTSD, but MMJ for PTSD is not without controversy and concern. The science and studies are mixed on whether there is a true efficacy around the use of marijuana for PTSD and there remain concerns about addiction, cannabis use disorder, and SUD for veterans who use marijuana. Whatever the outcome, one thing is clear: Veterans who have served the country deserve any assistance that modern science and medicine can offer. Perhaps the time has come to conduct a rigorous scientific study to find out whether marijuana actually helps people with PTSD.

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