Cannabis: Exit Drug to Neurotherapy

Waqas Rasheed[a*], Aamir Saeed Malik[b]

[a]*Department of Neurobiology and Behavior, University of California Irvine, Irvine, CA, United States*.
[b]*Department of Electrical & Electronic Engineering, University of Jeddah, Jeddah, Saudi Arabia*.

Abstract

This article reviews the use of cannabis for therapeutic purpose. Cannabis or marijuana had been used as a medicine in ancient China, but the illicit use of substance was stigmatized under the United Nations' single convention on narcotic drugs. Researchers have conducted limited preclinical and clinical studies using medical marijuana, mainly as curative for memory impairment, or exit drug for substance abuse cases. The use of Cannabis for Therapeutic Purposes (CTP) in several neurological disorders is also discussed together with respective details. Finally, the similarity of CTP objectives with neurofeedback, and future research recommendations are proposed. The information presented in this article shows potential and scope of CTP with complete references.

Keywords: Cannabis, Exit Drug, Neurotherapy, therapeutic, medicine, CTP, neurofeedback, severe pain relief.

ARTICLE INFO	
RECEIVED	February 10, 2020
REVIEWED	March 30, 2020
ACCEPTED	April 30, 2020

** Corresponding author.*

Email: *wrasheed@uci.edu*

1. Introduction

Although, cannabis (or marijuana) had been used in ancient China as a medicine (Li, 2974; Zuardi, 2006), the use of cannabis has been stigmatized worldwide since 1961, under the United Nations' single convention on narcotic drugs (Bayer & Ghodse, 1999). In the United States, National Organization for the Reform of Marijuana Laws (NORML) was founded in 1970, which seeked synthetic cannabinoids decriminalized in private possession; however, the legislation failed to change the drug abuse and controlled substance acts (Roffman, 2013). A compassionate use act was passed in 1996 by California state of the US, in order to defend medical use and cultivation of marijuana (Annas, 1997). Even when the federal court and the government opposed the act, medical use of cannabis remained in pracftice in California early 2000s, which also instigated other states to legalize cannabis for medical use. President Barrack Hussain Obama, during his second term, permitted the possession of small amounts of marijuana, and its prohibition under the controlled substance act no longer stayed a federal priority and a significant step towards more tolerant approach to cannabis (Harder, 2016). Contrarily, Trump administration, in 2018, reiterated marijuana to be a dangerous drug, and any activity involving its use or possession is a serious crime (Sessions, 2018). Presently, California bears a multi-billion dollar cannabis industry; whereas, the federal laws and many committed hardliner prohibitionists oppose it (Carroll, 2017). Similar situation has been observed in other countries after 1961 (DeCloedt, 2018). This legally ambiguous status and the under-researched knowledge related with cannabis has vexed the differentiation between medical and adulterous use of cannabis, which has barred the clinicians from practicing the commendable benefits of the cannabinoids (Islam, 2019).

Cannabis is extracted from a plant called cannabis sativa, which contains some 65 chemical compounds that alter neurotransmitter release in the brain (Newton, 2013). These compounds act on cannabinoid receptors, which are part of the endocannabinoid system, situated throughout the body, involved in a variety of physiological processes (e.g. appetite, mood, memory, and pain perception) (Aizpurua-Olaizola et al., 2017). Essentially, the cannabinoid receptors are categorized as CB_1 and CB_2 (Matsuda, Lolait, Brownstein, Young, & Bonner, 1990). CB_1 receptor is active in brain, lungs, liver, kidneys, and genitals; whereas, CB_2 is observed in the immune system and in hematopoietic cells with a limited presence in the brain (Preet et al., 2011).

Researchers have also been producing synthetic cannabinoids, which may not exist naturally, but imitate the physiological and pharmacological properties of the natural ones (Newton, 2013). Benefits of research for effects of cannabinoids on mammalian body and mind resulted in the form of medical drugs used to treat various physical and mental conditions. The most commonly known product is Marinol® (contains dronabinol), manufactured by United Pharmaceuticals Inc. Dronabinol is known to treat anorexia, nausea and vomiting associated with HIV/AIDS and cancer chemotherapy in pharmacoresistant cases (Badowski, 2017; Badowski & Yanful, 2018). Cesamet® (contins nabilone) is yet another example of synthetic cannabinoid product for medical use.

Considering cannabinoid receptors are active in the brain, there psychoactive effects have been researched, essentially studying clinical use of delta-9-tetrahydrocanabinol (THC). A non-psychoactive cannabinoid, cannabidiol (CBD), has also made it to the clinical studies; however, CBD is poorly characterized (Falkenham, 2018). THC shows affinity towards CB_1 receptor; however, CBD bears a partial affinity towards CB_1. Therefore, THC induces positive psychotic symptoms because it increases dopaminergic activitry in the mesolimbic reward pathway, which eventually leads to its addiction and abusive properties (Szabo, Siemes, & Wallmichrath, 2002) .

Research has reported benefits of THC for treating appetite loss in AIDS and Alzheimer's patients (Beal et al., 1997). It is also reported that cannabis suppresses spasticity and tremors that are observed in the patients suffering from multiple sclerosis or spinal cord injury (Clifford, 1983). Research also reports benefits of medical cannabinoids during care of Tourette's syndrome (Sandyk & Awerbuch, 1988). Another successful trial of canabinoids has been reported in glaucoma patients, where smoking marijuana help reduce the intraocular pressure (Hepler & Frank, 1971). This review focuses on the therapeutic benefits of medical cannabinoids for treatment of several neuronal disorders from central nervous system.

2. Literature Review

Although, the negative consequences of marijuana on physical and mental health are widely known (psychosis, memory and learning impairment, cancer, and respiratory diseases), research has demonstrated its neurotherapeutic effects on several neuronal dysfunctions, particularly for recovery from anxiety, epilepsy, post-traumatic stress disorder (PTSD), depression, attention deficit hyper disorder (ADHD), and psychosis (Aldington et al., 2008; Blows et al., 2005; Cairns, Yap, Pilkington, & Jorm, 2014; Fergusson, Horwood, & Beautrais, 2003; Gage, Hickman, & Zammit, 2016). Currently, the research for medical use of cannabinoids falls under a general term Cannabis for Therapeutic Purposes (CTP) (Walsh et al., 2013).

2.1. Cannabis Substitution for Problematic Substance use

Patients, engaged in licit or illicit drug use, prescription drug abuse, and alcohol, may seek recovery by using medical cannabis as a substitution substance (Reiman, 2009). This substitution of one psychoactive substance for another in order to reduce, control, or limit the negative outcomes is termed as harm reduction. The evidence suggests that cannabis may be used as an "exit drug" in order to reduce or limit any other substance abuse (Lucas et al., 2013; Reiman, 2009). The non-rewarding cannabinoid, CBD, may also be used as cannabis drug substitution substance, as it does not cause addiction. Epidiolex is a CBD based prescription drug in the US that is used to avert couple of childhood epilepsy issues, Dravet syndrome, and Lennox-Gastaut syndrome (Devinsky et al., 2016).

2.2. Severe Pain Relief

Neuropathic pain (NP) symptoms associated with multiple sclerosis (MS) are usually treated inadequately. Literature reports that Dronabinol is a long-term and safe treatment option (Schimrigk et al., 2017). Cannabis is also known to be prescroption drug for general severe pain relief (Bachhuber, Arnsten, & Wurm, 2019; Reiman, 2009).

2.3. Post-Traumatic Stress Disorder (PTSD) and Social Anxiety Disorder (SAD)

Literature reports significant results of CTP in cases with anxiety disorders; particularly, PTSD and SAD (Buckner et al., 2012). PTSD, usually observed after combat injuries or surviving life threatening situations, hampers the emotional response and alters perception of the surrounding world. In addition to standard treatment methods, psychotherapy and medication, cannabinoids has emerged as a side effect proof alternative, which prevent traumatic memories and help attain emotional stability (Fraser, 2009; Shishko, Oliveira, Moore, & Almeida, 2018). Similarly, characterization of anxiogenic and anxiolytic properties of cannabinoids are very useful to understand SAD, and research reports a decreases in SAD following CBD administration (Crippa et al., 2011; Millar et al., 2019).

2.4. Depression

Although, longitudinal studies suggest an association of heavy cannabis use with increased depressive symptoms among some cases, literature reports effective treatment of depressive and manic symptoms of bipolar disorder (Ashton, Moore, Gallagher, & Young, 2005; Degenhardt, Hall, & Lynskey, 2003; Scherma et al., 2018).

2.5. Schizophrenia

Although the available antipsychotic drugs have considerable limitation, they remain a key element of schizophrenia treatment. Essentially, CBD shows antipsychotic properties, and it may stabilize psychotomometic properties of THC. Therefore, there is a possibility that clinical cases at risk of schizophrenia or psychosis may benefit from cannabis in order to improve prodromal symptoms (Moore et al., 2007).

2.6. Alzheimer's Disease

Literature reports that a low dose of THC enhances mitochondria function and slows down β-amyloid proteins; assumed to be the chief contributors of Alzheimer's progression (Cao et al., 2014). This assumption is tested over a preclinical study using mouse model, and the results show that THC does slow down memory impairment (Aso, Andrés-Benito, Carmona, Maldonado, & Ferrer, 2016).

2.7. Epilepsy

Pharmacoresistant epilepsy cases, a third of the whole epileptic population, stand at risk of severe morbidity. Literature suggests that CBD reduces seizure frequency and maintains an adequate safety profile in treatment-resistant young epilepsy cases (Devinsky et al., 2016).

3. Inferences and Discussion

The review of literature associated with CTP clearly demonstrates the potential and scope of the cannabinoids in medical use. Despite the fact that the literature reports positive vibes about CTP, most of the preclinical research on the sensitivity, specificity, and efficacy of cannabinoids accounts for animal models, which indicates the need of clinical translation in order to validate the results for human subjects; yet there is plenty of room to determine the effective cannabinoid, its quantity, and effect size in insomnia, aggression, mood-swings, ADHD, Tourette's syndrome, and dementia.

A recent therapeutic method called neurofeedback tends to self-regulate brain function. Literature reports the significance of such neurotherapy for ADHD, pain, addiction, aggression, anxiety, autism, depression, schizophrenia, epilepsy, headaches, insomnia, Tourette's syndrome, PTSD, and dementia (Berman & Nichols, 2019; Chiba et al., 2019; Datko, Pineda, & Müller, 2018; Fielenbach, Donkers, Spreen, Visser, & Bogaerts, 2018; Ghaziri & Thibault, 2019; Harris, Hundley, & Lambie, 2019; Kumar, Duda, Mainali, Asghar, & Byler, 2018; Matthews & Schnyer, 2019; Melo, Carvalho, Prado, & Prado, 2019; Nigro, 2019; Orlov et al., 2018; Trudeau, 2020; Van Doren et al., 2019).

Granted that literature shows that neurofeedback is effective for treating substance abuse, most of the therapeutic goals of this neurotherapy match CTP research. Since both CTP and neurofeedback have limited literature to support their clinical effectiveness, it may be beneficial to study the combined or iterative effect of both therapeutic methods. Furthermore, longitudinal clinical studies with large sample size is required to establish the significance of the neurotherapeutic methods for the treatment of individual disorders, and again with comorbidities.

References

Aizpurua-Olaizola, O., Elezgarai, I., Rico-Barrio, I., Zarandona, I., Etxebarria, N., & Usobiaga, A. (2017). Targeting the endocannabinoid system: future therapeutic strategies. Drug Discovery Today, 22(1), 105–110. https://doi.org/10.1016/j.drudis.2016.08.005

Aldington, S., Harwood, M., Cox, B., Weatherall, M., Beckert, L., Hansell, A., Beasley, R. (2008). Cannabis use and risk of lung cancer: a case-control study. European Respiratory Journal, 31(2), 280–286. https://doi.org/10.1183/09031936.00065707

Annas, G. J. (1997). Reefer Madness — The Federal Response to California's Medical-Marijuana Law. New England Journal of Medicine, 337(6), 435–439. https://doi.org/10.1056/NEJM199708073370621

Ashton, C. H., Moore, P. B., Gallagher, P., & Young, A. H. (2005). Cannabinoids in bipolar affective disorder: a review and discussion of their therapeutic potential. Journal of Psychopharmacology (Oxford, England), 19(3), 293–300. https://doi.org/10.1177/0269881105051541

Aso, E., Andrés-Benito, P., Carmona, M., Maldonado, R., & Ferrer, I. (2016). Cannabinoid Receptor 2 Participates in Amyloid-β Processing in a Mouse Model of Alzheimer's Disease but Plays a Minor Role in the Therapeutic Properties of a Cannabis-Based Medicine. Journal of Alzheimer's disease, 51(2), 489–500. https://doi.org/10.3233/JAD-150913

Bachhuber, M., Arnsten, J. H., & Wurm, G. (2019). Use of Cannabis to Relieve Pain and Promote Sleep by Customers at an Adult Use Dispensary. Journal of Psychoactive Drugs, 51(5), 400–404. https://doi.org/10.1080/02791072.2019.1626953

Badowski, M. E. (2017). A review of oral cannabinoids and medical marijuana for the treatment of chemotherapy-induced nausea and vomiting: a focus on pharmacokinetic variability and pharmacodynamics. Cancer Chemotherapy and Pharmacology, 80(3), 441–449. https://doi.org/10.1007/s00280-017-3387-5

Badowski, M. E., & Yanful, P. K. (2018). Dronabinol oral solution in the management of anorexia and weight loss in AIDS and cancer. Therapeutics and Clinical Risk Management, Vol. 14, pp. 643–651. https://doi.org/10.2147/TCRM.S126849

Bayer, I., & Ghodse, H. (1999). Evolution of international drug control, 1945-1995. Bulletin on Narcotics, 51(1–2), 1–17.

Beal, J. E., Olson, R., Lefkowitz, L., Laubenstein, L., Bellman, P., Yangco, B., Shepard, K. V. (1997). Long-term efficacy and safety of dronabinol for acquired immunodeficiency syndrome-associated anorexia. Journal of Pain and Symptom Management, 14(1), 7–14. https://doi.org/10.1016/S0885-3924 (97) 00038-9

Berman, M. H., & Nichols, T. W. (2019). Treatment of Neurodegeneration: Integrating Photobiomodulation and Neurofeedback in Alzheimer's Dementia and Parkinson's: A Review. Photobiomodulation, Photomedicine, and Laser Surgery, 37(10), 623–634. https://doi.org/10.1089/photob.2019.4685

Blows, S., Ivers, R. Q., Connor, J., Ameratunga, S., Woodward, M., & Norton, R. (2005). Marijuana use and car crash injury. Addiction, 100(5), 605–611. https://doi.org/10.1111/j.1360-0443.2005.01100.x

Buckner, J. D., Heimberg, R. G., Schneier, F. R., Liu, S.-M., Wang, S., & Blanco, C. (2012). The relationship between cannabis use disorders and social anxiety disorder in the National Epidemiological Study of Alcohol and Related Conditions (NESARC). Drug and Alcohol Dependence, 124(1–2), 128–134. https://doi.org/10.1016/j.drugalcdep.2011.12.023

Cairns, K. E., Yap, M. B. H., Pilkington, P. D., & Jorm, A. F. (2014). Risk and protective factors for depression that adolescents can modify: a systematic review and meta-analysis of longitudinal studies. Journal of Affective Disorders, 169, 61–75. https://doi.org/10.1016/j.jad.2014.08.006

Cao, C., Li, Y., Liu, H., Bai, G., Mayl, J., Lin, X., Cai, J. (2014). The potential therapeutic effects of THC on Alzheimer's disease. Journal of Alzheimer's Disease : JAD, 42(3), 973–984. https://doi.org/10.3233/JAD-140093

Carroll, R. (2017, December 30). Hippy dream now a billion-dollar industry with California set to legalise cannabis. The Guardian. Retrieved from https://www.theguardian.com/us-news/2017/dec/30/california-legalise-cannabis-hippy-dream-billion-dollar-industry

Chiba, T., Kanazawa, T., Koizumi, A., Ide, K., Taschereau-Dumouchel, V., Boku, S., Kawato, M. (2019). Current Status of Neurofeedback for Post-traumatic Stress Disorder: A Systematic Review and the Possibility of Decoded Neurofeedback. Frontiers in Human Neuroscience, 13. https://doi.org/10.3389/fnhum.2019.00233

Clifford, D. B. (1983). Tetrahydrocannabinol for tremor in multiple sclerosis. Annals of Neurology, 13(6), 669–671. https://doi.org/10.1002/ana.410130616

Crippa, J. A. S., Derenusson, G. N., Ferrari, T. B., Wichert-Ana, L., Duran, F. L., Martin-Santos, R., … Hallak, J. E. C. (2011). Neural basis of anxiolytic effects of cannabidiol (CBD) in generalized social anxiety disorder: a preliminary report. Journal of Psychopharmacology, 25(1), 121–130. https://doi.org/10.1177/0269881110379283

Datko, M., Pineda, J. A., & Müller, R.-A. (2018). Positive effects of neurofeedback on autism symptoms correlate with brain activation during imitation and observation. European Journal of Neuroscience, 47(6), 579–591. https://doi.org/10.1111/ejn.13551

DeCloedt, M. (2018). The Decline of Prohibition: Human Rights and the Medicalization of Cannabis in the Contemporary West. Central European University.

Degenhardt, L., Hall, W., & Lynskey, M. (2003). Exploring the association between cannabis use and depression. Addiction (Abingdon, England), 98(11), 1493–1504. https://doi.org/10.1046/j.1360-0443.2003.00437.x

Devinsky, O., Marsh, E., Friedman, D., Thiele, E., Laux, L., Sullivan, J., Cilio, M. R. (2016). Cannabidiol in patients with treatment-resistant epilepsy: an open-label interventional trial. The Lancet Neurology, 15(3), 270–278. https://doi.org/10.1016/S1474-4422 (15) 00379-8

Falkenham, A. (2018). Marijuana: Judgement can preclude an honest dialogue in healthcare. Dalhousie Medical Journal, 45(1). https://doi.org/10.15273/dmj.vol45no1.8792

Fergusson, D. M., Horwood, L. J., & Beautrais, A. L. (2003). Cannabis and educational achievement. Addiction (Abingdon, England), 98(12), 1681–1692. https://doi.org/10.1111/j.1360-0443.2003.00573.x

Fielenbach, S., Donkers, F. C. L., Spreen, M., Visser, H. A., & Bogaerts, S. (2018). Neurofeedback Training for Psychiatric Disorders Associated with Criminal Offending: A Review. Frontiers in Psychiatry, 8. https://doi.org/10.3389/fpsyt.2017.00313

Fraser, G. A. (2009). The use of a synthetic cannabinoid in the management of treatment-resistant nightmares in posttraumatic stress disorder (PTSD). CNS Neuroscience & Therapeutics, 15(1), 84–88. https://doi.org/10.1111/j.1755-5949.2008.00071.x

Gage, S. H., Hickman, M., & Zammit, S. (2016). Association between cannabis and psychosis: Epidemiologic evidence. Biological Psychiatry, Vol. 79, pp. 549–556. https://doi.org/10.1016/j.biopsych.2015.08.001

Ghaziri, J., & Thibault, R. T. (2019). Neurofeedback: An inside perspective. In Casting Light on the Dark Side of Brain Imaging (pp. 113–116). https://doi.org/10.1016/B978-0-12-816179-1.00019-0

Harder, A. (2016). Reclaiming the right of beneficial use. University of Colorado Law Review, 963, 1–45.

Harris, S., Hundley, G., & Lambie, G. (2019). The Effects of Neurofeedback on Depression, Anxiety, and Academic Self-Efficacy. Journal of College Student Psychotherapy, 87568225.2019.1606689. https://doi.org/10.1080/87568225.2019.1606689

Hepler, R. S., & Frank, I. R. (1971). Marihuana smoking and intraocular pressure. JAMA, 217(10), 1392. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/5109652

Islam, A. (2019). Investigating the clinical decision-making process of physicians in rural Ontario: The perspective and attitudes on medical cannabis (University of Guelph). Retrieved from https://atrium.lib.uoguelph.ca/xmlui/bitstream/handle/10214/17364/Islam_Asiful_201909_Msc.pdf?sequence=7&isAllowed=y

Kumar, A., Duda, L., Mainali, G., Asghar, S., & Byler, D. (2018). A Comprehensive Review of Tourette syndrome and Complementary Alternative Medicine. Current Developmental Disorders Reports, 5(2), 95–100. https://doi.org/10.1007/s40474-018-0137-2

Li, H.-L. (2974). An archaeological and historical account of cannabis in China. Economic Botany, 28(4), 437–447.

Lucas, P., Reiman, A., Earleywine, M., McGowan, S. K., Oleson, M., Coward, M. P., & Thomas, B. (2013). Cannabis as a substitute for alcohol and other drugs: A dispensary-based survey of substitution effect in Canadian medical cannabis patients. Addiction Research & Theory, 21(5), 435–442. https://doi.org/10.3109/16066359.2012.733465

Matsuda, L. A., Lolait, S. J., Brownstein, M. J., Young, A. C., & Bonner, T. I. (1990). Structure of a cannabinoid receptor and functional expression of the cloned cDNA. Nature, 346(6284), 561–564. https://doi.org/10.1038/346561a0

Matthews, M. D., & Schnyer, D. M. (2019). Human performance optimization : the science and ethics of enhancing human capabilities. Retrieved from https://global.oup.com/academic/product/human-performance-optimization-9780190455132?prevSortField=9&sortField=9&start=1600&resultsPerPage=100&q=future&lang=en&cc=be#

Melo, D. L. M., Carvalho, L. B. C., Prado, L. B. F., & Prado, G. F. (2019). Biofeedback Therapies for Chronic Insomnia: A Systematic Review. Applied Psychophysiology and Biofeedback, 44(4), 259–269. https://doi.org/10.1007/s10484-019-09442-2

Millar, S. A., Stone, N. L., Bellman, Z. D., Yates, A. S., England, T. J., & O'Sullivan, S. E. (2019). A systematic review of cannabidiol dosing in clinical populations. British Journal of Clinical Pharmacology, 85(9), 1888–1900. https://doi.org/10.1111/bcp.14038

Moore, T. H., Zammit, S., Lingford-Hughes, A., Barnes, T. R., Jones, P. B., Burke, M., & Lewis, G. (2007). Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. The Lancet, 370(9584), 319–328. https://doi.org/10.1016/S0140-6736 (07) 61162-3

Newton, D. E. (2013). Background and History. In Marijuana: a reference handbook (Vol. 51, p. 7). https://doi.org/10.5860/choice.51-0036

Nigro, S. E. (2019). The Efficacy of Neurofeedback for Pediatric Epilepsy. Applied Psychophysiology and Biofeedback, 44(4), 285–290. https://doi.org/10.1007/s10484-019-09446-y

Orlov, N., Giampietro, V., O'Daly, O., Barker, G., Rubia, K., McGuire, P., Allen, P. (2018). T150. Real-Time fMRI Neurofeedback to Down-regulate Superior Temporal Gyrus Activity in Patients with Schizophrenia and Auditory Hallucinations: A Proof-of-Concept Study. Schizophrenia Bulletin, 44(suppl_1), S174–S174. https://doi.org/10.1093/schbul/sby016.426

Preet, A., Qamri, Z., Nasser, M. W., Prasad, A., Shilo, K., Zou, X., … Ganju, R. K. (2011). Cannabinoid receptors, CB1 and CB2, as novel targets for inhibition of non-small cell lung cancer growth and metastasis. Cancer Prevention Research (Philadelphia, Pa.), 4(1), 65–75. https://doi.org/10.1158/1940-6207.CAPR-10-0181

Reiman, A. (2009). Cannabis as a substitute for alcohol and other drugs. Harm Reduction Journal, 6(1), 35. https://doi.org/10.1186/1477-7517-6-35

Roffman, R. A. (2013). Legalization of marijuana: unraveling quandaries for the addiction professional. Frontiers in Psychiatry, 4(50). https://doi.org/10.3389/fpsyt.2013.00050

Sandyk, R., & Awerbuch, G. (1988). Marijuana and Tourette's syndrome. Journal of Clinical Psychopharmacology, 8(6), 444–445. https://doi.org/10.1097/00004714-198812000-00021

Scherma, M., Masia, P., Deidda, M., Fratta, W., Tanda, G., & Fadda, P. (2018). New Perspectives on the Use of Cannabis in the Treatment of Psychiatric Disorders. Medicines, 5(4), 107. https://doi.org/10.3390/medicines5040107

Schimrigk, S., Marziniak, M., Neubauer, C., Kugler, E. M., Werner, G., & Abramov-Sommariva, D. (2017). Dronabinol Is a Safe Long-Term Treatment Option for Neuropathic Pain Patients. European Neurology, 78(5–6), 320–329. https://doi.org/10.1159/000481089

Shishko, I., Oliveira, R., Moore, T. A., & Almeida, K. (2018). A review of medical marijuana for the treatment of posttraumatic stress disorder: Real symptom re-leaf or just high hopes? The Mental Health Clinician, 8(2), 86–94. https://doi.org/10.9740/mhc.2018.03.086

Szabo, B., Siemes, S., & Wallmichrath, I. (2002). Inhibition of GABAergic neurotransmission in the ventral tegmental area by cannabinoids. The European Journal of Neuroscience, 15(12), 2057–2061. https://doi.org/10.1046/j.1460-9568.2002.02041.x

Trudeau, D. (2020). My years with neurofeedback. In Neurofeedback (pp. 469–472). https://doi.org/10.1016/B978-0-12-817659-7.00058-0

Van Doren, J., Arns, M., Heinrich, H., Vollebregt, M. A., Strehl, U., & K. Loo, S. (2019). Sustained effects of neurofeedback in ADHD: a systematic review and meta-analysis. European Child & Adolescent Psychiatry, 28(3), 293–305. https://doi.org/10.1007/s00787-018-1121-4

Walsh, Z., Callaway, R., Belle-Isle, L., Capler, R., Kay, R., Lucas, P., & Holtzman, S. (2013). Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use. International Journal of Drug Policy, 24(6), 511–516. https://doi.org/10.1016/j.drugpo.2013.08.010

Zuardi, A. W. (2006). History of cannabis as a medicine: a review. Revista Brasileira de Psiquiatria (Sao Paulo, Brazil : 1999), 28(2), 153–157. https://doi.org/10.1590/s1516-44462006000020001