Research Paper: What Do Opioids and Marijuana Have in Common?

This paper is an attempt to describe the research that has been done on marijuana as it is metabolized and effects the chemical reactions in the human brain as an opiod receptor inhibitor. With this discussion it is hoped to stimulate the reader to do their own research and discover personally the decision and reasons to avoid what has become a part of the fabric of today's youth and a symbol of independence [see:"The Art of Self-expression: Marijuana Tattoos" http://www.growingmarijuanablog.com/marijuana-tattoos/ *and* "Celebrate Your Cannabis Independence with... WEED THE PEOPLE!" Posted by Wm.™ Steven Humphrey on Mon, Jun 8, 2015 at 1:59 PM http://www.portlandmercury.com/BlogtownPDX/archives/2015/06/08/celebrate-your-cannabis-independence-with-weed-the-people].

What are Opioids? Opioids are substances that act on the nervous system in a similar way to opiates such as morphine and codeine. In a medical context the term usually indicates medications that are artificially made rather than extracted from opium [see: D'Arcy, Pamela Stitzlein Davies, Yvonne (2012). Compact clinical guide to cancer pain management an evidence-based approach for nurses. New York: Springer. p. 55].

Understanding the term helps to put into perspective the effects the chemical compounds found in Marijuana, specifically, 1. cannabinoids such as tetrahydrocannabinol commonly known as THC, 2. cannabidiol (CBD), 3. tetrahydrocannabivarin (THCV), and 4. carsonagens. In addition, there are also similar compounds contained in cannabis that do not exhibit any psychoactive response but are

included as part of the functionality: cannabidiol (CBD), an isomer of THC; cannabinol (CBN), an oxidation product of THC; cannabivarin (CBV), an analog of CBN with a different side chain, cannabidivarin (CBDV), an analog of CBD with a different side chain, and cannabinolic acid. How these other compounds interact with THC is not fully understood.

It is also understood that there are about 400 different cannabinoids found in the various variants of cannabis of which THC has been attributed to psychological and physiologic factors on the human body. It is cannabidiol or CBD that has been shown used in small amounts that consumers claim alleviate pain in medical benefit studies [see: Whiting, PF; Wolff, RF; Deshpande, S; Di Nisio, M; Duffy, S; Hernandez, AV; Keurentjes, JC; Lang, S; Misso, K; Ryder, S; Schmidlkofer, S; Westwood, M; Kleijnen, J (23 June 2015). "Cannabinoids for Medical Use: A Systematic Review and Meta-analysis."].

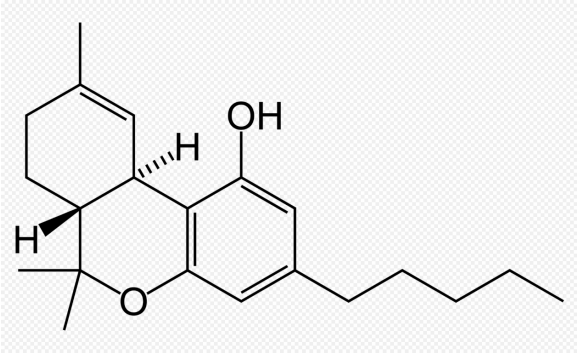
The nervous system of the human body is comprised of the brain, spinal cord, ganglion, nerves and in some studies includes the lymph nodes. The central nervous system (CNS) is so named because it integrates information it receives from, and coordinates and influences the activity of, all parts of the bodies. The mechanics of how this happens is complex but to put it simply, messages are carried across nodes in the nerve fiber called sensory receptors. The receptors recognize chemicals that the body maintains and when the chemicals present channel in sequences to the sensory receptors the information encoded is sent to the brain. The brain in turn sends messages back through the ganglia and a reaction to the stimulus occurs.

Inside the brain called the gray matter, there are millions of receptors that fire off information that are localized from many different parts of the brain. As studies increase and more is learned about the brain microscopy of the virtual learning process the effects of chemical messages and coded information storage understanding will improve [see: MacCallum, Don. "Peripheral Nervous System". Histology and Virtual Microscopy Learning Resources. University of Michigan Medical School. Retrieved 24 June 2014.].

The next section turns towards the topic of understanding how neural receptors work in the body and how the brain manages the stimulus from cannabinoids. The chemical process is a series of complex processes and it is hoped the description is an adequate enough model.

Cannabinoids and Cannabinoid Receptors

This is a structural model of the tetrahydrocammabinol molicule. The most prevalent chemical cannabinoids (as much as 29%) is THC. Other cannabinoids such as CBD as mentioned above are believed to have the effect to help the body metabolize the tetrahydrocammabinol and the help to regulate the body's metabolism by inactivating cytochrome P450 the class of enzymes used to



metabolize drugs. Interestingly enough, CBD has also been linked to lowering the body temperature, modulating the immune function and cellular production. THC is converted to 11-hydroxy-THC which is also a chemical activator so the drug effects outlasts the measurable THC levels in the blood. The body stores 11-hydroxy-THC molecule in the fatty tissues and metabolized over a longer period of months.

The cannabinoid receptor is a typical member of the largest known family of receptors called a G protein-coupled receptor. A signature of this type of receptor is the distinct pattern of how the receptor molecule spans the cell membrane seven times. The location of cannabinoid receptors exists on the cell membrane, and both outside (extracellularly) and inside (intracellularly) the cell membrane. CB1 receptors, the bigger of the two, are extraordinarily abundant in the brain: 10 times more plentiful than μ-opioid receptors, the receptors responsible for the effects of morphine [see: Rubino, T; Parolaro, D (2008). "Long lasting consequences of cannabis exposure in adolescence". Molecular and Cellular Endocrinology 286 (1–2 Suppl 1): S108–13. doi:10.1016/j.mce.2008.02.003. PMID 18358595.].

There are at least two types of cannabinoid receptors (CB1 and CB2) [see: Pertwee, Roger G. (January 1997). "Pharmacology of cannabinoid CB1 and CB2 receptors". Pharmacology & Therapeutics 74 (2): 129–180. doi:10.1016/S0163-7258(97)82001-3. PMID 9336020.]. The CB1 receptor is found primarily in the brain and mediates the psychological effects of THC. The CB2 receptor is most abundantly found on cells of the immune system. Cannabinoids act as immunomodulators at CB2 receptors, meaning they increase some immune responses and decrease others. Cannabinoids likely have a role in the brain's control of movement

and memory, as well as natural pain modulation. It is clear that cannabinoids can affect pain transmission and, specifically, that cannabinoids interact with the brain's endogenous opioid system and may affect dopamine transmission [see: H. Abadinsky (2004). Drugs: An Introduction (5th ed.). pp. 62–77; 160–166].

It should be noted that cannabis smoke contains thousands of organic and inorganic chemical compounds. This tar is chemically similar to that found in tobacco smoke or cigars. [see: Hashibe, M; Straif, K; Tashkin, DP; Morgenstern, H; Greenland, S; Zhang, ZF (April 2005). "Epidemiologic review of marijuana use and cancer risk.". Alcohol (Fayetteville, N.Y.) 35 (3): 265–75]. Over fifty known carcinogens have been identified in cannabis smoke. These include nitrosamines, reactive aldehydes, and polycylic hydrocarbons, including benzapyrene. [see: Tashkin, Donald (March 1997). "Effects of marijuana on the lung and its immune defenses". UCLA School of Medicine. Retrieved 2012-06-23) Marijuana smoke was listed as a cancer agent in California in 2009. ("Chemicals known to the state to cause cancer or reproductive toxicity" (PDF). ca.gov. 2012-07-20. Retrieved 2013-01-08]. It should be understood by the reader that the scope of this discussion is large and reason enough for developing another paper and in need of more exploration than what this paper provides.

From a psychological point the chemical actions effecting pathway to the brain responsible for interaction to pain, the movement or the body and memory all provide support to conclusions the effects of THC have the same action to the nervous system as other active drugs such as morphine and cocaine that have known addictive nature. The question under study is why some are addicted to the stimulus and others are not. It should also be noted these are some of the same reasons that the drug counter-culture

uses in order to base conclusions of non-morbidity [see: Is Weed Bad For You? The Arguments For and Against Marijuana's Supposed Health Risks Seth Millstein June 27, 2014 http://www.bustle.com/articles/29584-is-weed-bad-for-you-the-arguments-for-and-against-marijuanas-supposed-health-risks].

To understand this complex interaction and when asking why is there addiction to drugs, a paper this limited in scope cannot possibly introduce all the reasons. However, addictive behavior is described as the interaction of compulsive rewarding stimuli despite the consequences. This behavior has two leading reasons, 1. it is found to be biological, the propensity of the human brain to seek compulsive reward is heightened by the obsession on the reception of the reward over time and 2. nurture, the reinforcing or the likelihood of seeking repeated behavior by exposing the brain to the desirable reward. Addiction is a disorder of the brain's reward system which arises and increases in frequency of exposure over time [for more information please see: Nestler EJ (December 2013). "Cellular basis of memory for addiction". Dialogues Clin. Neurosci. 15 (4): 431–443.].

The gene transcription factor is a critical component and a common factor in the development of virtually all forms of behavioral and drug additions [see: Ruffle JK (November 2014). "Molecular neurobiology of addiction: what's all the (Δ)FosB about?". Am J Drug Alcohol Abuse 40 (6): 428–437]. Two decades of research into ΔFosB's role in addiction have demonstrated that addiction arises, and addictive behavior intensifies or attenuates, along with the genetic over expression of ΔFosB in the D1-type medium spiny neurons of the nucleus

accumbens [see: Nestler EJ (December 2013). "Cellular basis of memory for addiction". Dialogues Clin. Neurosci. 15 (4): 431–443.].

If you are wondering what ΔFosB is, that is the biomarker label given to the gene responsible for environmental factors in demonstrating addictive behavior. Dopamine is the primary neurotransmitter of the reward system in the brain. Nearly all addictive drugs, directly or indirectly, act upon the brain's reward system by heightening dopaminergic activity [see: National Institute on Drug Abuse: http://www.drugabuse.gov/publications/drugfacts/understanding-drug-abuse-addiction]. Dopamine plays a role in feelings of emotion, cognition, motivation and pleasure.

Nearly all behavior can be described by the function and interaction of brain's reward system. What makes the difference between reward and compulsive reward behavior is the presence of the gene ΔfosB and the quantities of CB1 and CB2 waiting to receive and process the stimulus. Although it is true that withdrawal from cannabis use for some is a minor inconvenience as described in Seth Millstein' article (June 27, 2014) on the topic of the health risks of marijuana use [see: Is Weed Bad For You? The Arguments For and Against Marijuana's Supposed Health Risks Seth Millstein June 27, 2014 http://www.bustle.com/articles/29584-is-weed-bad-for-you-the-arguments-for-and-against-marijuanas-supposed-health-risks]. For others it is much more than that and the act of withdrawl can lead to feeling of emptiness and depression [see: "Detoxing from Marijuana. Is marijuana a problem in YOUR life? Answer MA's Twelve Questions to see for yourself." ©1992 Marijuana Anonymous All Rights Reserved P-04. https://www.marijuana-anonymous.org/literature/pamphlets/detoxing-from-marijuana].

Conclusion

Writing this article was very thought provoking for me, I remember the attitudes and positions that I had on the issue and I can hear the echoes of the same arguments from my own son. I can hear the peace and trust he has in me when he discusses his reasons and the respect that I helped to foster in him with the expectation that I will help him along on his journey in life. I took the time to gather this data and quietly walk through my own journey of learning. It is my hope that my son will do the same. I am very proud of him, like I am so proud of my daughter. I am confident both my children are capable and confident to meet the challenges of life and make good decisions based on facts.

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