Marijuana

Cannabinoid Reception in the Brain

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2/16/2015

Cellular Neuroscience

Books, movies, songs, politics, schools, and just about every corner we turn to, marijuana is a hot topic in today's society. From hazy smoke to brownies, the plant is in high demand. Since 2007, marijuana use has been on the rise (Nationwide Trends, 2010). It is estimated that 18.9 million people were current marijuana users in 2012, which is just under the equivalent of the entire state of Florida. Of the 9.2% of the United States population over the age of 12 that used illicit drugs within the past month, 7.3% were marijuana users (Nationwide Trends, 2010). With the legality of marijuana in great debate all over the country, Colorado, Washington, Alaska and Oregon have all passed laws that make marijuana use recreationally and medically legal. If so many people currently use marijuana then why does it face continued opposition? A wide range of research is being done on marijuana's effects on the brain, but the basic mechanisms are known.

The Working Brain

The human brain is a complex machine, made up of around 100 billion neurons. Neurons are the cells of the nervous system. Neurons use gradients much like a car battery to send signals to other neurons (Lodish et al., 2000). Signaling occurs at the end of a neuron where extremely tiny particles called neurotransmitters are released from the neuron onto the neuron it is signaling. Neurotransmitters attach to receptors on the second neuron to cause a variety of responses based on their makeup (Lodish et al., 2000). There are many ways in which the effects that a neurotransmitter provides can be increased or decreased.

Drugs, whether they are prescribed or illicit, often work to alter some aspect of neuron function or transmitter release. Some drugs make neurons pump out more neurotransmitters which enhance the effects those neurotransmitters usually have. Others can stop neurons from releasing neurotransmitters, decreasing effects. Marijuana works in this way.

Early Marijuana Research

Marijuana comes in many different forms and stems from the plant *Cannabis sativa*. It is most often smoked but can be ingested through foods or even brewed (Chudler, 2010). Marijuana gets into the blood no matter how it is taken in. Once in the bloodstream is makes its way to the brain. The composition of the *Cannabis sativa* plant is what provides the effects of marijuana use. The main ingredients that alter brain activity are the psychoactive chemical, *delta-9-tetrahydrocannabinol* or THC and about 60 other cannabinoids. Psychoactive refers to an effect where brain function is altered resulting in short-term differences in mood, behavior, and perception (Greydanus, D. E., Hawver, Greydanus, M. M., and Merrick, 2013). Cannabinoids are the neurotransmitter-like particles in marijuana that can alter our normal neuron function.

Before discussing how these cannabinoids interact with the brain, it is necessary to fully understand the complexity of their makeup. Besides THC, the most widely known cannabinoids include cannabidiol (CBD), cannabigerol (CBG), and cannabinol (CBN) (Greydanus, D. E., Hawver, Greydanus, M. M., and Merrick, 2013). While THC is psychoactive, the other components of marijuana are not. THC and other cannabinoids can cause an increase in appetite, decrease in nausea, and also pain suppression (Cellular Biology: How Cannabis Works in the Body, 2013). Specifically, CBD can have anti-inflammatory, antiemetic, and anti-psychotic effects (Greydanus, D. E., Hawver, Greydanus, M. M., and Merrick, 2013). All of these effects are what create the "high" that is referred to by marijuana users. But how do cannabinoids actually interact with the brain?

Marijuana in the Brain: Mechanisms Reviewed

In the mid to late 20th century, research on the components of marijuana was in full swing and is a continued area of study. The human body has its own endocannabinoid system, which is

an internal system that produces the effects we associate with marijuana. We have the ability to create our own "high" if the right signals are sent without even coming into contact with marijuana. This system is made up of cannabinoid receptors which are a type of receptor that is found on a neuron or other cells. The internal particles that we make on our own are called 2-arachidonoyl glycerol (2-AG) and anandamide, also known as arachidonoyl ethanolamide (AEA) (Greydanus, D. E., Hawver, Greydanus, M. M., and Merrick, 2013). These homemade particles function just like the components we find in marijuana. The two main receptors that are found in our own bodies that respond to the homemade marijuana like particles are called CB-1 and CB-2. They are found widely throughout the body including the limbic system and other tissues like the heart and gastrointestinal tract (Greydanus, D. E., Hawver, Greydanus, M. M., and Merrick, 2013). Like marijuana components, 2-AG and AEA relate to the reward system in the brain and their levels are often altered during the use of drugs that are frequently abused. When we smoke or ingest marijuana, we add particles to our system that act like or enhance the effects of naturally occurring internal molecules like 2-AG and AEA to induce similar effects.

Current Areas of Research: Medical Applications

With the wide array of CB-1 and CB-2 receptors in the body and the equally wide array of potential effects that endocannabinoids can create, manipulation of this system for medical applications is in great debate. Figure 1 lists the plethora of possible benefits that medical marijuana could help. A study done on the effects of marijuana components on breast cancer found that they can freeze cancer growth to put it simply (Caffarel et al., 2012). The study also found that mice with cancer had their tumor growth slowed with the use of cannabinoids. Another study found that CBD from flax could reduce inflammation through the activation of a peripheral CB-2 receptor at the sight of inflammation (Styrczewska et al., 2012). The studies

listed above show promise to improve the issue of cancer which effects many people worldwide every day and is problem that needs further treatment options. In addition, the anti-inflammatory effects marijuana has could help in recovery time for surgeries or to bring down swelling in injuries.

Potential benefits of cannabis based on research studies
Remedy for inflammation
Remedy for pain (including chronic pain and neuropathic pain)
Remedy for diarrhea (as in Crohn's disease)
Treatment for dystonia
Treatment for multiple sclerosis
Treatment for rheumatoid arthritis
Treatment for glaucoma
Treatment for emesis due to chemotherapy
Treatment for epilepsy
Improvement of anorexia in AIDS patients
Treatment for Huntington's disease
Management of inflammatory bowel disease
Beneficial effect on atherosclerosis
Reduce brain infarct size
Block negative memories in posttraumatic stress disorder
Reduce cardiac reperfusion injury
Adjuvant treatment for prostate carcinoma
Others

Figure 1(Greydanus, et. al., 2013).

Some pharmaceutical companies have begun to produce prescription cannabis-containing products. Two of these, Marinol and Cesamet, both contain THC and are used to treat anorexia. The drugs act to reduce nausea through cannabinoids (Fernandez-Ruiz, 2012). Neurological problems like epilepsy and multiple sclerosis also see improvements with the use of cannabinoids. Epilepsy - reoccurring seizures – was recreated in lab during one study. It was found that, by manipulating the internal cannabinoid system, epilepsy could be treated (Hofmann and Frazier, 2011). Exactly how changing the internal system with the use of marijuana helps epilepsy patients isn't fully understood, many researchers believe the answer lies in the way the neurons create a charge and signal. Spasticity, a usual symptom of multiple sclerosis, is the condition of constant contraction of specific muscles. Research has found that marijuana use reduces spasticity in multiple sclerosis patients (Corey-Bloom et. al., 2012). All of these benefits seem to be promising, but like other prescription drugs marijuana has potential adverse properties.

Current Areas of Research: Adverse Properties

Marijuana use can lead to a long list of potential side effects. With the increase in appetite from cannabinoid receptor stimulation, long term marijuana use can lead to weight gain. The relaxing effects can also lead to a reduction in physical activity to add to the weight gain (Greydanus, D. E., Hawver, Greydanus, M. M., and Merrick, 2013). Studies have shown that marijuana can also reduce rapid eye movement as well as decrease EEG activity (DSM-IV-TR, 2000). Side effects like bronchitis and chronic cough can occur because of the irritation to lung tissues during the smoking of marijuana (Mallaret, Dal'Bo-Rohrer, Demattéis, 2005). These can lead to the development of asthma (Davis and Gunderson, 2012). Dental diseases can form from marijuana use because of the carcinogens found in the plant (Cho, Hirsch, and Johnstone, 2005). With the CB-1 and CB-2 receptors also found in the heart tissue, marijuana increases blood pressure and heart rate (Malinowska, Baranowska-Kuczko, and Schlicker, 2012). Like many other drugs, tolerance can occur in marijuana users (Budney, 2011). Tolerance happens when receptors are repeatedly over stimulated and the defense mechanism is to reduce the number of receptors on the cell.

Future Research in Marijuana:

Whether it be in the next feature film watched or a lyric from one of the many new songs on the radio, marijuana is a huge topic of everyday life. All the in's and out's of its uses and effects are still widely speculated and researched. Some of the areas for future research in marijuana are as follows. How marijuana effects neurons associated with epilepsy is still unknown. Another area for research is the exact functions of CB-1 and CB-2 receptors Also for further study, marijuana may be able to aid in the blockage of fear memory by CBD (Stern et. al., 2012). One underlying feature of most current research in this field is the need for human trials. Most research is currently being done with animal models or has been tested little in humans.

Overall, marijuana is a complex drug that needs further scrutiny and research to determine how to utilize its potential. Marijuana definitely should be reconsidered for its uses to help in medical situations but must be monitored closely to prevent abuse.

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