How CBD Works: The Endocannabinoid System

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Cannabis has two major cannabinoids—THC and CBD (cannabidiol). THC is the better-known psychoactive cannabinoid of cannabis, which is why marijuana provides intoxicating effects. CBD is a non-psychoactive cannabinoid, meaning it is non-intoxicating. Cannabinoids, like the ones found in cannabis, mimic the effects of the body's endocannabinoids. This is, in part, why they have such an interesting impact on us.

Originally, scientists thought the body's endocannabinoid receptors could only be found in the nerves and brain. Now they know they exist throughout the body. They're in our skin, bones, fat tissue, immune cells, heart, kidney, blood vessels, skeletal muscles, pancreas, liver, and gastrointestinal tract. As such, many of the body's processes involve the ECS. It plays a role in how we experience pain, our mood, memory, sleep, skin, stress, metabolism, appetite, immune system function, and reproductive function. This explains why cannabis seems to have such widespread and profound therapeutic effects. While more research is needed to understand the potential therapeutic benefits of consuming cannabis products like CBD fully, what is currently known is promising. In any case, there is no question that cannabis' effects have everything to do with the body's ECS.

What is the endocannabinoid system?

The ECS got its name because its discovery was a result of human use of cannabis. While cannabis has been used medicinally for thousands of years, it was not until 1964 when

scientists Yechiel Gaoni and Raphael Mechoulam figured out that THC was the primary active chemical in cannabis. They named THC a "cannabinoid." The discovery of THC led scientists to produce synthetic cannabinoids in an attempt to understand how cannabinoids worked. After that, scientists began exploring the effects of cannabis on the brain, discovering that THC had the power to bind firmly to specific parts of the brain. This meant that THC functioned by way of receptors in the body. Finally, in 1990, this theory was confirmed when Lisa Matsuda of the National Institute of Mental Health and her team were able to identify and successfully clone CB1, or cannabinoid receptor 1. Following that, they identified and cloned another, CB2. These are the two main cannabinoid receptors in the body, though there are others.

Endocannabinoids and endocannabinoid receptors are found throughout the human body and are responsible for various bodily tasks. The ultimate purpose of the ESC is maintaining a stable environment in the body, regardless of how the external environments we experience change. Along with this, the ECS (its endocannabinoids and cannabinoids) serves as a bridge between the body's different systems, making sure cells of all kinds can effectively communicate and coordinate with one another. Here is an example of how this works. Say you are injured. At the site of the injury, cannabinoids are there, reducing how many sensitizers and activators are released from the injured area. As a result, the nerves are calmer, less inflammation occurs, and less pain is felt.

The ECS also connects the body and the mind by way of how it acts on the nervous system, immune system, and each of the body's organs. This helps to explain how a person's mental state can affect their physical health. The increasing legality of cannabis allows for more research and, subsequently, more knowledge on how the ECS works. Current evidence suggests that it plays a role in the brain, vascular, reproductive, and immune function. In particular, it clearly influences memory, motor function, cognition, and the perception of pain.

These functions all contribute to homeostasis, which refers to the stability of your internal environment. For example, if an outside force, such as pain from an injury or a fever, throws off your body's homeostasis, your ECS kicks in to help your body return to its ideal operation.

How the endocannabinoid system works

Endocannabinoids, receptors, and enzymes are the three central components of the ECS.

Endocannabinoids, originally called endogenous cannabinoids, are made by the body. The difference between endocannabinoids and cannabinoids is that the body makes endocannabinoids while cannabinoids are not. The two major endocannabinoids discovered at this point are anandamide (AEA) and 2- arachidonoylglyerol (2-AG). The body makes them

only as necessary, so it is hard to determine their normal levels in the body. In any case, they help with internal bodily functions, making sure they are doing what they are supposed to do.

Then there are endocannabinoid and cannabinoid receptors found all around the body. The body has two major endocannabinoid and cannabinoid receptors, CB1 and CB2. The majority of CB1 receptors are found in the central nervous system (CNS), specifically in the neocortex, basal ganglia, hippocampus, amygdala, cerebellum, hypothalamus, and striatum, all regions of the brain. These regions are associated with lots of important behavior functions that include memory, learning, decision-making, motor and sensory response, and emotional reactions. The majority of CB2 receptors are found in the peripheral nervous system and mostly in immune cells—in white blood cells, the spleen, and the tonsils, regions associated with inflammation and cancer.

When endocannabinoids bind to endocannabinoid receptors, it is a signal to the ECS that it needs to start working. Endocannabinoids can bind to either CB1 or CB2. Which endocannabinoid binds to which receptor and where these are principle-determining factors for the impact this action will have on a person. To illustrate the concept, here is an example. Endocannabinoids bind to CB1 receptors in a spinal nerve to reduce pain. Endocannabinoids bind to CB2 receptors in immune cells to tell the ECS that the body is undergoing inflammation, consequently reducing the inflammation.

Enzymes are the final component of the ECS. Their job is to break down endocannabinoids when they have completed a task. Specifically, two enzymes play a part in this process. Fatty acid amide hydrolase breaks down AEA and monoacylglycerol acid lipase breaks down 2-AG.

How CBD and THC affect the endocannabinoid system?

Any substance that enters the body creates a physiological reaction. When cannabinoids like CBD and THC enters the body, they interact with the body's cannabinoid receptors. THC mainly binds to CB1 and CB2 receptors. It is important to note that these receptors are located in the central nervous and peripheral nervous systems. Therefore, it makes sense that consuming THC can alter perception, memory, and concentration, leaving people feeling intoxicated. CBD mainly binds to the other receptors in the body, of which there are many. This explains why CBD does not cause intoxication. Furthermore, CBD changes the way THC binds to CB1 receptors, so when a person consumes high amounts THC and CBD simultaneously, the intoxicating effects of THC are weakened.

Instead of binding to cannabinoid receptors, CBD binds to our serotonin receptors, and this is just one of many receptors with which CBD is interacting. Serotonin controls things like mood, the experience of pain, and sleep functions. CBD also binds to vanilloid receptors, which influence inflammation and perception of pain. Another way CBD interacts with the human body is by binding to orphan receptors. They play a role in how blood pressure is

regulated, the migration of cancer cells, and bone density and reabsorption. These are just examples of how CBD interacts with the body's receptors, and the specific ways CBD impacts us is still the subject of research.

Some believe that CBD binds to receptors that remain undiscovered, thus the mystery of CBD's functioning. Additionally, many professionals think that aside from just binding to receptors, CBD has other functions. It may prevent the breakdown of endocannabinoids, for example. What we do know is this. CBD seems to target more than 65 areas of the body. The body's mechanisms are not isolated. They overlap, which means the potential health benefits of CBD are extensive, even if they are currently uncertain.

By the sheer fact that CBD reaches so many areas of the body, contributes to the ongoing research that provides scientists and researchers confidence that CBD has widespread effects on health. That being said, keep in mind that not much has been confirmed about the therapeutic benefits of the cannabinoids THC and CBD. As a result, when you use cannabis for medical reasons, you are still doing so at your own risk. If you have concerns or if you plan to use CBD for a particular condition, consult your doctor. It is not currently recommended to use cannabis as a replacement for other medications prescribed by your doctor because of the lack of clinical studies to prove its effectiveness.

Explaining the CBD's potential benefits

CBD may be able to help treat anxiety and depression because it binds to the brain's serotonin receptors that play a role in regulating mood. There is a link between low levels of serotonin and anxiety. Preliminary studies by the National Institute of Drug Abuse (NIDA) and others found that CBD decreased anxiety levels in most participants, for instance, and that is just one of many studies that have had similar findings. Much anecdotal evidence concurs with these findings.

One of the most common uses of CBD is to treat pain, including chronic pain. CBD does not bind much to endocannabinoid receptors, though sometimes it does, and this is the current explanation for CBD's touted analgesic and anti-inflammatory abilities. This means CBD could be helpful to people suffering from many pain-related and inflammatory disorders, such as arthritis, diabetes, multiple sclerosis, bone diseases, and skin issues rooted in inflammation.

CBD's anti-inflammatory and anti-oxidative functions that come from its role as a receptor agonist might also be able to help prevent neurodegenerative diseases like Parkinson's and Alzheimer's disease.

Many people also use CBD to deal with sleep issues. It was thought that CBD could help with sleep issues based on its interaction with GABA and serotonin receptors. GABA receptors reduce brain activity, allowing relaxation, while serotonin regulates sleep. Another

important factor has to do with the link between anxiety and trouble sleeping. Therefore, indirectly, if CBD helps with anxiety, it may also help with sleep.

There is one area with conclusive research regarding the therapeutic benefits of CBD, and that is with epilepsy. CBD has been shown to reduce seizures based on how it prevents erratic firing in the body's sodium channels, where that erratic firing is linked to seizures. In fact, in 2018, the FDA approved a CBD-comprised drug called Epidolex to treat a rare and severe form of epilepsy.

Endocannabinoid deficiency

Clinical endocannabinoid deficiency (CED) is when the body has low endocannabinoid levels or possible dysfunction of the ECS. It's not a proven disease currently but a theory that was first proposed in 2001. It is based on the concept that several brain disorders, such as Alzheimer's and Parkinson's, are associated with neurotransmitter deficiencies. Therefore, it makes sense that deficient endocannabinoid levels would manifest as disorders through similar predictable channels.

Some experts think that an endocannabinoid deficiency could cause migraines, irritable bowel syndrome, and fibromyalgia. These three conditions have certain unified pathophysiological trends, including the fact that they are diagnoses of exclusion, their comorbidity (the symptoms of each condition often overlap), and the lifetime risk of developing one or both of the other conditions with the presence of one is very common.

Treating CED is difficult because messing with the ECS means you are messing with the body's homeostasis. Therefore, research suggests the best approach may be with cannabis, THC and CBD, which are weaker rather than full agonists of CB1. Using full synthetic agonists could easily disturb the system too much and lead to other health problems.

Wrapping up endocannabinoid function

The stability of the human body is largely dependent on the ECS. Scientists know this, though so much about the ECS remains a mystery based on limited studies. Continuous research is underway exploring the ways the ECS functions. THC and CBD can play a role in treating many health conditions, considering how much both interact with the ECS. Specifically, CBD does not come with serious side effects that other medications have, so using it as an alternative treatment (given it is proven effective) would be an ideal scenario. Additionally, many health conditions do not currently have effective treatment options. The use of cannabis in those cases may be a potential solution.

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