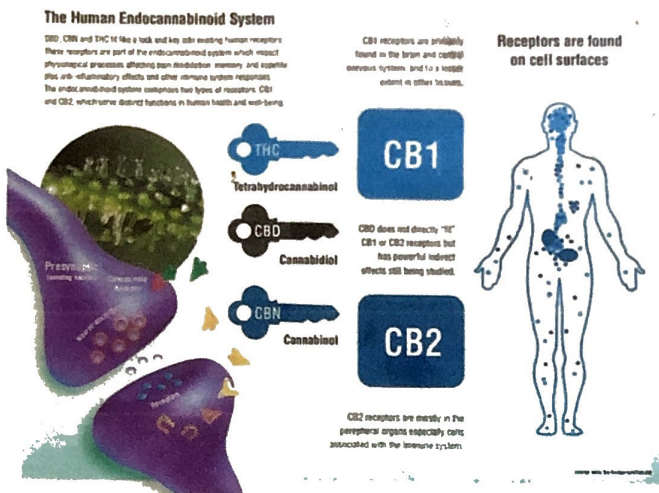


A Beginner's Guide To The Endocannabinoid System

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Introduction

The endocannabinoid system is a complex subject and hard for most laypeople to understand, since it's normally discussed using very scientific terminology and most of the literature available is aimed at researchers with a technical background in chemistry or biology.

To remedy this we wanted to create a guide in simple everyday language, detailed enough for those who want to understand the science behind it.

We will explain how the human endocannabinoid system works, how it evolved and the main functions it serves. We will explore the body's communication system using neurotransmitters or biochemicals that enable cells to "converse" with one another by providing instructions and feedback and how they interact with receptors found throughout the body and central nervous system.

With this understanding you will begin to appreciate how important the Endocannabinoid system is for human health and well-being. This is a relatively new field of science and much more research is needed to see how this system functions and interacts with our body mind system.

What is the Endocannabinoid System?

Definition

To understand the Endocannabinoid system we should first start with the actual word, how it was derived and what it means.

Endo is derived from the Greek meaning inside or within, it's similar in function to the Endocrine System (from endo- + -crine, from Greek krinein to separate) that refers to the body's hormone secreting glands in the circulatory system carrying chemical messages towards distant target organs.

Cannabinoid is named after the chemical compounds found inside the Cannabis or Indian Hemp plant.

The Endocannabinoid System

The endocannabinoid system is part of the body's immune system and is

a communication mechanism geared to maintaining homeostasis, driven by our own internally produced cannabinoids and cannabinoid receptors. It might be the most important system on the physiological level for creating and maintaining human health. Endocannabinoids and their corresponding receptors are found extensively throughout the human body. They are mainly concentrated in the brain, organs, glands, connective tissues and immune cells.

Understanding receptors and neurotransmitters

Before diving more deeply into the subject of the endocannabinoid system it's worthwhile having a little understanding about the mechanisms the body uses to communicate with itself. For a more detailed description check out [Brain Receptors-A Primer](#) by Kayt Sukel.

Synaptic transmission

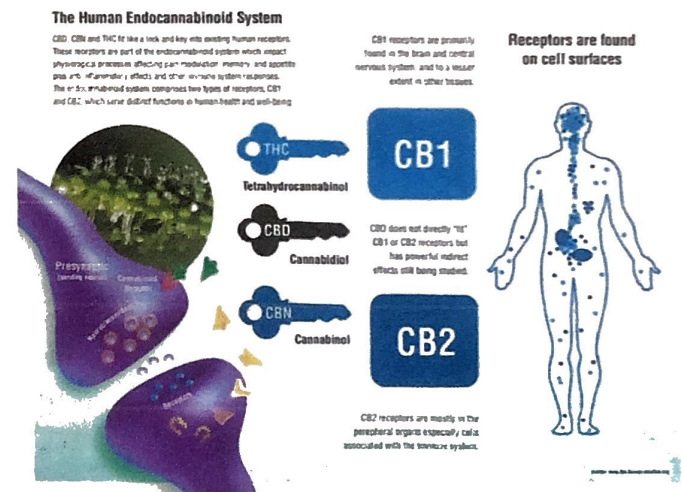
Synaptic transmission is the process where a neurochemical (brain chemical) is released into the synapse. The synapse is made up of two brain cells and the narrow space found between them. The transmission process is not complete until the neurochemical joins together with a receptor on the receiving postsynaptic neuron.

Lock and Key Metaphor

Neurotransmitters and receptors are often described by using a lock and key metaphor, the neurotransmitter being the key and the receptor being the lock. A single neurotransmitter may bind with several types of receptors and have a different effect depending on their location in the body.

Agonist and Antagonist

An agonist is a chemical that binds to a [receptor](#) and activates it causing a biological response. Conversely an [antagonist](#) blocks the action of the agonist suppressing the response.



There are three main types of [cannabinoids](#)

Endogenous cannabinoids

Endogenous cannabinoids are those produced naturally within the human body.

The two most common endogenous (internally produced) cannabinoids are [Anandamide](#) and 2AG (2-Arachidonoylglycerol) Anandamide is sometimes referred to as the bliss chemical, it's name is rooted from the ancient Indian Sanskrit "Ananda" meaning "happiness, bliss, joy or delight"

Synthetic cannabinoids

Synthetic cannabinoids are cannabinoids formulated in a laboratory environment e.g. Dronabinol or Marinol. The active ingredient in MARINOL® Capsules, is a synthetic form of delta-9-THC. Marinol has been used to treat people with AIDS by stimulating appetite and preventing unnecessary weight loss. It can also be used to treat severe nausea and vomiting caused by cancer chemotherapy.

After the CB1 and CB2 receptors were initially discovered in the early 90's many big pharmaceutical companies developed single molecule synthetic cannabinoids to target these receptors hoping to manipulate the body's response to disease. They discovered that the system is much more complex and that single cannabinoids were less effective than whole plant extracts due to the entourage effect where the cannabinoids regulate and support each other.

Phytocannabinoids

Phytocannabinoids are those found in plants. The most common phytocannabinoids are found in the marijuana (*Cannabis Indica*) and hemp plants (*Cannabis Sativa*). *Cannabis indica* has higher levels of THC compared to CBD, whereas *Cannabis sativa* has higher levels of CBD to THC but a huge variability exists within either species.

Phytocannabinoids are known to occur in several other plant species besides cannabis. These include *Echinacea* a plant known by herbalists to boost the body's immune system. Its uses include pain relief for toothaches, relief of colds, coughs and throat infections, and used externally for wounds, burns, and insect bites.

How does the Endocannabinoid System work?

The endocannabinoid system connects complex functions of our organs (physical), immune system (chemical), and nervous system (electrical) and acts as a bridge or gateway between our body and mind. Once we understand how this system works we can see the interconnectedness of states of consciousness and how they can promote health or disease and may be a key to our holistic understanding of the body/mind organism.

How Cannabinoids work differently from other Neurotransmitters

Brain cells communicate by sending chemical messages with each other and the rest of the body. These chemical transmissions regulate and control everything we feel, think and do.

Typically the chemicals or Neurotransmitters are released from a neuron (a presynaptic cell) they travel across the synapse or small gap and attach themselves to receptors on the surface of a nearby neuron (postsynaptic cell). The neuron is activated and the message is passed along.

The Endocannabinoid system works in reverse or backwards. Cannabinoids, the messenger chemicals of the body's endocannabinoid system are manufactured from fat cells in the postsynaptic neuron. They are then released backwards to the presynaptic neuron, where they then attach to cannabinoid receptors CB1 and CB2



How the Endocannabinoid System was discovered

The endocannabinoid system was discovered by Dr. Ralph Mechoulam an Israeli organic chemist famous for isolating and synthesizing THC, and explaining the chemical structure of cannabidiol in 1963.

In 1992, the first endocannabinoid, Anandamide, was discovered in Dr Mechoulam's laboratory in Israel. A second endocannabinoid 2-AG (2-Arachidonoylglycerol), was discovered in by Shimon Ben-Shabat, one of his PhD students and reported in 1994-1995.

The CB1 and CB2 receptors

The endocannabinoid system works through two types of receptors found in our body CB1 and CB2. Another receptor GPR55 may actually be a third cannabinoid receptor affecting blood pressure and bone density.

CB1 receptor

In 1990 the CB1 receptor was discovered by Professor Allyn Howlett and her graduate student William Devane, concentrated in the Brain and Central nervous system.

CB1 receptors are primarily found in the brain, nervous system and glands although they are also both present in the male and female reproductive organs. They modulate and moderate the perception of pain

These receptors were found to be concentrated in the hippocampus area of the brain related to our memory, cerebral cortex related to our higher cognition and brain functioning, the cerebellum that affects our motor coordination, basal ganglia affecting our physical movement, the hypothalamus related to appetite and the amygdala that influences our emotions. There are hardly any cannabinoid receptors in the brainstem which controls our breathing and heart rate.

CB2 receptor

The CB2 receptor was discovered in 1993 by a research group from Cambridge, they were searching for a second cannabinoid receptor that could explain the function and pharmacological properties of THC tetrahydrocannabinol. The discovery of this receptor helped explain on a molecular level the already known effects of cannabinoids on the immune system. The CB2 receptors populate the immune system and related peripheral organs.

How do the CB1 and CB2 receptors communicate

Earlier we discussed receptors and neurotransmitters. The CB1 and CB2 receptors are activated or suppressed by the body's neurochemicals and are also affected when we take cannabinoids like THC and CBD from external sources.

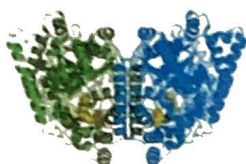
amide is an endocannab
receptor. THC is a ph
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Anandamide is an endocannabinoid produced by the body that activates the CB1 receptor. THC is a phytocannabinoid that also activates the CB1 receptor.

2-AG, the other main endocannabinoid activates both CB1 and CB2 receptors in the. CBN is a phytocannabinoid that also activates the CB2 receptor.

CBD is interesting since it **doesn't directly bind to the CB1 or CB2 receptors**. Instead it exerts its influence and medicinal effects through its **indirect chemical reactions** in the body and its effects on other brain receptors like, the vanilloid receptor (mediating pain perception, body temperature and inflammation), the adenosine receptor (broad anti-inflammatory properties) and the 5-HT serotonin receptor (multiple biological and neurological processes, including anxiety, addiction, appetite, sleep, pain perception, nausea and vomiting).

CBD affects the CB1 receptor indirectly by suppressing FAAH (fatty acid amide hydroxylase). This enzyme is normally responsible for breaking down anandamide, so by reducing FAAH the body's level of anandamide is increased for a longer time which means more CB1 signalling.



FAAH Enzyme

The mechanism is complex since all these receptors cause a regulating and balancing effect in other systems of the body, making research complex. Furthermore isolating cause and effect from single compounds proves very difficult due to the entourage effect which is where the interaction of different cannabinoids creates a sum greater than its parts.

The main functions of the Endocannabinoid System

The endocannabinoid system regulates a whole host of body functions that are directly related to health and wellbeing such as, memory, appetite, metabolism, stress response, energy levels, immune system functioning, autonomic nervous system, female reproductive functions, analgesia (pain perception), thermoregulation (body temperature) and sleep.

The three main functions of the Endocannabinoid System

1 . Neurogenesis and Neuroprotection

Neurogenesis (Brain formation)

The endocannabinoid system regulates the creation of brain cells when a baby is being formulated in the mother's womb, choreographing the creation of the central nervous system.

Neuroprotection (Brain cell replacement & regulation)

The endocannabinoid system also functions as a mechanism of neuroprotection, it aims to prevent or slow disease progression by stopping or at least slowing down the loss of neurons (Brain cells)

2 . Regulation of many different body functions and processes restoring Homeostasis

The endocannabinoid system is likened to a series of thermostats or dimmer switches regulating bone density, glucose metabolism, short-term & long-term memory, hunger, energy storage and nutrient transport, stress response, immune functions, female reproduction, pain control, sleep, temperature & heat regulation.

Examples :

Fever

When you get a fever your body temperature increases to create a fever to kill the virus. The endocannabinoid system tells the body when to reduce the temperature and bring the body back to balance again.

3. Regulation of the body's response to Stress

When you get stressed the brain releases a hormone called cortisol. The endocannabinoid system tells the body when to stop producing this chemical and bring the body systems back to equilibrium again. Stress can be from anything like the introduction of poisons or pollutants, a perceived increase in danger, or sudden exertion due to exercise like our fight or flight response.

Normal everyday stress in the body creates an increase in the body's natural cannabinoids but chronic stress over time depletes the body's natural cannabinoids making us more susceptible to disease.

Age

As you get older you are more likely to get sick because your endocannabinoid signalling system is weaker and its tone is depleted.

The Medicinal Properties of Cannabinoids found in Marijuana (Cannabis Indica) and Hemp plants (Cannabis Sativa)

Ongoing research is showing that phytocannabinoids found in Marijuana (Cannabis Sativa) and Hemp plants (Cannabis Indica) have a direct effect on the body's Endocannabinoid system. This exciting research shows promising results in a number of different health and medical situations. We suggest you do your own research and consult your doctor or health practitioner if

you intend to take cannabinoid supplements.

Tetrahydrocannabinol (THC)

THC is the most common cannabinoid, it is generally thought to be the main psychoactive component but its exact effect vary from person to person. Scientific studies have shown it has neuroprotective properties and brings an analgesic quality causing pain relief.

Cannabidiol (CBD)

CBD or Cannabidiol is the second most common cannabinoid. It has a whole range of medicinal properties. It is generally considered to be a non-psychoactive component that is believed to reduce and control the psychoactive effects of THC.

Tetrahydrocannabinolic Acid (THCA)

THCA is found in fresh green cannabis before it is dried and processed. In this form it is considered non psychoactive. Medicinally it's been shown to have neuroprotective and anti-inflammatory properties.

Cannabidiolic Acid (CBDA)

CBDA is the raw acidic form of CBD. It decomposes to CBD when heated. It is considered non-psychoactive and useful in treating the side effects of conventional cancer treatments since it can help reduce nausea and vomiting. Like CBD it also has anti-inflammatory properties.

Cannabinol (CBN)

CBN is reported to have an analgesic or sedative effect. It is non-psychoactive and is created after THC degrades and oxidizes after exposure to air, heat or ultraviolet light. It is normally only found in very small quantities. Medicinal qualities include : Pain relief, Anti-insomnia, Promotion of growth of bone

cells, Antibacterial, Anti-inflammatory, Anti-convulsive, Appetite stimulant

Cannabigerol (CBG)

CBG is a non psychoactive cannabinoid. Research shows it may potentially help with Glaucoma symptoms, digestive and bowel inflammation and may also have antibacterial properties.

Cannabichromene (CBC)

CBC is currently needing more research into understanding its properties. It may prove to be one of the most important cannabinoids as it affects bone growth, and inhibits pain and inflammation.

Cannabidivarin (CBDV)

CBDV may have similar effects to CBD in treating epilepsy. It is being researched by GW Pharmaceuticals because of its potential anti-epileptic and anti-convulsive properties.

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