

Cannabinoid Receptors

The primary cannabinoid receptors are identified as Cannabinoid type 1 receptors (CB1-R) and Cannabinoid type 2 receptors (CB2-R). The receptors can be “unlocked” by three kinds of cannabinoids:

1. **Endocannabinoids** – endogenous-fatty-acid cannabinoids produced naturally in the body (e.g., anandamide and 2-AG)
2. **Phytocannabinoids** – concentrated in the oily resin of the buds and leaves of plants such as cannabis (e.g., THC and CBD)
3. **Synthetic cannabinoids** – manufactured by artificial means such as in a laboratory

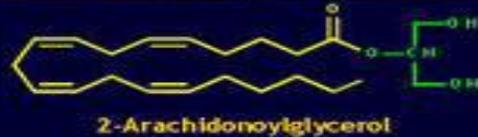
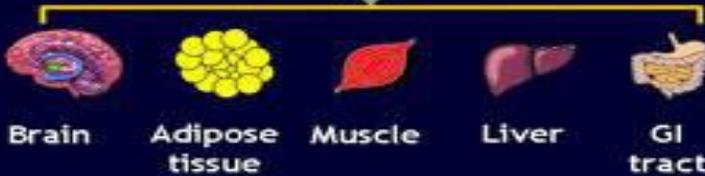
First detected in the brain, science now shows that CB1-R are also located in many other organs, connective tissues, gonads and glands. CB1-R are not found in the medulla oblongata (the part of the brain stem responsible for respiratory and cardiovascular functions). CB1-R play an important role in the coordination of movements, spatial orientation, sensory perceptions (taste, touch, smell, hearing), cognitive performance and motivation.

The most important function of the CB1-R is the reduction of excessive or inadequate signaling by the neurotransmitters (messengers) in the brain. By the activation of the CB1-R, the hyperactivity or hypoactivity of the messengers (e.g., serotonin, dopamine) is regulated back into balance. For example, when THC binds to CB1-R, activity in the pain circuits is inhibited, thus resulting in reduced pain. Many other symptoms such as nausea, muscle spasticity and seizures can be alleviated or diminished with cannabinoid therapy.

CB2-R are primarily associated with the immune system and found outside of the brain in such places as the gut, spleen, liver, heart, kidneys, bones, blood vessels, lymph cells, endocrine glands and reproductive organs. For example, CBD is keyed to CB2-R, and good evidence shows CBD is a beneficial therapeutic strategy to lessen the impact of inflammatory and neuro-inflammatory diseases. Until recently, it was believed that CB-2R played no role with nerve cells or bundles. However, studies now show that it also plays an important role in the signal processing of the brain.

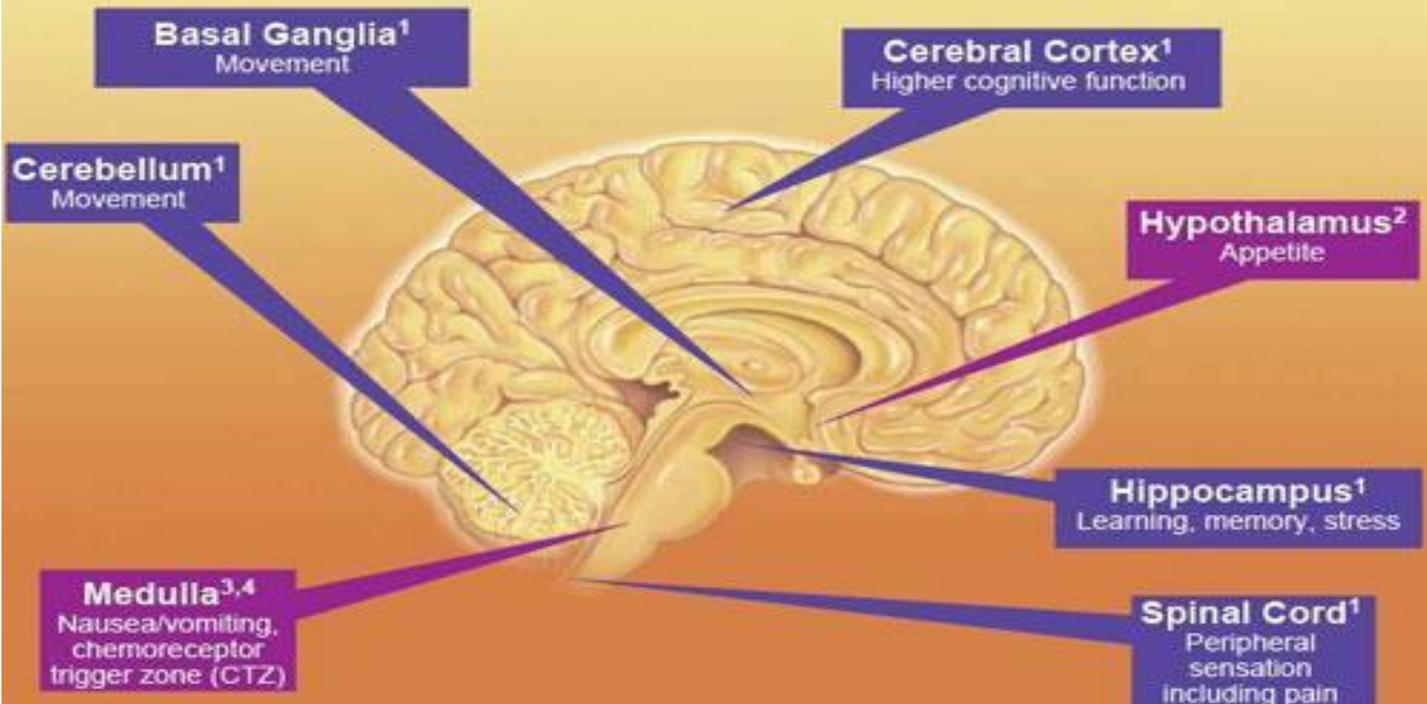
A third receptor that gets little attention is the transient receptor potential vanilloid-type one (TRPV1). The function of TRPV1 is to detect and regulate body temperature. In addition, TRPV1 is responsible for the sensations of extreme external heat and pain and is subject to desensitization. Therefore, if continuously stimulated, the pathway will eventually slow down or even stop. This raises therapeutic possibilities for agents to effectively treat certain kinds of neuropathic pain.

The Endocannabinoid System



Immune system

Concentrations of CB₁ receptors



1. Joy JE, et al, eds. *Marjuana and Medicine: Assessing the Science Base*. Washington, DC: National Academy Press, 1999:33-81. 2. Martin BR, et al. *J Support Oncol*. 2004;2(4):305-316. 3. Grotenharmen F. *Curr Drug Targets CNS Neurol Disord*. 2005;4(5):507-530. 4. Navari RM, et al. *Expert Opin Emerg Drugs*. 2006;11(1):137-151.

The Endocannabinoid System

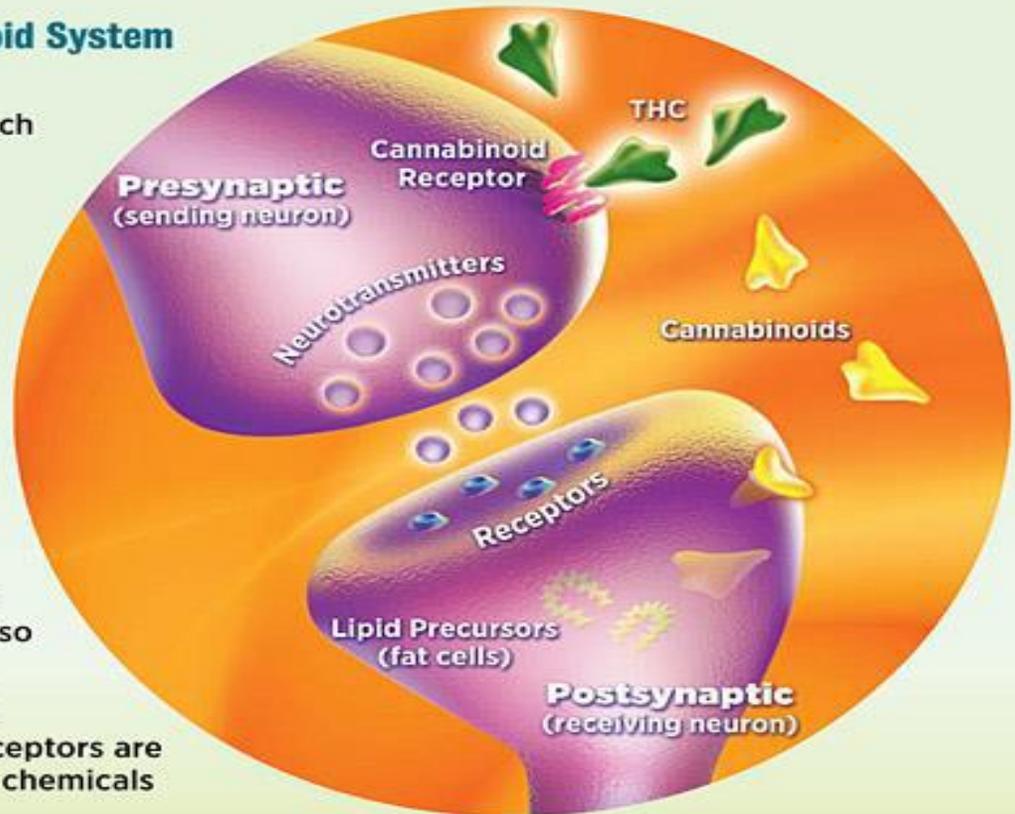
Brain cells (neurons) communicate with each other by sending chemical messages. The chemicals (neurotransmitters) cross a gap between neighboring neurons before attaching to their specific receptors.

Presynaptic: The neuron sending a message by releasing a chemical when signaled to do so

Postsynaptic: The neuron receiving the message when its receptors are activated by specific chemicals (neurotransmitters)

Neurotransmitters: The chemical messengers that travel from one brain cell to another

Receptors: Activated by neurotransmitters, receptors trigger a set of events that allows a message to be passed along to other neurons



Cannabinoids: Natural chemicals (anandamide and 2-AG) that bind to cannabinoid receptors in the brain and the body

THC: The main active ingredient in marijuana; THC, also a cannabinoid, interferes with the normal functioning of the endocannabinoid system

The Human Endocannabinoid System

CBD, CBN and THC fit like a lock and key into existing human receptors. These receptors are part of the endocannabinoid system which impact physiological processes affecting pain modulation, memory, and appetite plus anti-inflammatory effects and other immune system responses. The endocannabinoid system comprises two types of receptors, CB1 and CB2, which serve distinct functions in human health and well-being.

CB1 receptors are primarily found in the brain and central nervous system, and to a lesser extent in other tissues.

Receptors are found on cell surfaces



Tetrahydrocannabinol



Cannabidiol



Cannabinol

CB1

CBD does not directly "fit" CB1 or CB2 receptors but has powerful indirect effects still being studied.

CB2

CB2 receptors are mostly in the peripheral organs especially cells associated with the immune system.

