
# The Endocannabinoid System

# Endocannabinoid System

- For most of history, the effects of cannabis on the human body were little understood. Then, in the 1990's, scientists discovered endocannabinoids, the natural cannabis-like molecules produced by the human body. Scientists began to realize cannabis exerted its effects, in part, by mimicking our endocannabinoids. It appears the main function of the endocannabinoid system is to maintain bodily homeostasis—biological harmony in response to changes in the environment. Taxonomic investigation revealed that the endocannabinoid system is incredibly old, having evolved over 500 million years ago. Moreover, it is present in all vertebrates—mammals, bird, reptiles, amphibians, fish, etc., all produce endocannabinoids!
- Research initially suggested endocannabinoid receptors were only present in the brain and nerves, but scientists later found that the receptors are present throughout the body, including our skin, immune cells, bone, fat tissue, liver, pancreas, skeletal muscle, heart, blood vessels, kidney, and gastrointestinal tract. We now know the endocannabinoid system is involved in a wide variety of processes, including pain, memory, mood, appetite, stress, sleep, metabolism, immune function, and reproductive function. Endocannabinoids are arguably one of the most widespread and versatile signaling molecules known to man.

# Therapeutic Potential

- CBD (Epidiolex) is FDA approved to treat certain pediatric seizure disorders and was recently shown in a historic phase III clinical trial to reduce seizures in children with epilepsy disorders. In addition, early evidence has shown cannabinoids to have a range of effects that may be therapeutically useful, including **antioxidant, neuroprotective, anti-inflammatory, anti-pain, anti-tumor, anti-psychotic, anti-anxiety, and sleep modulating effects**. However, the current evidence is preliminary and often limited to animal studies–it will take rigorous human clinical trials before we can confirm these effects and determine which conditions they could possibly be used for.

- **A landmark review published in 2017 by the U.S. National Academy of Sciences, Engineering and Medicine concluded there was "substantial evidence" cannabinoids were effective for:**

- Chronic Pain
- Nausea and Vomiting during Chemotherapy
- Spasticity in Multiple Sclerosis.

- **They also concluded there was "moderate evidence" cannabinoids were effective for:**
- Improving sleep in people suffering from certain conditions, including chronic pain, obstructive sleep apnea, and fibromyalgia
- **Other areas demonstrating promise but where current evidence is more" limited" include:**
- Post-Traumatic Stress Disorder
- Tourette's Syndrome
- Social Anxiety
- Traumatic brain injury

- Source: UCLA Health Cannabis Research Initiative

# The ECS

- The **Endocannabinoid system** (**ECS**) is a biological system composed of endocannabinoids, which are endogenous lipid-based retrograde neurotransmitters that bind to cannabinoid receptors, and cannabinoid receptor proteins that are expressed throughout the vertebrate central nervous system (including the brain) and peripheral nervous system. The endocannabinoid system is involved in regulating a variety of physiological and cognitive processes including fertility, pregnancy, during pre- and postnatal development, appetite, pain-sensation, mood, and memory, and in mediating the pharmacological effects of cannabis.

- The ECS is also involved in mediating some of the physiological and cognitive effects of voluntary physical exercise in humans and other animals, such as contributing to exercise-induced euphoria as well as modulating locomotor activity and motivational salience for rewards.
  In humans, the plasma concentration of certain endocannabinoids (i.e., anandamide) have been found to rise during physical activity;- since endocannabinoids can effectively penetrate the blood–brain barrier, it has been suggested that anandamide, along with other euphoriant neurochemicals, contributes to the development of exercise-induced euphoria in humans, a state colloquially referred to as a runner's high.

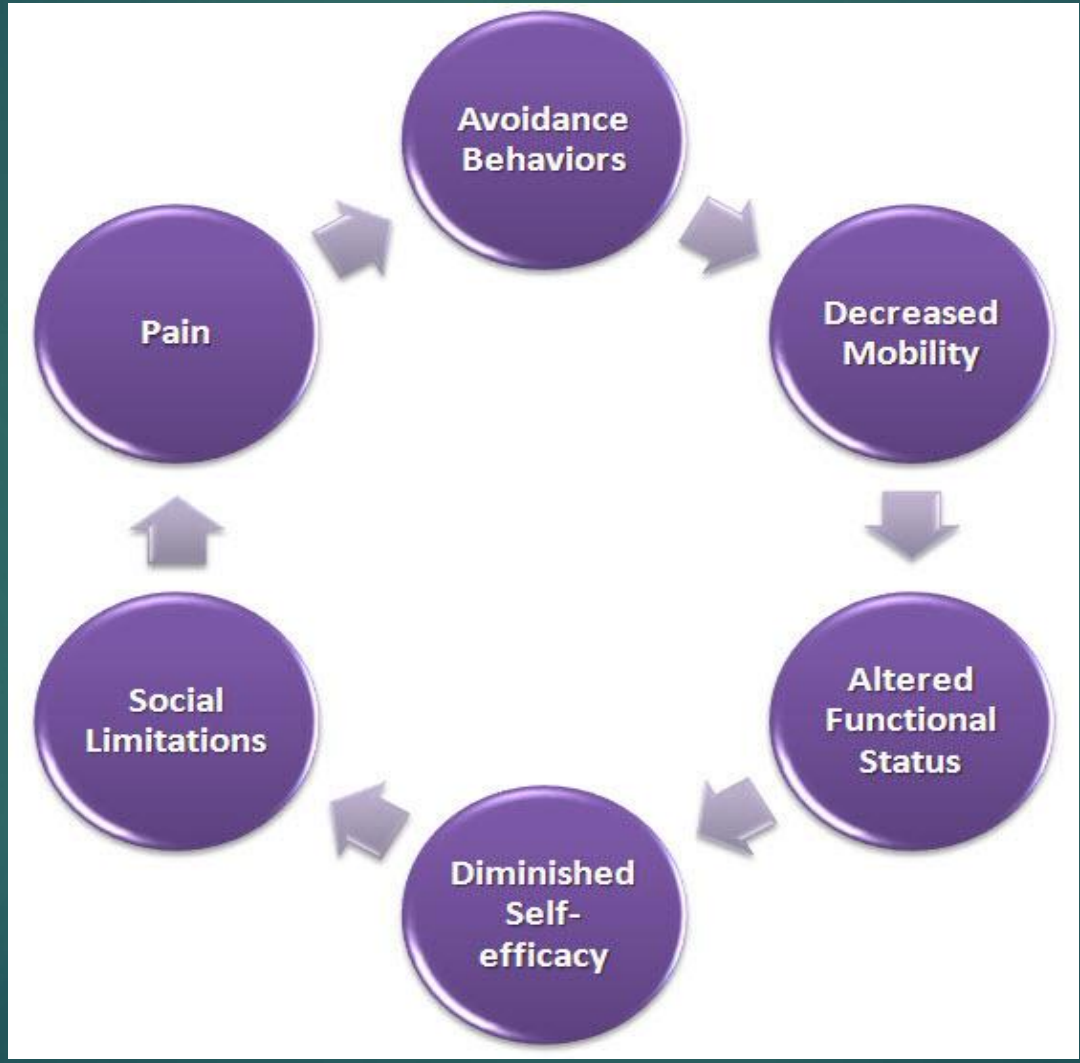
- Two primary endocannabinoid receptors have been identified: CB1, first cloned in 1990; and CB2, cloned in 1993. CB1 receptors are found predominantly in the brain and nervous system, as well as in peripheral organs and tissues, and are the main molecular target of the endocannabinoid ligand (binding molecule), anandamide. One other main endocannabinoid is 2-arachidonoylglycerol (2-AG) which is active at both cannabinoid receptors, along with its own mimetic phytocannabinoid, CBD. 2-AG and CBD are involved in the regulation of appetite, immune system functions and pain management

# Functions of the Endocannabinoid System

- Memory
- Appetite
- Energy Balance and Metabolism
- Stress Response
- Immune Function
- Female Reproduction
- Sleep
- Autonomic Nervous System
- Analgesia
- Thermoregulation
- Voluntary Physical Exercise

- Source: Wikipedia

# Vicious Cycle of Pain



# Consequence of Pain