Think of this system as the wizard behind the curtain. It underlies all the other systems, including the Autonomic Nervous System. Overall it influences well-being and the perception of well-being. It is involved in learning, memory, relaxation, eating, sleeping, forgetting and protection. Raphael Mechoulam calls it the “Global Protection System”.

Specifically the E.C. modulates:

- Embryological development
- Neural plasticity
- Neuroprotection
- Immunity
- Inflammation
- Apoptosis & Carcinogenesis
- Pain
- Blood sugar
- Cognition
- Forgetting of Fear
- Cardiovascular tone
- Hunger, feeding & Metabolism
- Emotional memory

**Components of the system**

**Ligands**: AEA, 2AG ~ think of them as the peptides of inner calm.

**Receptors**: CB1, CB2, CB3, CB4, CB5, GABA, Serotonin
The Ligands

**AEA (Arachidonylethanolamide)....“Anandamide” & 2AG (2-Arachidonylglycerol)**

Ligands are made in the phospholipid bilayer of the post-synaptic neuron on demand.

![Chemical Diagram](image_url)

- Found in the brain, spleen, heart and uterus.
- Uses CB1, CB2, TRP, PPAR, CB3 and GABA receptors.
- Binds receptors with less affinity than 2AG.

**Functions:**

- Inhibitory neurotransmitters
- Decrease: pain, nausea, wasting & brain damage
- Increases communication between amygdala and frontal cortex.
- Increases exploratory behavior *(the universe is safe enough)*
- Quicker learning when safe.
- Decreases anxiety.
- Calms neuronal function
- 2-AG is a true agonist and is 17-800X more present then Anandamide in brain.

**Receptors (CB1-CB5)**

Cannabinoid receptors are over 300 million years old. They are an old and widely used receptor type. Asters, conifers and of course, mushrooms, all bind this receptor type. Cannabis is only 34 million years old *(Compared to our 200,000 years to keep everything in perspective!)*. In general the highest density of receptors are in the hippocampus, cerebellum and basal ganglia. There are no receptors in the brainstem, so there is no risk of cessation of breathing or heart rate upon over consumption of chemicals binding the CB receptor.

The cannabinoid receptors are a class of receptors named G-coupled receptors located on the cell membrane. G-coupled receptors are ubiquitous. All organs and tissues contain this class of receptors. 50% of Pharmaceuticals use this class of protein receptors. *(Important to note here that “bullying” can occur at the molecular level. If one receptor type is over-activated (Over-used), it can steal parts from other receptor types. There are a limited amount of resources to make structures in the body).*

**CB1**

Where found:

- Most densely populated receptor in the brain!!
• Brain: substantia nigra, hippocampus, cerebral cortex, cerebellum, amygdala, thalamus
• Adipocytes
• Hepatocytes
• Skeletal muscles
• Bone/marrow
• Basophils
• Peripheral nerves
• Uterus
• Adrenals
• Lungs
• Bladder
• Mast cells

**Ligands that bind:**

• 2AG
• AEA
• THC
• CBD
• Terpenes

**Functions:**

• Temperature regulation
• Emotional response
• Learning and memory
• Sleep
• Pain response
• Language development
• Musical talent
• Appetite @hypothalamus
• Protects against: neurodegeneration, cirrhosis, nausea, pain, adipose build up, neuropathic pain, schizophrenia, cancer.

~ Animals without CB1 Receptor function are anxious, depressed, have increased morbidity & mortality, regressive, can’t enjoy pleasure, are afraid of the new and can’t forget/unlearn fear.

**CB2**

**Where found:**

Immune system and nervous system.

**Ligands that bind:**

• AEA
• 2AG
• THC
• CBD
• Echinacea
• Caryophyllene (Terpene in Black pepper)

Function:
• Protection against: osteoporosis, atherosclerosis, pain, chronic liver disease, neurodegeneration, possible metabolic disorders, & inflammation.
• Regulates cytokine activity.

**CB3**
Recognizes THC. Only 15% similar to CB!

**CB4 & CB5**
In early stages of research.

Clinical Endocannabinoid Deficiency Syndrome
CEDS is a suboptimal functioning of the ECS and could be linked to Migraines, IBS, Fibromyalgia, Anxiety, MS, Huntington’s, Chronic motion sickness, Anorexia, Schizophrenia, Parkinson’s and Failure to thrive.

In general, one could go about increasing the function of the ECS *and by the way any system with ligands), by either:

1. Increase the ECS ligand synthesis.
2. Decrease ligand degradation.
3. Increase receptor number and function.

Ways to Modulate the System
1. Dietary supplementation of Omega-3’s.
2. Dietary supplementation of probiotics.
3. Herbal Agonists of CB1 &CB2.

Copal Thujone
Curcumin Echinacea
Yagonin Black Pepper

4. Pesticides alter ECB function. *Pthalates*
5. Stress
    Acute vs. Chronic

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6. Opiates
   Acute vs. Chronic
7. Massage
8. Food intake and increased adipose tissue
9. Exercise
10. Alcohol
11. Caffeine
12. Cannabis
13. Breast milk