How CBD Affects the Brain

Let's start with the basics – The Endocannabinoid System (ECS)

The ECS is made up of three parts: 1) endocannabinoids, 2) receptors, and 3) enzymes.

1) Endocannabinoids are "messenger" molecules produced by your body that are similar to the cannabinoids found in cannabis (phytocannabinoids).

The job of cannabinoids (both endo and phyto cannabinoids) is to find receptors and bind to them.

2) When the cannabinoid binds to the receptor, the receptor becomes active. It then sends out a message to deliver what is needed for that area of the body. For example, if you're experiencing pain in your body due to arthritis or back pain, the receptor will stimulate the release of analgesic and anti-inflammatory peptides to relieve pain in that area.

The two main endocannabinoid receptors are CB1 receptors and CB2 receptors.

CB1 receptors are mostly found in the brain and central nervous system. They're responsible for controlling mood, emotion, pain, cognition, movement, coordination, memory, thinking and many other functions.

CB2 receptors are mostly found in immune cells. They regulate inflammatory and immune responses.

3) Enzymes are responsible for breaking down cannabinoids in the body.

Where does CBD come in?

CBD (cannabidiol) does *not* bind to the main CB1 and CB2 receptors like other cannabinoids. Instead, CBD works with the endocannabinoid system in an unusual way. CBD stimulates the ECS causing it to produces its own endocannabinoids, such as anandamide.

Anandamide is an endocannabinoid known as the "bliss molecule" (*ananda* is the Sanskrit word meaning *bliss*). Anandamide is responsible for feelings of pleasure and motivation.

CBD increases anandamide concentration in two ways: first is by inhibiting the fatty acid amide hydrolase (FAAH), that breaks down anandamide. The second way is by inhibiting the fatty acid binding protein (FABP) that carries anandamide away to be broken down. The result is an elevated feeling of pleasure and well-being.

Research has shown anandamide plays one of the most critical roles in the body. It's known to be the body's self-produced version of THC. It has profound effects such as upgrading the nervous system, brain function and immune system because it binds to both CB1 and CB2 receptors.

The benefits of anandamide range from elevated mood, pain-relief, mental clarity, improved memory, better sleep, relaxation and improved immune function—as well as decreased anxiety, depression and cognitive disorders such as schizophrenia, psychosis and Alzheimer's disease.

More Pleasure, Less Pain

CBD is found to directly affect serotonin and dopamine levels. 5-HT1A (hydroxytryptamine) is a G protein-coupled receptor (GPCR) that is activated by CBD, resulting in the increase to two critical "feel-good" neurotransmitters: serotonin and dopamine.

Serotonin helps improve your mood, regulate sleep, increases your appetite, makes you more social, improves memory—while curbing addiction, anxiety, pain perception, nausea and vomiting.

Dopamine causes us to feel good for doing things such as eating delicious food, sipping coffee, exercising. It's our brain's way of rewarding us so that we keep repeating those tasks, causing increased pleasure, motivation and mental performance—while alleviating depression.

When dopamine levels are out of balance, it's common to compensate by over indulging in food, drugs, sex etc., that may eventually lead to addiction. In extreme cases in which the brain does not produce enough dopamine, the resulting effect is Parkinson's disease.

CBD inhibits the TRPV1 (vanilloid 1) receptors that mediate inflammation, block pain and regulate body temperature. Interestingly, capsaicin inhibits the same TRPV1 receptors to mediate inflammation, block pain and raise your body temperature. You know the feeling if you've ever eaten a hot chili pepper, because capsaicin is the "hot" compound in chili peppers.

Another way CBD induces sedative effects is very interesting. Although CBD doesn't bind to CB1 and CB2 receptors, it controls how the receptors bind with other cannabinoids. According to studies, CBD can either enhance or inhibit how a receptor transmits a signal by changing the shape of the receptor.

Let's take GABA for example. GABA (gamma-Aminobutyric acid), like serotonin, is an inhibitory neurotransmitter. Its job is to block certain brain signals and decrease nervous system activity. GABA activity in the brain has a sedative effect, lowering the volume of anxiety. In the spinal cord, GABA allows for sensory information to integrate and thereby allowing your body to move smoothly.

Low GABA activity contributes to anxiety, depression, schizophrenia, autism, Huntington's disease, Dystonia (movement disorder) and muscle spasticity.

CBD modifies the shape of the GABA-A receptor. This increases activity between GABA and GABA-A receptors, raising GABA levels in the body. This function of modifying a receptor's shape to increase activity is known as "positive allosteric modulator".

Another example is with THC. CBD acts as a "negative allosteric modulator" whereby CBD alters the shape to weaken CB1 receptors. This weakening makes it difficult for THC to bind with these receptors, limiting excessive THC in the nervous system.

As a result, CBD/THC balanced products have therapeutic benefits along with a euphoric high, rather than paranoia and anxiety associated with overdoing THC.

Blood Pressure, Cancer and Bone Density

CBD has been found to reduce blood pressure, regulate bone density and inhibit cancer cell growth.

According to a few studies published by the National Institute of Health, CBD inhibits GPR55 (another G protein-coupled receptor), expressed mostly in the cerebellum. When the GPR55 receptor becomes overactive, it signals the breakdown of bone density through osteoclast cell function. The resulting effect is osteoporosis.

The GPR55 is also responsible for cancer cell proliferation.

CBD is found to block the GPR55 receptor thereby suppressing cancer growth and osteoporosis. (See study below: *The putative cannabinoid receptor GPR55 affects osteoclast function in vitro and bone mass in vivo* and *G protein-coupled receptor GPR55 promotes colorectal cancer and has opposing effects to cannabinoid receptor 1*)

In another study published by the National Institute of Health, CBD was found to have significant anti-cancer effects on various types of cancer such as glioma, breast cancer, lung cancer, colorectal cancer, leukemia and lymphoma, prostate cancer, cervical cancer, thyroid cancer and hepatocellular carcinoma to name a few from the study.

Here's a quote from the study: "CBD, alone or with other agents, has been shown to successfully induce cell death, inhibit cell migration and invasion in vitro, decrease tumor size, vascularization, growth, and weight, and increase survival and induce tumor regression in vivo." (See study below: *Cannabidiol (CBD) as a Promising Anti-Cancer Drug* in the sources)

Another study shows CBD reduces blood pressure in "hypertensive, overweight and hypercholesteremic patients". According to the study, CBD affects the PPAR-gamma and again the TRPV1 receptors resulting in CBD-induced relaxation and reduced hypertension.

Neuroprotective and Anti-Aging Effects

CBD is also shown to protect against the degradation of brain cells, making it a powerful antioxidant.

CBD activates receptors responsible for preventing brain cell degradation. Also, CBD increases anandamide concentration, strengthening the hippocampus by creating new neurons that are responsible for short-term and long-term memory.

In the case of Alzheimer's disease, the hippocampus is the first area of the brain to sustain neural damage. For this reason, CBD is often recommended to early onset Alzheimer's patients.

In addition to Alzheimer's, CBD is often prescribed to treat seizures, epilepsy, and neuropsychiatric disorders.

At high concentrations, CBD blocks the 5-HT1A receptors in the hippocampus and temporal neocortex. "This effect could modify neuronal excitation and reduce epileptic seizures in patients..." (See study below: *Cannabidiol Acts at 5-HT 1A Receptors in the Human Brain: Relevance for Treating Temporal Lobe Epilepsy*)

Many studies show that both CBD and THC are neuroprotective antioxidants. These potent cannabinoids slow down signs of aging by reducing free radicals causing oxidative damage in the brain.

Both CBD and THC were shown to prevent hydroperoxide-induced oxidative damage as well as or better than other antioxidants. They were also shown to protect equally well against neurotoxicity. CBD was shown to be more protective against glutamate neurotoxicity than both vitamin C and vitamin E. This indicates both cannabinoids are potent antioxidants, with CBD potentially being more potent of the two.

The study concludes, "These data also suggest that the naturally occurring, nonpsychotropic cannabidiol, may be a potentially useful therapeutic agent for the treatment of oxidative neurological disorders such as cerebral ischemia." (See study below: *Cannabidiol and (−)Δ9-tetrahydrocannabinol are neuroprotective antioxidants* in the sources)

The Synergistic Role of Terpenes

Imagine cutting into a fresh lemon...

The aroma you're smelling is limonene, beta-pinene and gamma-terpinene. Terpenes are what give plants and fruits their aroma and flavor. In cannabis, terpenes increase the effectiveness of cannabinoids' therapeutic qualities and also give cannabis strains their unique and wonderful aromas.

Like cannabinoids, terpenes are known to interact with receptors and neurotransmitters. Different cannabis strains contain a variety of different terpenoid and cannabinoid levels at varying ratios. For this reason, different strains produce a range of effects on mood, levels of alertness and sedation, flavor and aroma, and so on.

The three most abundant terpenes in cannabis are myrcene, beta-caryophyllene and limonene.

Myrcene has been found to decrease inflammation. Studies show that myrcene slows down the degeneration of cartilage and could be used to block the progression of osteoarthritis. It has a mildly sweet flavor profile found in mangos, thyme, parsley, bay leaf, hops, cardamom, lemongrass and juniper. (See study below: Evaluation of the anti-inflammatory, anti-catabolic and pro-anabolic effects of E-caryophyllene, myrcene and limonene in a cell model of osteoarthritis)

Beta-caryophyllene (β-caryophyllene) is a sesquiterpene, known to deliver oxygen directly into the cell to fuel the healing process. Beta-caryophyllene is considered an atypical cannabinoid because it's the only known terpene to bind to CB2 receptors that help relieve inflammation, pain, atherosclerosis, and osteoporosis. Studies show that beta-caryophyllene is directly beneficial for colitis, osteoarthritis, diabetes, cerebral ischemia, anxiety and depression, liver fibrosis, and Alzheimer-like disease types. (See study below: Caryophyllene). Beta-caryophyllene is found in cloves, hops, rosemary, black pepper and copaiba.

Limonene gives cannabis an uplifting feel and citrusy flavor. Not surprisingly, limonene is found in citrus peels. A study has shown limonene to neutralize pathogenic bacteria and viruses by increasing the production of antibody-producing cells used by the immune system. (See study below: *Immunomodulatory Activity of Naturally Occurring Monoterpenes Carvone, Limonene, and Perillic Acid*)

The Entourage Effect

I'd like to point out that the wide range of therapeutic benefits are by no means limited to CBD and terpenes. As mentioned earlier, CBD and THC work together and balance one another. THC is know to be a powerful analgesic with a huge list of other therapeutic benefits.

According to another study published by the National Institute of Health, CBN (cannabinol), CBG (cannabigerol), CBC (cannabichromene), THC and CBD "showed potent activity against a variety of methicillin-resistant Staphylococcus aureus (MRSA) strains of current clinical relevance." MRSA is resistant to antibiotics, making it difficult to treat. (See study below: *Antibacterial cannabinoids from Cannabis sativa: a structure-activity study*)

CBN is also a neuroprotectant and anti-inflammatory agent used for rheumatoid arthritis. (See study below: *Cannabinoids, inflammation, and fibrosis)*

CBG is the mother molecule from which all other phytocannabinoids are born. It's also a neuroprotectant, anti-inflammatory, used for pain relief, to relax muscles, anti-anxiety, to strengthen bones, and the list goes on...

There are over a hundred known cannabinoids, each having its own therapeutic gifts to offer.

Conclusion

CBD is found to be an effective analgesic, antioxidant, anti-cancer and antibacterial agent that is non-addictive and has zero known negative side effects. CBD runs its course through the body and is used only when and where it's needed. When the body has reached optimum health (homeostasis) CBD is simply broken down by enzymes and carried out of the body.

A common theme that is seen with cannabinoids is that they induce relaxation in so many ways, both directly and indirectly. This shows that relaxation is key. Relaxation switches on the parasympathetic nervous system responsible for DNA repair, healing, protecting against viruses and disease, and reversing biological age so that you look and feel younger and healthier.

It appears to me the reason why cannabinoids (and terpenes) are so effective is because they help the body repair itself.

The endocannabinoid system is a complex and intelligent organism. It knows how, where, and when to use each cannabinoid and terpene molecule. It's fortunate the legal issues surrounding cannabis have relaxed over the years, allowing access for many people to receive its benefits.

We're all participating in a massive paradigm shift. We will begin to see more positive changes happen as more of us raise our level of consciousness and realize *who* we are and *why* we are here at this time.

This research paper is for our friend, Virginia. Thank you so much for inspiring me to look into your question, "how does CBD affect the brain?". There were so many things I didn't know about the ECS. If it weren't for you, I may have never known how truly amazing this organism operates.

Much love to you,

Alex & Stephanie

Sources:

The Impact of Cannabidiol on Human Brain Function: A Systematic Review
https://pubmed.ncbi.nlm.nih.gov/33551817/

Effects of Cannabidiol (CBD) on the Brain (CBD)
https://clinicaltrials.gov/ct2/show/NCT04831294

The direct actions of cannabidiol and 2-arachidonoyl glycerol at GABA A receptors
https://pubmed.ncbi.nlm.nih.gov/28249817/

Cannabinoid Receptors in the Central Nervous System: Their Signaling and Roles in Disease
https://www.frontiersin.org/articles/10.3389/fncel.2016.00294/full

Antidepressant-like and anxiolytic-like effects of cannabidiol: a chemical compound of Cannabis sativa
https://pubmed.ncbi.nlm.nih.gov/24923339/

Cannabidiol Acts at 5-HT1A Receptors in the Human Brain: Relevance for Treating Temporal Lobe Epilepsy
https://www.frontiersin.org/articles/10.3389/fnbeh.2020.611278/full

Neural basis of anxiolytic effects of cannabidiol (CBD) in generalized social anxiety disorder: a preliminary report
https://pubmed.ncbi.nlm.nih.gov/20829306/

Alzheimer's disease; taking the edge off with cannabinoids?
https://pubmed.ncbi.nlm.nih.gov/17828287/

A Personal Retrospective: Elevating Anandamide (AEA) by Targeting Fatty Acid Amide Hydrolase (FAAH) and the Fatty Acid Binding Proteins (FABPs)
https://www.frontiersin.org/articles/10.3389/fphar.2016.00370/full

Cannabinoids in the management of difficult to treat pain
https://pubmed.ncbi.nlm.nih.gov/18728714/

Enzymatic Pathways That Regulate Endocannabinoid Signaling in the Nervous System
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3150828/

Role of the endocannabinoid system in the neuroendocrine responses to inflammation
https://pubmed.ncbi.nlm.nih.gov/24588819/

Cannabidiol is a negative allosteric modulator of the cannabinoid CB1 receptor
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4621983/

The putative cannabinoid receptor GPR55 affects osteoclast function in vitro and bone mass in vivo
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2737440/

Cannabinoid Receptors as Target for Treatment of Osteoporosis: A Tale of Two Therapies
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3001217/

G protein-coupled receptor GPR55 promotes colorectal cancer and has opposing effects to cannabinoid receptor 1
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5679368/

Cannabidiol (CBD) as a Promising Anti-Cancer Drug
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7693730/

Vasodilatory effects of cannabidiol in human pulmonary and rat small mesenteric arteries: modification by hypertension and the potential pharmacological opportunities
https://journals.lww.com/jhypertension/Fulltext/2020/05000/Vasodilatory_effects_of_cannabidiol_in_human.16.aspx

Immunomodulatory Activity of Naturally Occurring Monoterpenes Carvone, Limonene, and Perillic Acid
https://www.tandfonline.com/doi/abs/10.1081/IPH-120020476?journalCode=iipi20

Caryophyllene
https://www.sciencedirect.com/topics/medicine-and-dentistry/caryophyllene

Evaluation of the anti-inflammatory, anti-catabolic and pro-anabolic effects of E-caryophyllene, myrcene and limonene in a cell model of osteoarthritis
https://pubmed.ncbi.nlm.nih.gov/25622554/

Cannabidiol and (−)Δ9-tetrahydrocannabinol are neuroprotective antioxidants
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC20965/

Antibacterial cannabinoids from Cannabis sativa: a structure-activity study
https://pubmed.ncbi.nlm.nih.gov/18681481/

Cannabinoids, inflammation, and fibrosis
https://faseb.onlinelibrary.wiley.com/doi/full/10.1096/fj.201600646r