

The Impact of Cannabis Use on the Developing Brain

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Cannabis 101

- Cannabis refers to the entire plant, leaves, stock, flowers, etc.
- Species of Cannabis plant: C. sativa, C. indica, and C. ruderalis
- Strains of *C. sativa* and *C. indica* vary in their ratios of THC:CBD
- Hemp is a strain of *C. sativa* that has very low amounts of Δ9-THC (<0.3%) **Δ9-THC in marijuana
- Cannabinoids: the chemicals within the plant like THC, CBD, THCA, Δ 8-THC etc.





Endocannabinoid System – where THC interacts

The Endocannabinoid System:

- a) consists of cannabinoid receptors (CB1 and CB2) and endogenous ligands (eCBs)
- b) is highly active during adolescence particularly in the prefrontal cortex (executive function) and limbic circuitry (emotional brain).
- c) plays an essential role in central nervous system (CNS) maturation.
- d) acts on certain neurotransmitter systems (glutamate, GABA, dopamine). Regulates neurogenesis (growth of new neurons), formation of new synapses (communication between neurons), and synaptic pruning.





Endocannabinoids



- Endocannabinoids: a family of lipids (fats) that bind to the cannabinoid receptors (CB1 and CB2) in the body and illicit a biological response.
- The endocannabinoids are synthesized on demand.
- The endocannabinoids:
 - Regulate communication between neurons (specialized nerve cell) called synaptic communication
 - Play a role in synaptic plasticity (neuroplasticity)





Cannabinoid Receptors (CB1) in the Brain

Cannabinoid receptors regulate:

- Brain development
- Memory & cognition
- Motivational systems & reward
- Appetite
- Immunological function
- Reproduction
- Movement coordination
- Pain regulation & analgesia



CB1 receptors – primarily found in the central nervous system (CNS – brain and spinal cord)

CB2 receptors – primarily found in tissues associated with immune function



Cannabis (Marijuana) DrugFacts, NIDA, 2019.



The Expanded Cannabinoid System



Cristino et al, Nat. Rev. Neurology, 2020, 16, 9-29









Endocannabinoid System Communication



AEA or 2-AG are released from the *Post*synaptic (receiving) neuron and binds to the CB1 receptor on the *pre*synaptic (sending) neuron. This event modulates the communication between neurons releasing glutamate (excitatory), GABA (inhibitory) and dopamine (reward).

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Synaptic Pruning

The adolescent brain literally loses roughly half of its gray matter volume!





Bara et al. Cannabis and synaptic reprogramming of the developing brain, Nature Reviews Neuroscience, 22, 423-438 (2021)





Synaptic Pruning





Cannabis and the Adolescent Brain

Main chemical components in cannabis

Tetrahydrocannabinol (THC): the main psychoactive ingredient that gives the "high" feeling while smoking/ingesting cannabis



Cannabidiol (CBD): CBD does not produce a "high" feeling. CBD has been thought to help treat epilepsy, anxiety, and opioid withdrawal symptoms







Endocannabinoids vs. THC







Endocannabinoid System Communication







THC Concentrations Over the Years



Source: U. Miss. Potency Monitoring Project

What is considered high potency marijuana?

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A cannabis product that contains > 10% THC

Cannabis extracts with high concentrations of THC

Names	Form	Consistency	THC Level
batter, budder	liquid	thick, spreadable	90 to 99 percent
butane hash oil (BHO), butane honey oil, honey oil	liquid	gooey	70 to 85 percent
crystalline	solid	crystal	~99 percent
distillate	liquid	oily	~95 percent
honeycomb, crumble, crumble wax	solid	spongy	60 to 90 percent
pull-and-snap	solid	taffy-like	70 to 90 percent
shatter	solid	glass-like, brittle	70 to 90 percent
wax, earwax	liquid	thick, sticky	60 to 90 percent

Can be smoked, vaped, eaten, or rubbed onto skin



Hash Oil: A Cannabis Concentrate (healthline.com)

Delta-8-THC & Delta-9-THC

There is very little research on the benefits and side effects of Delta-8-THC and Delta-10-THC in humans.

Delta-8- and Delta-10-THC are made from CBD and are not evaluated for purity or approved by the FDA.

This means many unknown and possibly harmful chemicals can be found in store bought Delta-8- and Delta-10-THC products.

Where do Delta-8 and Delta-10 come from?







Delta-8-THC



Delta-10-THC









Recent Studies on Cannabis Use

Cannabis Hyperemesis Syndrome (CHS) is the result of long-term cannabis use that includes chronic severe vomiting, nausea, stomach pain, and dehydration. CHS does not respond to conventional antiemetic therapies.

Studies in Canada:

• Over 7.5 years, the rates of CHS ED visits increased 13-fold



- Pre-legalization in Canada (2014-2018)
- Legalization with retail store restrictions (2018-2020)
- Commercialization with new products and expanded stores (2020-2022) **Largest increase in CHS

JAMA Network Open. 2022;5(9):e2231937





Recent Studies on Cannabis Use

"THC activates cannabinoid receptors in the brain, thus interfering with the physiological actions of the endocannabinoids....endocannabinoid production is pivotal for correct processing of different brain functions such as higher-order cognition, memory, reward, mood, and stress sensitivity"

Albaugh et al., JAMA Psych., **2021**;78:1031-40.



"CUD was found to be associated with an increased risk of unipolar depression and bipolar disorder" *Jefsen et al.* JAMA Psych., **2023**; 80(8):803-810



"The more potent the THC concentration, the higher probability of developing psychosis, or a major depressive episode, or a major anxiety disorder later in life." Dr. Andrew Huberman, Neurobiologist, Stanford University





Recent Studies on Cannabis Use

Psychosis: Seeing of hearing things that are not there or extreme paranoia

"Overall, use of high potency cannabis, relative to lower potency cannabis, was associated with an increased risk of psychosis and cannabis use disorder." Petrilli *et al Lancet Psychiatry* (2022);9:736



"All BCN algorithms strongly suggested a **directional relationship from adolescent** cannabis use to accelerated Prefrontal cortical thinning." Owens *et al.*, Translational Psychiatry (2022);12:188

"Young males might be particularly susceptible to the effects of cannabis on schizophrenia. At a population level, assuming causality, **one-fifth of cases of schizophrenia among young males might be prevented by averting CUD**. *NIH Bulletin* 5-2023





Effects of THC exposure (2 weeks) on pyramidal neurons of adolescent rodents



Pyramidal neurons in the prelimbic subregion of the rodent ventromedial PFC This area of the brain helps with cognitive function, emotional regulation, and decision making

* Disruptions in this region's circuitry is implicated in psychiatric illness like schizophrenia

Miller er at., Mol. Psych. (2019) 24:588-600





Cannabis-Induced Psychosis

- Short term psychosis can occur with cannabis use and remain in effect until the cannabis is metabolized by the body.**
- People who experience seeing or hearing things that are not there, paranoia, and confusion about reality while "high" are more likely to develop a psychotic disorder like schizophrenia if they continue to use cannabis.*
- 15% of new cases of psychosis are attributable to cannabis**
- Teens who use cannabis are significantly more likely to develop psychotic disorders than those teens who have never used cannabis.*
- Consider avoiding or delaying use of cannabis until after the age of typical expression/onset of the illness (at least 25). Or avoid using high THC potency cannabis – especially during adolescence!!*
- Not everyone who uses cannabis develops psychosis**





* Bearden et al. UCLA, Cannabis Psychoeducational Brochure, Harm Reduction Approach **Connecticut Department of Mental Health & Addictive Services at Yale School of Medicine



Cannabis-Induced Psychosis









Anders Christian Meisenheimer

10/23/96 - 3/5/19









Money and Power

- "Legal cannabis sales in the U.S. totaled \$30 billion in 2022 and are projected to surpass \$35 billion in 2023."
- "If the pace of state-level legalization continues in the absence of federal policy reform, legal cannabis sales are projected to reach \$71 billion by 2030. If that pace stagnates, it would still reach \$58 billion."



https://newfrontierdata.com/cannabis-insights/u-s-cannabis-sales-could-total-71b-in-2030-without-federal-legalization/





Questions



Grief never ends but it changes. It is a passage not a place to stay. Grief is not a sign of weakness nor a lack of faith. It is the price of love.

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