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CANNABIS USE AND THE DEVELOPING BRAIN: HIGHS AND LOWS

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AGE: 15

THEODORE AGE: 13 Although cannabis is a naturally occurring plant with a long history of use by humans, the chemicals it contains, called cannabinoids, can act on the human body in many ways. Use of cannabis during important periods of development, such as during pregnancy and adolescence, can have a long-lasting impact on the way the brain forms and develops its systems to control emotions and other functions. This article gives an overview of some of the effects of cannabinoids on the developing brain, before birth and as teenagers, and provides information about how young people can prevent or minimize the negative effects of cannabis on their brains.

CANNABIS AFFECTS THE BRAIN—ESPECIALLY DURING DEVELOPMENT

Cannabis is a plant also known as weed, pot, grass, bud, dank, ganja, and flower. Cannabis use in America is increasing—more teenagers now use cannabis than smoke cigarettes, although cannabis remains illegal in many countries [1]. Cannabis contains more than 500 chemicals, at least 140 of which are called **cannabinoids**, the active ingredients of cannabis that are responsible for the way it affects people. The main cannabinoid that causes the "high" people experience from smoking or ingesting cannabis is called delta-9-tetrahydrocannabinol, commonly known as THC.

In our bodies, we have naturally occurring cannabinoids called **endocannabinoids**. Endocannabinoids influence the brain and body in a very controlled way. They play a role in many normal bodily processes, including emotion control, movement, memory, and the immune system, just to name a few [2]. In the developing brain, endocannabinoids help to establish healthy connections between nerve cells, so that these cells can communicate properly. Endocannabinoids do all these things by binding to specific molecules called **cannabinoid receptors**, which exist on the surfaces of many cells. When THC enters the body through cannabis use, it binds to cannabinoids do, and it overwhelms the body's natural cannabinoid system.

The potency (strength) of cannabis has been increasing over the years. Before 2000, the THC concentration in street cannabis was 4% or less. Since then, however, THC levels in cannabis have consistently doubled in concentration: from 4-8% in the early 2000s to 20% now. Highly potent products such as dabs or vape pens boost THC content even more—to 70% and higher.

Given the many effects cannabis can have on the body and brain and the increased potency of cannabis available to young people, understanding how cannabis use might impact the developing brain is extremely important. Two key stages of brain development are particularly critical in terms of cannabis exposure: the prenatal (before birth) period within the womb, and the teenage years. Exposure to cannabis at either of these critical periods can increase the risk of anxiety, depression, and addiction. So, how exactly do cannabis and THC affect the developing brain?

CANNABINOIDS

The chemical compounds found in cannabis.

ENDOCANNABINOIDS

Chemicals made within our own bodies that influence the brain and body in a very controlled way including emotion control, movement, memory.

CANNABINOID RECEPTORS

Specific molecules which exist on the surfaces of many cell types which bind our natural endocannabinoids and cannabis.

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THC EXPOSURE IN THE WOMB

Approximately 18% of pregnant women use cannabis during pregnancy and/or while breastfeeding, which exposes their unborn babies and newborns to THC. It is known that THC binds to cannabinoid receptors in the developing brain, and studies show that babies exposed to cannabis during pregnancy are more likely to be anxious, have depression, or to be more aggressive and impulsive in childhood and adolescence [3]. Other studies show that exposure to THC in the womb changes genes related to brain cell structure and the production of certain critical proteins that regulate behavior. For example, prenatal THC exposure can reduce the number of **dopamine** receptors on cells. Dopamine plays an important role in how we respond to "rewards"—things that make us feel good—and a reduction in dopamine receptors is associated with an increased risk of substance use disorder, commonly known as addiction.

How can prenatal THC exposure affect an individual's behavior after birth and as they grow up? One way involves a biological process called **epigenetics**, in which chemical changes are made to the DNA, which can turn genes on or off. These changes are long-lasting but may be reversible. Studies have demonstrated that, if animals are exposed to THC during pregnancy, the infants after birth show changes in the on/off patterns of genes that regulate their behavior in adulthood [4]. These epigenetic changes help to explain why THC can cause such long-term effects on the brain. Also, since epigenetic mechanisms are reversible, this information gives us hope that we can develop treatments to reverse the effects of cannabis.

Another study showed that exposure of babies to cannabis in the womb led to increased levels of the stress hormone **cortisol** in their bodies, increased anxiety, increased aggression, and an increase in disruptive behavior (Figure 1). Similar effects are seen in babies born to mothers who experience traumatic stress during pregnancy, such as coping with a natural disaster [3, 5]. This might mean that a mother who uses cannabis while pregnant might also be priming her baby's brain to overreact when exposed to stress later in life [6].

THC EXPOSURE DURING THE TEENAGE YEARS

There is a well-known link between cannabis use in teenage years and negative mental health outcomes such as mental illness, depression, anxiety, and addiction. Addiction to cannabis is called **cannabis use disorder (CUD)**. CUD is on the rise, and risks for developing CUD peak during the teenage years. However, not everyone who tries cannabis will become addicted, and it is important to understand what makes some people more vulnerable to CUD. Studies have shown that teens and young adults who have both anxiety *and* genes that are related

DOPAMINE

A body chemical that helps us feel good after "rewarding" behaviors.

EPIGENETICS

A biological process by which a person's environment or behavior impacts whether their genes are turned on or off.

CORTISOL

A hormone released by the body in times of stress, it can increase anxiety, aggression, and disruptive behavior.

CANNABIS USE DISORDER (CUD)

Addiction to cannabis or problematic use of cannabis.

Figure 1

Exposure of unborn babies to THC or stress can have an impact on them for their whole lives, from before birth into adulthood. Response to stress and THC exposure to unborn babies is similar. This figures shows the effects of stress or THC exposure before birth at different stages of life (\uparrow = increase; \downarrow = decrease).

↑ Risk low birth weight Effect on birth Risk of premature birth Risk of baby dying before birth Early character ↑ Fear ↑ Distress Reactivity to stress **Early behavior** ↑ Aggression ↑ Impulsive behavior **Time** 1 Anxiety **1** Depression ↑ Cortisol Steroid hormones ↑ Hormones ↓ Hormones that control sleep ↑ Sweating and Cardiovascular effects nervousness ↓ Time between heartbeats suggesting high stress Figure 1

to addiction were much more likely to develop CUD than those with anxiety alone or addiction-related genes alone [7].

One of the strongest influences for developing CUD is the age at which cannabis is first used—the younger a person is when they first use cannabis, the more likely they are to develop CUD. For every year a teenager delays cannabis use, the risk of developing CUD drops by about 10%. Use of cannabis during the teen years is not just associated with an increased risk of CUD, but with an increased risk of addiction in general. So, delaying cannabis use until later in life may decrease some of the negative effects on the brain and behavior. Of course, if the use of cannabis is avoided altogether, the risks of CUD or other negative brain effects due to cannabis will be zero.

Since the concentration of THC in cannabis has more than quadrupled over time, teens today might be exposed to stronger cannabis than teens of the past, so understanding the effects of high doses of THC is crucial. Studies in animals have shown that high doses of THC activate the brain's stress mechanisms more strongly than low-dose THC [8]. When these animals experienced a stressful event, such as being isolated from other animals, their reward-seeking behavior and social anxiety increased; and this was associated with changes in the structure of certain brain cells called **astrocytes**. Astrocytes support brain function by providing brain cells with nutrients, repairing them

ASTROCYTES

Star-shaped brain cells that perform a wide range of functions including providing nutrients to other brain cells and repairing them after injury. after injury, and helping them to communicate effectively. Changes to astrocytes caused by THC may contribute to increased anxiety, depression, and social avoidance [8].

DECREASING THE RISKS

How can we minimize the risk of cannabis on the developing brain (Figure 2)? The best way to minimize risk is to avoid or reduce the use of cannabis! Learning the facts about the negative effects of cannabis on brain development is vital because this information can prevent people from starting to use cannabis in the first place. Trusted adults should start conversations about cannabis with young people early, ideally in the pre-teen years. Most often, we do not know whether we have the genes that contribute to addiction, or whether our mothers experienced stress or drug use during pregnancy—things that might influence our response to cannabis. As a result, we cannot know if exposing ourselves to cannabis in our teenage years will build on those unknowns and negatively impact our behavior, our mental health, or our future urge to use dangerous drugs.

What can be done to protect the developing brain from cannabis use? Start to educate and discuss Listen to young people to cannabis and other drugs early understand their perspectives, pressures, and issues with young people Early, honest, non-judgmental conversations about cannabis are needed with young people, by parents and in schools · What is it? · What can it do to my brain? How can it affect my behavior now and in the future? What can young people do • What can it mean for my future brain? to avoid cannabis harm? Understand that the goal is to minimize harm The most effective way to avoid harm from cannabis is to avoid it all together · Delay trying cannabis beyond teenage years Avoid cannabis with high THC content (this includes vape products, edibles, and dabs) · Cut down or cut out use of cannabis in pregnancy or if there is a possibility of pregnancy Figure 2

Teenagers who are at high risk for cannabis use or are currently using cannabis in a problematic way should get treatment as soon as possible. Early treatment is most successful. If teenagers are unwilling to attend treatment, parents and caregivers should attend on their own—parental attendance has been shown to increase the willingness of young people to get treatment themselves.

Figure 2

Since cannabis can affect the developing brain, it is critical for young people to minimize harm from cannabis use. This figure gives some ideas of how this might be achieved.

SUMMARY

Exposure to THC during important periods of brain development, particularly in the womb or during the teenage years, can cause long-lasting changes to the brains and behaviors of children—both in childhood and beyond (Figure 3). Avoiding the use of cannabis completely, or at least delaying its use until after the teenage years, is the best way to protect the brain. When we understand the effects of cannabis we can make informed choices—choices that can benefit our future brains and bodies!

Natural cannabinoids in the body -Cannabis contains >500 control communication between cells chemicals and ~140 cannabinoids They are essential for THC, the most studied development of brain cells cannabinoid, hijacks the body's and brain pathways own systems Cannabis use in pregnancy is increasing THC in cannabis is now 4 16% pregnant mothers use cannabis times higher than in the 1980s every day ~4% to 10-20% 15% among breastfeeding mothers THC exposure changes genes, which THC exposure change brain function changes brain and behavior cell structures in unborn babies THC exposure in teenage animals 1 anxiety † depression risky behavior What is the impact † impulsive behavior People exposed † mental illness of cannabis on the to THC in the substance use disorder (addiction) womb are more developing brain likely to abuse in the womb and substances In animals as teenagers? later in life Low-dose THC caused addiction-like behavior High-dose THC increased sensitivity to stress Babies born to mothers under extreme stress or exposed to cannabis have increased levels of the stress hormone cortisol High dose THC + stress = ^ * social anxiety ↑ anxiety Why? ↑ aggression Astrocytes are vital brain ٥, ↑ disruptive behaviour cells that support brain cell function and communication THC alters the genes and structure Babies born to mothers exposed to of astrocytes, so they are no longer both have 11 behavioural problems effective communicators **Disrupting astrocytes may** cause behavior changes TAN Future treatments might reverse genetic including anxiety, depression, changes - research is underway and avoiding social situations Figure 3

ACKNOWLEDGMENTS

This article was conceived, authored, and reviewed by the authors following the On the Shoulders of Giants virtual symposium 2021 organized by the Child Mind Institute. The symposium

Figure 3

Summary of the effects of cannabis on the developing brain. (\uparrow = increase; $\uparrow\uparrow$ = significant increase/greater-thanexpected increase), THC, tetrahydrocannabinol. can be accessed at https://childmind.org/science/initiatives/on-theshoulders-of-giants-science-symposium/2021-program/. The On the Shoulders of Giants Event is made possible through the generosity of Sarah and Geoff Gund, who provided the Sarah Gund Prize for Research and Mentorship in Child Mental Health to YH, as well as Phyllis Green and Randolph Cowen, Joseph P. Healey, Drs. Gail, and Leonard Saltz, and the Stavros Niarchos Foundation. The authors are grateful to the Child Mind Institute for funding the development of this manuscript. The authors gratefully acknowledge facilitation of the roundtable workshop at the On the Shoulders of Giants symposium by Dr. Wilson M Compton of the National Institute on Drug Abuse (NIDA) on which this manuscript is based. Editorial support was provided by Brandfish Limited, UK.

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SUBMITTED: 17 March 2022; **ACCEPTED:** 26 July 2023; **PUBLISHED ONLINE:** 16 August 2023.

EDITOR: Nico Sollmann, University of California, San Francisco, United States

SCIENCE MENTORS: Christina Dalla and Sok King Ong

CITATION: Hurd YL, Ferland J-MN, Nomura Y, Hulvershorn LA, Gray KM and Thurstone C (2023) Cannabis Use and the Developing Brain: Highs and Lows. Front. Young Minds 11:898445. doi: 10.3389/frym.2023.898445

CONFLICT OF INTEREST: KG has provided consultation to Jazz Pharmaceuticals.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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YOUNG REVIEWERS

LI JIA, AGE: 15

I enjoy reading, watching shows, and learning new things. I find science particularly fascinating due to it being all around us.





Born in Athens but raised in London, Theodore enjoys Maths and creative writing, playing video games, being social, eating souvlaki, and Japanese ramen and sushi. He also likes reading books, traveling, and watching comedy.

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