



# HHS Public Access

Author manuscript

*Front Young Minds*. Author manuscript; available in PMC 2023 November 09.

Published in final edited form as:

*Front Young Minds*. 2023 August ; 11: . doi:10.3389/frym.2023.898445.

## CANNABIS USE AND THE DEVELOPING BRAIN: HIGHS AND LOWS

**Yasmin L. Hurd<sup>1</sup>, Jacqueline-Marie N. Ferland<sup>1</sup>, Yoko Nomura<sup>1,2,3,4</sup>, Leslie A. Hulvershorn<sup>5</sup>, Kevin M. Gray<sup>6</sup>, Christian Thurstone<sup>7</sup>**

<sup>1</sup>Departments of Neuroscience and Psychiatry, Addiction Institute of Mount Sinai, Icahn School of Medicine at Mount Sinai, New York, NY, United States

<sup>2</sup>Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, United States

<sup>3</sup>Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York, NY, United States

<sup>4</sup>Department of Psychology, Queens College and Graduate Center, City University of New York, New York, NY, United States

<sup>5</sup>Department of Psychiatry, Indiana University School of Medicine, Indianapolis, IN, United States

<sup>6</sup>Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC, United States

<sup>7</sup>Behavioral Health—Adolescent Outpatient, Denver Health and Hospital Authority and University of Colorado School of Medicine, Denver, CO, United States

### Abstract

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.

### Graphical Abstract

---

This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](#). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

**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.



## 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 cannabinoid receptors more strongly than our own internal endocannabinoids 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?

## 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 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 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.

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.

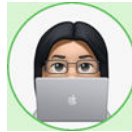
## SUMMARY

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!

## ACKNOWLEDGMENTS

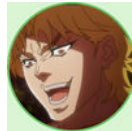
This article was conceived, authored, and reviewed by the authors following the On the Shoulders of Giants virtual symposium 2021 organized by the Child Mind Institute. The symposium can be accessed at <https://childmind.org/science/initiatives/on-the-shoulders-of-giants-science-symposium/2021-program/>. 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.

## 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.



THEODORE, AGE: 13

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.

## AUTHORS



YASMIN L. HURD

Dr. Yasmin Hurd is Professor of Psychiatry and Director for the Addiction Institute at the Icahn School of Medicine at Mount Sinai in New York. She is an internationally renowned neuroscientist whose translational research examines the neurobiology of drug abuse and related psychiatric disorders with primary focus on opioid abuse and the developmental effects of cannabis. Based on her high scientific accomplishments and her advocacy of drug addiction education and health, Dr. Hurd was inducted into both the National Academy of Sciences and the National Academy of Medicine. \*yasmin.hurd@mssm.edu



#### JACQUELINE-MARIE N. FERLAND

Dr. Jacqueline-Marie Ferland is an Instructor at the Icahn School of Medicine at Mount Sinai. Her research investigates the impact of adolescent cannabis exposure and cannabis use on cognition and psychiatric vulnerability. She holds a PhD. in Neuroscience from the University of British Columbia where her research investigated the involvement of decision making on addiction susceptibility. In addition to being an academic, Dr. Ferland enjoys communicating science to a broader audience where the facts can have an impact and science can improve public health.



#### YOKO NOMURA

Dr. Yoko Nomura is a tenured Professor in the Department of Psychology (in behavioral neurosciences and clinical psychology) Queens College, CUNY, and Professorial lecturer in the Department of Psychiatry Icahn School of Medicine at Mount Sinai. She is the Principal Investigator of a population based, longitudinal research study in developmental psychopathology, known as the Stress in Pregnancy (SIP) Study that focuses on the gestational period (during pregnancy), which is a critical, but often overlooked, stage for optimal child development.



#### LESLIE A. HULVERSHORN

Dr. Leslie A. Hulvershorn is a child and adolescent and addiction psychiatrist, Chair of the Department of Psychiatry at the IU School of Medicine and Director of the Division of Child and Adolescent Psychiatry at the Riley Hospital for Children. Dr. Hulvershorn is an active researcher and clinician and has authored numerous publications on various topics in child psychiatry. She has received multiple grants to study the neurobiological basis of addiction risk in children. She has directed Indiana's Department of Child Services Psychotropic Medication Consultation Program and serves as the consulting Medical Director for Indiana's Division of Mental Health and Addiction.



KEVIN M. GRAY

Kevin M. Gray, M.D., a child and adolescent psychiatrist, is a Professor in the Department of Psychiatry and Behavioral Sciences at the Medical University of South Carolina (MUSC) and Co-Director of the MUSC Youth Collaborative, leading research, clinical, and educational efforts to understand and address substance use disorders in adolescents and young adults.



CHRISTIAN THURSTONE

Christian Thurstone, M.D., is a child psychiatrist and addiction psychiatrist and is a professor at the University of Colorado School of Medicine. He also serves as the medical director for an adolescent substance treatment program located in eight school-based health centers and a hospital-based location.

## Glossary

### **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

### **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)**

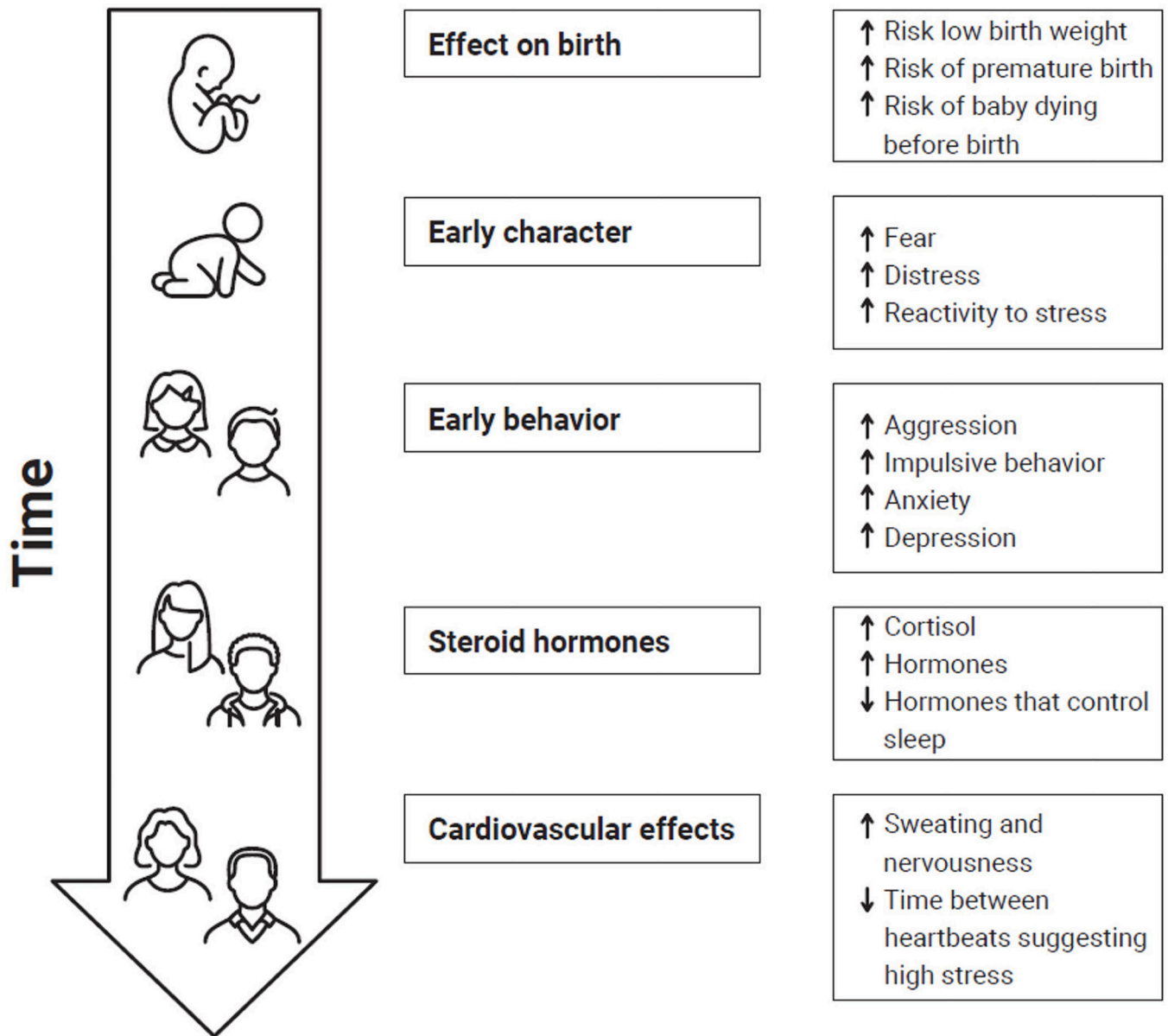
Addiction to cannabis or problematic use of cannabis

**ASTROCYTES**

Star-shaped brain cells that perform a wide range of functions including providing nutrients to other brain cells and repairing them after injury

**REFERENCES**

1. American Academy of Child and Adolescent Psychiatry. 2019. Marijuana and Teens. Available online at: [https://www.aacap.org/AACAP/Families\\_and\\_Youth/Facts\\_for\\_Families/FFF-Guide/Marijuana-and-Teens-106.aspx](https://www.aacap.org/AACAP/Families_and_Youth/Facts_for_Families/FFF-Guide/Marijuana-and-Teens-106.aspx) (accessed October 31, 2022).
2. Berghuis P, Rajnicsek AM, Morozov YM, Ross RA, Mulder J, Urbán GM, et al. 2007. Hardwiring the brain: endocannabinoids shape neuronal connectivity. *Science*. 316:1212–6. doi:10.1126/science.1137406 [PubMed: 17525344]
3. Rompala G, Nomura Y, and Hurd YL 2021. Maternal cannabis use is associated with suppression of immune gene networks in placenta and increased anxiety phenotypes in offspring. *Proc. Natl. Acad. Sci. U. S. A.* 118:e2106115118. doi:10.1073/pnas.2106115118
4. Ellis RJ, Bara A, Vargas CA, Frick AL, Loh E, Landry J, et al. 2021. Prenatal tetrahydrocannabinol exposure in males leads to motivational disturbances related to striatal epigenetic dysregulation. *Biol. Psychiat.* 92:127–38. doi:10.1016/j.biopsych.2021.09.017 [PubMed: 34895699]
5. Nomura Y, Rompala G, Pritchett L, Aushev V, Chen J, Hurd YL 2021. Natural disaster stress during pregnancy is linked to reprogramming of the placenta transcriptome in relation to anxiety and stress hormones in young offspring. *Mol. Psychiat.* 26:6520–30. doi: 10.1038/s41380-021-01123-z
6. Nomura Y, Ham J, Pelme P, Wong WM, Pritchett A, Ravinowitz S, et al. .2022. Synergistic impact of maternal exposure to a natural disaster stress and cannabis on elevated risk for developmental psychopathology among offspring. *Br. J. Psych. Open.* doi: 10.1192/bjo.2022.595. [Epub ahead of print].
7. Wittchen H-U, Frölich C, Behrendt S, Gunther A, Rehm J, Zimmermann P, et al. 2007. Cannabis use and cannabis use disorders and their relationship to mental disorders: a 10-year prospective-longitudinal community study in adolescents. *Drug Alcohol Depend.* 88:S60–70. doi: 10.1016/j.drugalcdep.2006.12.013 [PubMed: 17257779]
8. Ferland JN, Ellis RJ, Rompala G, Landry JA, Callens JE, Ly A, et al. .2022. Dose mediates the protracted effects of adolescent THC exposure on reward and stress reactivity in males relevant to perturbation of the basolateral amygdala transcriptome. *Mol. Psychiat.* doi: 10.1038/s41380-022-01467-0. [Epub ahead of print].



**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 figure shows the effects of stress or THC exposure before birth at different stages of life (↑ = increase; ↓ = decrease).



## What can be done to protect the developing brain from cannabis use?

Start to educate and discuss cannabis and other drugs early with young people

Listen to young people to understand their perspectives, pressures, and issues

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 it mean for my future brain?



## What can young people do to avoid cannabis harm?

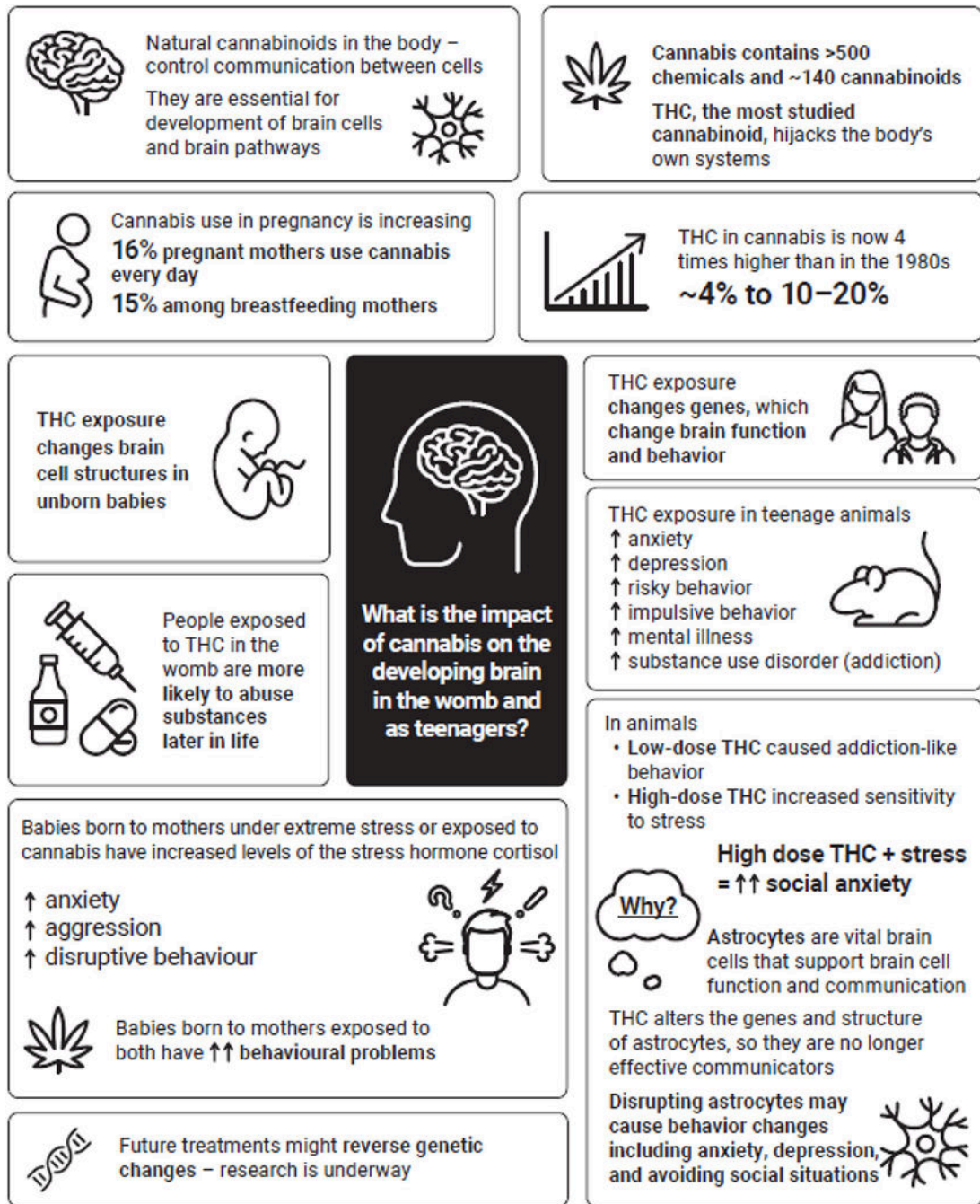
Understand that the goal is to minimize harm

- 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.

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.



**Figure 3.** Summary of the effects of cannabis on the developing brain. (↑ = increase; ↑↑ = significant increase/greater-than-expected increase), THC, tetrahydrocannabinol.