**Cannabis consumption in <u>pregnancy</u>** might be associated with restrictions in growth of the fetus, miscarriage, and cognitive deficits.

Fonseca BM, Correia-da-Silva G, Almada M, Costa MA, Teixeira NA (2013). "The Endocannabinoid System in the Postimplantation <u>Period: A Role during Decidualization</u> and Placentation". Int Endocrinol (Review). **2013**: 510540. doi:10.1155/2013/510540. PMC 3818851. PMID 24228028.

The <u>American Congress of Obstetricians and Gynecologists</u> recommended that cannabis use be stopped before and during <u>pregnancy</u>, Committee on Obstetric Practice (July 2015).

"Committee Opinion No. 637: Marijuana Use During Pregnancy and Lactation". *Obstetrics & Gynecology*. **126**(1): 234–238. doi:10.1097/01.AOG.0000467192.89321.a6. Cannabis is the most commonly used illicit substance among pregnant women. [3]

- Although it is difficult to draw firm conclusions, there is some evidence that prenatal exposure to marijuana may be associated with <u>deficits in language</u>, <u>attention</u>, <u>cognitive performance</u>, and delinquent behaviors. [4] Irner TB (2012). "Substance exposure in utero and developmental consequences in adolescence: a systematic review". *Child Neuropsychol* (Review). **18** (6): 521–49. <u>doi:10.1080/09297049.2011.628309</u>. <u>PMID 22114955</u>.
- THC exposure in rats during the prenatal developmental phase may cause <u>epigenetic</u> changes in gene expression, but there is limited knowledge about the risk for psychiatric disorders because of ethical barriers to studying the developing human brain. Morris CV, DiNieri JA, Szutorisz H, Hurd YL (November 2011). "Molecular mechanisms of maternal cannabis and cigarette use on human <u>neurodevelopment</u>". *Eur. J. Neurosci.* (Review). **34** (10): 1574—83. doi:10.1111/j.1460-9568.2011.07884.x. PMC 3226730. PMID 22103415.
- While animal studies cannot take into account factors that could influence the effects of cannabis on human maternal exposure, such as environmental and social factors, [6]
- Campolongo *et al.*(2011) added that "clinical studies report hyperactivity, cognitive impairments and altered emotionality in humans exposed in utero to cannabis" *Campolongo P, Trezza V, Ratano P, Palmery M, Cuomo V (March 2011).* "Developmental consequences of perinatal cannabis exposure: behavioral and neuroendocrine effects in adult rodents". Psychopharmacology (Review). **214** (1): 5–15. doi:10.1007/s00213-010-1892-x. PMC 3045519. PMID 20556598.

a 2011 review of <u>rodent studies</u> by Campolongo *et al.* said there was "... increasing evidence from animal studies showing that cannabinoid drugs ... induce enduring neurobehavioral abnormalities in the exposed offspring ..." Campolongo *et al.* added that "clinical studies report hyperactivity, cognitive impairments and altered emotionality in humans exposed <u>in utero</u> to cannabis". [6]

Martin *et al.* investigated recent trends in substance abuse treatment admissions for cannabis use in pregnancy in the US, based on Treatment Episodes Data Set (TEDS) from 1992 to 2012, and discovered that, while the proportion of treatment admissions for pregnant women was stable (about 4%), the admissions for women who were

- pregnant and reported any marijuana use grew from 29% to 43%.<sup>[7]</sup> A 2015 review found that cannabis use by pregnant mothers impaired brain maturation in their children, and that it also predisposed their children to <u>neurodevelopmental disorders</u>.<sup>[8]</sup>
- A 2015 review found that cannabis use by pregnant mothers impaired brain maturation in their children, and that it also predisposed their children to neurodevelopmental disorders. Alpár, A; Di Marzo, V; Harkany, T (25 September 2015). "At the Tip of an Iceberg: Prenatal Marijuana and Its Possible Relation to Neuropsychiatric Outcome in the Offspring". Biological Psychiatry. 79: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3739026/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3739026/</a> utras-Aswad D, DiNieri JA, Harkany T, Hurd YL (October 2009). "Neurobiological consequences of maternal cannabis on human fetal development and its neuropsychiatric outcome". Eur Arch Psychiatry Clin Neurosci (Review). 259 (7): 395–412. doi:10.1007/s00406-009-0027-z. PMID 19568685.

At the Tip of an Iceberg: Prenatal Marijuana and Its Possible Relation to Neuropsychiatric

Outcome in the Offspring

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Abstract

Endocannabinoids regulate brain development via modulating neural proliferation, migration, and the differentiation of lineage-committed cells. In the fetal nervous system, (endo)cannabinoid-sensing receptors and the enzymatic machinery of endocannabinoid metabolism exhibit a cellular distribution map different from that in the adult, implying distinct functions. Notably, cannabinoid receptors serve as molecular targets for the psychotropic plant-derived cannabis constituent  $\Delta^9$ -tetrahydrocannainol, as well as synthetic derivatives (designer drugs). Over 180 million people use cannabis for recreational or medical purposes globally. Recreational cannabis is recognized as a niche drug for adolescents and young adults. This review combines data from human and experimental studies to show that long-term and heavy cannabis use during pregnancy can impair brain maturation and predispose the offspring to neurodevelopmental disorders. By discussing the mechanisms of cannabinoid receptor-mediated signaling events at critical stages of fetal brain development, we organize histopathologic, biochemical, molecular, and behavioral findings into a logical hypothesis predicting neuronal vulnerability to and attenuated adaptation toward environmental challenges (stress, drug exposure, medication) in children affected by in utero cannabinoid exposure. Conversely, we suggest that endocannabinoid signaling can be an appealing druggable target to dampen neuronal activity if pre-existing pathologies associate with circuit hyperexcitability. Yet, we warn that the lack of critical data from longitudinal follow-up studies precludes valid conclusions on possible delayed and adverse side effects.

Overall, our conclusion weighs in on the ongoing public debate on cannabis legalization, particularly in medical contexts.

Tibor Harkany och hans medarbetare fann att cannabinoidreceptorn finns i hjärnbarken i den omogna hjärnan hos människofostret redan från vecka 11 och då bildas de första nätverken. Gemensamt för de endogena molekylerna är att de binder till samma receptor som tar emot en av de substanser, THC (tetrahydrocannabinol), som går in i kroppen vid cannabisrökning. Det cannabis gör är alltså att bryta in i det signalsystem som är viktigt för kommunikationen mellan hjärnans olika delar. Om receptorn blockeras kan det uppstå kaos i hjärnan.

Nästa steg var att undersöka om, och i så fall hur, cannabisrökning påverkar hjärnans utveckling.

Ingen hade studerat detta tidigare.

- Vi kunde konstatera att om mamman under graviditeten röker cannabis kan det ge bestående skador hos barnet.

Då cannabisämnet THC ockuperar cannabinoidreceptorerna, bryts kommunikationen mellan nervcellerna, dessa kopplas ihop felaktigt och hjärnans nätverk utvecklas inte normalt. Ju mer omogen hjärnan är desto större blir skadan.

## Endocannabinoid signaling in female reproductive events: a potential therapeutic target?

Mauro Maccarrone (Professor)

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- Here, the main features of the eCB system are presented, in order to put in a better perspective the relevance of eCB signaling in virtually all steps of human reproduction and to highlight emerging hopes that elements of this system might indeed become novel targets to combat fertility problems.
- It has been shown that CB<sub>1</sub> and CB<sub>2</sub> are expressed in the preimplantation embryos, and that their activation by uterine AEA can interfere with embryo development. Notably, oviductal transport of the fertilized egg and its development to the morula stage are controlled by a gradient of AEA concentration (increasing from ampulla to isthmus), that is kept by increasing NAPE-PLD and decreasing FAAH expression in epithelial cells of the oviduct

https://www.livescience.com/52015-marijuana-lowers-sperm-counts.html

## Marijuana Use May Lower Sperm Counts 'Quite a Lot'

By Agata Blaszczak-Boxe, Contributing Writer | August 28, 2015 12:17pm ET

Smoking marijuana more than once a week may lower men's sperm counts by about a third, according to a new study.

Researchers found that the men in the study who smoked marijuana more than once a week had sperm counts that were 29 percent lower, on average, than those who did not smoke marijuana, or used the drug less frequently.

The researchers thought that amount of reduction in sperm count "was quite a lot," said study author Tina Kold Jensen, of the University of Copenhagen in Denmark.

They also found that the sperm concentrations (which is measured slightly differently than sperm count) were 28 percent lower in the men who smoked marijuana more than once a week.

It is not clear why marijuana use may decrease a man's sperm count and concentration, but it may have something to do with how <a href="https://example.com/THC">THC — marijuana's psychoactive ingredient</a>— interacts with certain receptors in the testes, the researchers said. In the study, the researchers asked 1,215 Danish men ages 18 to 28 whether they used marijuana and other drugs like amphetamine, ecstasy and cocaine within the past three months, and if so, how often. [11 Odd Facts About Marijuana]

The researchers also collect semen samples, to measure the men's sperm counts and concentrations.

About 45 percent of the men in the study said they had smoked marijuana in the past three months. About 10 percent of the study participants had used marijuana as well as recreational drugs during this time.

Moreover, in the men in the study who smoked marijuana and used other recreational drugs, the sperm counts were reduced by 55 percent, and the sperm concentrations were reduced by 52 percent, compared with men who hadn't used the drugs.

The researchers found that the men who had smoked marijuana in the past three months were also more likely to smoke cigarettes, and consumed more alcohol and caffeine than those who had not.

These lifestyle factors also could have affected the <u>men's sperm levels</u>, so the researchers took them into account, and the link between marijuana and lower sperm levels held. However, the study still does not prove that the drug caused the lower sperm counts, Jensen said.

"We cannot exclude the possibility that the men who used marijuana generally have an unhealthier lifestyle and health behavior, which may also affect their semen quality and hormone levels," the researchers said in the study.

"It is ... important to note that marijuana users were distinct in several ways from nonusers," Dr. Michael L. Eisenberg of Stanford University School of Medicine, who was not involved in the new study, wrote in an editorial accompanying the study in the journal. And although the researchers adjusted for these differences, such as higher rates of cigarette smoking and alcohol consumption, they could have still confounded the potential <a href="effects of marijuana on sperm">effects of marijuana on sperm</a>, he wrote.

Still, the new study "provides important information for patients and providers regarding the negative association between marijuana use and semen quality," Eisenberg wrote.

The study was published Aug. 16 in the American Journal of Epidemiology.