

New research questions safety of cannabidiol for pregnant women

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Cannabidiol (CBD), one of the active ingredients in cannabis, is thought

to be safe as it does not cause a "high." Increasing numbers of pregnant women take CBD, believing that it can help alleviate symptoms such as morning sickness, insomnia, anxiety and pain.

However, research presented today (Tuesday) at the Federation of European Neuroscience Societies ([FENS](#)) Forum 2024, suggests that it may affect offspring. Two studies in mice have shown that gestational exposure to CBD alters the behavior of offspring and also affects the nerve cells (neurons) in the insular cortex (IC) of the brain that is involved in processing emotions and signals from the senses.

Dr. Daniela Iezzi and Alba Caceres Rodriguez, a Ph.D. student, work in the team "Sex differences in developmental vulnerability to neuropsychiatric diseases" at INSERM Université Aix-Marseille, France, directed by Pascale Chavis. Caceres Rodriguez says that the last International Cannabis Policy Study reported that one in five pregnant women reported using CBD.

"Scientific evidence has proven that CBD crosses the placenta, can reach the brain of rodents and [human embryos](#) and is also present in [breast milk](#); therefore, it's a public health priority to understand the impact of CBD on the developing nervous system as we don't yet know the consequences of CBD exposure to the brain during development," she says.

"An important part of the research that we are conducting in mice is a longitudinal follow-up of the behavioral consequences of gestational exposure to CBD, and we are also investigating what is happening to the neurons in the brain that may be the basis of such changes in behavioral traits."

Dr. Iezzi and Cáceres Rodríguez injected pregnant female mice subcutaneously with a low dose of CBD (3mg/kg) from day 5 to day

18—almost the entire gestational period of a mouse. Injections meant they could be sure the mice received the same concentrations of CBD each day. Another group of pregnant mice were not treated with CBD and acted as the control group.

After the pups were delivered, the researchers waited for them to become adults and then tested their behaviors with a technology that uses infra-red, depth-sensing cameras and machine learning (or artificial intelligence, AI) called "Live Mouse Tracker." This allowed them to detect a large range of behaviors when the mice were placed in a new environment for several days.

"We found a number of behavioral changes among the mice exposed to CBD," says Caceres Rodriguez. "CBD-exposed females tended to move around their new environment more compared to females that didn't receive CBD during gestation. Furthermore, compared to control mice, both male and female mice treated with CBD established more physical contacts with each other.

"These findings indicate that prenatal exposure to CBD alters specific behaviors of groups of mice and that this depends on their sex. A strength of our study is that we are able to reproduce a more naturalistic environment, which permits us to study group dynamics that would be impossible to unmask with other conventional tasked-based tests. In addition, a follow-up of several days enables us to analyze the development and progression of such dynamics. This study serves as a good starting point to dive deeper to understand the actual consequences of these changes in overall social interactions in the long term."

This research is carried out in mice so caution is necessary when considering any implications for humans. However, in addition to what is known about CBD crossing the placenta and being present in breast milk in both mice and humans, it is also known that cannabis intake can

affect brain development in mice and humans.

A limitation of the study is that mice had a controlled amount of CBD administered for more than two-thirds of their pregnancy, whereas humans might be more likely to take CBD intermittently to help with symptoms that might vary over the course of the pregnancy, and might take considerably larger doses.

Dr. Iezzi investigated how CBD affected two parts of the insular cortex in the brain: the anterior IC (aIC), which is responsible for processing emotional and social signals, and the posterior IC (pIC), which processes perceptions of pain and the physical and emotional state of the body.

"In 2022, we used [artificial intelligence](#) to demonstrate for the first time that prenatal exposure to a low dose of CBD can modify the early communication and cognition during the early stages of development in mice. So, we wanted to go deeper into the impact of this substance in the brain and, specifically, the insular cortex, which is known to be a region in the brain responsible for emotions and sensory perception," she says.

Dr. Iezzi studied the brains from adult mice that had been exposed to CBD during gestation in the same way as in Caceres Rodriguez's research. She compared them with the brains from the control group of mice that had not been exposed to CBD.

"We examined specific brain cells called [pyramidal neurons](#) in both aIC and pIC and discovered noteworthy distinctions between these neurons in adult male and female mice exposed or not to CBD," she says.

"Our results reveal that prenatal exposure to CBD profoundly changes the functionality of neurons in the [insular cortex](#). We saw differences according to sex and also according to the IC sub-regions. In particular, pyramidal neurons in the pIC lose their cellular identity following

prenatal exposure to CBD and no longer behave like typical pIC neurons.

"This could have negative consequences on specific functions of the pIC. These neurons specialize in integrating sensory information from the environment and the internal state of the body in order to generate an appropriate behavioral response. Therefore, a loss of pIC differentiation following [prenatal exposure](#) to CBD can have a considerable impact on the ability to understand and react properly to the environment.

"These findings have significant implications for understanding the effects of CBD on fetal life, changing the general idea that CBD is a universally safe compound, and revealing the need for additional studies on the effect of prenatal CBD exposure. Furthermore, several studies have shown that IC dysfunction increases the risk of developing psychiatric disorders, including anxiety, addiction, depression and schizophrenia."

Dr. Iezzi and Caceres Rodriguez are now joining forces to find the possible molecular and cellular mechanisms that would explain their results.

Professor Richard Roche, Deputy Head of the Department of Psychology at Maynooth University, Maynooth, County Kildare, Ireland, is chair of the FENS communication committee and was not involved in the research. He said, "Just because cannabidiol is legal and available in most countries does not mean that it is safe for women to consume during pregnancy. The consequences of exposing developing brains of fetuses to CBD has not been thoroughly researched so far.

"These two studies carried out in [mice](#) show that exposure to CBD during gestation does affect offspring. More research is required to be sure about the possible effects in humans, but these findings are an early indication that women should not take CBD during pregnancy until more

is known. In addition, more information and better data are needed to understand the prevalence of CBD use during pregnancy, particularly in Europe."

More information: PS03-27AM-619."The influence of prenatal CBD exposure on group dynamics and social behaviours in adult offspring", Ms Alba Caceres Rodriguez, Poster session 03 – Late-breaking abstracts, Thursday 27 June, 09:30-13:00 hrs, Poster area:

fens2024.abstractserver.com/presentations/4793

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