

Study implicates marijuana use in pregnancy problems

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New research indicates marijuana-like compounds called endocannabinoids alter genes and biological signals critical to the formation of a normal placenta during pregnancy and may contribute to pregnancy complications like preeclampsia.

A study in the Sept. 14 edition of The [Journal of Biological Chemistry](#) offers new evidence that abnormal biological signaling by endocannabinoid [lipid molecules](#) produced by the body disrupts the movement of early embryonic cells important to a healthy pregnancy, in particular trophoblast cells that form the placenta. Abnormal placental function is common in preeclampsia – a medical condition of unknown cause that is a danger to mother and child.

The research – from scientists in the Division of Reproductive Sciences at Cincinnati Children's Hospital Medical Center – analyzed mouse preimplantation embryos mutated to alter endocannabinoid signaling. They found that either silencing or enhancing endocannabinoid signaling adversely affects trophoblast stem cell migration.

"The findings of our investigation raise concerns that exposure to cannabis products may adversely affect early embryo development that is then perpetuated later in pregnancy," said Sudhansu K. Dey, PhD., principal investigator on the study and division director. "Also, given that endocannabinoid signaling plays a key role in the [central nervous system](#), it would be interesting in future studies to examine whether affected cell migration-related genes in early embryos also participate in

neuronal [cell migration](#) during brain development."

Along with co-first authors Huirong Xie and Xiaofei Sun, Dey and other members of the research team studied mouse embryos that had not yet implanted inside the uterus of the mother. Previous research by Dey's laboratory has shown the timing of critical events in [early pregnancy](#), including when and how well an [embryo implants](#) in the uterus, is vital to a healthy pregnancy and birth.

In the current study, researchers conducted [DNA microarray](#) analyses to determine how the expression levels of genes important to healthy embryo development were affected in embryos with abnormal endocannabinoid signaling.

In one group of embryos endocannabinoid signaling was silenced by deleting the gene *Cnr1*, which activates endocannabinoid signaling processes. A second group of mice was mutated to produce elevated endocannabinoid levels similar to that observed in wild type mice treated with tetrahydrocannabinol (THC), the active psychotropic agent in cannabis. This was done by deleting the gene *Faah*, which breaks down molecules that activate endocannabinoid signaling.

In both groups, the expression of numerous genes known to be important to cell movement and embryo development was lower than in normal wild type mice. This included the development and migration of trophoblast stem cells. Trophoblast cells help anchor the conceptus with the uterus and also form much of the placenta, critical to establishment of maternal-fetal circulation and exchange of nutrients.

Researchers said mouse models developed for the current study (with silenced and elevated endocannabinoid signaling) may help advance more extensive studies on the causes of preeclampsia.

Provided by Cincinnati Children's Hospital Medical Center

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