Project title

Impact of maternal cannabis use in utero on the neurodevelopment of the gut-brain axis

Investigators

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Statement of purpose

The project will determine if exposure to cannabis in utero results in structural and functional changes in the neurodevelopment of the gut-brain axis.

Project summary

Recreational use of cannabis has been legalized in Canada since 2018. Increasing numbers of women are using cannabis while pregnant, with reported rates >10%. There is a disconnect with societal perceptions, with up to one third of women believing that cannabis is safe to use for symptom management during pregnancy, but with preclinical and clinical studies demonstrating negative neurodevelopmental outcomes, including defects in axon growth and synapse formation, and consequences including developmental delay, cognitive changes, and challenges with mental health.

The gut-brain axis, composed of the enteric nervous system and bidirectional communication via the vagus nerve, is critical for normal gastrointestinal homeostasis. A key component of gut-brain axis regulation is found in the endocannabinoid system (ECS). Alterations in the gut-brain axis form the pathophysiological basis of the well-characterized disorders of gut-brain interaction, which can present as early as infancy. While early life factors such as *in utero* drug exposure and alterations in the gut microbiota are known to influence components of the gut-brain axis, the potential for maternal cannabis use to impact gut-brain neurodevelopment is a knowledge gap of growing clinical and societal importance.

Specific Aims:

1. **Determine the mechanisms by which cannabis exposure *in utero* can modulate the structure and function of the gut-brain axis.** As smoking is the most common method of reported cannabis use in Canada, our experiments use a “real-world” model of a validated in-house cannabis smoke exposure system. Timed-pregnant female mice will be exposed to cannabis smoke from after implantation to delivery; female and male fetuses and pups from exposed and control dams will be studied at a range of development stages for biometric and gut-brain axis outcomes (molecular methods, histology, *in vivo* models).
2. **Determine how cannabis exposure *in utero* can impact the neonatal microbiome and the formation of the microbiota-gut-brain axis.** Stool from cannabis smoke exposed and control offspring will be collected and processed for bacterial community profiling of 16S rRNA genes. Potential metabolomic changes due to alterations in microbiota will be assessed by measuring fecal levels of short-chain fatty acids by mass spectroscopy.

The clinical and societal relevance of these proposed studies in animal models will be leveraged with a funded clinical study to measure neurodevelopmental outcomes in babies exposed to cannabis. Our translational research team anticipate that our findings will generate novel understanding of the potential for cannabis exposure to impact gut-brain axis neurodevelopment and further inform public health strategies and anticipatory care.