2018

Role of microglia signaling in brain circuit development and cognition

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Western BrainsCAN
Transforming brain research.

Project **Summary**

KNOWLEDGE MOBILIZATION & IMPACT

Role of microglia signaling in brain circuit development and cognition

Background

Microglia are the resident immune cells of the central nervous system. They help the brain respond to injury and infections and remove damaged cells. During brain development, they play a key role eliminating weak neuronal communication sites (synapses), a process called synaptic pruning. In mice, the critical period when microglia engulf synaptic material is between days 8-28 after birth. When synaptic pruning is impaired during this period, it leads to autism-like behaviour in adult mice.

The Problem

We don't fully understand the mechanisms behind microglia control of this synaptic pruning of central synapses. Microglia express a wide range of receptors that allows them to receive and respond to signals provided by neurons, other cells as well as the brain environment. Many of these receptors are 'G protein coupled receptors' (GPCRs). They respond to specific proteins and this protein signalling causes changes in microglia function. Two specific G-protein classes are known as G_q and G_i. Our hypothesis is that the signaling pathways for these G_q and G_i class proteins are vital for normal microglial function, particularly for controlling synaptic pruning. Disruption of either of these pathways during the critical postnatal pruning period underlies abnormal cognitive behaviour in adults in some forms of autism.

The Project

We have generated two mouse models in which we can control the G_q and G_i signalling in microglia during specific periods of brain development so we can explore the mechanisms behind abnormal microglial function.

Using our mouse models, we can stimulate these signalling pathways during the critical period of postnatal brain development to understand whether they impact adult cognition by influencing normal synaptic pruning. Mouse models of autism show issues with social memory, attention, sociability and hyperactivity. We will therefore assess those behaviors in our mouse models to determine if any autism-like behaviours are present.

Funding Program

BrainsCAN Accelerator Grant: Stimulus
Awarded: $90,000

Additional BrainsCAN Support

Rodent Cognition Core

Western Faculty, Group or Institution

Robarts Research Institute, Schulich School of Medicine & Dentistry

Keywords

Mental health, memory, mood & emotion & social behaviour

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