Linking the Immune System to Behaviour and Brain Development

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Immune-brain Communication

- continual
- bidirectional
- neural, humoral and cellular communication pathways
- influences brain development
- influences behaviour
- share molecules and signaling pathways
Immune-brain Communication

- neuron
- microglia
- immune system
- microbiota
- T cells
- Monocytes
Immune-brain Communication

• microglia are the brain’s resident immune cell
• microglia are critical to normal brain development, particularly in wiring the brain and synaptic connections
• research in animal models and in clinical populations show sex differences in microglial function
• infections and other insults activate microglia
• shifts in the microglia-neuronal communication pathways can lead to changes in behavior and influence the trajectory of brain development
All of the surfaces of your body are covered with microbes, including bacteria, viruses, fungi, protozoa, and parasites.

Bacteria are the best studied microbes.

Trillions of viable bacteria are found in your gut and influence immune development and function.

Gut microbiota influence immune development and bi-directional communication between microbes and the immune system.

Bi-directional communication between microbes and the immune system influence brain development.

QUESTION: Are there any effective treatments for autism involving the gut?
QUESTION: Are there any effective treatments for autism involving the gut?

- Microbiota composition and diversity is changed in some individuals with autism

- GI disturbances often are present in individuals with autism

- Ongoing research on microbiota-targeted strategies includes diet interventions, probiotics, and fecal microbiota transplant

- [www.probioticchart.ca](http://www.probioticchart.ca) - a good resource for evidence for benefits of probiotics in Canada
Immune-brain Communication

- The peripheral immune system communicates with the brain through neural, humoral, and cellular pathways.
- Immune cells release inflammatory mediators into the bloodstream that can signal the brain.
- Circulating immune cells influence normal brain development.
- Infection and other triggers can activate the peripheral immune system and influence immune-brain communication.
- Individual differences in the immune system may influence behaviour and brain development.
- We can measure features of an individual's peripheral immune system from a blood sample.
Immune & Neurodevelopmental Disorders

OCTOBER 22, 2019

Inflammation and autism—an important piece of the puzzle
by Delthia Ricks, Medical Xpress

Researchers receive $3.2 million NIH grant to pursue a deeper understanding of Down syndrome

Brain Immune Cells Linked to OCD and Anxiety

Brain immune cells may protect against OCD, anxiety

Oct 24, 2019
Benefits of looking at immune phenotype in brain health and neurodevelopment disorders

• Identification of biomarkers that will help understand biological differences and help subgroup individuals based on their shared biology

• Provide new biological targets for the development of new drugs or therapies

• Expansion and development of diet, prebiotic, probiotic, or other intervention strategies for neurodevelopment disorders

• Develop precision medicine approaches to match individuals to the best treatment approach for them
Which immune biomarkers?

1. PERIPHERAL IMMUNE CELLS

• Use flow cytometry analysis to phenotype peripheral immune cells including T cells, B cells, natural killer cells, and monocytes/macrophages

• Sample preparation - whole blood collected - separation of peripheral blood mononuclear cells (PBMC); frozen/biobanked for later analysis
Which immune biomarkers?

2. CYTOKINES

• Use standard ELISA/protein assay methods to measure levels of several cytokines and chemokines in peripheral blood

• Sample preparation - plasma collected from EDTA-whole blood sample; frozen/biobanked for later analysis
3. CIRCULATING BACTERIAL FACTORS

- Use colourimetric reporter bioassay to detect LPS and MDP in serum samples; use PCR to detect the presence of bacterial DNA in serum.

- Sample preparation - serum collected from whole blood sample; frozen/biobanked for later analysis.
Clinical White Blood Cell Differentials - standard clinical assessment of number and type of blood cells

Plasma - inflammatory mediators

Peripheral Blood Mononuclear Cells (PBMC) - lymphocytes (T cells, B cells, NK cells) and monocytes

Granulocytes - neutrophils, eosinophils, basophils

Serum - immune and endocrine markers

2nd blood draw - 3 months later
POND Immune/Endocrine Platform

• Samples banked at McMaster University (Foster Lab)
• Over 300 samples banked to date
• Analysis of PBMCs for monocyte cell numbers, maturation, and function ongoing
• Analysis of inflammatory mediators in plasma ongoing
Questions?

neuron

microglia

immune system

microbiota

T cells

Monocytes