

Hopewell M.I.N.D. Prize Finalists

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Project Title: Gut-Brain Axis Communication to Nourish and Cleanse the CNS: Limiting Disease and Improving Cognition

A healthy brain requires steady nourishment and clearance of waste products which is assured by brain blood flow. Surprisingly, the relationships between brain blood flow and the availability of nutrients in the gut and blood remain poorly understood. Little is known about how brain blood flow changes when we shift from being satiated, to fasting, or when we overconsume food during the day. Many studies have shown the profound health benefits of fasting and consuming food only within a 12 hour active period. In contrast, eating food in excess and beyond the 12 hour active period has deleterious effects to health. The gut microbiome - the collection bacteria, viruses, fungi and other micro-organisms that live in the intestinal track of humans and other mammals - has emerged as a powerful regulator of body functions.

Here we propose that gut-brain communication helps coordinate bodily energy status and brain blood flow by responding to the availability of nutrients (or lack thereof). Using animal models, we will test if fasting-related eating patterns improve cerebral blood flow in a manner that depends on the proper functioning of the gut microbiome. More specifically, we will explore if fasting causes the gut microbiome to release blood-borne factors to communicate with brain cells to improve brain blood flow. Additionally, deficits in cerebral blood flow are deeply connected with several neurological conditions, including Alzheimer's disease. Given this, we will also test our hypothesis in a common mouse model of Alzheimer's. We will employ the latest light microscope methods to interrogate brain blood flow in a manner not possible previously, including cellular level observations in awake and sleeping mice. Examining sleep is important because sleep is when the brain cleanses and restores itself. Our research plan will discover previously unknown fundamental relationships between energy substrate delivery and brain maintenance via nutrient sensing in the gut microbiome. We propose that this system is essential for health and limiting the progression of several neuropathologies. We will identify new signaling pathways involved in gut-brain axis communication that improve brain health by cleansing the MIND.