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The Effect of a Probiotic Diet on htauE14 in a Rodent Model of Alzheimer's Disease

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Abstract : Alzheimer's Disease (AD) is a progressive neurodegenerative disorder affecting broad areas of the cerebral cortex and hippocampus. More than 95% of AD cases are representative of sporadic AD, where both genetic and environmental risk factors play a role. The main pathological features of AD include the widespread deposition of amyloid-beta and neurofibrillary tau tangles in the brain. The earliest brain pathology related to AD has been defined as hyperphosphorylated soluble tau in the noradrenergic locus coeruleus (LC) neurons, characterized by Braak. However, the cause of this pathology and the ultimate progression of AD is not understood. Increasing research points to a connection between the gut microbiota and the brain, and mounting evidence has shown that there is a bidirectional interaction between the two, known as the gut-brain axis. This axis can allow for bidirectional movement of neuroinflammatory cytokines and pathogenic misfolded proteins, as seen in AD. Prebiotics and probiotics have been shown to have a beneficial effect on gut health and can strengthen the gut-barrier as well as the blood-brain barrier, preventing the spread of these pathogens across the gut-brain axis. Our laboratory has recently established a pretangle tau rat model, in which we selectively express pseudo-phosphorylated human tau (htauE14) in the LC neurons of TH-Cre rats. LC htauE14 produced pathological changes in rats resembling those of the preclinical AD pathology (reduced olfactory discrimination and LC degeneration). In this work, we will investigate the effects of pre/probiotic ingestion on AD behavioral deficits, blood inflammation/cytokines, and various brain markers in our experimental rat model of AD. Rats will be infused with an adeno-associated viral vector containing a human tau gene pseudophosphorylated at 14 sites (common in LC pretangles) into 2-3 month TH-Cre rats. Fecal and blood samples will be taken at pre-surgery, and various post-surgery time points. A collection of behavioral tests will be performed, and immunohistochemistry/western blotting techniques will be used to observe various biomarkers. This work aims to elucidate the relationship between gut health and AD progression by strengthening gut-brain relationship and aims to observe the overall effect on tau formation and tau pathology in AD brains.

Keywords : alzheimer's disease, aging, gut microbiome, neurodegeneration
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