

More than a gut feeling: The implication of gut microbiota in the pathology of Alzheimer's Disease



The gut microbiome comprises a complex system of microorganisms that reside in our gastrointestinal tract and plays a crucial role for host immunity. Imbalance between different microbiota species and their released metabolites and toxins can affect the gut barrier function, thereby enabling bacterial entry along with metabolites and toxins into the circulation resulting in systemic inflammation. Moreover, gut microbiota-derived metabolites can impact the integrity of the blood-brain barrier (BBB), which acts as a gatekeeper to control the passage of molecules and cells between the circulatory system and the brain parenchyma. Consequently, modifications in the gut microbiota composition does not solely affect intestinal disorders but also central nervous system disorders such as Alzheimer's disease (AD). AD, the most common form of dementia, is a neurodegenerative disorder characterized by cognitive impairment and abnormal cerebral accumulation of β -amyloid and tau protein [1].

A recent study by Verhaar et al, investigated associations among patients with AD pathology and their gut microbiota [2]. Fecal samples were collected in a total of 170 AD patients and the link between the gut microbiome composition and the presence of AD biomarkers such as cerebrospinal fluid,

β -amyloid and phosphorylated tau and MRI visual scores was assessed using a sequencing approach and machine learning models.

Results showed that AD markers were overlapping with lower abundance of short chain fatty acid (SCFA)-producing microbes including anaerobic bacteria from the *Firmicutes* phylum and *Eubacterieae*, *Ruminococcaceae* and *Lachnospiraceae* families. SCFAs are produced by bacteria during fermentation of dietary fibers and are known for their immunomodulatory activities. Therefore, the reduction of SCFAs might have an indirect effect on the development and progression of AD by inducing peripheral inflammation or modulating the BBB integrity [2].

This study demonstrates that the gut microbiome composition is linked to biomarkers of AD pathology and suggests that imbalance of microbial taxa and their metabolites is associated with altered immune and BBB functions, thereby promoting inflammatory processes in the pathogenesis of AD. Therefore, restoring the gut microbiota composition, e.g. by fecal microbiota transplantation from healthy donors to diseased subjects, may open new avenues for future therapeutic and preventive options in AD.

References:

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