Analysis of the Gut-Brain Axis in Aging: Implications in Alzheimer Disease

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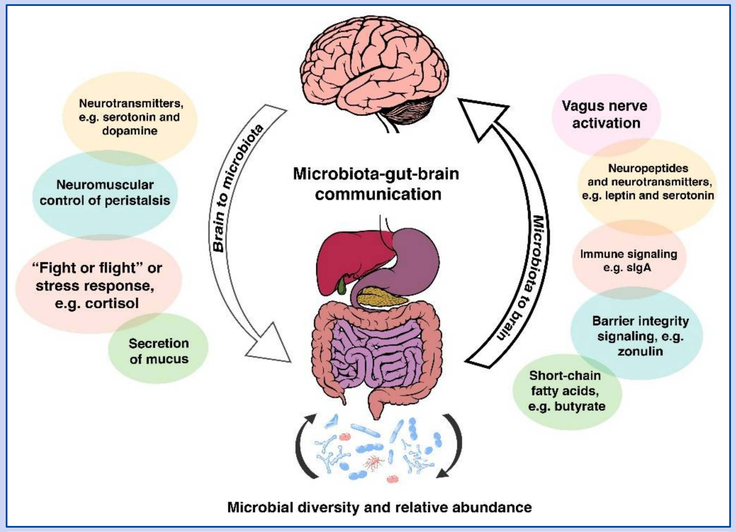
ABSTRACT

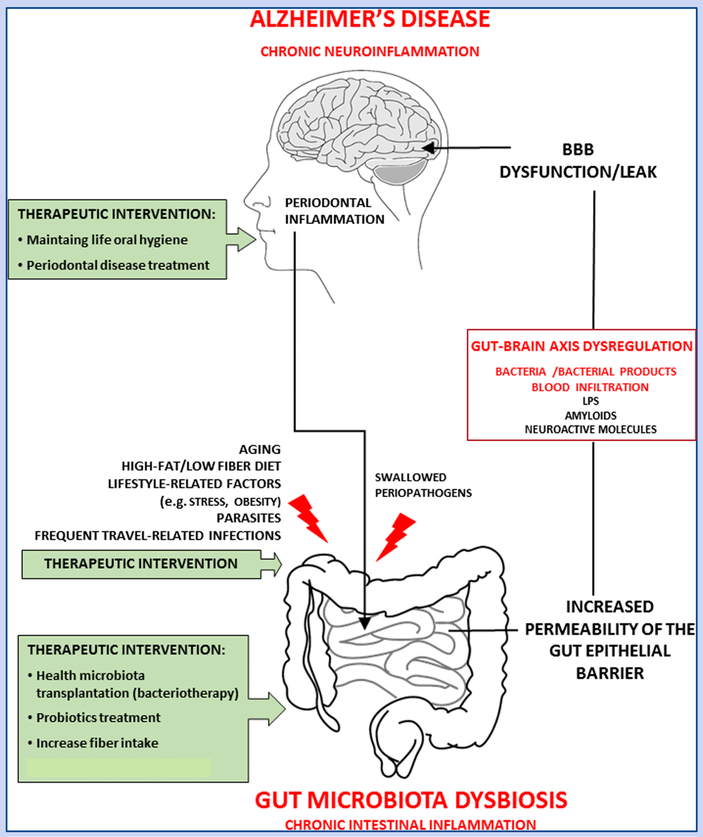
The gut microbiome consists of the shared genome of the community of trillions of commensal, symbiotic, and pathogenic microorganisms residing in the gastrointestinal ecosystem. The interaction between the host and its gut microbiome, as well as the Gut-Bran Axis (GBA), is a complex relationship whose management could prove critical to preventing or treating not only various gut disorders, such as irritable bowel syndrome (IBS) or behavioral health disorders like general depression and anxiety, but also central nervous system (CNS) disorders, such as Alzheimer's (AD) and Parkinson's (PD) diseases. The purpose of this review is to summarize what is currently known about the gut microbiome, how it is connected to the development of disease pathology and to identify the bacterial and biochemical targets/pathways that should be the focus of future research. In identifying, exploring, and understanding the mechanisms behind the activity and propagation of the gut microbiome, this will provide us new insights that are likely to pave the way for increased novel therapeutic strategies.

- Dysbiosis in the gut microbiome and microbial metabolites is known to be associated with abnormalities in the gut mucosal barrier integrity and enhanced pro-inflammatory cytokines
- Changes in the aging gut microbiome that impact the gut-brain axis can also lead to problems with neural, endocrine, nutrient, and immunological signals between the gut and the brain via the enteric nervous system
- It is possible to use a pro-biotics, pre-biotics, and psycho-biotics as a treatment to aid in slowing psychological/behavioral decline linked to gut dysbiosis or signaling problems between the ENS/CNS
- It has been found that *Fecalibacterium* and *Butyricoccus*, which are potentially probiotic genera associated with inflammation suppression, and butyrate production, respectively, were higher in cognitively unimpaired subjects
- Psycho-biotics are beneficial bacteria (a class of probiotics) or support for such bacteria (prebiotics) that influence bacteria–brain relationships
- Elevated serum levels of C-reactive protein (CRP) in middle age is associated with an increased risk for both Alzheimer's Disease and vascular dementia, which supports the theory that inflammatory markers are involved in dementia and act through both peripheral and cerebral vascular pathways
- Age-related changes in microbial composition and metabolism are consistent with the concept of "inflamm-aging," which associates chronic low-grade inflammation as a common basis for a widespread range of age-related pathologies, including cognitive decline, neurodegeneration general CNS disease



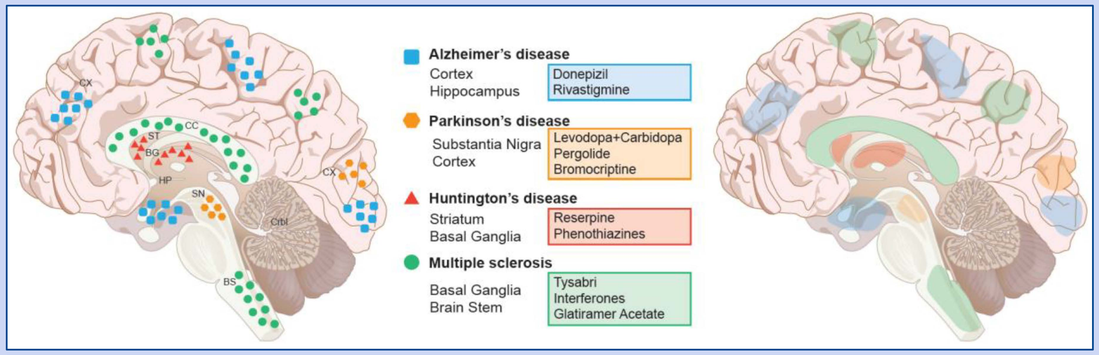
The bi-directional relationship of the gut/gut microbiota and the brain/central nervous system (CNS).

Modified from: https://www.straightfromascientist.com/the-microbiota-gut-brain-axis-from-eubiosis-to-dysbiosis-and-back-useful-biomarkers-for-clinical-treatment/figure-2-miguels/



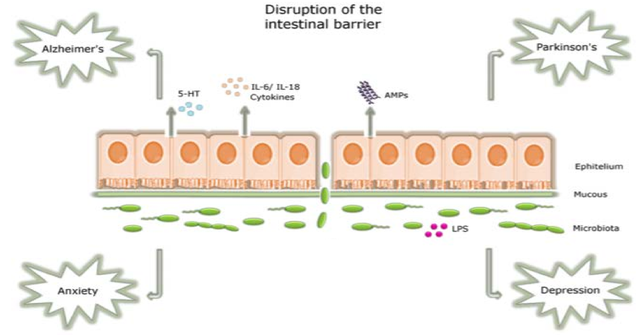
Interaction of the host health and immune function, diet, neurotransmitters, metabolites, environmental factors, and the gut microbiome as it pertains to the pathology of Alzheimer's Disease.

Modified from: https://link.springer.com/article/10.1007/s12035-018-1188-4



Areas of the brain affected by CNS-based disease pathologies and medications/therapies commonly used to treat symptoms in affected persons.

Modified from: https://www.mdpi.com/2076-3425/8/9/177/htm



Several inflammatory factors such as cytokines and endotoxins, as well as neurotransmitters, and antimicrobial peptides, play a significant role in the development or potential mitigation of various pathologies and are present and active in the gut microbiota.

Modified from: https://www.semanticscholar.org/paper/Neuromicrobiology%3A-How-Microbes-Influence-the-Fuente-Nu%C3%B1ez-Meneguetti/c2deb682f76a962b30e29f562a8cd97e2d1c61bc

Lessons Learned

- In aging, the blood brain barrier begins to weaken, facilitating the allowance of a large spectrum of pathogens (viruses, bacteria, fungi), immune cells, and their products into the brain
- Dietary changes, such as including more vegetables containing polyphenols and monounsaturated fatty acids has shown to be beneficial in improving verbal fluency and memory
- Variation of gut microbiota through personalized diet or beneficial microbiota intervention alter microbes and their products, including amyloid protein, and may prove to become a novel approach to the treatment and potential slowing of the effects of Alzheimer's Disease
- Over time, various conditions lead to an inflammatory response shift from beneficial to detrimental in the form of systemic chronic inflammation, specifically in the brain
- Aβ deposits as well as varying microbes and their products (LPS, amyloids) crossing into the brain might be an initiating factor of the neuroinflammation and neurodegenerative changes observed in Alzheimer's Disease

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