Tiny Friends and Foes: The Gut-Brain Axis and Alzheimer's Disease

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Abstract

In a remarkable work of symbiosis, the gut microbiota coordinate with the brain to regulate multiple bodily functions, including those of the immune system, through bidirectional communication with the gut-brain axis. This symbiotic process has been shown to affect human health and disease pathology as certain inflammatory responses correlate with the composition and general disruption of the gut microbiome. To name a few, neurological disorders, gut-based inflammatory disorders, and cancer have been linked, in part, to dysfunction of the gut-brain axis. Previous literature on the gut-brain axis stems from *in vivo* and *in vitro* models, which have worked to understand the connection between the microbiome and disease pathology. Emerging evidence from these studies has continued to become more convincing regarding the importance of the bidirectional relationship in human health. In this review, evidence focusing on the intricate connections between the gut-brain axis and Alzheimer's disease will be discussed. How this information can be utilized, including what has been or could be done in the clinic to improve the outcomes of patients with inflammatory-related diseases, will be highlighted so that continued advances in this newer aspect of medicine might lead to direct benefits for human health.

Introduction

- The microbiota is a community of commensal microorganisms that live symbiotically in and on our bodies
- Microbes contribute more genes needed for human survival than human's own genome with more diversity (Gilbert et al., 2018)
- Proposed to outnumber our own cells (Gilbert et al., 2018)
- Often thought to just play a role in the gut but may be connected to risk factors for Alzheimer's Disease via the gut-brain axis
- The gut-brain axis describes a bidirectional relationship that regulates key homeostatic and physiological functions (Mayer et al., 2022)

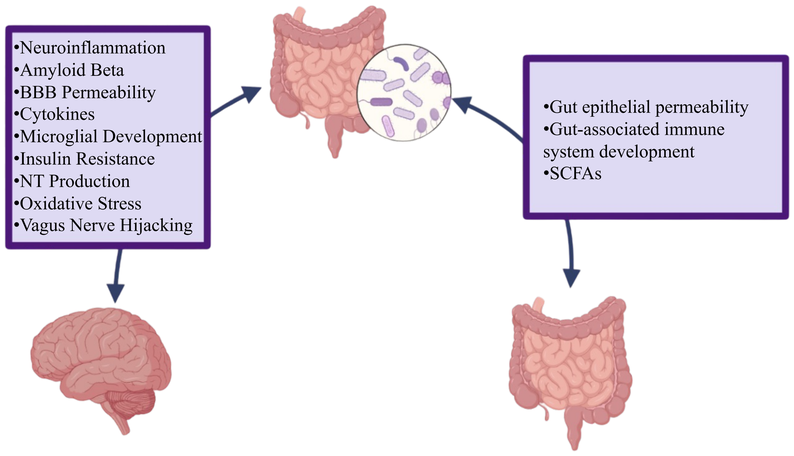


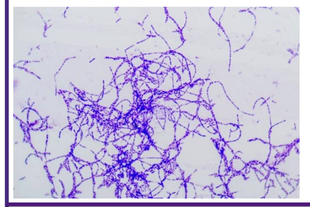
Figure 1: Two-way effects of microbiota on the gut and on the brain that could contribute to Alzheimer's disease pathology. Dysbiosis of the gut microbiota leads to many of the observed pathogenic effects and occurs as the healthy, commensal bacteria are replaced by harmful alternatives.

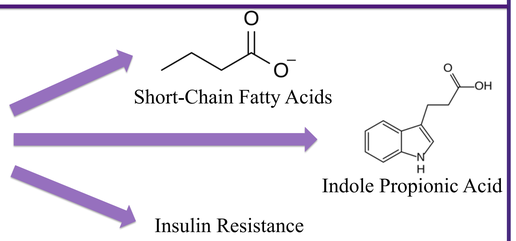
Phyla Associated with AD

	Phyla	Family	Genus
Increased Microbial Numbers in AD Patients	Firmicutes	Gemellaceae	Blautia Phascolarctobacterium Gemella
	Bacteroidetes	Bacteroidaceae Rikenellaceae	Bacteroides Alistipes
	Proteobacteria	Enterobacteriaceae	Bilophila Escherichia
Decreased Microbial Numbers in AD Patients	Firmicutes	Ruminococcaceae Turicibacteraceae Peptostreptococcaceae Clostridiaceae Mogibacteriaceae	Clostridiaceae SMB53 Dialister Clostridium Turicibacter Erysipelotrichaceae cc115
	Actinobacteria	Bifidobacteriaceae	Bifidobacterium Adlercreutzia

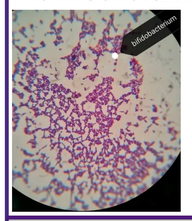
Table 1: Several differences in microbiome composition between Alzheimer's disease patients and age matched controls were found. There are four main phyla that seem to either increase or decrease in Alzheimer's disease that vary in effects.

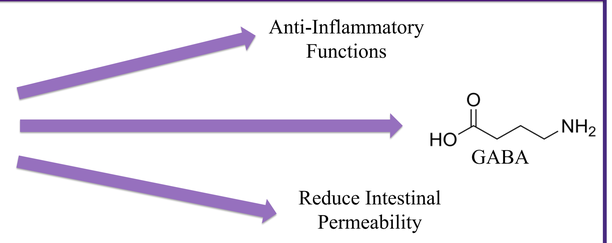
Firmicutes



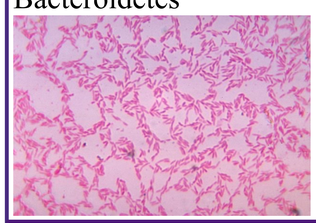


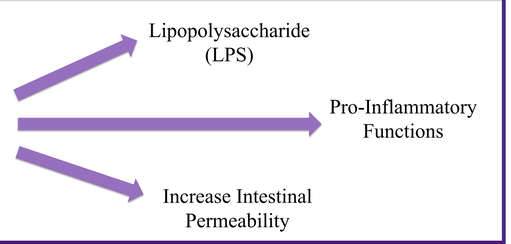
Actinobacteria



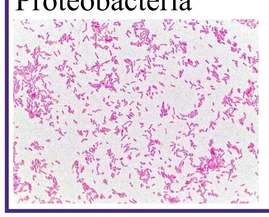


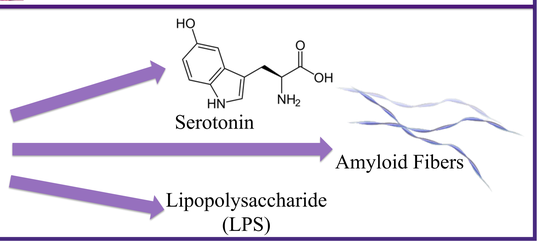
Bacteroidetes





Proteobacteria





Significance

Diagnostics

- If there are composition differences, then we might be able to use this for diagnosis even before symptoms begin since Alzheimer's disease symptoms have been found to take over 20 years to show (Alzheimer's Disease Association, 2023)

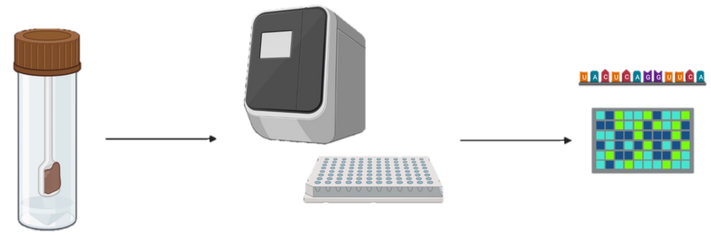
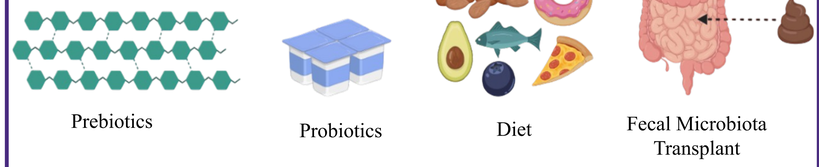


Figure 2: The main way to look at microbiota composition is via fecal samples that are run through PCR and then sequenced

Therapies



- **Prebiotics**: Non-digestive short chain carbohydrates that possess the ability to change composition and metabolism
- **Probiotics**: Living microorganisms that confer benefits to the hosts
- **Diet**: High-fiber diets, such as the Mediterranean diet, improve the production of short-chain fatty acids, such as butyrate.
- **Fecal Microbiota Transplant**: Transfers healthy donor's gut microbiome through regulated feces to the recipient

Conclusions

- Microbiome composition could contribute to Alzheimer's disease development and pathology
- There appears to be a relationship between our lifestyle choices, such as diet, and our risk or avoidance of Alzheimer's disease
- These results bode well for continued research into the gut-brain axis in regard to disease diagnosis and therapy

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