WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Connecting the Dots: Microbiota-Gut-Brain Axis in Alzheimer's Disease Pathogenesis – A Review of Current Insights and Future Directions

Yousef Sawikr*[1], Souad A M Moftah*[2], Abdelhakim A. Eljaki*[3]

[1]Pharmacology and Toxicology Department, Medicine Faculty, Ajdabiya University, Libya.
[2]Department of Physjology, Faculty of Medicine Elmarj Campus, University of Benghazi, Benghazi, Libya
[3]Department of Microbiology, Faculty of Science, University of Benghazi, Benghazi, Libya
DOI: https://doi.org/10.55248/gengpi.4.1223.123543

Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline and neuronal loss. It is the most common cause of dementia, affecting over 50 million people worldwide (Alzheimer's Disease International, 2021). With increasing life expectancy, the prevalence of AD is projected to rise dramatically in the coming decades. However, the complex pathophysiology underlying AD is still not fully understood. Recent research has focused on the role of the microbiota-gut-brain axis – the bidirectional communication pathway between the gastrointestinal (GI) tract microbiota and the central nervous system (CNS). This review summarizes current evidence on the involvement of the microbiota-gut-brain axis in AD pathogenesis.

Definition of AD

AD involves the accumulation of amyloid beta (Aβ) plaques and neurofibrillary tangles of hyperphosphorylated tau protein in the brain, resulting in inflammation and neurodegeneration (DeTure & Dickson, 2019). It is characterized by progressive impairment in memory, cognition, and behavior that interfere with daily living. While several hypotheses have been put forth regarding AD causes, factors such as genetics, lifestyle, environment, inflammation, and microbiota dysbiosis may all play a role (Cheung et al., 2018).

Increasing Prevalence of AD

The global prevalence of dementia due to AD and other causes was estimated at over 55 million in 2019 (Alzheimer's Disease International, 2021). This figure is expected to rise to 78 million by 2030 and 139 million by 2050 as life expectancy increases, posing substantial social and economic burdens. Developing effective preventive and therapeutic strategies for AD is therefore imperative.

Complex Pathophysiology

The complex pathophysiology of AD involves deposition of amyloid plaques and neurofibrillary tangles, neuroinflammation, immune system activation, blood-brain barrier impairment, and oxidative stress (Kowalski & Mulak, 2019). Additionally, growing evidence from human and animal studies supports gut microbiota alterations influencing brain function and playing a role in AD (Bhattacharjee & Lukiw, 2013).

Microbiota-Gut-Brain Axis

The microbiota-gut-brain axis consists of bidirectional pathways linking the GI tract microbiota to the CNS (Cenit et al., 2017). This communication system includes immune, neural, endocrine and metabolic pathways. The gut microbiota can interact with the brain via microbial secretions, gene expression modulation, vagus nerve stimulation and tryptophan metabolism. Reciprocally, the brain can influence gut microbiota composition through endocrine, immune and neural signals (Caracciolo et al., 2014).

Gut Microbiota Changes in AD

Studies have revealed changes in microbiota composition and diversity in AD patients compared to controls. These include decreased abundance of anti-inflammatory bacteria and increased pro-inflammatory species (Vogt et al., 2017). Such dysbiosis can impact the CNS by producing neurotoxins, reducing neuroprotective metabolites, and promoting inflammation.

Mechanisms Linking Gut Microbiota to AD

Several mechanisms have been proposed through which gut dysbiosis may contribute to AD (Figure 1). These include increased intestinal permeability, systemic inflammation, heightened immune responses, amyloid and tau aggregation, oxidative stress, and decreased production of beneficial microbial metabolites like short chain fatty acids (SCFAs) (Bhattacharjee & Lukiw, 2013; Pistollato et al., 2016).

Modulating Gut Microbiota in AD

Given the lack of effective AD treatments currently, modulation of gut microbiota represents a promising disease management approach. Strategies such as probiotics, prebiotics, diet and fecal microbiota transplantation may help restore microbial balance in AD patients (Hu et al., 2016). However, more studies are needed to validate these interventions.

Conclusion

In summary, a growing body of clinical and preclinical evidence suggests that gut microbiota play a crucial role in AD pathogenesis through the microbiota-gut-brain axis. Dysbiosis of gut microbiota may contribute to AD via pathways involving inflammation, amyloid deposition, impaired gut-blood-brain barriers, and altered microbial metabolites. Further elucidating these mechanisms is key for developing novel microbiota-targeted diagnostics and therapeutics for AD. Modulating the gut microbiome composition could provide new avenues for managing this global health crisis.

References

Alzheimer's Disease International. (2021). Dementia statistics. https://www.alzint.org/about/dementia-facts-figures/dementia-statistics/

Bhattacharjee, S., & Lukiw, W. J. (2013). Alzheimer’s disease and the microbiome. Frontiers in cellular neuroscience, 7, 153. https://doi.org/10.3389/fncel.2013.00153

Caracciolo, B., Xu, W., Collins, S., & Fratiglioni, L. (2014). Cognitive decline, dietary factors and gut–brain interactions. Mechanisms of ageing and development, 136, 59-69. https://doi.org/10.1016/j.mad.2013.11.011

Cenit, M. C., Sanz, Y., & Codoñer-Franch, P. (2017). Influence of gut microbiota on neuropsychiatric disorders. World journal of gastroenterology, 23(30), 5486. https://doi.org/10.3748/wjg.v23.i30.5486

Cheung, G., Kuh, D., & Richards, M. (2018). Childhood cognition and age-related cognitive change in later life. Gerontology, 64(4), 388-396. https://doi.org/10.1159/000486024

DeTure, M. A., & Dickson, D. W. (2019). The neuropathological diagnosis of Alzheimer's disease. Molecular neurodegeneration, 14(1), 1-18. https://doi.org/10.1186/s13024-019-0333-5

Hu, X., Wang, T., & Jin, F. (2016). Alzheimer’s disease and gut microbiota. Science China Life Sciences, 59(10), 1006-1023. https://doi.org/10.1007/s11427-016-5083-9

Kowalski, K., & Mulak, A. (2019). Brain-gut-microbiota axis in Alzheimer's disease. Journal of neurogastro enterology and motility, 25(1), 48. https://doi.org/10.5056/jnm18087

Pistollato, F., Sumalla Cano, S., Elio, I., Masias Vergara, M., Giampieri, F., & Battino, M. (2016). Role of gut microbiota and nutrients in amyloid formation and pathogenesis of Alzheimer disease. Nutrition reviews, 74(10), 624-634. https://doi.org/10.1093/nutrit/nuw023

Vogt, N. M., Kerby, R. L., Dill-McFarland, K. A., Harding, S. J., Merluzzi, A. P., Johnson, S. C., ... & Rey, F. E. (2017). Gut microbiome alterations in Alzheimer's disease. Scientific reports, 7(1), 1-11. https://doi.org/10.1038/s41598-017-13601-y