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ARTICLE

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MICROBIOME-BASED NEUROPROTECTION: PROBIOTICS IN ALZHEIMER'S DISEASE (AD) AND PARKINSON'S DISEASE (PD)

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Parkinson's disease (PD) and Alzheimer's disease (AD) are major neurodegenerative disorders whose progression is influenced by gut microbiota, stress, and diet. This study evaluates the therapeutic effects of probiotics on cognition and neuroinflammation in AD and PD, and examines how microbiota-derived short-chain fatty acids (SCFAs) modulate immune, endocrine, and neuronal pathways. Probiotics enhance barrier integrity, regulate neurotransmission, improve metabolic and inflammatory markers, and counter HPA-axis hyperactivation, while SCFAs further support neuroprotection by modulating microglia, gut hormones, and neurotransmitter synthesis.

Introduction

Parkinson's disease (PD) and Alzheimer's disease (AD) are the two most common neurodegenerative disorders and major contributors to global disability among older adults. Global estimates indicate millions affected: PD case counts in recent Global Burden of Disease studies and WHO reports are in the millions (with rising prevalence over recent decades), and there are ~55–57 million people living with dementia worldwide (AD being the most common cause). These burdens are projected to rise substantially with population ageing[1].

The probiotics influence brain function via three main function: immune modulation, endocrine pathways and neuronal regulation. Small chain fatty acids (SCFAs), the main metabolites produced by the fermentation of gut microbiota, suppress pro-inflammatory mediators while upregulating the anti-inflammatory mediators. Via endocrine pathways, probiotics activate the hypothalamic-pituitary-adrenal (HPA) axis, stimulate adrenal release of cortisol, which is the most potent anti-inflammatory hormone. Probiotics also stimulate the production of glucagon-like-peptide-1 (GLP-1) and peptide (PYY) hormones YY enteroendocrine L-cells (EECs). Further, by intestine probiotics secrete certain neurotransmitters such as glutamate (GLU) or modulate the secretion of[1] neurotransmitters via enterochromaffin cells (EC) such as serotonin (5-HT). These neurotransmitters and neuroactive metabolites exert neuroprotective effects in concert, preventing neuronal apoptosis[2].

Probiotics exert a beneficial effect on the gut-brain-microbiota axis by preventing the hyperactivation of hypothalamic-pituitary-adrenal axis following a gut microbiota dysbiosis and inflammatory processes. Investigation of the different strains of Lactobaccilus identified that probiotic *Lactobacillus rhamnosus* decreased the corticosterone levels and anxiety-like behaviour in non-stressed mice . Although HPA dysregulation is believed to be associated with stress, the exact mechanism remains unclear. Probiotic *Bifidobacterium pseudocatenulatum* reduces stress-induced inflammation and improved glucocorticoid sensitivity in murine model of chronic stress induced by maternal separation[3].

Short-chain fatty acids (SCFAs)—acetate, propionate and butyrate—produced by gut microbial fermentation modulate brain function via immune, endocrine and neuronal pathways. They enhance gut barrier integrity,

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reduce pro-inflammatory cytokines, and cross the BBB to influence microglial activity and neuroinflammation. SCFAs stimulate GLP-1 and PYY release, supporting neuroprotection and appetite regulation. They also regulate neurotransmitter systems by promoting 5-HT and GABA synthesis from enterochromaffin cells and influence CNS signalling partly through vagal nerve activation[3].

Objectives

The objectives of this study are **t**o assess the therapeutic impact of probiotic supplementation on cognition and neuroinflammation in AD and PD and to examine how gut microbiota–derived SCFAs modulate neuroinflammation, endocrine signaling, *neurotransmission, and the gut–brain axis in neurodegeneration.*

To Assess the Therapeutic Impact of Probiotic Supplementation on Cognition and Neuroinflammation in AD and PD

Parkinson's disease (PD) was already known in ancient India under the name of "Kampavata." Parkinson's disease (PD) is a common motor disorder of mysterious etiology. It is due to the progressive degeneration of the dopaminergic neurons of the substantia nigra and is accompanied by the appearance of intraneuronal inclusions enriched in á-synuclein, the Lewy bodies. Responsible genes for PD include SNCA, LRRK2, DJ-1 (PARK7), PRKN (Parkin), and PINK1.

The occurrence of these diseases relies heavily on age, the most significant risk factor. Genetics also play a crucial role, especially in familial or early-onset cases of Alzheimer's and Parkinson's diseases. Environmental exposures like pesticides and head trauma increase risk. Other reasons include high blood uric acid levels, certain medications, smoking, and psychological stress, all identified as potential risk factors[3].

Alzheimer's disease (AD) is associated with initial memory loss, followed by impairments in cognitive function, language, visuospatial skills, and executive function, coupled with behavioral changes. Terminally, patients may become bedridden, incontinent, and unable to communicate. Responsible genes for AD include APP, PSEN1, PSEN2, APOE, etc.[3].

PD is characterized by classical motor signs including bradykinesia, rigidity, rest tremor, and postural instability. Non-motor symptoms including anosmia, constipation, REM sleep behavior disorder, and depression may predate motor features. Degeneration of striatonigral dopaminergic neurons along with α-synuclein–laden Lewy bodies appear as the major pathology in PD. Although multiple genetic and environmental factors have been implicated, the pathophysiology continues to evolve[3].

Global dietary heterogeneity shaped by geography, environment, and culture contributes to differing risks of neurodegenerative diseases. Diets rich in antioxidants, vitamins, fruits, vegetables, and fish are associated with reduced PD and AD risk, while vitamin B6 supplementation may lower PD risk and B12 deficiency is common in PD patients. Polyphenol-rich foods such as tea confer neuroprotection in preclinical PD studies. High-carbohydrate and high–glycemic index diets may elevate brain dopamine and reduce PD risk, whereas diets high in animal fat, saturated fats, and dairy increase oxidative stress, neuroinflammation, and both PD and AD risk. Additional PD risk factors include exogenous á-synuclein from meat, pesticide residues in milk, and urate reduction linked to dairy consumption[4].

FDA-approved Therapies and Their Limitations

FDA-approved Alzheimer's disease (AD) therapies primarily relieve symptoms without modifying disease progression. Acetylcholinesterase inhibitors—galantamine, donepezil, rivastigmine, and the now-withdrawn tacrine—preserve acetylcholine by preventing its breakdown. Memantine, an NMDA receptor antagonist, reduces glutamate-mediated excitotoxicity, while suvorexant is used to manage AD-related sleep disturbances. However, their overall benefit remains limited because most drugs poorly penetrate the blood–brain barrier, restricting effective CNS delivery and diminishing therapeutic impact[5].

Effects of Probiotics on AD and PD

Probiotics reinforce the intestinal mucosal barrier and influence gut immunity. They show minimal effects on digestion, absorption, and propulsion, but significantly improve barrier integrity, reduce permeability, stimulate mucosal immunity, reduce mucus degradation, and interact with inflammatory mediators. Yogurt may help lactose digestion, and some bacteria may accelerate intestinal transit (Fig. 1)[1].

How Gut Microbiota–derived SCFAs Modulate Neuroinflammation, Endocrine Signaling, Neurotransmission, and the Gut–brain Axis in Neurodegeneration

Alteration of the gut microbiome (gut dysbiosis) may lead to low-grade inflammation, increased oxidative stress,

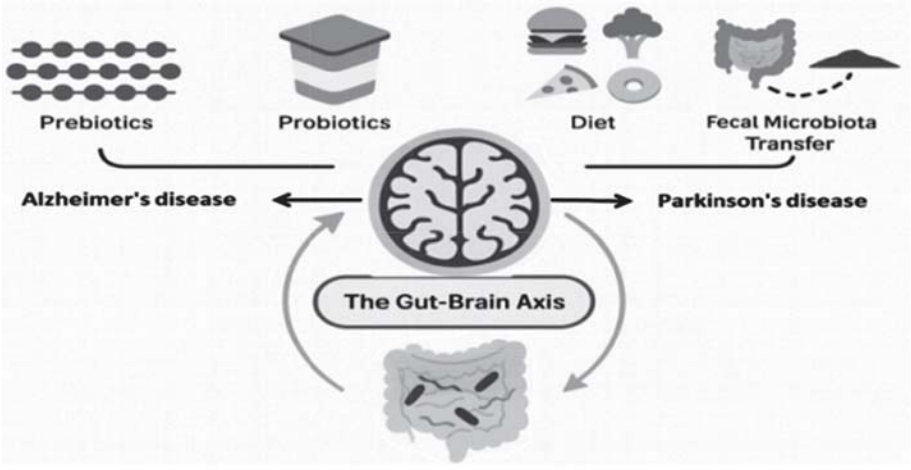

Fig. 1: Probiotics in Alzheimer's disease (AD) and Parkinson's disease (PD)

cellular degeneration, and compromised blood–brain barrier (BBB) integrity. Intestinal microbiota also modify short-chain fatty acid metabolism, microglial activation, and α-synuclein aggregation. Alpha-synuclein originating from the enteric nervous system may travel to the brain via the vagus nerve and the dorsal motor nucleus of the vagus (Fig. 1)[2].

Short-chain fatty acids (SCFAs)—acetate, butyrate, and propionate—are produced by fermentation mediated by Bacteroides, Clostridium, Lactobacillus, Bifidobacterium, and Eubacterium species. SCFAs influence the brain through immune pathways, endocrine pathways, and neuronal pathways[2].

Immune Modulation

SCFAs modulate immunity by strengthening gut barrier integrity and supporting mucus production, while also regulating cytokine secretion and guiding immune cell proliferation and differentiation. They suppress pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α and promote anti-inflammatory responses[6]. SCFAs can cross the blood–brain barrier via monocarboxylate transporters and enhance its integrity by upregulating tight junction proteins. Within the CNS, they influence microglial activity, thereby reducing neuroinflammation and protecting neurons from degeneration[2].

Endocrine Effects

SCFAs also act through endocrine pathways by stimulating the secretion of gut hormones such as GLP-1 and PYY via G-protein-coupled receptors. GLP-1, produced by intestinal L-cells and certain brainstem neurons, exerts strong neuroprotective effects by reducing neuronal apoptosis. PYY not only regulates appetite but also demonstrates neuroprotective actions in Alzheimer's disease models through PI3K-XBP1-Gip78/BIP signaling, inhibition of caspase-3 and caspase-4 activities, reduction of oxidative stress, and modulation of BDNF levels[2].

Neuronal and Neurotransmitter Effects

Gut microbiota can produce neurotransmitters or their precursors, and SCFAs play a key role in regulating 5-HT and GABA synthesis through enterochromaffin (EC) cells. Butyrate and propionate specifically enhance 5-HT biosynthesis, as demonstrated by Yano et al. (2015). EC cells additionally generate neuroactive metabolites such as PYY, tryptophan, and histamine, some of which can cross the BBB and contribute to CNS neurotransmitter production. Gut microbes also modulate vagal nerve signaling, influencing activity in the dorsal motor nucleus[3].

HPA Axis and Stress Mechanisms

Long-term stress is a significant risk factor for Alzheimer's disease and can accelerate its progression through chronic activation of the hypothalamic–pituitary–adrenal (HPA) axis, leading to elevated glucocorticoid levels that cross the BBB and act on brain receptors. Probiotics help counteract this stress-driven HPA hyperactivation by mitigating dysbiosis and inflammation. Lactobacillus rhamnosus has been shown to reduce corticosterone levels and anxiety-like behavior in mice, while Bifidobacterium pseudocatenulatum lessens stress-induced inflammation and improves glucocorticoid sensitivity in maternal separation models (Fig. 1)[3].

Conclusion

Probiotic supplementation offers a promising, low-risk adjunct strategy for supporting gut–brain axis function in Alzheimer's disease and Parkinson's disease. Evidence indicates modest benefits in reducing inflammation, improving metabolic markers, enhancing gut barrier integrity, and supporting neurotransmitter and hormone regulation through SCFA-mediated pathways. Although early clinical studies show improvements in cognitive and non-motor symptoms, current data remain insufficient to

confirm disease-modifying effects. Diets that promote microbiome diversity, such as the Mediterranean diet, provide stronger supportive evidence. Large, standardized clinical trials integrating mechanistic biomarkers are essential to establish the therapeutic value of probiotics in neurodegenerative diseases..

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References

1. V. Mishra, D. Yadav, K.S. Solanki and B. Koul, *J. Alzheimers Dis. Rep.*, **8**(1), 1–21 (2024).
2. S. Xiang, J. Chen, X. Wang, Y. Liu, Y. Zhang and J. Li, *Front. Aging Neurosci.*, **14**, 814001 (2022).
3. G. Zhu, J. Zhao, H. Zhang, W. Chen and G. Wang, *Aging Dis.*, **12**(7), 1735–1750 (2021).
4. R. Naomi, H. Embong, F. Othman, H. F. Ghazi, N. Maruthey and H. Bahari, *Nutrients*, **14**(20), 4210 (2022).
5. H. Sun, J. Chen, Y. Jiang and X. Wang, *Neurosci. Lett.*, **808**, 136828 (2023).
6. A.H. Tan, *J. Parkinsons Dis.*, **11**(2), 414–419 (2021).