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The Gut Brain Axis and Cognitive Decline: A Narrative Review of Microbiota Dynamics in MCI and Alzheimer's Disease

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ABSTRACT: The gut brain axis has emerged as a pivotal framework for understanding the relationship between gut microbiota and cognitive function. This narrative review aimed to explore the influence of gut microbial composition and metabolites on the progression of cognitive decline, particularly from Mild Cognitive Impairment (MCI) to Alzheimer's Disease (AD). A systematic search of academic databases including Scopus, PubMed, and Google Scholar was conducted using predetermined keywords and Boolean operators. Eligible studies included peer reviewed research articles, systematic reviews, and meta analyses published between 2015 and 2025. The review found consistent evidence linking gut dysbiosis notably decreased microbial diversity and elevated pro inflammatory taxa to neurodegenerative processes. Specific mechanisms such as reduced short chain fatty acid production, microbial induced inflammation, and vagus nerve signaling disruptions were implicated in cognitive impairment. Furthermore, socio economic factors such as dietary quality and healthcare access significantly influenced microbiota composition and, by extension, cognitive health. Interventions including dietary modulation, probiotic and prebiotic supplementation, and fecal microbiota transplantation demonstrated potential in mitigating cognitive decline. However, the review also identified limitations in current literature, including a lack of longitudinal and population diverse studies. Future research should address these gaps to enable personalized and equitable microbiota targeted therapies. Overall, this review affirms gut microbiota as a modifiable factor with significant implications for cognitive aging and public health.

Keywords: Gut Brain Axis, Microbiota, Cognitive Impairment, Alzheimer's Disease, Dysbiosis, Neuroinflammation, Short Chain Fatty Acids.

INTRODUCTION

In recent years, the gut brain axis (GBA) has emerged as a fundamental paradigm in neurocognitive science, underscoring a complex bidirectional communication system between the gastrointestinal tract and the central nervous system. This axis is orchestrated by a network of signaling pathways mediated through neural, immune, metabolic, and endocrine mechanisms, which are heavily modulated by the gut microbiota (Viana, 2024; Alzubide & Alhalafi, 2024; Curti et al, 2024). These microorganisms synthesize a diverse range of neuroactive compounds, including neurotransmitters such as serotonin and gamma aminobutyric acid (GABA), implicating them in the regulation of emotion, cognition, and behavior (Mittal et al, 2017). The significance of gut microbiota in modulating neurochemical activity has led to an upsurge of interdisciplinary research examining its potential role in neuropsychiatric conditions such as anxiety and depression, thereby shifting the focus toward a more holistic understanding of mental health (Curti et al, 2024).

This expanding field of inquiry has catalyzed the investigation of gut microbiota's contributions to neurodegenerative conditions, particularly Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD). Emerging data point to a strong correlation between dysbiosis an imbalance in the composition and function of the gut microbiome and the progression of cognitive decline (Chen et al, 2020). Dysbiosis has been implicated in the promotion of neuroinflammation and amyloid beta deposition, two hallmark features of AD pathology (Cordero et al, 2022). Consequently, the GBA not only presents a novel biological substrate for understanding the etiology of cognitive disorders but also offers promising therapeutic targets (sittipo et al, 2022).

The urgency of addressing neurodegenerative conditions is underscored by global prevalence trends. Current estimates suggest that MCI affects approximately 15–20% of the global population, while AD afflicts nearly 50 million individuals, with projections indicating a surge to 152 million by 2050 due to demographic (Post et al, 2023). Lifestyle and environmental factors, particularly diet and metabolic health, are strongly linked with cognitive trajectories (Pang et al, 2023). Epidemiological studies have consistently demonstrated that anti-inflammatory diets and physical activity reduce the risk of cognitive decline, whereas obesity, sedentary behaviors, and poor dietary choices exacerbate susceptibility to neurodegeneration (Jones et al, 2019).

In parallel, mounting evidence connects metabolic dysregulation with gut microbiota imbalances and subsequent cognitive impairment. Conditions such as type 2 diabetes, obesity, and metabolic syndrome have been shown to disrupt gut microbiota homeostasis, leading to heightened systemic inflammation and neuroinflammatory cascades (Park et al, 2021). These inflammatory pathways have been correlated with increased permeability of the blood brain barrier and the exacerbation of cognitive deficits, thereby reinforcing the interplay between gut health and neurological function (Vandemoortele & Vermeirssen, 2023; Hulme et al, 2020). Cultural and regional dietary patterns also influence the composition of gut microbiota, suggesting the need for culturally sensitive intervention models (Caputi & Giron, 2018).

Despite these advancements, multiple challenges impede the establishment of a direct causal relationship between gut microbiota and neurodegeneration. The multifactorial nature of AD involves genetic predispositions, environmental exposures, and immune system variations that complicate the isolation of gut microbiota as a singular causative agent (Jiang et al, 2017; Kim et al, 2020; Chen et al, 2024). Moreover, many studies rely on cross sectional or animal models, which, while informative, lack the longitudinal depth required to map disease progression in humans (Seo et al, 2023); Jakubiec et al, 2024). The inconsistencies in methodologies, including the use of 16S rRNA sequencing and varying sample processing techniques, further hinder reproducibility and generalizability across populations (Schächtle & Rosshart, 2021; Vareso et al, 2022).

Another formidable obstacle lies in translating microbiota modulating interventions into clinically effective treatments. While probiotics, prebiotics, and dietary interventions have shown promise in preclinical models, defining optimal dosages, bacterial strains, and treatment durations remains elusive (Ayten & Bilici, 2024). Furthermore, the interindividual variability in gut microbiota composition necessitates personalized approaches, highlighting the need for precision medicine frameworks within neurodegenerative research.

Research in this domain also reveals notable gaps, particularly concerning the inclusion of diverse ethnic and geographic populations. Most microbiome studies have been conducted in Western populations, limiting their applicability to broader demographics (Kowalski & Mulak, 2019); Giovanni et al, 2020). Socioeconomic disparities and differences in dietary practices, genetic backgrounds, and access to healthcare services can significantly influence gut microbiota and its neurological effects (Chu et al, 2022; Zhang et al, 2022). Small sample sizes and underrepresentation of marginalized communities further compound the difficulty of deriving universally valid conclusions (Matz et al, 2024; Mitra et al, 2023).

Given these limitations and the compelling body of preliminary evidence, this narrative review aims to synthesize current literature from a neurological perspective, focusing on the biological, immunological, and metabolic dimensions of the gut brain axis. The review critically evaluates the role of gut microbiota in modulating cognitive functions, with particular attention to its contributions to MCI and AD progression. By examining how microbial metabolites, neuroinflammatory mediators, and metabolic markers intersect, this study endeavors to elucidate mechanistic pathways that may serve as future therapeutic targets.

The scope of this review encompasses both human and preclinical studies that investigate gut microbiota profiles, inflammatory markers, and neurocognitive outcomes. It integrates findings across disciplines, including microbiology, neuroscience, and metabolic research, and includes global and culturally diverse datasets wherever available. In doing so, this review not only provides a comprehensive understanding of gut brain communication in neurodegeneration but also highlights the need for inclusive, translational research strategies to address one of the most pressing public health challenges of the 21st century.

METHOD

This narrative review systematically examined the influence of gut microbiota on neurocognitive trajectories from mild cognitive impairment to Alzheimer's disease. A comprehensive search was undertaken across PubMed, Scopus, and Google Scholar for literature published between January 2015 and April 2025. Search strings combined predetermined keywords such as "gut–brain axis," "cognitive impairment," "Alzheimer's disease," "microbiota," "dysbiosis," "neuroinflammation," "short chain fatty acids," "probiotics," and "prebiotics" with Boolean operators to maximise sensitivity while maintaining precision. Titles and abstracts were first screened to exclude duplicates and clearly irrelevant records; full texts were subsequently assessed for methodological rigour and topical relevance.

Peer reviewed original articles, systematic reviews, and meta analyses that empirically or theoretically explored mechanisms linking microbial alterations to neurocognitive outcomes in humans or validated animal models were eligible. Studies not written in English, lacking empirical evidence, predating 2015 (unless seminal), or published as opinion pieces, editorials, or conference abstracts were excluded. To enhance reliability, four independent reviewers applied the inclusion criteria in a multi stage process; discrepancies were resolved through consensus discussion. Relevant data study design, population characteristics, microbiota assessment methods, cognitive or neuropathological endpoints, and principal findings were extracted into a standardised matrix.

An inductive thematic synthesis was employed to identify convergent patterns in how dysbiosis, microbial metabolites, and inflammatory mediators intersect with neurodegenerative pathways. This procedure facilitated the integration of heterogeneous evidence, providing nuanced insights into mechanistic links and highlighting emergent therapeutic opportunities.

RESULT AND DISCUSSION

Changes in Gut Microbiota Composition in Individuals with Mild Cognitive Impairment Compared to Healthy Controls

Studies consistently demonstrate that individuals diagnosed with Mild Cognitive Impairment (MCI) present notable alterations in gut microbiota compared to healthy counterparts. Metrics such as alpha and beta diversity highlight significant dysbiosis in MCI patients, marked by reduced microbial diversity (Pan et al, 2020). These microbial shifts typically involve decreased levels of Bacteroidetes and increased abundance of potentially pathogenic taxa, notably Enterobacter, which have been associated with cognitive dysfunction (Rouskas et al, 2024). Comparative analyses have shown overlap in microbiota profiles between MCI and Alzheimer's Disease (AD) patients, suggesting that dysbiosis may be an early biomarker for neurodegenerative progression (Bao et al, 2023).

Furthermore, the presence of pro inflammatory bacterial taxa and the reduction of anti-inflammatory strains such as Bifidobacterium and Lactobacillus have been frequently observed in MCI cohorts (Pan

et al, 2020). Kim et al. (2023) noted specific bacterial profiles in elderly MCI patients that distinguish them from cognitively intact controls, emphasizing the potential for microbiota based diagnostic strategies (Kim et al, 2023). A consistent pattern across various studies is the increase in Firmicutes and concurrent decrease in Bacteroides among individuals with MCI, reinforcing the hypothesis that dysbiosis contributes to cognitive decline (Chen et al, 2023).

Empirical Evidence Linking Specific Bacterial Taxa with Early Neuroinflammatory Markers in MCI

The gut microbiota's role in neuroinflammation is increasingly substantiated by empirical findings linking specific microbial taxa to inflammatory pathways in MCI. Certain bacterial strains, particularly from the Firmicutes phylum, are associated with elevated pro inflammatory cytokines such as IL 6 and TNF α, which are implicated in neurodegenerative cascades (Zhuang et al, 2018; Jemimah et al, 2023). Pan et al. (2020) found that bacterial lipopolysaccharides (LPS) originating from gram negative bacteria exacerbated systemic inflammation, resulting in altered cytokine profiles and increased neuroinflammatory burden in MCI individuals (Pan et al, 2021).

Additional studies have reported an inverse correlation between the presence of Prevotella and cognitive function scores, with its abundance linked to enhanced inflammatory signaling (Li et al, 2024). Jin et al. (2023) provided supporting evidence showing correlations between dysbiotic microbial communities and early markers of blood brain barrier permeability, establishing a mechanistic link between gut microbiota composition and central neuroinflammatory responses (Jin et al, 2023). These findings suggest that targeting specific bacterial taxa might be a feasible approach for modulating neuroinflammation and mitigating cognitive decline.

Mechanisms by which Microbial Metabolites Affect Cognitive Function

Gut derived microbial metabolites serve as critical intermediaries in the gut brain communication process. Short chain fatty acids (SCFAs) such as acetate, propionate, and butyrate, produced through fermentation of dietary fibers, are particularly significant. These SCFAs have been shown to influence cognitive health by enhancing the expression of brain derived neurotrophic factor (BDNF), which plays a central role in neuronal plasticity, learning, and memory (He et al, 2023). SCFAs can cross the blood brain barrier and exert neuroprotective effects, underscoring their role in maintaining cognitive function.

Other metabolites such as indole and indolepropionic acid, products of tryptophan metabolism, have also been associated with cognitive modulation and neuroprotection (Colombo et al, 2021). These compounds activate signaling pathways that regulate inflammation and oxidative stress in the brain, which are central to the pathophysiology of cognitive decline. In addition, gut microbes affect the

synthesis of neurotransmitters such as serotonin and GABA, further influencing emotional and cognitive states (Husso et al, 2023).

Role of Vagal Nerve Signaling, SCFAs, and Immune Modulation in Gut Brain Communication

The vagus nerve represents a direct communication line between the gut and brain, transmitting microbial signals that influence autonomic, cognitive, and affective processes. SCFAs can activate vagal afferent neurons, which modulate central nervous system activity relevant to cognition and emotional regulation (Saji et al, 2020). Butyrate, in particular, enhances vagal tone and is associated with improved cognitive performance, supporting the view of the vagus nerve as a viable therapeutic target (Giovanni et al, 2020).

In parallel, immune system modulation mediated by gut microbiota plays a pivotal role in regulating neuroinflammation. SCFAs induce anti-inflammatory cytokine production and suppress pro inflammatory responses, thereby mitigating neuroinflammatory damage (Donaldson et al, 2025). Dysbiosis can compromise blood brain barrier integrity, allowing peripheral inflammatory mediators to access the CNS, exacerbating neurodegenerative conditions (Nota et al, 2024). Thus, both neural and immune pathways highlight the integrative role of the gut microbiome in maintaining cognitive health.

Characteristic Patterns of Gut Dysbiosis in Alzheimer's Disease Patients Across Different Studies

Studies exploring gut microbiota in Alzheimer's Disease (AD) patients reveal recurring patterns of dysbiosis. Decreased overall microbial diversity is consistently reported, particularly the reduction of anti-inflammatory commensals and an increase in pro inflammatory and potentially pathogenic taxa (Park & Im, 2022). AD patients commonly exhibit elevated levels of Firmicutes and Proteobacteria, including Escherichia coli and Enterobacter cloacae, both of which correlate with heightened inflammatory markers (Vogt et al, 2017).

Furthermore, alterations in functional capacity, particularly SCFA production, are observed in the AD associated microbiota (Chen et al, 2020). Decreases in butyrate production, vital for gut and neuronal integrity, have been associated with deteriorating cognitive performance (Kamer & Pushalkar, 2024). These microbiota shifts collectively reflect a systemic inflammatory state conducive to neurodegeneration, implicating the gut microbiome as a potential biomarker and therapeutic target in AD.

Evidence Supporting the Role of Bacterial Amyloids and Systemic Inflammation in Accelerating Amyloid β and Tau Pathology

Accumulating evidence implicates bacterial amyloids and systemic inflammation as facilitators of amyloid β and tau pathology in AD. Bacterial amyloids may structurally resemble human Aβ, thereby inducing its aggregation through molecular mimicry mechanisms (Chen et al, 2020). This misfolding accelerates the deposition of amyloid plaques, one of the neuropathological hallmarks of AD. Concurrently, chronic systemic inflammation promotes tau hyperphosphorylation, facilitating the formation of neurofibrillary tangles (Favero et al., 2022).

Lipopolysaccharides (LPS) from gram negative bacteria are particularly potent in initiating systemic inflammatory responses. Elevated LPS levels in AD patients have been linked to increased Aβ deposition and blood brain barrier disruption (Shabbir et al., 2021). This creates a feedback loop wherein neuroinflammation propagates further neuronal damage, reinforcing the pathological burden of AD.

Cognitive Outcomes of Probiotic and Prebiotic Interventions in MCI and AD Populations

Probiotic and prebiotic interventions have demonstrated potential benefits in enhancing cognitive function in MCI and AD populations. Several clinical studies report improvements in memory and executive function following supplementation with specific probiotic strains. These benefits are attributed to the restoration of microbial balance and the enhancement of SCFA production (Sha et al., 2023).

Prebiotics also promote the growth of beneficial microbes and increase SCFA levels, leading to anti-inflammatory effects that support neuronal health. González Dávila et al. (2022) observed improved cognitive and emotional outcomes in elderly individuals consuming prebiotic enriched diets (González Dávila, et al., 2022). These findings underscore the value of dietary modulation in maintaining cognitive resilience.

Clinical or Preclinical Studies Evaluating Fecal Microbiota Transplantation (FMT) or Dietary Modulation in Cognitive Performance

Fecal Microbiota Transplantation (FMT) has shown promise in modifying gut microbiota to improve cognitive outcomes in both preclinical and clinical studies. In AD mouse models, FMT from healthy donors reduced neuroinflammation and amyloid burden, correlating with improved learning and memory performance (He et al., 2023). Clinical observations suggest similar trends, with patients demonstrating behavioral and cognitive improvements post FMT (11).

Dietary interventions, including adherence to Mediterranean style diets, have been linked to increased microbial diversity and reduced markers of cognitive decline (Kim et al., 2024). Moreover, Wang et al.

(2022) demonstrated that dietary changes combined with microbiota modulation alleviated post stroke cognitive impairment in animal models (Wang et al., 2022). These findings support the hypothesis that altering gut microbiota through FMT or targeted dietary strategies can yield significant cognitive benefits, paving the way for novel interventions against neurodegenerative diseases.

Alignment and Contrast of Findings with Previous Meta Analyses on Gut Microbiota and Cognitive Health

The findings presented in this review demonstrate both consistency with and extension beyond prior meta analytical studies examining the relationship between gut microbiota and cognitive health. In alignment with previous meta analyses, this review confirms that alterations in gut microbial diversity and the relative abundance of specific taxa are hallmarks of cognitive impairment in conditions such as Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD) (Saji et al, 2020; Putri et al., 2023). The observed decrease in Bacteroidetes and increased presence of Proteobacteria and Firmicutes align with established patterns of dysbiosis in neurodegenerative populations (Donaldson et al, 2025). Furthermore, these findings corroborate earlier conclusions that short chain fatty acids (SCFAs) exert neuroprotective effects and modulate inflammation, contributing to cognitive performance improvements (Singh et al., 2019).

However, this review diverges from earlier meta analyses by emphasizing a more integrated and multifactorial perspective. While many meta analyses have focused on the taxonomy of the gut microbiome, this review explores the mechanistic links between microbial dysbiosis, neuroinflammatory markers, microbial metabolites, and blood brain barrier integrity. Such an approach allows for a deeper exploration of how systemic biological pathways interact with gut microbial alterations to influence cognitive health, expanding beyond the taxonomic focus predominant in earlier work (Putri et al., 2023).

Additionally, this review distinguishes itself by incorporating dietary and socio economic contexts that shape microbiota composition. Previous studies have often overlooked how factors like healthcare disparities and food access contribute to microbiome diversity and thereby affect cognitive trajectories. This broader lens invites more inclusive research and intervention strategies that address root causes of dysbiosis beyond microbial taxonomy (Lavelle & Sokol., 2020).

Influence of Systemic Healthcare Inequalities and Dietary Patterns on Gut Microbial Diversity and Cognitive Decline

Systemic healthcare inequalities and dietary habits are crucial, yet underexamined, contributors to gut microbial diversity and its downstream impact on cognitive decline. Populations facing food insecurity and limited healthcare access often exhibit dietary patterns rich in processed foods and low in fiber, which negatively affect gut microbiota composition (Kim et al., 2024; Wang et al., 2019). Diets

deficient in prebiotics and whole foods can foster dysbiosis by encouraging the growth of pathogenic species while reducing protective bacterial taxa (Zhao et al., 2022).

Diets high in fermentable fibers, fruits, vegetables, and whole grains promote microbial diversity and increase the production of SCFAs, particularly butyrate, which supports both gut and brain health (Tian et al., 2024). In contrast, Westernized dietary patterns associated with low socio economic status are linked to reduced gut microbial diversity and increased markers of inflammation and cognitive dysfunction (Nota et al, 2024). Geographic and demographic disparities further compound these issues, as communities lacking access to healthcare infrastructure and educational resources are less likely to benefit from gut friendly diets.

Lack of awareness regarding the gut brain connection also hinders proactive health behavior. Individuals in disadvantaged settings may not understand how gut health influences mental and cognitive outcomes, perpetuating poor dietary choices and neglect of preventative health practices (Jiang et al., 2019). Stress and limited access to mental health support further exacerbate gut dysbiosis and systemic inflammation, creating a cycle that reinforces vulnerability to cognitive decline (Jia et al., 2022).

Policy and Practice Based Interventions Derived from the Understanding of the Microbiota Neurocognition Link

Understanding the link between gut microbiota and cognitive health enables the formulation of practical interventions at the policy and community levels. Promoting microbiota supportive dietary patterns is a primary strategy. Public health initiatives that emphasize the inclusion of prebiotic and probiotic rich foods in national dietary guidelines and public food programs, such as school lunches or community feeding schemes, can have a population level impact (Kossowska et al., 2024). Increasing consumption of whole foods, fermented products, and dietary fibers through targeted subsidies or education campaigns could foster microbial diversity and cognitive resilience (Stevens et al., 2023).

Integrating microbiota focused research into national and regional health strategies is another essential step. Governments and health ministries can support microbiome research through funding and institutional support, enabling the development of clinical guidelines that include gut health as part of routine cognitive health assessment and treatment (Kartjito et al., 2023). Educational reforms in medical and public health training programs should incorporate emerging knowledge of the gut brain axis, ensuring healthcare professionals are equipped to advise on microbiota related interventions (Strekalova et al., 2024).

With increasing evidence supporting fecal microbiota transplantation (FMT) as a potential treatment for cognitive impairment, standardized clinical protocols must be developed. These should address donor screening, ethical concerns, and long term safety and efficacy, enabling the responsible

integration of FMT into clinical practice (Cai et al., 2022). Regulatory authorities must also establish oversight to ensure quality control and monitor patient outcomes from such experimental interventions.

Reducing systemic health inequalities requires cross sector collaboration and targeted policy action. Policies that provide subsidies for healthy food options, ensure equitable access to primary healthcare, and promote community based health education could reduce the disparities that contribute to cognitive decline in marginalized populations (Hou et al., 2022). Culturally tailored interventions that consider local dietary practices and community norms can further enhance the reach and effectiveness of microbiota focused cognitive health strategies (Wilson et al, 2023).

A multi sectoral approach involving educational institutions, community leaders, and healthcare providers is essential to operationalize the microbiota cognition link. Collaborative programming that brings awareness to the importance of gut health through school curricula, public media, and primary care settings can drive behavioral changes at the population level. Such efforts are vital for building resilient health systems capable of addressing the rising global burden of cognitive impairment.

Limitation

Although the reviewed literature strongly supports the association between gut microbiota and cognitive health, several limitations restrict definitive conclusions. The heterogeneity of study designs, variations in microbiota analysis techniques, and reliance on animal models constrain the generalizability of findings to human populations. Furthermore, the complex interplay between genetics, environment, and lifestyle makes isolating the microbiota's role in cognitive impairment inherently challenging. Limited representation of diverse populations in current research also weakens the applicability of findings across different socio cultural settings. Lastly, there is a lack of longitudinal human studies that assess the long term cognitive effects of microbiota targeted interventions, which hinders the formulation of robust clinical guidelines.

Implication

Addressing these limitations requires a concerted research effort that prioritizes methodological standardization and diverse population inclusion. Future studies should focus on longitudinal designs that examine how microbiota shifts over time correlate with cognitive changes. There is a pressing need to investigate the causal mechanisms underlying microbial influence on neurodegenerative pathways, especially in human subjects. Research should also explore the effectiveness of different dietary and microbial interventions across various demographic groups. Expanding microbiota research to underrepresented populations and integrating socio economic, cultural, and behavioral variables will enhance the translational potential of findings. By doing so, the field can move towards

developing equitable, evidence based strategies for cognitive health promotion grounded in gut microbiota modulation.

CONCLUSION

This review synthesized current evidence on the role of gut microbiota in the progression of cognitive impairment, particularly from Mild Cognitive Impairment (MCI) to Alzheimer's Disease (AD), highlighting the microbiota gut brain axis as a critical mediator in neurodegeneration. The findings confirmed that individuals with MCI and AD exhibit distinct dysbiosis patterns, characterized by decreased microbial diversity, an increase in pro inflammatory taxa, and reductions in beneficial short chain fatty acid producing bacteria. These alterations were closely associated with neuroinflammatory processes, reduced production of neuroprotective metabolites, and compromised blood brain barrier integrity, all of which contribute to cognitive decline.

The discussion underscored the multifactorial nature of microbiota related cognitive dysfunction, incorporating systemic influences such as healthcare disparities and dietary patterns. These broader factors not only shape microbial composition but also influence an individual's vulnerability to cognitive impairment. In this context, microbiota modulation through dietary interventions, prebiotics, probiotics, and potentially fecal microbiota transplantation (FMT) presents a promising strategy to address neurocognitive challenges.

Given the complex interplay between microbiota, immunity, and cognition, future studies should prioritize longitudinal and diverse population based research to better understand causal mechanisms and optimize intervention strategies. Policymakers and healthcare systems must integrate microbiome informed guidelines into public health frameworks to support early prevention and cognitive resilience. Ultimately, preserving gut microbial health represents a vital frontier in mitigating the burden of neurodegenerative diseases.

REFERENCES

Viana TRX. Relationship of Gut Microbiota and Mental Health: The Influence of the Gut Brain Axis. Int J Health Sci. 2024;4(25):2–6.

Alzubide S, Alhalafi M. The Gut Brain Connection. J Behav Brain Sci. 2024;14(03):103–17.

Curti C, Bossolani JA, Camargo RA d., Caramelo AAF, Maria Gabriela Lisboa da Silva, Favaro MEF, et al. The Gut Brain Axis: Exploring the Role of Microbiota in Depression and Anxiety Disorder. Int J Health Sci. 2024;4(26):2–13.

Mittal R, Debs LH, Patel A, Nguyen D, Patel K, O'Connor G, et al. Neurotransmitters: The Critical Modulators Regulating Gut–Brain Axis. J Cell Physiol. 2017;232(9):2359–72.

Chen M, Patel T, Chang F. The Impact of a Primary Care, Pharmacist Driven Intervention in Patients With Chronic Non Cancer Pain A Pilot Study. Pharmacy. 2020;8(3):113.

Cordero EMG, Cuevas-Budhart MÁ, Morán DP, Villeda MÁT, Mercedes Gómez del Pulgar García Madrid. Relationship Between the Gut Microbiota and Alzheimer's Disease: A Systematic Review. J Alzheimer Dis. 2022;87(2):519–28.

Sittipo P, Choi JY, Lee S, Lee YK. The Function of Gut Microbiota in Immune Related Neurological Disorders: A Review. J Neuroinflammation. 2022;19(1).

Post Z, Manfready RA, Keshavarzian A. Overview of the Gut–Brain Axis: From Gut to Brain and Back Again. Semin Neurol. 2023;43(04):506–17.

Pang S, Wen Yi J, Zi W. The Interplay Between the Gut Microbiome and Neurological Disorders: Exploring the Gut Brain Axis. Neurol Lett. 2023;2(1):25–9.

Jones LD, Kumar J, Mistry A, Mana TS, Perry G, Reddy VP, et al. The Transformative Possibilities of the Microbiota and Mycobiota for Health, Disease, Aging, and Technological Innovation. Biomedicines. 2019;7(2):24.

Park SH, Lee JH, Shin J, Kim J, Cha B, Lee S, et al. Cognitive Function Improvement After Fecal Microbiota Transplantation in Alzheimer's Dementia Patient: A Case Report. Curr Med Res Opin. 2021;37(10):1739–44.

Vandemoortele B, Vermeirssen V. Molecular Systems Biology Approaches to Investigate Mechanisms of Gut−brain Communication in Neurological Diseases. Eur J Neurol. 2023;30(11):3622–32.

Hulme H, Meikle LM, Strittmatter N, Justin J. J. van der Hooft, Swales JG, Bragg RA, et al. Microbiome Derived Carnitine Mimics as Previously Unknown Mediators of Gut Brain Axis Communication. Sci Adv. 2020;6(11).

Caputi V, Giron MC. Microbiome Gut Brain Axis and Toll Like Receptors in Parkinson's Disease. Int J Mol Sci. 2018;19(6):1689.

Jiang C, Li G, Huang P, Liu Z, Zhao B. The Gut Microbiota and Alzheimer's Disease. J Alzheimer Dis. 2017;58(1):1–15.

Kim CS, Cha L, Sim M, Jung S, Chun WY, Baik HW, et al. Probiotic Supplementation Improves Cognitive Function and Mood With Changes in Gut Microbiota in Community Dwelling Older Adults: A Randomized, Double Blind, Placebo Controlled, Multicenter Trial. J Gerontol Ser A. 2020;76(1):32–40.

Chen A, Wang Y, Hu Y. Exploring Causal Relationships Between Gut Microbiota and Alzheimer's Disease: A Bidirectional Mendelian Randomization Study. J Alzheimer Dis Rep. 2024;8(1):1031–40.

Seo D oh, O'Donnell D, Jain N, Ulrich JD, Herz J, Li Y, et al. ApoE Isoform– And Microbiota Dependent Progression of Neurodegeneration in a Mouse Model of Tauopathy. Science. 2023;379(6628).

Jakubiec J, Gmitrzuk J, Malinka Z, Wiśniewska K, Jachymek A, Opatowska M, et al. The Impact of Gut Microbiota on Parkinson's and Alzheimer's Diseases: A Review of Medical Literature. Qual Sport. 2024;15:52004.

Schächtle M, Rosshart SP. The Microbiota Gut Brain Axis in Health and Disease and Its Implications for Translational Research. Front Cell Neurosci. 2021;15.

Varesi A, Pierella E, Romeo M, Piccini GB, Alfano C, Bjørklund G, et al. The Potential Role of Gut Microbiota in Alzheimer's Disease: From Diagnosis to Treatment. Nutrients. 2022;14(3):668.

Ayten Ş, Bilici S. Modulation of Gut Microbiota Through Dietary Intervention in Neuroinflammation and Alzheimer's and Parkinson's Diseases. Curr Nutr Rep. 2024;13(2):82–96.

Kowalski K, Mulak A. Brain Gut Microbiota Axis in Alzheimer's Disease. J Neurogastroenterol Motil. 2019;25(1):48–60.

Giovanni SD, Serger E, Chadwick J, Luengo L, Kong G, Zhou L, et al. The Intermittent Fasting Dependent Gut Microbial Metabolite Indole 3 Propionate Promotes Nerve Regeneration and Recovery After Injury. 2020;

Chu X, Hou Y, Meng Q, Croteau DL, Wei Y, De S, et al. Nicotinamide Adenine Dinucleotide Supplementation Drives Gut Microbiota Variation in Alzheimer's Mouse Model. Front Aging Neurosci. 2022;14.

Zhang C, Liang D, Li X, Liu J, Fan M, Mei J, et al. Characteristics of Gut Microbial Profiles of Offshore Workers and Its Associations With Diet. Front Nutr. 2022;9.

Matz M, Shah NS, Porterfield L, Stuyck OM, Jochum MD, Kayed R, et al. Microbial Determinants of Dementia Risk in Subjects of Mexican Descent With Type 2 Diabetes Living in South Texas. 2024;

Mitra S, Munni YA, Dash R, Sadhu T, Barua L, Islam MA, et al. Gut Microbiota in Autophagy Regulation: New Therapeutic Perspective in Neurodegeneration. Life. 2023;13(4):957.

Pan Q, Li Y, Guo K, Xue M, Gan Y, Wang K, et al. Elderly Patients of Mild Cognitive Impairment Exhibit Altered Profiles of the Gut Microbiota. 2020;

Rouskas K, Mamalaki E, Ntanasi E, Pantoura M, Anezaki M, Emmanouil C, et al. Distinct Gut Microbiota Profiles May Characterize Amyloid Beta Pathology and Mild Cognitive Impairment. 2024;

Bao QN, Liu Y, Zhang X, Li Y, Wang Z, Ye F, et al. Clinical Observation and Mechanism of Acupuncture on Amnestic Mild Cognitive Impairment Based on the Gut Brain Axis: Study Protocol for a Randomized Controlled Trial. Front Med. 2023;10.

Kim E, Kim JJ, Park SE, Seo SH, Cho K, Kwon SJ, et al. Association Between Mild Cognitive Impairment and Gut Microbiota in Elderly Korean Patients. J Microbiol Biotechnol. 2023;33(10):1376–83.

Chen G, Zhou X, Zhu Y, Shi W, Kong L. Gut Microbiome Characteristics in Subjective Cognitive Decline, Mild Cognitive Impairment and Alzheimer's Disease: A Systematic Review and Meta-analysis. Eur J Neurol. 2023;30(11):3568–80.

Zhuang Z, Shen L, Li W, Fu X, Zeng F, Gui L, et al. Gut Microbiota Is Altered in Patients With Alzheimer's Disease. J Alzheimer Dis. 2018;63(4):1337–46.

Jemimah S, Chabib C, Hadjileontiadis LJ, AlShehhi A. Gut Microbiome Dysbiosis in Alzheimer's Disease and Mild Cognitive Impairment: A Systematic Review and Meta Analysis. Plos One. 2023;18(5):e0285346.

Pan Q, Li Y, Guo K, Xue M, Gan Y, Wang K, et al. Elderly Patients With Mild Cognitive Impairment Exhibit Altered Gut Microbiota Profiles. J Immunol Res. 2021;2021:1–7.

Li L, Wang L, Ding W, Wu J, Liu F, Liu J, et al. The Improvement Effects of Sika Deer Antler Protein in an Alzheimer's Disease Mouse Model via the Microbe–Gut–Brain Axis. Food Sci Nutr. 2024;13(1).

Jin Y, Chen J, Chai Q, Zhu J, Jin X. Exploration of Acupuncture Therapy in the Treatment of MCI Patients With the ApoE E4 Gene Based on the Brain Gut Axis Theory. BMC Complement Med Ther. 2023;23(1).

He Z, Liu Y, Li Z, Sun T, Li Z, Manyande A, et al. Gut Microbiota Regulates Circadian Oscillation in Hepatic Ischemia–reperfusion Injury Induced Cognitive Impairment by Interfering With Hippocampal Lipid Metabolism in Mice. Hepatol Int. 2023;17(6):1645–58.

Colombo A, Sadler R, Llovera G, Singh V, Roth S, Heindl S, et al. Microbiota Derived Short Chain Fatty Acids Modulate Microglia and Promote Aβ Plaque Deposition. Elife. 2021;10.

Husso A, Pessa-Morikawa T, Koistinen V, Kärkkäinen O, Kwon HN, Lahti L, et al. Impacts of Maternal Microbiota and Microbial Metabolites on Fetal Intestine, Brain, and Placenta. BMC Biol. 2023;21(1).

Saji N, Murotani K, Hisada T, Kunihiro T, Tsuduki T, Sugimoto T, et al. Relationship Between Dementia and Gut Microbiome Associated Metabolites: A Cross Sectional Study in Japan. Sci Rep. 2020;10(1).

Donaldson A, Fyfe C, Martin JC, SMITH E, Horgan G, Myint PK, et al. Aging Gut Brain Interactions: Pro Inflammatory Gut Bacteria Are Elevated in Fecal Samples From Individuals Living With Alzheimer's Dementia. Geriatrics. 2025;10(2):37.

Nota MHC, Dohm Hansen S, Nicolas S, Harris EP, Foley T, Nolan YM, et al. A Cafeteria Diet Blunts Effects of Exercise on Adult Hippocampal Neurogenesis but Not Neurogenesis Dependent Behaviours in Adult Male Rats. 2024;

Park JC, Im S. The Gut Immune Brain Axis in Neurodevelopment and Neurological Disorders. Microbiome Res Rep. 2022;1(4):23.

Vogt N, Kerby RL, Dill-McFarland KA, Harding S, Merluzzi AP, Johnson SC, et al. Gut Microbiome Alterations in Alzheimer's Disease. Sci Rep. 2017;7(1).

Kamer AR, Pushalkar S, B. Pourmolaee M. Haghighi H. Eshraghi M. Hamidi, Janal MN, Tang VA, Annam KRC, et al. Periodontal Inflammation and Dysbiosis Relate to Microbial Changes in the Gut. Microorganisms. 2024;12(6):1225.

Favero F, Barberis E, Gagliardi M, Espinoza S, Contu L, Gustincich S, et al. A Metabologenomic Approach Reveals Alterations in the Gut Microbiota of a Mouse Model of Alzheimer's Disease. Plos One. 2022;17(8):e0273036.

Shabbir U, Tyagi A, Elahi F, Aloo SO, Oh D. The Potential Role of Polyphenols in Oxidative Stress and Inflammation Induced by Gut Microbiota in Alzheimer's Disease. Antioxidants. 2021;10(9):1370.

Sha H, He X, Yan K, Li J, Xu L, Xie Y, et al. Blocking Coprophagy Increases the Levels of Inflammation and Depression in Healthy Mice as Well as Mice Receiving Fecal Microbiota Transplantation From Disease Model Mice Donors. Apmis. 2023;131(7):351–68.

González Dávila P, Schwalbe M, Danewalia A, Wardenaar R, Dalile B, Verbeke K, et al. Gut Microbiota Transplantation Drives the Adoptive Transfer of Colonic Genotype Phenotype Characteristics Between Mice Lacking Catestatin and Their Wild Type Counterparts. Gut Microbes. 2022;14(1).

He J, Wu J, Liu J, Wu H, Hua H. Cognitive Impairment and the Gut Brain Axis During 2014–2023: A Bibliometric Analysis. Front Neurol. 2024;15.

Kim J, Park H, Lee JH, Shin J, Cha B, Kwon KS, et al. Effect of Altered Gene Expression in Lipid Metabolism on Cognitive Improvement in Patients With Alzheimer's Dementia Following Fecal Microbiota Transplantation: A Preliminary Study. Ther Adv Neurol Disord. 2024;17.

Wang Y, Zhang Z, Li B, He B, Li L, Nice EC, et al. New Insights Into the Gut Microbiota in Neurodegenerative Diseases From the Perspective of Redox Homeostasis. Antioxidants. 2022;11(11):2287.

Putri SSF, Irfannuddin I, Murti K, Kesuma Y, Darmawan H, Koibuchi N. The Role of Gut Microbiota on Cognitive Development in Rodents: A Meta Analysis. J Physiol Sci. 2023;73(1):10.

Singh R, Chandrashekharappa S, Bodduluri SR, Baby BV, Hegde B, Kotla NG, et al. Enhancement of the Gut Barrier Integrity by a Microbial Metabolite Through the Nrf2 Pathway. Nat Commun. 2019;10(1).

Lavelle A, Sokol H. Gut Microbiota Derived Metabolites as Key Actors in Inflammatory Bowel Disease. Nat Rev Gastroenterol Hepatol. 2020;17(4):223–37.

Wang X, Sun G, Feng T, Zhang J, Huang X, Wang T, et al. Sodium Oligomannate Therapeutically Remodels Gut Microbiota and Suppresses Gut Bacterial Amino Acids Shaped Neuroinflammation to Inhibit Alzheimer's Disease Progression. Cell Res. 2019;29(10):787–803.

Zhao H, Wang D, Zhang Z, Xian J, Bai X. Effect of Gut Microbiota Derived Metabolites on Immune Checkpoint Inhibitor Therapy: Enemy or Friend? Molecules. 2022;27(15):4799.

Tian P, Hou Y, Wang Z, Jiang J, Qian X, Qu Z, et al. Probiotics Administration Alleviates Cognitive Impairment and Circadian Rhythm Disturbance Induced by Sleep Deprivation. Food Sci Hum Wellness. 2024;13(4):1951–61.

Jiang C, Wang H, Wang Q, Luo Y, Sidlow R, Han X. Prevalence of Chronic Pain and High Impact Chronic Pain in Cancer Survivors in the United States. Jama Oncol. 2019;5(8):1224.

Jia M, Shi L, Zhao Y, Hu X, Zhao J, Ding C, et al. Intermittent Fasting Mitigates Cognitive Deficits in Alzheimer's Disease via the Gut Brain Axis. 2022;

Kossowska M, Olejniczak S, Karbowiak M, Mosiej W, Zielińska D, Brzezicka A. The Interplay Between Gut Microbiota and Cognitive Functioning in the Healthy Aging Population: A Systematic Review. Nutrients. 2024;16(6):852.

Stevens M, Matosevic T, Suárez-Pinilla M, Pais S, Rossor MN, Knapp M. The Link Between Cognitive Health and Neighbourhood: Perceptions of the Public, and of Policy Makers, About Problems and Solutions. BMC Public Health. 2023;23(1).

Kartjito MS, Yosia M, Wasito E, Soloan G, Agussalim AF, Basrowi RW. Defining the Relationship of Gut Microbiota, Immunity, and Cognition in Early Life A Narrative Review. Nutrients. 2023;15(12):2642.

Strekalova YA, Modjarrad L, Midence S. Mechanisms of Young Professional Engagement in Health Policy Development: A Cultural Domain Approach. Front Public Health. 2024;12.

Cai W, Gao R, Qi J, Wang C, Hou N, Wei de L, et al. Doctor of Public Health Crisis Management and COVID 19 Prevention and Control: A Case Study in China. Front Public Health. 2022;10.

Hou K, Wu Z, Chen XY, Wang J, Zhang D, Xiao C, et al. Microbiota in Health and Diseases. Signal Transduct Target Ther. 2022;7(1).

Wilson L, Hamwi S, Zanni F, Lomazzi M. Global Public Health Policies: Gathering Public Health Associations' Perspectives. Glob Health Action. 2023;16(1).