# Visual Analysis of Research Trends in the Relationship Between Neurological Diseases and Gut Microbiota from 2000–2024: Postprint

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## Abstract

Background Nervous system diseases severely impair patients' quality of life, and their complex etiology involves multiple factors including genetics, infection, and immunity. In recent years, research on the involvement of gut microbiota in the pathogenesis of nervous system diseases through the gut-brain axis has garnered considerable attention, yet the hotspots and development trends of related research remain to be systematically reviewed. Objective To conduct visual analysis of literature related to nervous system diseases and gut microbiota, to understand the current status of domestic and international research, explore its hotspots and frontier trends, and provide reference for future research. Methods Relevant literature from the Web of Science Core Collection database from 2000-01-01 to 2024-07-29 were retrieved, and CiteSpace software was used to conduct visual analysis from multiple aspects including publication volume, document co-citation, highly cited literature, citation burst literature, keyword co-occurrence, country collaboration, institution collaboration, and author collaboration. Results A total of 5,239 articles were included. Since 2012, the annual publication volume has increased annually, surpassing 1,000 articles in 2022. Research hotspots primarily focus on Parkinson' s disease, Alzheimer' s disease, ischemic stroke, and amyotrophic lateral sclerosis. Document co-citation analysis indicates that the relationship between gut microbiota and nervous system diseases is becoming a research focus in recent years. Keyword co-occurrence analysis further identifies the frequent emergence of important research themes such as short-chain fatty acids, gut-brain axis, and gut microbiota dysbiosis, reflecting high attention to these directions. Analysis of highly cited articles and citation burst literature indicates that research trends mainly focus on the mechanisms through which gut microbiota influences neurodegenerative diseases and other central nervous system diseases, particularly the regulatory roles of short-chain fatty acids, gut microbiota diversity, and the gut-brain axis.

Conclusion Based on bibliometric analysis using CiteSpace, potential associations between gut microbiota and multiple nervous system diseases (such as Parkinson' s disease, Alzheimer' s disease, multiple sclerosis, etc.) are revealed. Intervening in microbiota dysbiosis holds promise for opening new avenues for treating nervous system diseases. Further longitudinal studies and clinical trials will be instrumental in validating this perspective and revealing the mechanisms of gut microbiota' s role in nervous system diseases.

## Full Text

**Original Article · Special Topic Research**

# A Bibliometric and Visualized Analysis of Research Trends in the Relationship between Neurological Disorders and Gut Microbiota (2000–2024)

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## Abstract

**Background:** Neurological disorders severely impact patients' quality of life, with complex etiologies involving genetic, infectious, immunological, and other factors. In recent years, research on the involvement of gut microbiota in the pathogenesis and progression of neurological diseases through the gut-brain axis has attracted widespread attention, yet the research hotspots and development trends in this field have not been systematically reviewed.

**Objective:** This study aims to conduct a visualized analysis of literature related to neurological disorders and gut microbiota to understand the current research landscape both domestically and internationally, explore hotspots and emerging trends, and provide a reference basis for future research.

**Methods:** Relevant literature was retrieved from the Web of Science Core Collection database from January 1, 2000 to July 29, 2024. Using CiteSpace software, visualized analysis was performed from multiple perspectives including publication volume, document co-citation, highly cited literature, citation burst literature, keyword co-occurrence, national collaboration, institutional collaboration, and author collaboration.

**Results:** A total of 5,239 articles were included. Since 2012, the annual publication volume has increased year by year, exceeding 1,000 articles in 2022. Research hotspots primarily focus on Parkinson' s disease, Alzheimer' s disease, ischemic stroke, and amyotrophic lateral sclerosis. Co-citation analysis reveals that the relationship between gut microbiota and neurological diseases is becoming a key research focus in recent years. Keyword co-occurrence analysis further identifies important research themes such as short-chain fatty acids, gut-brain axis, and gut microbiota dysbiosis, reflecting high attention to these directions. Analysis of highly cited articles and citation burst literature shows that research trends concentrate on the mechanisms through which gut microbiota influence neurodegenerative diseases and other central nervous system disorders, particularly the regulatory roles of short-chain fatty acids, gut microbiota diversity, and the gut-brain axis.

**Conclusion:** CiteSpace-based bibliometric analysis reveals potential associations between gut microbiota and various neurological diseases (such as Parkinson' s disease, Alzheimer' s disease, and multiple sclerosis). Intervening in microbiota dysbiosis may open new therapeutic avenues for neurological disorders. Further longitudinal studies and clinical trials will help validate this perspective and elucidate the mechanisms by which gut microbiota influence neurological diseases.

**Key words:** Nervous system diseases; Gut microbiota; CiteSpace; Bibliometrics; Visual analysis

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## Introduction

Neurological disorders represent a broad group of diseases affecting the central and peripheral nervous systems, including common conditions such as Alzheimer' s disease (AD), Parkinson' s disease (PD), epilepsy, multiple sclerosis (MS), and stroke [1-5]. These diseases may involve genetic, infectious, traumatic, immune system dysregulation, or environmental factors in their etiology. Depending on the underlying cause and affected areas, these disorders can lead to various symptoms including muscle weakness, numbness, memory loss, language difficulties, and behavioral changes, severely impacting patients' daily functioning and social activities [6].

Despite significant progress in understanding the etiology and pathogenesis of these diseases, challenges remain in early diagnosis, effective treatment, and dis-

ease progression intervention. In recent years, mounting evidence has demonstrated a close bidirectional interaction between gut microbiota and the nervous system, which importantly influences brain activity, behavior, and levels of neurotransmitter receptors and neurotrophic factors [7-11]. The gut-brain axis serves as a critical pathway connecting the gut and central nervous system, participating in the occurrence and development of multiple neurological diseases [6,12-15]. Gastrointestinal physiology and motility are subject to bidirectional influence from both local intestinal and central nervous system signals. Neurotransmitters, immune signals, hormones, and neuropeptides produced in the gut can in turn regulate brain function [16]. The gut, often termed the "second brain," communicates with the brain through complex neural, immune, and endocrine pathways [17]. Gut microbiota imbalance may exacerbate neurological disease progression by modulating immune responses, affecting neurotransmitter metabolism and release, and even influencing central nervous system function through microbial metabolites such as short-chain fatty acids (SCFAs) [5,18-20]. For example, research has found that gut microbial dysbiosis in PD patients correlates with $\alpha$-synuclein aggregation in the brain, a typical pathological feature of PD [21]. Studies on AD have also shown that changes in gut microbiota correlate with abnormal deposition of amyloid-$\beta$ and tau proteins in the brain, key pathological features of AD [22]. Additionally, immune-related neurological diseases such as MS also demonstrate correlations between gut microbiota and immune dysfunction [4]. Therefore, studying the relationship between gut microbiota and neurological diseases not only helps understand disease pathological mechanisms but also provides potential directions for exploring new therapeutic strategies.

As research on the relationship between neurological diseases and gut microbiota gradually deepens, systematic literature analysis becomes crucial for understanding research progress and future trends in this field. Bibliometrics and scientific knowledge mapping provide researchers with effective methods to reveal research hotspots, knowledge structures, and evolutionary trends through quantitative analysis of large volumes of literature [23]. Tools such as CiteSpace have been widely applied in biomedical research to help researchers visually identify academic frontiers and potential research opportunities [24].

This study utilizes the information visualization software CiteSpace to conduct a comprehensive knowledge mapping analysis of literature in the field of neurological diseases and gut microbiota from 2000–2024, aiming to reveal research hotspots, academic development trends, and future research directions. Through this analysis, we hope to provide researchers with a panoramic review of the field and offer theoretical basis and data support for future basic and clinical research.

### 1.1 Literature Sources

This study conducted literature retrieval through the Web of Science Core Collection database using advanced search mode, focusing on the subject terms

"neurological disorders" and "gut microbiota." The specific search strategies were as follows:

**#1: Neurological disorders**
TS=( "Neurodegenerative disease" OR "Neurological disorder" OR "Central nervous system disorder" OR Neuroinflammation OR "Alzheimer' s disease" OR "Parkinson' s disease" OR "Multiple sclerosis" OR "Amyotrophic lateral sclerosis" OR ALS OR "Huntington' s disease" OR Epilepsy OR Dementia OR "Cognitive impairment" OR Stroke OR "Brain injury" OR "Spinal cord injury" OR "Peripheral neuropathy" OR "Tourette syndrome" OR "Cerebrovascular disease" OR "Ischemic stroke" OR "Hemorrhagic stroke" OR "Transient ischemic attack" OR TIA OR "Vascular dementia" OR "Cerebral small vessel disease" OR "Intracerebral hemorrhage" OR "Subarachnoid hemorrhage" OR "Cavernous malformation" OR "Arteriovenous malformation" OR Neurofibromatosis OR "Brain tumor" OR Glioma OR Glioblastoma OR Astrocytoma OR Meningioma OR Medulloblastoma OR "Pituitary adenoma" OR Schwannoma OR Neuroblastoma OR Ependymoma OR "Primary CNS lymphoma" OR "Spinal cord tumor" OR "Spinal glioma" OR "Spinal meningioma" OR "Spinal schwannoma" OR "Spinal ependymoma" OR "Metastatic brain tumor" )

**#2: Gut microbiota**
TS=( "Gut microbiota" OR "Gut microbiome" OR "Gut microorganisms" OR "Gut bacteria" OR "Gut metagenome" OR "Gut fungi" OR "Gut pathogens" OR "Gut beneficial bacteria" OR "Gut viruses" OR "Gut microbiota metabolites" OR "Gut bacteriophages" OR "Gut probiotics" OR "Gut symbiotic bacteria" OR "Gut microecology" OR "Gut microenvironment" OR "Microbiota-gut-brain axis" OR "Brain-gut axis" OR "Lung-gut axis" OR "Kidney-gut axis" OR "Fecal microbiota transplantation" OR "Gut microbiota colonization" )

All search terms used exact retrieval methods, with the search timeframe ranging from January 1, 2000 to July 29, 2024. Document types were limited to original research and reviews, while conference papers were excluded. Search results included only English literature.

### 1.2 Research Tools and Methods

This study utilized the information visualization software CiteSpace 6.3.R6, designed and developed by CHEN et al. [24-25], to create visual knowledge maps of the included literature. The analysis encompassed research hotspots and trends (keyword clustering analysis, document co-citation analysis, keyword co-occurrence and burst analysis), national/regional and institutional collaboration network analysis, and author collaboration network analysis.

Specific parameter settings were as follows: time span 2000–2024, single time slice of 1 year; threshold set at Top N=50, with pathfinder network pruning method applied.

## Results

### 2.1 Publication Volume Statistics in Neurological Diseases and Gut Microbiota Field (2000–2024)

From 2000–2024, a total of 85,278 articles on gut microbiota were published (annual publication trends shown in [Figure 1: see original paper]). Analysis of gut microbiota research across different disciplines revealed that neuroscience and clinical neurology fields published 2,987 (3.50%) and 1,073 (1.26%) articles respectively, ranking 11th and 34th among all disciplines (see [Figure 2: see original paper]). Statistical results for literature specifically related to neurological diseases and gut microbiota showed that from 2000–2024, the field demonstrated a steady increase in publication volume, with citations reaching 124 times, reflecting the growing academic influence and annual expansion of research in this domain (see [Figure 3: see original paper]).

### 2.2 Co-citation Clustering Network of Neurological Diseases and Gut Microbiota Literature

The visualized clustering map of the reference co-citation network generated by CiteSpace is shown in [Figure 4: see original paper]. The co-citation network is divided into multiple clusters, with closely connected references within the same cluster and relatively loose connections between different clusters. Cluster labels were generated using the log-likelihood ratio (LLR) test method. The network' s modularity value (Q value) is 0.8144, indicating clear classification in the professional scientific domain [23]. Meanwhile, the average silhouette value (S value) of clusters is 0.9341, reflecting high consistency and reliability of the clustering results [23]. Generally, Q>0.3 and S>0.5 indicate good clustering effects, demonstrating that this study' s clusters have significant structure and high reliability [26].

The 16 largest literature clusters in the co-citation network, sorted by member quantity, are: PD, depression, AD, autoimmunity, multiple sclerosis, ischemic stroke, obesity, asthma, epilepsy, amyotrophic lateral sclerosis, gut microbiota, short-chain fatty acids, *Akkermansia muciniphila*, preterm, minerals, and immune signaling (see ). All clusters demonstrate high homogeneity and high silhouette scores, indicating good internal consistency of clustering results. The average publication year of clusters further reflects the cutting-edge nature and timeliness of these research fields.

Temporal trend analysis shows that since 2020, PD, AD, ischemic stroke, and amyotrophic lateral sclerosis remain concentrated research areas (see [Figure 5: see original paper]). The relationship between these diseases and gut microbiota continues to attract widespread attention, indicating that research in this field maintains high activity and has important clinical significance.

### 2.3 Analysis of Highly Cited Articles

Among highly cited literature, research in the PD field is particularly prominent (see [Figure 6: see original paper]), with 4 of the top 10 most frequently cited articles (see ) focusing on this area, reflecting strong research interest in PD gut microbiota. SAMPSON et al. [21] demonstrated that $\alpha$-synuclein aggregation is closely related to motor dysfunction in PD, with gut microbiota playing a key role in this process. The study found that antibiotics could alleviate PD symptoms, but reintroduction of microbes might exacerbate the condition, revealing the central role of the gut-brain axis in PD. Similarly, SCHEPERJANS et al. [27] found through gut microbial analysis of PD patients and healthy controls that significant reduction of Prevotellaceae correlated with motor symptom severity, further highlighting the important position of gut microbiota in PD pathogenesis. UNGER et al. [28] supplemented this field by noting that SCFA levels were significantly decreased in PD patients, suggesting that microbial changes might affect PD development through influencing intestinal function. Additionally, KESHAVARZIAN et al. [29] showed that $\alpha$-synuclein aggregation and inflammatory changes in the colon of PD patients reflected that pro-inflammatory dysbiosis of gut microbiota might be closely related to disease progression. These studies consistently emphasize the potential role of gut microbiota in PD, providing important biomarkers and intervention targets for future therapeutic strategies.

Beyond PD, gut microbiota is also crucial for maintaining central nervous system homeostasis and regulating immune function. ERNY et al. [30] demonstrated that microbiota deficiency leads to microglial dysfunction in germ-free mice, revealing the important role of gut microbiota in maintaining microglial homeostasis. SCFAs are confirmed as important molecules regulating microglial function, suggesting that host microbiota may regulate neural health and immune homeostasis through SCFAs. Furthermore, studies have found that germ-free mice exhibit increased blood-brain barrier (BBB) permeability from fetal stage, and exposure to pathogen-free gut microbiota can improve this permeability, showing the long-term interaction between gut microbiota and BBB [31]. These studies provide new directions for understanding how gut microbiota regulates neural function and immune balance.

AD-related research also reveals significant changes in gut microbiota. Studies show that AD patients have markedly decreased microbial diversity, accompanied by reduced Firmicutes and Bifidobacteria and increased Bacteroidetes, which correlate with AD biomarkers in cerebrospinal fluid, suggesting the potential role of gut microbiota in AD progression [32]. Meanwhile, cognitively impaired patients show increased pro-inflammatory gut microbiota (e.g., *Escherichia/Shigella*), elevated pro-inflammatory cytokines, and reduced anti-inflammatory cytokines. This gut microbiota imbalance is closely related to brain amyloid deposition and peripheral inflammation [22]. These findings provide potential targets for early diagnosis and intervention of AD.

In MS research, changes in gut microbiota are also closely related to immune regulation. JANGI et al. [4] analyzed gut microbiota of MS patients and healthy controls, finding increased abundance of *Methanobrevibacter* and *Akkermansia* and significant reduction of *Butyricimonas* in MS patients. These changes were closely related to immune-related gene expression, revealing that gut microbiota may participate in MS pathogenesis by regulating T cell and monocyte functions. Additionally, increased methane levels in exhaled breath correlated with increased intestinal *Methanobrevibacter*, further suggesting the important role of gut microbiota in MS.

In recent years, gut-brain axis research has received increasing attention, with the microbiome being widely studied as a key regulator of this axis. CRYAN et al. [33] demonstrated that gut microbiome communicates with the brain through multiple mechanisms such as the immune system, tryptophan metabolism, and vagus nerve. These mechanisms are influenced by various factors in early life, such as infection, antibiotic use, and environmental stress, which significantly alter microbiome composition in later stages, thereby affecting neurodevelopment and function. These findings not only associate gut microbiota with various neuropsychiatric disorders but also provide insights for future microbiota-based therapeutic strategies.

### 2.4 Citation Bursts

Recent research has primarily focused on the role of gut microbiota in neurodegenerative diseases. Literature from 2022–2024 in the field of neurological diseases and gut microbiota was sorted by citation burst intensity, with results shown in [1-3,34-42]. In PD, ROMANO et al. [2] found significant dysbiosis in PD patients' gut microbiota, characterized by enrichment of *Lactobacillus*, *Akkermansia*, and *Bifidobacterium*, and reduction of SCFA-producing bacteria such as *Faecalibacterium*, potentially leading to pro-inflammatory states and gastrointestinal symptoms. AHO et al. [34] compared fecal samples from PD patients and healthy controls, finding elevated calprotectin levels and reduced SCFA levels in PD patients, which correlated with age and symptoms, revealing potential changes in microbe-host interactions.

Additionally, SRIVASTAV et al. [35] showed that probiotic mixtures could protect dopaminergic neurons and increase butyrate levels, thereby improving neurodegeneration. In AD research, KESIKA et al. [3] noted that gut microbiota influences disease mechanisms through the gut-brain axis, and improving microbial composition may become a preventive strategy for AD. COLOMBO et al. [36] found that SCFAs promote A$\beta$ deposition in AD mouse models, emphasizing their important role in the gut-brain axis. LING et al. [37] analyzed fecal microbiota of AD patients and found significantly reduced microbial diversity, suggesting that gut microbiota imbalance may serve as a non-invasive biomarker for AD. MARIZZONI et al. [38] found that blood levels of lipopolysaccharide and SCFAs positively correlated with AD-related brain pathology. DEN et al. [39] conducted a meta-analysis showing that probiotics could significantly

improve cognitive performance in AD patients, possibly by reducing inflammatory and oxidative biomarkers. Regarding stroke, TAN et al. [1] found that gut microbiota and SCFAs were dysregulated in acute ischemic stroke patients, suggesting SCFAs may serve as prognostic markers. XU et al. [40] demonstrated that post-stroke gut microbiota dysbiosis correlates with stroke prognosis, emphasizing the potential value of the gut-brain axis in treatment. These studies collectively reveal the importance of gut microbiota in neurodegenerative diseases and its prospects as an intervention target.

### 2.5 Keyword Co-occurrence

Keywords provide accurate depiction of research hotspots during specific periods and can clearly show research status. [Figure 7: see original paper] displays keywords with high co-occurrence rates, where larger font size indicates higher keyword frequency. Frequent appearance of gut microbiota, PD, AD, multiple sclerosis, oxidative stress, SCFAs, and microbiota-gut-brain axis reflects the main research focuses in this field.

### 2.6 Collaboration Network

A total of 104 countries/regions have published related papers. Ranked by publication quantity, the top 5 countries/regions are China (1,953 articles), United States (1,336 articles), Italy (409 articles), United Kingdom (256 articles), and Germany (230 articles). [Figure 8: see original paper] shows the collaboration network among countries/regions, containing 104 nodes and 396 connecting lines. Nodes and lines represent countries/regions and their collaborative relationships respectively. Larger nodes indicate more publications; wider lines indicate stronger collaborations.

### 2.7 Collaborating Institutions

From 2006–2024, 515 institutions published papers in this field. The top 9 institutions (with >50 publications) are Zhejiang University, Harvard Medical School, Capital Medical University, Shanghai Jiao Tong University, Southern Medical University, Chinese Academy of Sciences, Central South University, Nanjing Medical University, and University of California, San Francisco. The generated institutional network diagram shows 515 nodes and 1,740 connecting lines, representing institutions and their collaborative relationships, demonstrating active cooperation among different institutions (see [Figure 9: see original paper]).

### 2.8 Collaborating Authors

From 2006–2024, a total of 696 authors published papers in this field. Among them, ZHANG XIN had the most publications (20), ranking first, followed by LIU JIAMING (18); LI JING, KIM DONG-HYUN, and SUN JING tied for third (16 each). The author collaboration network is shown in [Figure 10: see

original paper], containing 696 nodes and 971 collaboration lines, with relatively limited collaboration among individual authors.

## Discussion

This study conducted a bibliometric analysis of literature on gut microbiota and neurological disorders since 2000 using CiteSpace, revealing potential connections between gut microbiota and neurological diseases and systematically summarizing research hotspots and trends in this field. Although the relationship between gut microbiota and neurological diseases has received widespread attention, current research remains in preliminary stages, requiring further exploration of specific mechanisms and providing clearer guidance for future research priorities.

### 3.1 Trends in Highly Cited Literature and Citation Bursts

Analysis of highly cited literature reveals that some studies on gut microbiota and neurological diseases have established a solid theoretical foundation in recent years. Particularly, certain studies have elucidated the mechanisms of the gut-brain axis through animal models and clinical trials, such as the close relationships between SCFAs, gut microbiota diversity, dysbiosis, and neurodegenerative diseases (e.g., PD, AD) [21,29]. These studies have not only produced profound academic impact but also provided potential intervention targets for clinical treatment.

Citation burst analysis shows that with advances in gut microbiota research, some articles have received numerous citations within short timeframes. These articles typically focus on specific mechanisms linking gut microbiota to central nervous system diseases, particularly regarding SCFA functions, gut microbiota regulation of immune responses, and direct effects on brain function [1,34,36,40]. Additionally, clinical trials targeting gut microbiota interventions have begun receiving increasing attention [35], indicating that research in this field is gradually transitioning from basic science to clinical applications.

### 3.2 Research Hotspots: Gut Microbiota, SCFAs, and Gut-Brain Axis

Through keyword co-occurrence analysis, this study further reveals the frequent appearance of research themes including gut microbiota, SCFAs, and gut-brain axis, reflecting the main concerns in this field. SCFAs, particularly butyrate, acetate, and propionate, are considered biologically important metabolites produced by gut microbiota [35]. Increasing evidence shows that SCFAs can affect the nervous system through influencing intestinal barrier function and modulating the immune system, and may also regulate neurotransmitter levels in the brain, thereby influencing the occurrence and development of neurodegenerative diseases [5,18-20].

The gut-brain axis, as a bridge between gut microbiota and the central ner-

vous system, has become an important research direction in this field. Gut microbes communicate with the brain through neural, immune, and endocrine pathways, influencing neurodevelopment, behavior, emotional regulation, and disease processes. This mechanism provides new perspectives for understanding the association between gut microbiota and neurological diseases and may offer theoretical basis for future clinical interventions.

### 3.3 In-depth Analysis: Relationship between Microbiota Dysbiosis and Neurological Diseases

Increasing evidence indicates that gut microbiota dysbiosis has become an important risk factor for various neurological diseases. Neurological disorders including AD, PD, MS, and ischemic stroke all exhibit characteristics associated with specific gut microbiota disturbances. Microbiota participate in neuropathological processes through multiple mechanisms including influencing inflammatory responses, neurotransmitter metabolism, barrier system homeostasis, and microbial metabolites, suggesting the key role of the microbiota-gut-brain axis in neurological diseases.

**3.3.1 Microbiota Dysbiosis Associated with Early Diagnosis, Inflammation, and Metabolic Disorders in AD** A study of 476 Chinese participants (covering 5 pathological stages of AD) through fecal metagenomic analysis found that over 10% of microbial species and gene families changed significantly during AD progression, closely related to neuroinflammation and neurotransmitter disorders [43]. Specific microbial gene families (e.g., those involved in carbohydrate and amino acid metabolism) showed high discriminative ability in AD diagnosis (cross-validation AUC=0.80, independent validation AUC=0.75) and were associated with genera such as *Alistipes* and *Bacteroides*. Fecal microbiota transplantation (FMT) experiments further confirmed that microbiota from AD patients could accelerate cognitive decline in 5xFAD mice, suggesting gut microbiota may become an important target for intervening in AD progression [43]. Additionally, a team from Capital Medical University led by LIU Xicheng found that in AD model mice, reduced *Bacteroides ovatus* and increased *Clostridium* correlated positively with A$\beta$ deposition. Supplementation with *B. ovatus* or its metabolite lysophosphatidylcholine (LPC) could improve cognitive impairment and reduce AD pathology by regulating ferroptosis-related pathways through the GPR119 receptor [44]. Another study in 3×Tg-AD mice revealed that with aging, butyrate-producing bacteria decreased and cecal butyrate levels declined, preceding cognitive impairment and tau protein abnormalities. Oral administration of the butyrate prodrug tributyrin could improve memory function and delay pathological progression [45].

**3.3.2 Intertwined Mechanisms of Microbiota-Amino Acid Metabolism-Inflammation in PD** PD-related research indicates that gut microbiota plays an important role in its pathogenesis and progression. A study of 106 PD patients and 114 controls found that plasma branched-chain amino

acids (BCAA) and aromatic amino acids (AAA) levels were significantly decreased in PD patients, negatively correlating with clinical stages. Gut function analysis suggested that genes involved in BCAA biosynthesis (e.g., *ilvB*, *ilvC*, *ilvD*, *ilvN*) were less abundant in advanced PD patients, indicating that microbiota metabolic disorders and amino acid imbalance may be one of the PD pathogenic mechanisms [46]. A prospective metabolomics study from the EPIC4PD cohort further noted that pre-onset microbial metabolites (e.g., valine, butyrate, propionate metabolic pathways) were associated with PD risk, particularly significant in males, smokers, and obese individuals, suggesting these metabolites may serve as early predictive biomarkers for PD [47].

In clinical interventions, a Chinese randomized double-blind placebo-controlled study showed that FMT treatment could significantly improve autonomic and gastrointestinal symptoms in mild-to-moderate PD patients and increase gut microecological complexity without serious adverse events [48]. However, results from another Finnish randomized controlled trial were inconsistent, with the FMT group showing no advantage in clinical score improvement and higher gastrointestinal adverse reactions (53% vs. 7%), suggesting donor selection may be an important factor affecting FMT efficacy [49]. These discrepancies may also be related to different study designs, such as different primary endpoint assessment dimensions (overall symptoms vs. single motor symptoms), FMT administration methods differences (nasointestinal tube vs. enema combined with oral capsules), sample sizes, and follow-up durations. Additionally, donor microbiota composition and its matching with recipients may also critically influence FMT clinical outcomes.

Experimental studies also support the role of gut microbiota in PD pathogenesis. For example, supplementation with the butyrate-producing bacterium *B. producta* could inhibit microglial activation and improve motor dysfunction in PD model mice by regulating the RAS-NF- B signaling pathway [50]; while transplanting microbiota from PD patients into mice could induce loss of tyrosine hydroxylase-positive neurons in the midbrain, motor dysfunction, and reduction of Th17 cells, suggesting microbiota may affect the central nervous system through immune-inflammatory mechanisms [51].

**3.3.3 Exploration of Microbial Mechanisms in Other Neurological Diseases** Besides AD and PD, other neurological diseases also show close associations with gut microbiota. For example, MS patients have significantly reduced bile acid-metabolizing microbiota, and these metabolites can induce Treg differentiation and inhibit Th17 inflammation, suggesting their key role in immune homeostasis [52]. The acute phase of ischemic stroke can lead to gut microbiota dysbiosis and intestinal barrier damage, triggering "leaky gut," endotoxemia, and bacterial translocation; while microbial metabolites (such as SCFAs, TMAO, lipopolysaccharide) can activate inflammatory pathways and affect brain function [53]. Multiple barrier systems in the microbiota-gut-brain axis (intestinal epithelial barrier, blood-brain barrier, blood-cerebrospinal fluid

barrier) play central roles in maintaining nervous system homeostasis. Barrier function integrity depends on regulation by SCFAs, tryptophan metabolites, bile acids, polyamines, and other microbial metabolites. Increased barrier permeability is a key pathological link in various neurological diseases (such as AD, PD, stroke), further illustrating the potential of microbiota-regulated barrier function in preventing neurodegenerative diseases [54].

Existing studies have preliminarily revealed the close connection between gut microbiota dysbiosis and neurological diseases, covering multiple aspects including metabolic pathway disorders, inflammatory activation, and barrier dysfunction. However, most current evidence still comes from animal experiments or cross-sectional studies, lacking large-scale, long-term follow-up population studies and standardized clinical trials. Therefore, future research should further explore the mechanisms of gut microbiota dysbiosis in neurological diseases and develop intervention strategies targeting gut microbiota, such as dietary regulation, microbiome modulation, and miRNA-based precision therapy, to find new prevention and treatment approaches for neurological diseases.

## Conclusion

Through bibliometric analysis, this study systematically summarized the potential associations between gut microbiota and neurological diseases and revealed research hotspots and frontier trends in this field. Based on CiteSpace analysis results, gut microbiota intervention may open new directions for neurological disease treatment, but requires further validation through more longitudinal studies and clinical trials. Future research should strengthen translation from basic to clinical science and promote the application of gut microbiota in neurological disease treatment.

**Author Contributions:** GUO Yangyang was responsible for literature data analysis, figure production, quality control and verification, manuscript writing and revision, and overall responsibility for the paper; ZHANG Linlin was responsible for literature retrieval, screening, and deduplication; SHI Guangzhi was responsible for data verification, quality control, and manuscript revision; ZHANG Jindong was responsible for topic selection, manuscript revision, overall structural control, final approval, and overall responsibility for the paper.

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