International Journal of Creative and Open Research in Engineering and Management
ISSN: **3108-1754 (Online)**
Volume 02 Issue 06 June-2026 | Impact Factor: 3.5

"Role of Gut Microbiota in Neurotransmitter Regulation and Brain Function: A Review"

Gunlu Gangmei[1] , Jackricky N.Sangma[2] ,H.Suraj Singha[2] ,Marli Ango[2] , Hmangte Wendy Kom[2], Samir Moirangthem[2]

1Affiliation: Medical Lab. Technologist , Department of pathology ,AIIMS Bathinda Punjab, India
Email id: gangmeigungun529@gmail.com
2Affiliation: Faculty of Allied & Healthcare Sciences, Assam down town University, Sankar Madhab Path, Gandhi Nagar, Panikhaiti, Guwahati, Assam, India, PIN – 781026
Email id: sangmajackricky@gmail.com
2Affiliation: Faculty of Allied & Healthcare Sciences, Assam down town University, Sankar Madhab Path, Gandhi Nagar, Panikhaiti, Guwahati, Assam, India, PIN – 781026
Email id: suraj.singha@adtu.in
2Affiliation: Faculty of Allied & Healthcare Sciences, Assam down town University, Sankar Madhab Path, Gandhi Nagar, Panikhaiti, Guwahati, Assam, India, PIN – 781026
Email id: marliango99@gmail.com
2Affiliation: Faculty of Allied & Healthcare Sciences, Assam down town University, Sankar Madhab Path, Gandhi Nagar, Panikhaiti, Guwahati, Assam, India, PIN – 781026
Email id: hmangtewendy@gmail.com
2Affiliation: Faculty of Allied & Healthcare Sciences, Assam down town University, Sankar Madhab Path, Gandhi Nagar, Panikhaiti, Guwahati, Assam, India, PIN – 781026
Email id: samirthem1999@gmail.com

How to Cite this Article:

Gangmei, G., N.Sangma, J., Singha, H., Ango, M., Kom, H. W. & Moirangthem, S. (2026). "Role of Gut Microbiota in Neurotransmitter Regulation and Brain Function: A Review". International Journal of Creative and Open Research in Engineering and Management, 02(6). https://doi.org/10.55041/ijcope.v2i6.376

https://doi.org/ 10.55041/ijcope.v2i6.376

Abstract

Background: The gut microbiota constitutes a complex ecosystem of trillions of microorganisms that exert profound effects on host physiology, including brain function and behavior. The bidirectional communication network between the gastrointestinal tract and the central nervous system, termed the gut-brain axis, has emerged as a critical regulator of neurological health.

Objective: This review synthesizes current evidence from peer-reviewed literature on the mechanisms by which gut microbiota modulate neurotransmitter systems and influence brain function, with emphasis on clinical translation and diagnostic applications.

Methods: A systematic literature search was conducted using PubMed and Scopus databases (2015–2026) with Boolean operators: ("gut microbiota" OR "gut microbiome") AND ("neurotransmitters" OR "serotonin" OR "dopamine" OR "GABA") AND ("brain function" OR "gut-brain axis"). Inclusion criteria comprised peer-reviewed original research and review articles in English, with preference for studies published in the last decade. The selection process followed PRISMA guidelines, yielding 127 articles for full-text review and 68 for final synthesis.

Results: Emerging evidence demonstrates that gut bacteria produce or modulate multiple neuroactive compounds, including serotonin, dopamine, gamma-aminobutyric acid (GABA), and short-chain fatty acids. Commensal species such as *Enterococcus faecalis* synthesize

dopamine, while *Escherichia coli* and *Blautia producta* generate GABA. Microbial metabolites influence brain function through neural (vagus nerve), endocrine (hypothalamic-pituitary-adrenal axis), and immune pathways. Dysbiosis is consistently associated with neuropsychiatric conditions including depression, anxiety, and neurodegenerative diseases such as Alzheimer's and Parkinson's disease. Clinical applications, including microbiome-based biomarkers and therapeutic interventions (probiotics, prebiotics, fecal microbiota transplantation), show promise but require validation through large-scale randomized controlled trials.

Conclusion: The gut microbiota represents a modifiable target for neurological and psychiatric interventions. Future research must establish causality through mechanistic studies and develop standardized protocols for clinical translation.

Keywords: *gut microbiota; gut-brain axis; neurotransmitters; GABA;; neuroinflammation*

1. Introduction

The human gastrointestinal tract harbors a vast and dynamic community of microorganisms bacteria, archaea, fungi, and viruses collectively termed the gut microbiota. This microbial ecosystem, comprising over 150 times the genetic material of the human genome, has co-evolved with its host to establish a mutually beneficial relationship essential for metabolic, immunological, and neurological homeostasis [1, 2]. The concept of the microbiota-gut-brain axis (MGBA) has emerged from accumulating evidence demonstrating bidirectional communication between the gut and the central nervous system (CNS), mediated by neural, endocrine, immune, and metabolic pathways [3].

Groundbreaking studies in germ-free animal models established that the absence of microbiota leads to profound neurodevelopmental abnormalities, altered stress responses, and behavioral changes that can be partially reversed by microbial colonization [4]. These findings provided the first causal evidence linking gut microbes to brain function. Subsequent research has identified specific microbial species and their metabolites including short-chain fatty acids (SCFAs), tryptophan derivatives, and neurotransmitter-like molecules as key mediators of gut-brain communication [5].

The clinical relevance of the MGBA is underscored by consistent observations of gut dysbiosis in patients with neuropsychiatric and neurodegenerative disorders, including major depressive disorder (MDD), anxiety disorders, autism spectrum disorder (ASD), Parkinson's disease (PD), and Alzheimer's disease (AD) [1, 6]. These associations have sparked intense interest in microbiome-targeted interventions as potential therapeutic strategies. However, significant gaps remain in our mechanistic understanding, and the translation of preclinical findings to clinical practice faces substantial challenges.

This review aims to provide a comprehensive synthesis of current evidence on the role of gut microbiota in neurotransmitter regulation and brain function, with emphasis on: (1) the composition and functional capacity of the gut microbiota, (2) mechanistic pathways of gut-brain communication, (3) microbial regulation of specific neurotransmitter systems, (4) implications for brain function and disease, and (5) clinical and diagnostic applications in medical laboratory technology. By critically evaluating the available literature and identifying research gaps, this review seeks to inform future investigations and facilitate the development of microbiome-based precision medicine approaches.

2. Methodology

2.1 Search Strategy

A systematic literature search was conducted using PubMed and Scopus databases, with the final search performed in March 2026. The following Boolean search strategy was employed:

```
("gut microbiota" OR "gut microbiome" OR "intestinal microbiota" OR "gastrointestinal microbiome")
AND
("neurotransmitters" OR "serotonin" OR "5-HT" OR "dopamine" OR "GABA" OR "gamma-aminobutyric acid" OR "short-chain fatty acids" OR "SCFAs")
AND
("brain function" OR "gut-brain axis" OR "microbiota-gut-brain axis" OR "neuroinflammation" OR "cognition" OR "mood disorders")
```

Additional hand-searching of reference lists from included articles was performed to identify relevant studies not captured by the initial database search.

2.2 Inclusion and Exclusion Criteria

Inclusion criteria:

- Peer-reviewed original research articles and systematic reviews
- Articles indexed in PubMed or Scopus
- Published between January 2015 and March 2026 (landmark studies published prior to 2015 considered if essential)
- English language publications
- Studies investigating gut microbiota composition, function, or interventions in relation to neurotransmitter systems or brain function
- Human studies, animal models, and in vitro investigations

Exclusion criteria:

- Non-peer-reviewed sources (conference abstracts, editorials, commentaries, blog posts)
- Articles not indexed in PubMed or Scopus
- Grey literature, including theses and institutional reports
- Studies published in predatory journals as identified by established criteria
- Articles with insufficient methodological detail or unverifiable data

2.3 Study Selection Process

The study selection process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [7]. Initial database searches yielded 847 records (PubMed: 412; Scopus: 435). After removal of duplicates (n = 203), 644 records underwent title and abstract screening. Two independent reviewers screened the records against inclusion criteria, with disagreements resolved by consensus or consultation with a third reviewer. Following screening, 127 full-text articles were assessed for eligibility. Of these, 59 were excluded: 23 for insufficient relevance to neurotransmitter regulation, 18 for methodological quality concerns, 12 for duplication of findings, and 6 for inability to verify data sources. The final synthesis included 68 articles, comprising 34 original research studies, 28 systematic reviews or meta-analyses, and 6 landmark foundational studies.

Table 1. PRISMA Flow Summary

Stage	Records (n)
Records identified through PubMed	412
Records identified through Scopus	435
Total records identified	847
Duplicates removed	203
Records screened (title/abstract)	644
Records excluded	517
Full-text articles assessed for eligibility	127
Full-text articles excluded (total)	59
- Insufficient relevance	23
- Methodological quality concerns	18

- Duplication of findings	12
- Data source unverifiable	6
Studies included in final synthesis	68

2.4 Data Extraction and Synthesis

Data were extracted from included studies using a standardized form capturing: first author and year, study design, sample characteristics, microbiota analysis methods, neurotransmitter or metabolite measurements, brain function outcomes, and key findings. Given the heterogeneity of study designs and outcome measures, a narrative synthesis approach was adopted, organizing findings by thematic categories corresponding to the review objectives.

3. Review of Literature

3.1 Overview of Gut Microbiota Composition

The human gut microbiota is dominated by six bacterial phyla: *Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria,* and *Verrucomicrobia* [1, 8]. Firmicutes and Bacteroidetes typically constitute 70–90% of the total microbial community, with the remaining phyla present in lower relative abundance. This composition varies along the gastrointestinal tract, with Bacilli and Actinobacteria predominating in the small intestine, while Bacteroidetes and Lachnospiraceae dominate the colon [9].

The functional capacity of the gut microbiota extends far beyond taxonomic composition. Metagenomic analyses have revealed that the collective microbial genome the microbiome encodes enzymes and metabolic pathways absent from the human genome, enabling the degradation of complex polysaccharides, synthesis of vitamins, and production of a diverse array of bioactive metabolites [5, 10]. Key functional modules include:

- Carbohydrate-active enzymes (CAZymes) for dietary fiber fermentation
- Tryptophan metabolism pathways for indole derivative production
- Bile acid transformation enzymes
- Neurotransmitter synthesis and degradation pathways

3.2 Gut-Brain Axis Mechanisms

The gut-brain axis encompasses multiple, interconnected pathways through which the gut microbiota communicates with the CNS [3, 11].

3.2.1 Neural Pathways

The vagus nerve serves as the primary neural conduit for gut-brain signaling. Afferent vagal fibers, which constitute approximately 80% of vagal nerve fibers, sense mechanical and chemical stimuli from the gastrointestinal tract and transmit this information to the nucleus tractus solitarius in the brainstem [12]. Importantly, vagal afferents do not directly contact the gut lumen but instead respond to signals from enteroendocrine cells, enteric neurons, and microbial metabolites that reach the basolateral compartment [11].

Microbial metabolites, including SCFAs, lipopolysaccharides (LPS), and GABA, activate vagal afferents through specific receptors on enteroendocrine cells and enteric neurons [13]. Studies employing vagotomy have demonstrated that the behavioral effects of certain probiotic strains, such as *Lactobacillus rhamnosus,* are abrogated following vagal disruption, confirming the necessity of this pathway for microbiota-brain communication [14].

3.2.2 Endocrine Pathways

The hypothalamic-pituitary-adrenal (HPA) axis constitutes the central endocrine stress response system. Gut microbiota influence HPA axis activity through multiple mechanisms: (1) microbial metabolites modulate corticotropin-releasing hormone (CRH) expression, (2) SCFAs enhance glucocorticoid receptor sensitivity, and (3) microbial products regulate adrenal steroidogenesis [15].

Enteroendocrine cells (EECs), scattered throughout the intestinal epithelium, function as chemosensory cells that detect microbial metabolites and release hormones including serotonin (5-hydroxytryptamine, 5-HT), glucagon-like peptide-1 (GLP-1), and peptide YY (PYY) [16]. These hormones signal to the CNS via vagal afferents or enter the circulation to exert central effects.

3.2.3 Immune Pathways

The gut microbiota critically shapes systemic immune function. Microbial products, particularly SCFAs, promote the differentiation of regulatory T cells (Tregs) and modulate cytokine production [17]. Dysbiosis leads to increased intestinal permeability often termed "leaky gut" allowing translocation of bacterial products, including LPS, into the circulation. Circulating LPS activates Toll-like receptor 4 (TLR4) on immune cells and brain endothelial cells, triggering neuroinflammation through the release of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) [18].

3.3 Microbial Regulation of Neurotransmitters

Table 2. Gut Bacterial Species with Neurotransmitter-Modulating Activity

Bacterial Species	Neuroactive Compound	Mechanism	Reference
Enterococcus faecalis	Dopamine, Tyramine	Direct synthesis from tyrosine	[5]
Escherichia coli	GABA, L-DOPA	Glutamate decarboxylase; tyrosine conversion	[5, 19]
Blautia producta	GABA, L-DOPA	Glutamate decarboxylase; tyrosine conversion	[5]
Lactococcus lactis	L-DOPA	Tyrosine conversion	[5]
Clostridium symbiosum	L-DOPA	Tyrosine conversion	[5]
Bacteroides fragilis	L-DOPA	Tyrosine conversion	[5]
Prevotella copri	L-DOPA	Tyrosine conversion	[5]
Spore-forming Clostridium spp.	Serotonin (indirect)	TPH1 induction via SCFAs	[20]
Lactobacillus rhamnos	GABA (indirect)	Vagal activation; GABA receptor modulation	[14]

Abbreviations: GABA, gamma-aminobutyric acid; L-DOPA, levodopa; SCFAs, short-chain fatty acids; TPH1, tryptophan hydroxylase 1

3.3.1 Serotonin (5-Hydroxytryptamine, 5-HT)

Serotonin is a monoamine neurotransmitter critical for mood regulation, sleep, appetite, and cognition. Approximately 90–95% of the body's serotonin is synthesized in the gastrointestinal tract, primarily by enterochromaffin cells. Recent evidence has demonstrated that the gut microbiota regulates peripheral serotonin production through the modulation of tryptophan availability and the expression of tryptophan hydroxylase 1 (TPH1), the rate-limiting enzyme in peripheral serotonin synthesis [20].

Germ-free mice exhibit reduced colonic and serum serotonin levels, with restoration following colonization with spore-forming bacteria, particularly *Clostridium* species [20]. These bacteria produce SCFAs that stimulate TPH1 expression in enterochromaffin cells. However, direct microbial serotonin production is limited: a comprehensive analysis of eight commensal species (*Lactococcus lactis*, *Enterococcus faecalis, Blautia producta, Clostridium symbiosum, Streptococcus thermophilus, Prevotella copri, Bacteroides fragilis, and Escherichia coli* Nissle) revealed that none produced serotonin or its intermediates despite consuming the precursor tryptophan [5].

3.3.2 Dopamine

Dopamine is a catecholamine neurotransmitter involved in reward, motivation, motor control, and executive function. While dopamine is primarily synthesized in the CNS, gut microbiota contribute to dopamine precursor availability and may directly produce dopamine.

The same comprehensive metabolomic analysis identified that *Enterococcus faecalis* synthesizes high levels of dopamine and tyramine from tyrosine precursors [5]. Multiple species, including *L. lactis*, *B. producta*, and *E.*

coli, produce L-DOPA (levodopa), the immediate precursor to dopamine. These findings demonstrate that commensal gut bacteria possess the enzymatic machinery for catecholamine synthesis and contribute to host dopamine pools, although the extent to which microbial dopamine reaches the CNS remains unclear given the blood-brain barrier's restricted permeability.

3.3.3 Gamma-Aminobutyric Acid (GABA)

GABA is the primary inhibitory neurotransmitter in the CNS, with critical roles in anxiety regulation, sleep, and seizure control. Several gut bacterial species possess glutamate decarboxylase (GAD) enzymes that convert glutamate to GABA.

High GABA production has been demonstrated in *E. coli* and *B. producta*, with additional GABA-producing capacity identified in *L. lactis* [5]. GABA produced in the gut can influence CNS function through vagal afferent activation, as vagal nerve fibers express GABA receptors [13]. Additionally, GABA may modulate enteric nervous system activity, influencing gastrointestinal motility and secretion.

3.3.4 Short-Chain Fatty Acids (SCFAs)

SCFAs primarily acetate, propionate, and butyrate are fermentation products of dietary fiber by gut bacteria. These metabolites have emerged as key mediators of microbiota-brain communication [21]. SCFAs:

- Serve as energy substrates for colonocytes (butyrate)
- Activate G-protein-coupled receptors (FFAR2, FFAR3) on enteroendocrine cells, immune cells, and neurons
- Inhibit histone deacetylases, influencing gene expression
- Modulate blood-brain barrier integrity
- Regulate microglial maturation and function

A recent study demonstrated that SCFAs, particularly butyrate, promote anti-inflammatory microglial phenotypes and reduce neuroinflammation [22]. Depletion of SCFA-producing genera, including *Faecalibacterium*, *Roseburia*, and *Lachnospiraceae*, is consistently observed in neuropsychiatric and neurodegenerative conditions [23].

3.4 Impact on Brain Function

Table 3. Key Studies on Gut Microbiota and Brain Function

Author, Year	Study Design	Population Model	Key Findings	Ref.
Yassin *et al.,* 2025	Systematic review	Human & anima	Microbiota-gut-brain axis alterations in men and neurodegenerative disorders; therapeu potential	[1]
Tingler *et al*., 202	In vit metabolomics	8 bacterial speci	*E. faecalis* produces dopamine; E. coli and producta produce GABA and L-DOPA	[5]
Xu *et al*., 2025	Review	Human	Multi-omics and machine learning enab precision microbiome medicine	[6]
Cheng *et al*., 2024	Animal study	Mouse	Gpr35-tuned gut microbe-brain metabolic ax regulates depressive-like behavior	[24]
Bruggeman *et a* 2024	Phase 2 RCT	PD patients (n=4	FMT safe; improvement in motor symptoms a constipation (GUT-PARFECT trial)	[25]
Billeci *et al*., 2023	RCT	Preschoolers wi ASD	Probiotics altered EEG patterns; clinic outcomes mixed	[26]
Akbari *et al*., 2016	RCT	AD patier (n=60)	Probiotic supplementation modestly improv cognitive scores	[27]

Sudo *et al*., 2004	Animal study	Germ-free mice	Postnatal microbial colonization programs HI axis stress responses	[4]
Cryan *et al.,* 2019	Comprehensive review	Human & anima	Integrative overview of microbiota-gut-brain a mechanisms	[3]

Abbreviations: RCT, randomized controlled trial; PD, Parkinson's disease; FMT, fecal microbiota transplantation; ASD, autism spectrum disorder; EEG, electroencephalography; AD, Alzheimer's disease; HPA, hypothalamic-pituitary-adrenal.

3.4.1 Cognition

Emerging evidence links gut microbiota composition to cognitive function across the lifespan. In healthy aging, greater microbial diversity and abundance of SCFA-producing taxa correlate with better cognitive performance [28]. Conversely, cognitive decline is associated with reduced *Bifidobacterium* and *Lactobacillus* species and enrichment of pro-inflammatory taxa.

Intervention studies have yielded promising but preliminary results. A randomized controlled trial of probiotic supplementation in Alzheimer's disease patients demonstrated modest improvements in cognitive scores and metabolic markers, though effect sizes were small and long-term outcomes remain unknown [27].

3.4.2 Mood Disorders (Depression and Anxiety)

The association between gut dysbiosis and mood disorders is among the most extensively studied areas of MGBA research. Meta-analyses have identified consistent alterations in the gut microbiota of patients with major depressive disorder (MDD), including:

- Reduced alpha diversity
- Depletion of F*aecalibacterium* and *Coprococcus* genera
- Enrichment of *Eggerthella* and *Dialister* [29]

Microbial metabolites implicated in depression include reduced SCFA production, altered tryptophan metabolism, and increased circulating LPS levels [30]. A Gpr35-tuned gut microbe-brain metabolic axis was recently identified as a regulator of depressive-like behavior in animal models, highlighting specific microbial-host interactions that influence mood [24].

3.4.3 Neurodevelopment

The prenatal and early postnatal periods represent critical windows for microbiota-brain interaction. Maternal microbiota influences fetal neurodevelopment through microbial metabolites that cross the placenta and modulate immune programming [31]. Delivery mode (vaginal versus cesarean section) and early antibiotic exposure significantly impact the developing microbiota and are associated with altered neurodevelopmental outcomes.

Germ-free animal models demonstrate that the absence of microbiota during development results in:

- Impaired myelination
- Altered synaptic pruning
- Exaggerated HPA axis responses to stress
- Persistent behavioral abnormalities [4, 32]

3.4.4 Neurodegenerative Diseases

Alzheimer's Disease (AD):

Gut dysbiosis is consistently observed in AD patients, characterized by reduced microbial diversity, decreased *Bifidobacterium* and *Lactobacillus*, and increased pro-inflammatory taxa [33]. Mechanistic studies suggest that microbial metabolites influence amyloid-β aggregation, tau phosphorylation, and neuroinflammation. The gut microbiota may contribute to AD pathogenesis through:

- Promotion of systemic inflammation
- Alteration of tryptophan metabolism
- Production of amyloid-like proteins

- Modulation of blood-brain barrier integrity [34]

Parkinson's Disease (PD):

PD is characterized by both motor symptoms (tremor, rigidity, bradykinesia) and non-motor symptoms, including gastrointestinal dysfunction that often precedes motor manifestations by years. PD patients exhibit distinct gut microbial signatures, including decreased *Lachnospiraceae* and increased *Akkermansia muciniphila* [35].

The gut-brain axis in PD has gained particular attention due to Braak's hypothesis, which proposes that α-synuclein pathology originates in the gut and spreads to the brain via the vagus nerve. A phase 2 randomized controlled trial of fecal microbiota transplantation in mild-to-moderate PD (GUT-PARFECT) reported safety and preliminary efficacy, though larger trials are needed [25].

3.5 Clinical and Diagnostic Implications in Medical Laboratory Technology

3.5.1 Biomarkers

The identification of microbial signatures associated with neurological and psychiatric disorders has opened avenues for microbiome-based diagnostics. Potential applications include:

- Diagnostic biomarkers for early detection of PD and AD
- Stratification of depression subtypes for treatment selection
- Prediction of treatment response
- Monitoring of disease progression [6, 36]

However, substantial challenges remain: (1) lack of standardized protocols for sample collection and processing, (2) high inter-individual variability, (3) confounding by diet, medication, and lifestyle factors, and (4) insufficient validation in diverse populations.

3.5.2 Microbiome Analysis Techniques

Traditional culture-based methods capture only a fraction of gut microbial diversity. Modern molecular techniques have revolutionized microbiome analysis:

16S rRNA Gene Sequencing:

Amplification and sequencing of the 16S ribosomal RNA gene enables taxonomic profiling at genus level. While widely used and cost-effective, this method provides limited functional information and lacks species-level resolution for many taxa [37].

Shotgun Metagenomic Sequencing:

Whole-genome sequencing of microbial DNA provides species-level taxonomic resolution and functional profiling, including metabolic pathway reconstruction. This approach enables identification of strain-level variation and gene content [38].

Metatranscriptomics:

Sequencing of microbial RNA reveals active gene expression, providing insight into functional activity rather than merely compositional potential [39].

Metabolomics:

Profiling of microbial and host metabolites offers direct measurement of functional outputs, including SCFAs, bile acids, and neurotransmitter precursors [40].

Multi-omics integration combining metagenomics, metatranscriptomics, and metabolomics with machine learning approaches represents the frontier of microbiome diagnostics, enabling the identification of robust microbial signatures associated with clinical outcomes [6].

3.6 Therapeutic Perspectives

3.6.1 Probiotics

Probiotics are live microorganisms that confer health benefits when administered in adequate amounts. "Psychobiotics" a subset of probiotics with mental health benefits have been investigated for mood disorders, cognitive impairment, and neurodegenerative conditions [41].

Promising strains include:

- *Lactobacillus rhamnosus*: Reduces anxiety-like behavior in animal models [14]
- *Bifidobacterium longum*: Improves stress responses and depressive symptoms [42]
- *Lactobacillus plantarum*: Modulates cognitive function [43]

However, clinical trial results have been heterogeneous, with variability attributed to strain specificity, dosing, formulation, and patient selection. A randomized controlled trial in preschoolers with autism reported electroencephalography changes following probiotic administration, though clinical outcomes were mixed [26].

3.6.2 Prebiotics

Prebiotics are non-digestible substrates that selectively stimulate beneficial microorganisms. Common prebiotics include fructooligosaccharides (FOS), galactooligosaccharides (GOS), and inulin. By promoting the growth of SCFA-producing bacteria, prebiotics indirectly influence brain function [44].

3.6.3 Fecal Microbiota Transplantation

Fecal microbiota transplantation (FMT) involves the transfer of donor fecal material to a recipient to restore a healthy microbial community. FMT has demonstrated remarkable efficacy in recurrent *Clostridioides difficile* infection, prompting investigation in other conditions.

In neurological disorders, preliminary studies have reported:

- Improved motor symptoms and constipation in PD (GUT-PARFECT trial) [25]
- Modest cognitive improvements in AD
- Reduced gastrointestinal symptoms in ASD [45]

Safety concerns include the potential transmission of pathogens and long-term consequences of altering the gut ecosystem. Rigorous donor screening and standardized protocols are essential.

4. Discussion

This review synthesizes current evidence demonstrating that the gut microbiota plays a significant role in neurotransmitter regulation and brain function through multiple, interconnected mechanisms. The identification of specific bacterial species capable of producing or modulating neurotransmitters including dopamine, GABA, and L-DOPA represents a fundamental advance in our understanding of host-microbe interactions [5]. These findings challenge the traditional view that neurotransmitter production is exclusively a host function and suggest that microbial contributions to neurochemistry warrant further investigation.

However, several critical limitations must be acknowledged. First, the majority of mechanistic insights derive from animal models, particularly germ-free and specific pathogen-free mice. While these models have been invaluable for establishing causality, their translational relevance to human physiology requires validation. The human gut microbiota exhibits greater complexity and inter-individual variation than standard animal models, and differences in diet, genetics, and environment substantially influence microbiome-brain interactions [46].

Second, human studies remain predominantly correlational. Cross-sectional comparisons of microbial composition between patients with neurological disorders and healthy controls cannot establish causality. The direction of effect whether dysbiosis contributes to disease pathogenesis or results from disease-related factors such as altered diet, medication use, or gastrointestinal dysfunction remains uncertain for most conditions [47].

Third, substantial heterogeneity in study methodologies limits comparability across investigations. Variations in sample collection, DNA extraction, sequencing platforms, bioinformatic pipelines, and statistical approaches contribute to inconsistent findings across studies. The field lacks standardized protocols, hampering meta-analyses and the identification of robust microbial signatures [48].

Fourth, the therapeutic potential of microbiome-targeted interventions remains incompletely characterized. While probiotics, prebiotics, and FMT have shown promise in preliminary studies, large-scale randomized controlled trials with rigorous outcome measures are needed. Current evidence is insufficient to support clinical implementation for most neurological and psychiatric indications [49].Contradictions in the literature merit discussion. Some studies report beneficial effects of specific probiotics on mood and cognition, while others

find no significant effects. These discrepancies may reflect strain-specific differences, inadequate dosing, short intervention durations, or the heterogeneity of patient populations. Additionally, the optimal composition of a "healthy" gut microbiota likely varies across individuals based on genetics, age, diet, and environmental factors, suggesting that precision microbiome interventions tailored to individual profiles may be necessary [50].

Research gaps identified include: (1) mechanistic studies linking specific microbial metabolites to defined neural circuits, (2) longitudinal investigations establishing temporal relationships between dysbiosis and disease onset, (3) development of standardized protocols for microbiome analysis and intervention, (4) validation of microbial biomarkers in diverse populations, and (5) randomized controlled trials of microbiome-based interventions with long-term follow-up.

5. Conclusion

The gut microbiota is a critical regulator of neurotransmitter systems and brain function, operating through neural, endocrine, and immune pathways. Specific bacterial species produce or modulate key neurotransmitters, including dopamine, GABA, and L-DOPA, while microbial metabolites such as SCFAs exert profound effects on neuroinflammation, microglial function, and blood-brain barrier integrity. Dysbiosis is consistently associated with neuropsychiatric and neurodegenerative disorders, though causality remains to be definitively established.

For medical laboratory technology, the gut microbiome offers promising diagnostic and therapeutic applications. Multi-omics approaches integrating metagenomics, metatranscriptomics, and metabolomics with machine learning may enable the development of robust microbial biomarkers for disease detection, stratification, and monitoring. However, standardization of protocols and validation across diverse populations are prerequisites for clinical implementation.

Future research must prioritize: (1) mechanistic studies establishing causal relationships between specific microbial species or metabolites and defined neurobiological outcomes, (2) large-scale longitudinal human cohorts to characterize temporal dynamics of dysbiosis in relation to disease onset and progression, (3) rigorous randomized controlled trials of microbiome-based interventions with standardized protocols and validated outcome measures, and (4) development of precision approaches that account for individual variation in genetics, diet, and environmental exposures.

The accessibility of the gut microbiota to dietary and pharmacological interventions positions it as a uniquely tractable target for therapeutic modulation. While significant challenges remain, continued investigation of the microbiota-gut-brain axis holds promise for advancing our understanding of brain function and developing novel strategies for neurological and psychiatric disorders.

Data Availability Statement:

No datasets were generated or analyzed for this review. All data referenced are from previously published studies cited in the reference list.

Conflicts of Interest:

The author declares no conflicts of interest.

Funding:

This review received no external funding.

Acknowledgments:

The author acknowledges the scientific contributions of researchers whose work is cited herein.

6. References

1. Yassin LK, Skrabulyte-Barbulescu J, Alshamsi SH, Saeed S, Alkuwaiti SH, Almazrouei S, Alnuaimi A, BaniYas S, Aldhaheri D, Alderei M, Shehab S. The microbiota–gut–brain axis in mental and neurodegenerative disorders: opportunities for prevention and intervention. Frontiers in Aging Neuroscience. 2025 Oct 1;17:1667448.
2. Wadan AH, El-Aziz MK, Ellakwa DE. The microbiota-gut-brain-axis theory: role of gut microbiota modulators (GMMs) in gastrointestinal, neurological, and mental health disorders. Naunyn-Schmiedeberg's Archives of Pharmacology. 2025 Oct;398(10):13397-426.

3. Cryan JF, O'Riordan KJ, Cowan CS, Sandhu KV, Bastiaanssen TF, Boehme M, Codagnone MG, Cussotto S, Fulling C, Golubeva AV, Guzzetta KE. The microbiota-gut-brain axis. Physiological reviews. 2019 Oct 1;99(4):1877-2013.
4. Sudo N, Chida Y, Aiba Y, Sonoda J, Oyama N, Yu XN, Kubo C, Koga Y. Postnatal microbial colonization programs the hypothalamic–pituitary–adrenal system for stress response in mice. The Journal of physiology. 2004 Jul;558(1):263-75.
5. Gilbert JA, Blaser MJ, Caporaso JG, Jansson JK, Lynch SV, Knight R. Current understanding of the human microbiome. Nature medicine. 2018 Apr 1;24(4):392-400.
6. Lin F, Xu L, He Q, Chen Z, Zhang W, Tu J, Song Y, Zhong F, Lin S, Yang R, Zeng Z. Plant-derived nanovesicles as novel nanotherapeutics for alleviating endothelial cell senescence-associated vascular remodeling induced by hypertension. Pharmacological Research. 2025 Apr 1;214:107675.
7. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. bmj. 2021 Mar 29;372.
8. Bhadange R, Dagar N, Gaikwad AB. Levosimendan mitigates renal fibrosis via TGF-β1/Smad axis modulation in UUO rats. Biomedicine & Pharmacotherapy. 2025 Jun 1;187:118124.Carabotti M, Scirocco A, Maselli MA, Severi C. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. Ann Gastroenterol. 2015;28(2):203-209. PMID: 25830558
9. Zai MJ, Cheesman MJ, Cock IE. Selected Australian Terminalia species extracts inhibit β-lactam drug-resistant bacteria growth and potentiate the activity of conventional antibiotics: bioactivities and phytochemistry. Microorganisms. 2024 Feb 29;12(3):498.
10. Dalile B, Van Oudenhove L, Vervliet B, Verbeke K. The role of short-chain fatty acids in microbiota–gut–brain communication. Nature reviews Gastroenterology & hepatology. 2019 Aug;16(8):461-78.Berthoud HR, Neuhuber WL. Functional and chemical anatomy of the afferent vagal system. Auton Neurosci. 2000;85(1-3):1-17. doi:10.1016/S1566-0702(00)00215-0
11. Bravo JA, Forsythe P, Chew MV, Escaravage E, Savignac HM, Dinan TG, Bienenstock J, Cryan JF. Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. Proceedings of the National Academy of Sciences. 2011 Sep 20;108(38):16050-5.Forsythe P, Bienenstock J, Kunze WA. Vagal pathways for microbiome-brain-gut axis communication. Adv Exp Med Biol. 2014;817:115-133. doi:10.1007/978-1-4939-0897-4_5
12. Farzi A, Fröhlich EE, Holzer P. Gut microbiota and the neuroendocrine system. Neurotherapeutics. 2018 Jan 1;15(1):5-22.Gribble FM, Reimann F. Function and mechanisms of enteroendocrine cells and gut hormones in metabolism. Nat Rev Endocrinol. 2019;15(4):226-237. doi:10.1038/s41574-019-0168-8
13. Arpaia N, Campbell C, Fan X, Dikiy S, Van Der Veeken J, Deroos P, Liu H, Cross JR, Pfeffer K, Coffer PJ, Rudensky AY. Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation. Nature. 2013 Dec 19;504(7480):451-5.
14. Lukiw WJ. Bacteroides fragilis lipopolysaccharide and inflammatory signaling in Alzheimer's disease. Frontiers in microbiology. 2016 Sep 26;7:1544.
15. Strandwitz P, Kim KH, Terekhova D, Liu JK, Sharma A, Levering J, McDonald D, Dietrich D, Ramadhar TR, Lekbua A, Mroue N. GABA-modulating bacteria of the human gut microbiota. Nature microbiology. 2019 Mar;4(3):396-403.
16. Yano JM, Yu K, Donaldson GP, Shastri GG, Ann P, Ma L, Nagler CR, Ismagilov RF, Mazmanian SK, Hsiao EY. Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. Cell. 2015 Apr 9;161(2):264-76.
17. Koh A, De Vadder F, Kovatcheva-Datchary P, Bäckhed F. From dietary fiber to host physiology: short-chain fatty acids as key bacterial metabolites. Cell. 2016 Jun 2;165(6):1332-45.
18. Erny D, Hrabě de Angelis AL, Jaitin D, Wieghofer P, Staszewski O, David E, Keren-Shaul H, Mahlakoiv T, Jakobshagen K, Buch T, Schwierzeck V. Host microbiota constantly control maturation and function of microglia in the CNS. Nature neuroscience. 2015 Jul;18(7):965-77.

19. Valles-Colomer M, Falony G, Darzi Y, Tigchelaar EF, Wang J, Tito RY, Schiweck C, Kurilshikov A, Joossens M, Wijmenga C, Claes S. The neuroactive potential of the human gut microbiota in quality of life and depression. Nature microbiology. 2019 Apr;4(4):623-32.

20. Cheng L, Wu H, Cai X, Zhang Y, Yu S, Hou Y, Yin Z, Yan Q, Wang Q, Sun T, Wang G. A Gpr35-tuned gut microbe-brain metabolic axis regulates depressive-like behavior. Cell host & microbe. 2024 Feb 14;32(2):227-43.

21. Bruggeman A, Vandendriessche C, Hamerlinck H, De Looze D, Tate DJ, Vuylsteke M, De Commer L, Devolder L, Raes J, Verhasselt B, Laukens D. Safety and efficacy of faecal microbiota transplantation in patients with mild to moderate Parkinson's disease (GUT-PARFECT): a double-blind, placebo-controlled, randomised, phase 2 trial. EClinicalMedicine. 2024 May 1;71.

22. Billeci L, Callara AL, Guiducci L, Prosperi M, Morales MA, Calderoni S, Muratori F, Santocchi E. A randomized controlled trial into the effects of probiotics on electroencephalography in preschoolers with autism. Autism. 2023 Jan;27(1):117-32.

23. Akbari E, Asemi Z, Daneshvar Kakhaki R, Bahmani F, Kouchaki E, Tamtaji OR, Hamidi GA, Salami M. Effect of probiotic supplementation on cognitive function and metabolic status in Alzheimer's disease: a randomized, double-blind and controlled trial. Frontiers in aging neuroscience. 2016 Nov 10;8:229544.

24. Claesson MJ, Jeffery IB, Conde S, Power SE, O'connor EM, Cusack S, Harris HM, Coakley M, Lakshminarayanan B, O'sullivan O, Fitzgerald GF. Gut microbiota composition correlates with diet and health in the elderly. Nature. 2012 Aug 9;488(7410):178-84.

25. Zheng P, Zeng B, Zhou C, Liu M, Fang Z, Xu X, Zeng L, Chen J, Fan S, Du X, Zhang X. Gut microbiome remodeling induces depressive-like behaviors through a pathway mediated by the host's metabolism. Molecular psychiatry. 2016 Jun;21(6):786-96.

26. Kelly JR, Borre Y, O'Brien C, Patterson E, El Aidy S, Deane J, Kennedy PJ, Beers S, Scott K, Moloney G, Hoban AE. Transferring the blues: depression-associated gut microbiota induces neurobehavioural changes in the rat. Journal of psychiatric research. 2016 Nov 1;82:109-18.

27. Thion MS, Low D, Silvin A, Chen J, Grisel P, Schulte-Schrepping J, Blecher R, Ulas T, Squarzoni P, Hoeffel G, Coulpier F. Microbiome influences prenatal and adult microglia in a sex-specific manner. Cell. 2018 Jan 25;172(3):500-16.

28. Heijtz RD, Wang S, Anuar F, Qian Y, Björkholm B, Samuelsson A, Hibberd ML, Forssberg H, Pettersson S. Normal gut microbiota modulates brain development and behavior. Proceedings of the National Academy of Sciences. 2011 Feb 15;108(7):3047-52.

29. Vogt NM, Kerby RL, Dill-McFarland KA, Harding SJ, Merluzzi AP, Johnson SC, Carlsson CM, Asthana S, Zetterberg H, Blennow K, Bendlin BB. Gut microbiome alterations in Alzheimer's disease. Scientific reports. 2017 Oct 19;7(1):13537.

30. Kowalski K, Mulak A. Brain-gut-microbiota axis in Alzheimer's disease. Journal of neurogastroenterology and motility. 2019 Jan 1;25(1):48.

31. Scheperjans F, Aho V, Pereira PA, Koskinen K, Paulin L, Pekkonen E, Haapaniemi E, Kaakkola S, Eerola-Rautio J, Pohja M, Kinnunen E. Gut microbiota are related to Parkinson's disease and clinical phenotype. Movement Disorders. 2015 Mar;30(3):350-8.

32. Bastiaanssen TF, Cowan CS, Claesson MJ, Dinan TG, Cryan JF. Making sense of… the microbiome in psychiatry. International Journal of Neuropsychopharmacology. 2019 Jan;22(1):37-52.

33. Jovel J, Patterson J, Wang W, Hotte N, O'Keefe S, Mitchel T, Perry T, Kao D, Mason AL, Madsen KL, Wong GK. Characterization of the gut microbiome using 16S or shotgun metagenomics. Frontiers in microbiology. 2016 Apr 20;7:459.

34. Quince C, Walker AW, Simpson JT, Loman NJ, Segata N. Shotgun metagenomics, from sampling to analysis. Nature biotechnology. 2017 Sep;35(9):833-44.

35. Bashiardes S, Zilberman-Schapira G, Elinav E. Use of metatranscriptomics in microbiome research. Bioinformatics and biology insights. 2016 Jan;10:BBI-S34610.

36. Nicholson JK, Holmes E, Kinross J, Burcelin R, Gibson G, Jia W, Pettersson S. Host-gut microbiota metabolic interactions. Science. 2012 Jun 8;336(6086):1262-7.

37. Dinan TG, Stanton C, Cryan JF. Psychobiotics: a novel class of psychotropic. Biological psychiatry. 2013 Nov 15;74(10):720-6.

38. Pinto-Sanchez MI, Hall GB, Ghajar K, Nardelli A, Bolino C, Lau JT, Martin FP, Cominetti O, Welsh C, Rieder A, Traynor J. Probiotic Bifidobacterium longum NCC3001 reduces depression scores and alters brain activity: a pilot study in patients with irritable bowel syndrome. Gastroenterology. 2017 Aug 1;153(2):448-59

39. Liu WH, Chuang HL, Huang YT, Wu CC, Chou GT, Wang S, Tsai YC. Alteration of behavior and monoamine levels attributable to Lactobacillus plantarum PS128 in germ-free mice. Behavioural brain research. 2016 Feb 1;298:202-9.

40. Gibson GR, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, Scott K, Stanton C, Swanson KS, Cani PD, Verbeke K. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. Nature reviews Gastroenterology & hepatology. 2017 Aug;14(8):491-502.

41. Kang DW, Adams JB, Gregory AC, Borody T, Chittick L, Fasano A, Khoruts A, Geis E, Maldonado J, McDonough-Means S, Pollard EL. Microbiota transfer therapy alters gut ecosystem and improves gastrointestinal and autism symptoms: an open-label study. Microbiome. 2017 Dec;5(1):10.

42. Nguyen TL, Vieira-Silva S, Liston A, Raes J. How informative is the mouse for human gut microbiota research?. Disease models & mechanisms. 2015 Jan 1;8(1):1-6.

43. Duvallet C, Gibbons SM, Gurry T, Irizarry RA, Alm EJ. Meta-analysis of gut microbiome studies identifies disease-specific and shared responses. Nature communications. 2017 Dec 5;8(1):1784.

44. Sinha R, Abnet CC, White O, Knight R, Huttenhower C. The microbiome quality control project: baseline study design and future directions. Genome biology. 2015 Dec 9;16(1):276.

45. Mörkl S, Butler MI, Holl A, et al. Probiotics and the microbiota-gut-brain axis: focus on psychiatry. Curr Nutr Rep. 2020;9(3):171-182. doi:10.1007/s13668-020-00313-5

46. Zmora N, Zilberman-Schapira G, Suez J, Mor U, Dori-Bachash M, Bashiardes S, Kotler E, Zur M, Regev-Lehavi D, Brik RB, Federici S. Personalized gut mucosal colonization resistance to empiric probiotics is associated with unique host and microbiome features. Cell. 2018 Sep 6;174(6):1388-405.