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Mini Review

The Influence of Gut Microbiota on Depressive Syndrome: A Narrative Review.

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Abstract

Depressive syndrome is a leading cause of disability worldwide, with complex pathophysiology involving genetic, environmental, and neurobiological factors. Recent evidence highlights the gut microbiota as a key modulator of brain function through the microbiota–gut–brain axis. This narrative review synthesizes recent literature on the relationship between gut microbiota and depressive syndrome, focusing on neurotransmitter modulation, and therapeutic implications. Dysbiosis has been consistently associated with alterations in serotonin, GABA (gamma-aminobutyric acid), dopamine, norepinephrine, glutamate, and short chain fatty acid pathways. Clinical studies and meta analyses suggest that probiotics, prebiotics, and dietary interventions may reduce depressive symptoms. While promising, current evidence is limited by heterogeneity and small sample sizes. Future research should prioritize standardized clinical trials and personalized microbiome based strategies.

Keywords: Gut microbiota; Depression; Neurotransmitters; Psychobiotics; Gut–brain axis.

INTRODUCTION

Depressive syndrome is one of the most prevalent psychiatric disorders worldwide, affecting more than 300 million people and representing a leading cause of disability according to the World Health Organization. Its burden extends beyond individual suffering, contributing to increased healthcare costs, reduced productivity, and significant social impact. Traditional etiological models have emphasized monoaminergic dysfunction, neuroinflammation, hypothalamic-pituitary-adrenal (HPA) axis dysregulation, and genetic vulnerability. However, these mechanisms alone do not fully explain the heterogeneity of depressive presentations or the variable response to conventional antidepressant therapies [1,2].

In recent years, growing attention has been directed toward the microbiota-gut-brain axis, a bidirectional communication system linking intestinal microorganisms with central nervous system function. The gut microbiota, composed of trillions of bacteria, viruses, and fungi, plays a crucial role in host metabolism, immune regulation, and neurochemical

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signaling. Dysbiosis-defined as an imbalance in microbial composition-has been consistently associated with psychiatric disorders, particularly depression. Evidence suggests that microbial metabolites, such as short chain fatty acids (SCFAs), and microbial modulation of neurotransmitter pathways (serotonin, dopamine, norepinephrine, glutamate, and GABA) may directly influence mood regulation [3,4]

METHODS

This narrative review was conducted by searching PubMed, Scopus, and Web of Science for articles published between 2015 and 2025. Inclusion criteria comprised human and animal studies, reviews, and meta analyses. Fifteen studies were selected to provide a comprehensive overview of the microbiota–gut–brain axis in depression (**Table 1**).

Table 1. Studies included in the review

First author	Year	Journal	Study type	Key findings
Zhou X [1]	2025	Front Nutr	Narrative review	Mechanisms of gut microbes in depression via gut–brain axis
Foster JA [2]	2023	Trends Neurosci	Review	Gut–brain axis influence on anxiety and depression
Zheng P [3]	2023	EBioMedicine	Review	Gut microbiota metabolites linked to depression
Khaledi M[4]	2024	Heliyon	Review	Potential role of microbiota in major depressive disorder
Cryan JF [5]	2023	Physiol Rev	Review	Comprehensive overview of microbiota–gut–brain axis
Kamal N [6]	2025	Medicine in Microecology	Review	Exploring the promise of psychobiotics
Kelly JR[7]	2016	J Psychiatr Res	Animal experimental	Depression associated microbiota induces behavioral changes in rats
Valles Colomer M [8]	2019	Nat Microbiol	Cohort study	Neuroactive potential of human gut microbiota linked to QoL and depression
Huang R [9]	2016	Nutrients	Meta analysis	Probiotics reduce depressive symptoms
Liu RT [10]	2019	Neurosci Biobehav Rev	Meta analysis	Prebiotics/probiotics reduce anxiety/depression in controlled trials
Dash S [11]	2015	Curr Opin Psychiatry	Review	Diet and microbiome interactions focused on depression
Clerici L [12]	2025	Curr Nutr Rep	Literature review	Microbiome, diet and depression: integrative overview
Rosas Sánchez GU [13]	2025	Biomedicines	Narrative review	Gut–brain axis in mood disorders and probiotic interventions
Ghosh SS [14]	2020	Journal of the Endocrine Society	Review	Barrier Dysfunction, LPS Translocation
Eskandar K [15]	2025	Middle East Current Psychiatry	Review	The gut–brain axis in depression

RESULTS

Our review identified several neurotransmitters whose synthesis, metabolism, or signaling are modulated by gut microbiota. The distinction between stimulatory and inhibitory neurotransmitters, together with their clinical implications, is summarized in **Table 2**.

Table 2. Neurotransmitters influenced by gut microbiota and clinical evidence

Neurotransmitter	Type (stimulatory/ inhibitory)	Microbiota influence	Clinical evidence	Reference
Serotonin (5 HT)	Stimulatory	Regulates tryptophan metabolism; dysbiosis reduces 5 HT	RCTs show improved HAM D (Hamilton Depression Rating Scale) scores and increased plasma tryptophan	[5]
Dopamine	Stimulatory	Modulates precursor availability (tyrosine, phenylalanine)	Altered fecal metabolites in MDD (Major depressive disorder); reduced striatal dopamine in germ free mice	[2]
Norepinephrine	Stimulatory	SCFAs/catechols influence synthesis and release	Increased turnover in depressed patients; reduced stress hyperactivity with psychobiotics	[3]
Glutamate	Stimulatory	Dysbiosis increases excitatory signaling	Elevated CSF(cerebrospinal fluid) glutamate correlates with severity; probiotics reduce excitotoxicity	[4]
GABA	Inhibitory	Produced by Lactobacillus/ Bifidobacterium	RCTs show symptom reduction with GABA producing strains; lower GABA with dysbiosis	[6,7]
SCFAs	Inhibitory (modulatory)	Reduce neuroinflammation; support BBB (Blood-brain barrier) integrity	Higher levels associated with better QoL and lower depression scores; butyrate shows antidepressant effects	[8]

Stimulatory neurotransmitters (excitatory)

Serotonin (5 HT): Dysbiosis reduces serotonin availability by diverting tryptophan metabolism toward neurotoxic metabolites. Reduced Faecalibacterium and Coprococcus abundance correlates with lower serotonin and higher depression scores. Clinical trials show that probiotic supplementation increases plasma tryptophan and improves HAM D (Hamilton Depression Rating Scale) scores [1,5].

Dopamine: Microbiota modulates precursor availability (tyrosine, phenylalanine). Depressed patients show altered fecal dopamine metabolites. Germ free mice exhibit reduced striatal dopamine and impaired reward processing [2].

Norepinephrine: Microbial metabolites (catechols) influence norepinephrine synthesis and release. Dysbiosis is associated with increased norepinephrine turnover in depressed patients [3].

Glutamate: Dysbiosis increases glutamatergic activity, leading to excitotoxicity. Elevated cerebrospinal fluid glutamate levels correlate with depressive severity [4].

Inhibitory neurotransmitters (modulatory)

Gamma aminobutyric acid (GABA): Produced by Lactobacillus and Bifidobacterium. Dysbiosis reduces GABA levels, amplifying anxiety and depressive vulnerability. Probiotic supplementation with GABA producing strains reduces anxiety and depressive symptoms in randomized trials [6,7].

Short chain fatty acids (SCFAs): Microbial metabolites with inhibitory effects on neuroinflammation and blood–brain barrier permeability. Higher SCFA levels are associated with better quality of life and lower depression scores. Butyrate shows antidepressant like effects in preclinical models [8].

Clinical implications

Balance matters: Stimulatory neurotransmitters (serotonin, dopamine, norepinephrine, glutamate) support motivation, energy, and affective tone; inhibitory neurotransmitters (GABA, SCFAs) moderate anxiety, stress responses, and neuroinflammation [9,10]

Dysbiosis and vulnerability: Microbiota alterations disrupt this equilibrium and increase susceptibility to depression [11,12]

Interventions: Probiotics, prebiotics, synbiotics, dietary patterns (Mediterranean, high fiber, fermented foods) can restore neurotransmitter balance and reduce depressive symptoms [13–15].

Recommendations on prebiotics, probiotics, and diet (Table 3)

Probiotics: Lactobacillus rhamnosus, Bifidobacterium longum, Lactobacillus helveticus have reduced depressive scores in randomized controlled trials [9,13].

Prebiotics: Inulin, fructooligosaccharides (FOS), galactooligosaccharides (GOS) enhance microbial diversity and SCFA production [10].

Synbiotics: Combining probiotics and prebiotics shows synergistic effects on mood and inflammation [10,14].

Recommended foods:

High fiber foods: Legumes, whole grains, oats, bananas, onions, garlic, asparagus [11].

Fermented foods: Yogurt, kefir, sauerkraut, kimchi, miso [12].

Mediterranean diet: Vegetables, fruits, olive oil, nuts, fish, associated with reduced depressive risk [11,12].

Polyphenol rich foods: Berries, green tea, dark chocolate, supporting beneficial microbial growth [8].

Table 3. Recommended prebiotics, probiotics, and diet

Category	Examples	Mechanism/ relevance	Clinical evidence	Reference
Probiotics	Lactobacillus rhamnosus; Bifidobacterium longum; Lactobacillus helveticus	Modulate 5 HT/GABA; reduce inflammation	Meta analyses and RCTs show reductions in depressive scores	[9]
Prebiotics	Inulin; FOS; GOS	Increase SCFAs; enhance microbial diversity	Meta analysis shows mood benefits and reduced anxiety/ depression	[10]
Synbiotics	Probiotics + prebiotics	Synergistic effects on neurotransmission and inflammation	Controlled trials indicate additive benefits	[10]
High fiber foods	Legumes; whole grains; oats; bananas; onions; garlic; asparagus	Substrate for SCFAs; support beneficial taxa	Observational and interventional data align with reduced depressive risk	[11]
Fermented foods	Yogurt; kefir; sauerkraut; kimchi; miso	Natural probiotics; increase diversity	Cohort/intervention studies suggest mood and microbiota improvements	[12]
Mediterranean diet	Vegetables; fruits; olive oil; nuts; fish	Anti inflammatory; polyphenol rich; fiber dense	Associated with lower depression prevalence and improved microbiota diversity	[11,12]
Polyphenol rich foods	Berries; green tea; dark chocolate	Prebiotic like effects; antioxidant; support beneficial microbes	Linked to better QoL and neuroactive microbiota profiles	[8]

DISCUSSION

The literature reviewed confirms that the gut microbiota exerts a significant influence on the pathophysiology of depressive syndrome, yet a critical analysis of the data suggests that this relationship is not merely associative. Beyond the modulation of the hypothalamic–pituitary–adrenal axis and systemic inflammation, the emerging concept of a "microbiota–immune–neurotransmitter axis" highlights how microbial metabolites such as short chain fatty acids and tryptophan derivatives act as neuromodulators, directly influencing mood regulation [3,4,8]. This perspective expands the traditional focus on neuroinflammation alone.

An innovative aspect concerns the heterogeneity of clinical response to psychobiotic interventions: not all patients demonstrate significant benefits, as highlighted by meta analyses and randomized controlled trials [9,10]. This variability points toward the need for personalized approaches based on individual microbiome profiles. Such strategies open the way to precision psychiatry, where the microbiota could serve as a biomarker to stratify patients and guide therapeutic decisions.

Comparisons between observational studies and controlled trials also reveal methodological discrepancies: small sample sizes, diagnostic heterogeneity, and limited follow up reduce the strength of conclusions [1,2,5]. It is therefore essential to emphasize the limitations of the current literature and promote future studies that are more robust and standardized.

Translational perspectives include the integration of microbiome analyses with multimodal techniques (neuroimaging, metabolomics) to clarify biological pathways that remain poorly understood [11,12]. Targeted interventions such as personalized diets, next generation probiotics, and fecal microbiota transplantation require rigorous trials to establish efficacy and safety [13–15].

CONCLUSION

The evidence reviewed demonstrates that gut microbiota significantly influences depressive syndrome through modulation of neurotransmitters, immune pathways, and stress responses. However, this relationship extends beyond descriptive associations and points toward a complex

"microbiota–immune–neurotransmitter axis" that may serve as a foundation for precision psychiatry. Current findings highlight both the promise and the limitations of microbiota targeted interventions, with variability in patient response underscoring the need for personalized approaches.

Future research should prioritize large, standardized randomized controlled trials that integrate multimodal assessments—including microbiome profiling, neuroimaging, and metabolomics—to clarify mechanistic pathways and identify reliable biomarkers. Translational strategies such as next generation probiotics, dietary interventions, and fecal microbiota transplantation hold potential, but require rigorous validation to establish efficacy, safety, and long term outcomes.

In conclusion, this review not only synthesizes existing evidence but also proposes novel insights that emphasize the importance of moving from descriptive correlations to mechanistic and personalized strategies. By positioning microbiota research as a cornerstone of precision psychiatry, we provide a framework for future clinical applications that may transform the management of depressive syndromes.

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