Review

GUT MICROBIOME AND MENTAL HEALTH: FROM MECHANISMS TO APPLICATIONS

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ABSTRACT

Aims: This review aims to summarize current evidence on the relationship between gut microbiota alterations and mood disorders, particularly depression and anxiety, and to highlight the potential of targeting the gut microbiome to develop interventions that improve outcomes in these conditions.

Methods: Relevant studies investigating gut microbiota composition, microbial metabolites, and microbiome-based interventions in depression and anxiety were analyzed to synthesize current findings and research directions.

Results: Compared with healthy individuals, patients with depression and/or anxiety exhibit reduced bacterial diversity and imbalances in genera such as *Lactobacillus* and *Bifidobacterium*. These alterations in microbial diversity are closely linked to the hypothalamic–pituitary–adrenal (HPA) axis, neurotransmitter modulation, and immune activity, and may contribute to the pathogenesis of mood disorders. Recent studies have also reported that microbiome-based strategies, including probiotics, prebiotics, and fecal microbiota transplantation, show potential as supportive treatments for mental health conditions.

Conclusion: Although growing evidence supports the role of the gut microbiome in mental health regulation, findings remain inconsistent across different populations. Further longitudinal and well–controlled studies are required to clarify causal relationships and support the development of personalized treatments.

Keywords: *Gut microbiome, Microbial diversity, Depression, Anxiety, Gut–brain axis, Neurotransmitters*

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I. INTRODUCTION

Depression and anxiety disorders are significant global health burdens, affecting approximately 280 million and 301 million people worldwide, respectively [1, 2]. While traditional psychiatric research has focused on neurotransmitter imbalances and psychological factors, growing evidence suggests that the gut microbiota plays a crucial role in the regulation of brain function through the bidirectional interaction of the gut-brain axis [3, 4]. The human gut harbors a complex ecosystem of approximately 3.8×10^{13} microorganisms, which influence host physiology via metabolic, immune, and neuronal signaling pathways [5]. These findings indicate that gut microbiota, particularly species of *Lactobacillus* and *Bifidobacterium*, may contribute to the pathogenesis of psychiatric disorders, highlighting the potential for probiotics to be used as adjuncts to treatment.

The gut-brain axis is a complex network linking the central nervous system (CNS) and the enteric nervous system. This bidirectional communication is executed through neural, endocrine, and immune pathways [4]. Neural pathways primarily function via the vagus nerve, transmitting signals between the enteric and CNS to regulate appetite, emotional states, and inflammatory responses in the gastrointestinal tract. Several gut bacteria, including *L. rhamnosus, L. helveticus,* and *B. longum*, have been shown to modulate gamma-aminobutyric acid (GABA) receptor expression in the brain via the vagus nerve, thereby reducing anxiety in mouse models.

Within the endocrine system, gut bacteria influence the regulation of the stress response in the HPA axis. Imbalances in the microbiome can increase cortisol levels, a stress hormone, which in turn affects cognitive function and mood [6]. Additionally, gut bacteria and their metabolites, such as short-chain fatty acids (SCFAs), can modulate the inflammatory response through their effects on immune cells and the balance between pro-inflammatory cytokines (IL-6, TNF-α) and anti–inflammatory cytokines (IL-10) [7, 8]. As a result, microbiome dysbiosis could lead to chronic inflammation, which is considered a risk factor for depression and anxiety [9].

These mechanisms together suggest that the gut microbiota is not only involved in digestion but also plays a crucial role in regulating neural function and behavior, offering a new approach to understanding and treating mental health disorders. Although there is growing evidence of a link between gut microbiota and mental disorders, data on specific changes in fecal bacterial composition, particularly across different populations with varying geographic regions, diets, and lifestyles, remain inconsistent. Some studies have shown an imbalance in certain bacterial genera, such as *Lactobacillus, Bifidobacterium,* or *Prevotella*, in individuals with depression and anxiety; however, the underlying mechanisms remain incompletely understood [6, 10, 11]. Particularly, in the

Vietnamese population, there is limited research on the gut microbial diversity in patients with mental health disorders.

Although previous reviews have explored the association between the gut microbiome and mental health, findings related to specific microbial alterations remain inconsistent across studies and populations. Therefore, this review aims to synthesize current evidence regarding alterations in gut microbiota composition in patients with depression and anxiety, with particular emphasis on findings derived from fecal sample analysis. By integrating findings on microbial composition with current knowledge of gut–brain communication mechanisms, this review seeks to provide a clearer overview of how microbial alterations may contribute to the pathophysiology of these disorders. In addition, the article discusses the mechanistic pathways underlying gut –brain communication and evaluates the emerging potential of probiotic-based interventions as adjunctive strategies in the treatment of these disorders.

II. METHODS

The review examined the relationship between gut microbiota and mental health disorders, with particular focus on the underlying biological mechanisms and therapeutic implications. Relevant publications were retrieved from Google Scholar, PubMed, ScienceDirect, and Nature. The structured literature search used the following keywords: gut microbiome, gut microbial diversity, depression, anxiety, gut-brain axis, neurotransmitter modulation, SCFAs, and inflammation.

Publications from 2015–2025 were prioritized, emphasizing recent peer-reviewed articles. Original human studies, animal experiments, and clinical trials investigating microbial composition, functional alterations, and microbiome-based interventions were included. Review articles were screened for additional primary studies. Research lacking clear diagnostic criteria or microbiome analytical methods was excluded. Eligible papers were synthesized narratively, with emphasis on current microbial patterns, proposed mechanisms, and translational implications, while considering methodological variation across studies.

III. RESULTS

3.1. The composition and functional roles of human gut microbiota

The intestinal microbiota, with its diverse roles in digestion, immune regulation, and neuronal activity, plays a crucial role in human health. This gut bacterial community ferments the complex carbohydrates, such as dietary fiber, which are indigestible by human enzymes, to produce SCFAs such as acetate, propionate, and butyrate [12]. These SCFAs not only provide energy for intestinal epithelial cells but also participate in the regulation of glucose and lipid metabolism, enhance the integrity of the intestinal mucosal barrier, and reduce inflammatory responses [7, 12, 13]. Intestinal bacteria also contribute to the synthesis of essential vitamins, such as species of the genus *Bacteroides*,

which produce vitamin K and several B vitamins, important for metabolism, blood clotting, and erythropoiesis [14]. These roles of gut bacteria have been further highlighted in patients with inflammatory bowel disease, whose dysbiosis greatly affects their conditions [15].

These functions extend beyond the gastrointestinal system and have profound effects on the CNS via the gut–brain axis, suggesting a potential role for microbiota in mental health [16]. Commensal bacteria help maintain the integrity of the intestinal epithelial barrier, promote the differentiation of T cells, and regulate the production of pro– and anti–inflammatory cytokines, thereby supporting the maintenance of immune tolerance in the host [6, 17]. Through the gut–brain axis, gut bacteria can influence the CNS by regulating the metabolism and synthesis of certain neurotransmitters, such as serotonin and GABA, which in turn affect host behavior and emotions [3]. Numerous studies have demonstrated a strong link between gut dysbiosis and neurodevelopmental or psychiatric disorders, such as bipolar disorder, anxiety, and depression, underscoring the role of the gut microbiome in maintaining overall health [4, 15, 18].

Four bacterial phyla predominantly form the human gut microbiota, including Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria [8, 19]. Specifically, approximately 90% of this bacterial community is contributed by Firmicutes and Bacteroidetes [20]. However, among individuals, significant differences in gut bacterial composition were observed in lower taxonomic levels. For example, the genus *Bacteroides* is often highly abundant in many stool samples but shows considerable variability in proportions between individuals [21]. At the species level, several bacteria, such as *Faecalibacterium prausnitzii, Roseburia intestinalis,* and *Bacteroides* uniformis, are commonly reported as prevalent in the gut microbial community [22]. However, in many individuals, the proportions of these species may be less than 0.5% of the total gut bacteria.

Gut microbial communities exhibit heterogeneity both longitudinally and laterally across the gastrointestinal tract [23]. Physiological differences along the intestinal tract, including pH, nutrient concentrations, oxygen levels, and immune activity, significantly influence microbial composition and distribution. For example, the small intestine has relatively higher oxygen concentrations and distinct pH conditions than the large intestine and is also rich in bile salts [24]. These conditions favor the growth of facultative anaerobes, which can grow rapidly, withstand environmental stress, and compete effectively with the host and other bacteria for carbohydrate utilization. In the small intestine, *Lactobacillaceae* and *Veillonellaceae* are reported as major bacterial families, while in the colon, *Bacteroidaceae* and *Lachnospiraceae* are predominant [25].

In addition to longitudinal differences, a study by Nava et al. (2011) also noted the heterogeneous distribution of bacteria across the cross-section of the intestinal tract using laser tomography combined with 16S rRNA gene sequencing in a mouse model [26]. Due

to the characteristic mucosal structure with many folds, the intestine forms distinct microenvironmental regions, such as the inter–fold regions and the central intestinal region (digesta region). The results showed that the *Lachnospiraceae* and *Ruminococcaceae* predominated in the interfold regions, while *Bacteroidaceae*, *Enterococcaceae*, and *Lactobacillaceae* were more common in the central intestinal region. These spatial distribution characteristics highlight that the intestinal microbiota is not only diverse in composition but also highly flexible and dependent on the microenvironment at each specific location in the digestive tract. Despite these findings, most human studies still rely on stool sample analysis, which primarily reflects the microbiome in the distal colon, due to its convenience and noninvasiveness [26].

3.2. Alterations of the gut microbiota in depression and anxiety

Table 1. *Gut microbiota alterations in depression and anxiety compared with healthy controls*

Condition	Changes in microbial group	Representative taxa	Potential implication for host physiology	Ref.
Depression and anxiety disorders	↓ SCFA - producing and beneficial bacteria	*Bifidobacterium*, *Lactobacillus*, *Faecalibacterium*, *Ruminococcus*	Reduced SCFA production, potentially affecting immune regulation, intestinal barrier integrity, and gut - brain communication.	[6, 7, 10, 27]
Depression	↓ Major gut microbial phyla	*Firmicutes*, *Actinobacteria*	Reduced representation of bacteria involved in metabolic and anti - inflammatory functions.	[25, 28]
Depression	↑ Dysbiosis - associated taxa	*Bacteroides*, *Parabacteroides*, *Alistipes*	Altered microbial metabolism and potential effects on inflammatory pathways and tryptophan - serotonin metabolism.	[28–31]
Depression and anxiety disorders	↓ SCFA - producing bacterial families and genera	*Prevotellaceae*, *Ruminococcaceae*, *Eubacterium*, *Coprococcus*, *Faecalibacterium*	Reduced microbial metabolites involved in immune balance and gut - brain signaling.	[6, 32]
Anxiety disorder	↑ Dysbiosis - associated taxa	*Escherichia*, *Bacteroides*	Increase representation of taxa associated with microbial imbalance and inflammatory profiles.	[6]

Arrows indicate the direction of alterations in bacterial abundance relative to healthy controls: ↓ decrease; ↑ increase.

Compared to healthy controls, several papers have indicated alterations in the gut microbiota composition in patients with depression and anxiety, including decreased microbial diversity and shifts in the relative proportions of specific taxa. Representative microbial patterns reported across studies are summarized in Table 1.

One of the first studies offering evidence of these microbial changes was a work conducted by Aizawa et al. in 2016. The study demonstrated that depressed patients had a marked reduction in the abundance of *Bifidobacterium* and *Lactobacillus*, two bacterial genera known for their positive effects in regulating stress and reducing depressive symptoms [27]. Moving to 2019, a systematic review by Cheung et al. on the association between gut microbiota and depression further noted a decrease in the genera *Faecalibacterium* and *Ruminococcus*, bacteria that play important roles in maintaining gut health and neurological function [10]. In major depressive disorder patients, gut dysbiosis is frequently marked by a reduced proportion of the phyla *Firmicutes* and *Actinobacteria*, families *Bifidobacteriaceae* and *Defluviitaleaceae* [25, 28]. Conversely, reports have indicated increased ratios of phyla *Bacteroidetes* and *Proteobacteria*, genera *Bacteroides*, *Parabacteroides*, and *Alistipes* [28, 29]. *Parabacteroides* have been associated with social stress responses in mice, while *Alistipes* may affect tryptophan metabolism, disrupting serotonin synthesis, implicated in depression [30, 31]

Anxiety disorder also exhibits distinct microbiological characteristics. Studies have shown that patients with this disorder often have increased proportions of the *Escherichia* and *Bacteroides* genera, with members causing several inflammatory conditions in the digestive system [6]. In contrast, reduced ratios have been observed in bacteria belonging to the phylum *Firmicutes*, families *Prevotellaceae* and *Ruminococcaceae*, and genera *Eubacterium*, *Coprococcus*, and *Faecalibacterium* [6, 32]. Bacteria such as *Ruminococcus*, *Faecalibacterium*, *Bifidobacterium*, and *Lactobacillus* produce SCFAs such as acetate, propionate, butyrate, and valerate [7, 12, 13]. These SCFAs play essential roles in immune regulation, support T–cell differentiation, participate in neurotransmitter synthesis, and can cross the blood–brain barrier to directly affect the brain. Therefore, the decrease in SCFA–producing bacteria in patients with depression and anxiety may contribute to the immune and neuronal imbalances associated with mood disorders.

In individuals with depression and anxiety, common influencing factors include diet, medications, and lifestyle. Diets high in sugar and fat, and low in fiber, reduce microbial diversity, alter species ratios, and increase intestinal permeability, while promoting the growth of inflammatory bacteria such as *Bilophila wadsworthia* [4]. In contrast, diets rich in whole grains, vegetables, legumes, and healthy fats increase the proportion of *Bacteroides* and *Clostridia*, while decreasing the proportion of *Proteobacteria*, thereby reducing the risk of neurological and psychiatric diseases, especially depression [4]. Prolonged use of antibiotics can cause dysbiosis, reducing the proportion of

Bifidobacterium and *Lactobacillus* and increasing the likelihood of developing antibiotic-resistant strains [33, 34]. Additionally, alcohol and tobacco negatively affect gut microbiota by reducing diversity and causing disturbances [35]. Although diet, medication, and lifestyle play important roles in explaining changes in bacterial composition, analyses of the independent relationship between microbiota and mental disorders are still limited due to numerous confounding factors. To better understand this link, further large-scale studies and repeated microbiological evaluations are therefore required.

3.3. Mechanistic pathways linking gut microbiota to mental health

The gut microbiota influences neurological and psychiatric functions through multiple pathways, with neurotransmitter regulation being a key mechanism [3]. Gut bacteria directly synthesize or modulate neurotransmitters such as serotonin, dopamine, and GABA, all of which are linked to the pathogenesis of depression and anxiety [3, 16, 36]. Approximately 90–95% of serotonin is produced in the gastrointestinal tract by enterochromaffin cells. Gut bacteria play a crucial role in regulating serotonin synthesis by stimulating these cells and producing mediators like tryptophan [3, 37]. In addition, bacterial strains such as *Lactobacillus*, *Bacillus*, and *Bifidobacterium* can directly produce dopamine and GABA [3, 38]. These neurotransmitters can affect the CNS directly through systemic circulation or indirectly through vagal nerve signals [39].

Additionally, gut microbiota is involved in immune regulation, another crucial pathway linked to mental health. Several studies have identified neuroinflammation and systemic inflammation as key pathophysiological mechanisms underlying depression and anxiety [7, 40]. Gut bacteria help maintain balance and protect the integrity of the intestinal barrier, preventing lipopolysaccharides and antigens from harmful bacteria from entering the circulation, thereby reducing inflammation [6, 15, 41]. Bacteria also influence immune cell activity by activating or inhibiting cytokine production. Dendritic cells in the intestinal mucosa receive signals from bacteria and can increase the production of IL-10, a cytokine that regulates inflammation and maintains immune balance [17]. Beneficial bacteria in the gut also participate in the activation and proliferation of regulatory T cells, which help maintain immune response balance, especially in hypersensitive inflammatory reactions induced by proinflammatory cytokines such as IL-6, IL-1β, and TNF-α [8, 15].

Furthermore, gut microbiota is also closely associated with the HPA axis, the central stress response system. Dysfunction of the HPA axis can lead to chronically elevated cortisol levels in individuals with depression, resulting in inflammation, increased intestinal permeability, and subsequent health issues [6, 7, 42]. Elevated cortisol also affects serotonin and dopamine receptors, disrupting their signaling pathways [17]. Gut bacteria, through their immune-modulating roles, can mitigate inflammation, thereby alleviating HPA axis overactivity [7, 42, 43]. Additionally, metabolites such as SCFAs and neurotransmitters produced by gut

bacteria can help restore neurotransmitter balance in depressed individuals and regulate cortisol hypersecretion by the HPA axis [13].

3.4. Methodological approaches and limitations in gut microbiota research

Advances in genomic sequencing technologies have significantly improved the study of gut microbiota diversity and function. Among these approaches, 16S rRNA gene sequencing and shotgun metagenomics are commonly used techniques, each with distinct advantages and limitations [44]. 16S rRNA gene sequencing targets the DNA sequence encoding the 16S ribosomal subunit, particularly the variable regions V3–V4, enabling cost effective profiling of bacterial communities [19, 45]. However, this method typically provides taxonomic resolution only at the genus level and does not offer information on microbial functional genes. In contrast, shotgun metagenomics sequences the entire genetic content of microbial communities by analyzing all the DNA in samples [44]. This approach provides detailed identification at the species and even strain level, and allows functional characterization, including genes associated with antibiotic resistance and metabolic pathways. Nevertheless, shotgun metagenomics requires greater sequencing depth and complex data analysis, making it more expensive and time-consuming. Therefore, the choice of sequencing approach should be guided by specific research objectives, considering factors such as taxonomic resolution, functional information, budget, and available analytical resources. Combining 16S rRNA screening with shotgun metagenomics may provide a more comprehensive understanding of the gut microbiota composition and function.

Methodological factors such as stool sample collection and DNA extraction procedures may also influence microbiome analysis. Stool samples are typically collected fresh, transported to the laboratory within 30 minutes, and stored at low temperatures (-80°C), ensuring consistency in collection equipment [46]. In addition, different DNA extraction kits may introduce bias by preferentially degrading certain bacterial cell components. Consequently, it is essential to optimize the sample collection process as well as the DNA extraction in the experimental design.

Finally, host related factors may complicate the interpretation of microbiome findings, particularly in patients with psychiatric disorders. Medication and lifestyle factors could substantially influence gut microbiota composition. Antidepressants, including Amitriptyline and selective serotonin reuptake inhibitors, have been reported to negatively affect the gut microbiota [4, 34, 35]. Additionally, lifestyle factors such as poor diet, physical inactivity, and smoking may contribute to microbial alterations [4, 34]. These variations highlight the importance of standardized protocols and careful consideration of confounding factors to improve comparability across gut microbiota studies.

3.5. Emerging clinical applications and therapeutic potential

Probiotic and prebiotic interventions have shown considerable promise in the management of mood disorders by modulating gut microbiota [4, 9, 47]. A meta-analysis of 34 randomized controlled trials reported that probiotic supplementation significantly reduced depressive symptoms compared with placebo [47]. Several studies have documented the mental health-promoting effects of *Lactobacillus* and *Bifidobacterium* strains, with *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175 exhibiting anti–anxiety and antidepressant properties in both humans and animals [48, 49]. Additionally, prebiotic supplementation supports the growth of beneficial gut bacteria and may enhance the production of SCFAs, which influences the gut–brain axis [12].

Beyond probiotic supplements, fecal microbiota transplantation (FMT) has been explored as a potential treatment for neuropsychiatric disorders, including depression and anxiety [50]. Animal studies have shown that FMT from depressed patients can induce depressive-like behaviors, while FMT from healthy donors can reverse these effects [51, 52]. For example, research demonstrated that FMT from healthy rats alleviated depressive-like behaviors in rats receiving FMT from depressed patients. However, evidence supporting the therapeutic application of FMT in human mental disorders remains limited, as most studies focus primarily on bacterial composition rather than clinical outcomes [50].

Besides therapeutic interventions, the gut microbiome may also provide potential biomarkers for the diagnosis and classification of depression and anxiety. Studies have identified significant alterations in the gut bacterial composition of patients compared to healthy individuals, including reduced bacterial diversity and changes in the abundance of specific bacterial phyla [10, 11]. Techniques such as 16S rRNA sequencing and shotgun metagenomics can detect these markers, suggesting their potential as complementary diagnostic tools alongside traditional psychiatric assessments [52, 53]. However, achieving consistent replication of these biomarkers across diverse populations remains a significant challenge.

Additionally, advances in microbiome research have also encouraged the development of personalized medicine approaches targeting the gut microbiome, which offer promising treatments for depression and anxiety. By analyzing microbiome composition individually through metagenomic techniques, clinicians may design tailored therapeutic strategies. These plans may include prescribing specific probiotics, recommending dietary adjustments with prebiotics and appropriate nutrients, or, in certain cases, FMT to restore microbial balance. For example, patients with low levels of SCFA-producing bacteria might benefit from a high-fiber diet, while those exhibiting specific dysbiosis patterns could be prescribed targeted probiotic formulations [4]. Advances in bioinformatics and microbiome sequencing are accelerating the development of such personalized therapies [53, 54].

IV. DISCUSSION

Current evidence suggests that alterations in the gut microbiota are consistently associated with depression and anxiety, particularly reduced microbial diversity and a decline in SCFA-producing bacteria. Across studies, immune dysregulation, impaired intestinal barrier integrity, and HPA axis overactivity emerge as intersecting pathways through which microbial imbalance may influence CNS function. Rather than being a single causal factor, the gut microbiome may function as a dynamic regulator of neuroimmune balance and stress responses. This integrative perspective aligns with findings that microbial metabolites, immune signaling, and neuroendocrine pathways interact bidirectionally within the gut–brain axis. However, the complexity of these interactions suggests that microbiome alterations may be only one component within an interconnected network underlying mood disorder.

Nevertheless, the interpretation of current findings remains constrained by important conceptual and methodological challenges. Most current studies rely on cross-sectional designs, which cannot establish temporal relationships nor determine whether alterations in the microbiome are causes or consequences of mental disorders [6]. Heterogeneity across geographic regions, diets, and clinical populations further complicates the identification of consistent microbial signatures. In addition, reliance on stool samples primarily reflects the distal colonic microbiome and may not capture region-specific microbial dynamics along the gastrointestinal tract. Differences in sequencing approaches, including 16S rRNA gene profiling versus shotgun metagenomics, also influence taxonomic resolution and functional inference. Together, these factors underscore the need for cautious interpretation and highlight the complexity of establishing robust microbiome-based biomarkers for mental health disorders.

Despite several promising prospects of microbiome-based applications, several challenges must be addressed before these methods can be widely implemented in clinical practice. Personalized microbiome-based medicine could raise important ethical, legal, and social considerations. These issues include informed consent, privacy and data security, and unequal access to costly techniques. Addressing these challenges requires careful consideration of appropriate regulatory frameworks and the development of equitable healthcare strategies to support the responsible integration of microbiome-based therapies.

Future research should prioritize longitudinal cohort designs with repeated microbial sampling to clarify temporal relationships and identify potential sensitive windows across the lifespan [55, 56]. Integrating multi–omics approaches may provide a more comprehensive understanding of host-microbiome interactions and functional consequences [57]. Although probiotic interventions and microbiome–guided strategies show therapeutic potential, their clinical translation requires greater mechanistic

clarity, standardized protocols, and replication across diverse populations. Advancing toward microbiome-based precision psychiatry would depend on rigorous study design, improved reproducibility, and careful consideration of ethical and regulatory frameworks. Overall, these efforts may help define the extent to which microbiome modulation can complement existing strategies for the prevention and management of depression and anxiety.

V. CONCLUSION

The gut microbiome is becoming acknowledged as a critical factor affecting the onset and progression of depression and anxiety. Studies have identified distinct microbial patterns in individuals with these conditions, including lower bacterial diversity and changes in beneficial bacterial genera such as *Lactobacillus* and *Bifidobacterium*. These alterations are associated with dysregulation of neurotransmitter production, immune function, and stress regulation through the gut-brain connection, potentially contributing to mood disorders. While treatments like probiotics and FMT show promise, further research is needed to address inconsistencies between studies and optimize therapeutic approaches. Long-term studies and personalized medicine will be essential to understanding causal relationships and developing targeted microbiome-based treatments. By integrating multi-omics data and advancing clinical applications, gut microbiome research presents a promising possibility to enhance mental health care. This review emphasizes the potential of microbiome research in psychiatry while underscoring the need for rigorous mechanistic studies and translational validation to bridge the gap between scientific findings and clinical applications.

References

1. World Health Organization. Depressive disorder (depression). Accessed March 28, 2025. Available from: https://www.who.int/news-room/fact-sheets/detail/depression
2. World Health Organization. Anxiety disorders. Accessed March 28, 2025. Available from: https://www.who.int/news-room/fact-sheets/detail/anxiety-disorders
3. Strandwitz P. Neurotransmitter modulation by the gut microbiota. Brain Res. 2018;1693 (Pt B):128. doi:10.1016/j.brainres.2018.03.015
4. Clerici L, Bottari D, Bottari B. Gut Microbiome, Diet and Depression: Literature Review of Microbiological, Nutritional and Neuroscientific Aspects. Curr Nutr Rep. 2025;14(1):1-14. doi:10.1007/S13668-025-00619-2
5. Rosenberg E. Diversity of bacteria within the human gut and its contribution to the functional unity of holobionts. npj Biofilms Microbiomes. 2024;10(1):5. doi:10.1038/s41522-024-00580-y
6. Simpson CA, Diaz-Arteche C, Eliby D, Schwartz OS, Simmons JG, Cowan CSM. The gut microbiota in anxiety and depression–A systematic review. Clin Psychol Rev. 2021;83:101943. doi:10.1016/j.cpr.2020.101943
7. Peirce JM, Alviña K. The role of inflammation and the gut microbiome in depression and anxiety. J Neurosci Res. 2019;97(10):1223-1241. doi:10.1002/jnr.24476
8. Nguyễn TTN, Đoàn TTH, Lưu ĐNA. Lợi khuẩn-cytokines và trầm cảm. Thai Binh Journal of Medicine and Pharmacy. 2023;(06).
9. Kumar A, Pramanik J, Goyal N, et al. Gut Microbiota in Anxiety and Depression: Unveiling the Relationships and Management Options. Pharmaceuticals. Multidisciplinary

Digital Publishing Institute (MDPI). 2023;16(4). doi:10.3390/ph16040565

10. Cheung SG, Goldenthal AR, Uhlemann AC, Mann JJ, Miller JM, Sublette ME. Systematic Review of Gut Microbiota and Major Depression. Front Psychiatry. 2019;10(FEB):34. doi:10.3389/fpsyt.2019.00034
11. Sanada K, Nakajima S, Kurokawa S, et al. Gut microbiota and major depressive disorder: A systematic review and meta-analysis. J Affect Disord. 2020;266:1-13. doi:10.1016/j.jad.2020.01.102
12. Silva YP, Bernardi A, Frozza RL. The Role of Short-Chain Fatty Acids From Gut Microbiota in Gut-Brain Communication. Front Endocrinol (Lausanne). 2020;11:25. doi:10.3389/fendo.2020.00025
13. O'Riordan KJ, Collins MK, Moloney GM, et al. Short chain fatty acids: Microbial metabolites for gut-brain axis signalling. Mol Cell Endocrinol. Elsevier Ireland Ltd. 2022;546. doi:10.1016/j.mce.2022.111572
14. Tarracchini C, Lugli GA, Mancabelli L, et al. Exploring the vitamin biosynthesis landscape of the human gut microbiota. Gilbert JA, ed. mSystems. 2024;9(10):e00929-24. doi:10.1128/msystems.00929-24
15. Hou K, Wu ZX, Chen XY, et al. Microbiota in health and diseases. Signal Transduct Target Ther. Springer Nature. 2022;7(1). doi:10.1038/s41392-022-00974-4
16. Qu S, Yu Z, Zhou Y, et al. Gut microbiota modulates neurotransmitter and gut-brain signaling. Microbiol Res. 2024;287:127858. doi:10.1016/j.micres.2024.127858
17. Choden T, Cohen NA. The gut microbiome and the immune system. Open Exploration. 2022;3(3):219-233. doi:10.37349/emed.2022.00087
18. Järbrink-Sehgal E, Andreasson A. The gut microbiota and mental health in adults. Curr Opin Neurobiol. 2020;62:102-114. doi:10.1016/j.conb.2020.01.016
19. Hoang TH, Le HD, Nguyen TTN, Nguyen TN. The first step comparative analysis of gut microbiota in human with type 2 diabetes and non-diabetic in Vietnam. In: Vietnam National Conference on Biotechnology. 2021.
20. Rinninella E, Raoul P, Cintoni M, et al. What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms. 2019;7(1). doi:10.3390/microorganisms7010014
21. Sheng Y, Wang J, Gao Y, et al. Combined analysis of cross-population healthy adult human microbiome reveals consistent differences in gut microbial characteristics between Western and non-Western countries. Comput Struct Biotechnol J. 2024;23:87-95. doi:10.1016/j.csbj.2023.11.047
22. Adak A, Khan MR. An insight into gut microbiota and its functionalities. Cellular and Molecular Life Sciences. Birkhauser Verlag AG. 2019;76(3):473-493. doi:10.1007/s00018-018-2943-4
23. Donaldson GP, Lee SM, Mazmanian SK. Gut biogeography of the bacterial microbiota. Nature Reviews Microbiology. 2015;14(1):20-32. doi:10.1038/nrmicro3552
24. Jensen BAH, Heyndrickx M, Jonkers D, et al. Small intestine vs. colon ecology and physiology: Why it matters in probiotic administration. Cell Rep Med. Cell Press. 2023;4(9). doi:10.1016/j.xcrm.2023.101190
25. Dieterich W, Schink M, Zopf Y. Microbiota in the Gastrointestinal Tract. Med Sci (Basel). NLM (Medline). 2018;6(4). doi:10.3390/medsci6040116
26. Nava GM, Friedrichsen HJ, Stappenbeck TS. Spatial organization of intestinal microbiota in the mouse ascending colon. ISME J. 2011;5(4):627-638. doi:10.1038/ismej.2010.161
27. Aizawa E, Tsuji H, Asahara T, et al. Possible association of Bifidobacterium and Lactobacillus in the gut microbiota of patients with major depressive disorder. J Affect Disord. 2016;202:254-257. doi:10.1016/J.JAD.2016.05.038
28. Zhao Q, Baranova A, Cao H, Zhang F. Gut microbiome and major depressive disorder: insights from two-sample Mendelian randomization. BMC Psychiatry. 2024;24(1):493. doi:10.1186/s12888-024-05942-6
29. Jiang H, Ling Z, Zhang Y, et al. Altered fecal microbiota composition in patients with major depressive disorder. Brain Behav Immun. 2015;48:186-194. doi:10.1016/J.BBI.2015.03.016
30. Parker BJ, Wearsch PA, Veloo ACM, Rodriguez-Palacios A. The Genus Alistipes: Gut Bacteria With Emerging Implications to

Inflammation, Cancer, and Mental Health. Front Immunol. Frontiers Media S.A. 2020;11. doi:10.3389/fimmu.2020.00906

31. Gomez-Nguyen A, Basson AR, Dark-Fleury L, et al. Parabacteroides distasonis induces depressive-like behavior in a mouse model of Crohn's disease. Brain Behav Immun. 2021;98:245-250. doi:10.1016/j.bbi.2021.08.218
32. Butler MI, Kittel-Schneider S, Wagner-Skacel J, Mörkl S, Clarke G. The Gut Microbiome in Anxiety Disorders. Current Psychiatry Reports. 2025;27(5):347-361. doi:10.1007/s11920-025-01604-w
33. Huang C, Feng S, Huo F, Liu H. Effects of Four Antibiotics on the Diversity of the Intestinal Microbiota. Microbiol Spectr. 2022;10(2):e01904-21. doi:10.1128/spectrum.01904-21
34. Lathakumari RH, Vajravelu LK, Satheesan A, Ravi S, Thulukanam J. Antibiotics and the gut microbiome: Understanding the impact on human health. Medicine in Microecology. 2024;20:100106. doi:10.1016/j.medmic.2024.100106
35. Cussotto S, Clarke G, Dinan TG, Cryan JF. Psychotropics and the Microbiome: a Chamber of Secrets. Psychopharmacology. 2019;236(5):1411-1432. doi:10.1007/S00213-019-5185-8
36. Huang F, Wu X. Brain Neurotransmitter Modulation by Gut Microbiota in Anxiety and Depression. Front Cell Dev Biol. Frontiers Media S.A. 2021;9. doi:10.3389/fcell.2021.649103
37. Yano JM, Yu K, Donaldson GP, et al. Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. Cell. 2015;161(2):264-276. doi:10.1016/j.cell.2015.02.047
38. Doenyas C, Clarke G, Cserjési R. Gut–brain axis and neuropsychiatric health: recent advances. Sci Rep. 2025;15(1):1-4. doi:10.1038/s41598-025-86858-3
39. Olsen LK, Solis E, McIntire LK, Hatcher-Solis CN. Vagus nerve stimulation: mechanisms and factors involved in memory enhancement. Front Hum Neurosci. Frontiers Media SA. 2023;17. doi:10.3389/fnhum.2023.1152064
40. Han KM, Ham BJ. How Inflammation Affects the Brain in Depression: A Review of Functional and Structural MRI Studies. J Clin Neurol. 2021;17(4):503. doi:10.3988/jcn.2021.17.4.503
41. Di Vincenzo F, Del Gaudio A, Petito V, Lopetuso LR, Scaldaferri F. Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review. Intern Emerg Med. Springer Science and Business Media Deutschland GmbH. 2024;19(2):275-293. doi:10.1007/s11739-023-03374
42. Bertollo AG, Santos CF, Bagatini MD, Ignácio ZM. Hypothalamus-pituitary-adrenal and gut-brain axes in biological interaction pathway of the depression. Front Neurosci. Frontiers Media SA. 2025;19. doi:10.3389/fnins.2025.1541075
43. Wallace CJK, Milev R. The effects of probiotics on depressive symptoms in humans: A systematic review. Ann Gen Psychiatry. 2017;16(1):1-10. doi:10.1186/S12991-017-0138-2
44. Laudadio I, Fulci V, Palone F, Stronati L, Cucchiara S, Carissimi C. Quantitative Assessment of Shotgun Metagenomics and 16S rDNA Amplicon Sequencing in the Study of Human Gut Microbiome. OMICS. 2018;22(4):248-254. doi:10.1089/omi.2018.0013
45. Ranjan R, Rani A, Metwally A, McGee HS, Perkins DL. Analysis of the microbiome: Advantages of whole genome shotgun versus 16S amplicon sequencing. Biochem Biophys Res Commun. 2016;469(4):967-977. doi:10.1016/j.bbrc.2015.12.083
46. Carruthers L V., Moses A, Adriko M, et al. The impact of storage conditions on human stool 16S rRNA microbiome composition and diversity. PeerJ. 2019;(12):e8133. doi:10.7717
47. Liu RT, Walsh RFL, Sheehan AE. Prebiotics and probiotics for depression and anxiety: A systematic review and meta-analysis of controlled clinical trials. Neurosci Biobehav Rev. 2019;102:13. doi:10.1016/j.neubiorev.2019.03.023
48. Morales-Torres R, Carrasco-Gubernatis C, Grasso-Cladera A, Cosmelli D, Parada FJ, Palacios-García I. Psychobiotic Effects on Anxiety Are Modulated by Lifestyle Behaviors: A Randomized Placebo-Controlled Trial on Healthy Adults. Nutrients. 2023;15(7). doi:10.3390/nu15071706
49. Ferrari S, Mulè S, Parini F, et al. The influence of the gut-brain axis on anxiety and depression:

A review of the literature on the use of probiotics. J Tradit Complement Med. National Taiwan University. 2024;14(3):237-255. doi:10.1016/j.jtcme.2024.03.011

50. Chinna Meyyappan A, Forth E, Wallace CJK, Milev R. Effect of fecal microbiota transplant on symptoms of psychiatric disorders: A systematic review. BMC Psychiatry. 2020;20(1):1-19. doi:10.1186/S12888-020-02654-5

51. Kelly JR, Borre Y, O' Brien C, et al. Transferring the blues: Depression-associated gut microbiota induces neurobehavioural changes in the rat. J Psychiatr Res. 2016;82:109-118. doi:10.1016/j.jpsychires.2016.07.019

52. Zheng P, Zeng B, Zhou C, et al. Gut microbiome remodeling induces depressive-like behaviors through a pathway mediated by the host's metabolism. Molecular Psychiatry. 2016;21(6):786-796. doi:10.1038/mp.2016.44

53. Jovel J, Patterson J, Wang W, et al. Characterization of the Gut Microbiome Using 16S or Shotgun Metagenomics. Front Microbiol. 2016;7(APR):459. doi:10.3389/fmicb.2016.00459

54. El-Salhy M, Mazzawi T. Fecal microbiota transplantation for managing irritable bowel syndrome. Expert Rev Gastroenterol Hepatol. 2018;12(5):439-445. doi:10.1080/17474124.2018.1447380

55. Vaher K, Bogaert D, Richardson H, Boardman JP. Microbiome-gut-brain axis in brain development, cognition and behavior during infancy and early childhood. Developmental Review. Elsevier Inc. 2022;66. doi:10.1016/j.dr.2022.101038

56. Fox M, Lee SM, Wiley KS, et al. Development of the infant gut microbiome predicts temperament across the first year of life. Dev Psychopathol. 2022;34(5):1914-1925. doi:10.1017/S0954579421000456

57. Wu J, Singleton SS, Bhuiyan U, Krammer L, Mazumder R. Multi-omics approaches to studying gastrointestinal microbiome in the context of precision medicine and machine learning. Front Mol Biosci. Frontiers Media SA. 2023;10. doi:10.3389/fmolb.2023.133737