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INTERACTIONS BETWEEN GUT MICROBIOTA AND DEPRESSIVE AND ANXIETY DISORDERS: A COMPREHENSIVE REVIEW

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ABSTRACT

Background. Depressive and anxiety disorders are major challenges in modern medicine and are increasingly linked to gut dysbiosis. Evidence indicates that affected patients often exhibit reduced microbial diversity, lower levels of SCFA-producing bacteria, and increased pro-inflammatory taxa. Proposed mechanisms include altered SCFA production, neurotransmitter modulation, vagus nerve signaling, immune activation, HPA axis dysregulation, and impaired gut and blood–brain barrier integrity

Aim. This review summarizes current evidence on the gut-brain axis and how it impacts mood disorders.

Material and methods. The review analyzed English-language studies published between 2015 and 2025 using PubMed, SpringerLink, and Elsevier, focusing primarily on human research examining the gut microbiota, gut–brain axis, and their association with depressive and anxiety disorders.

Results. The review highlights the potential of microbiota-based therapies for mood disorders. Probiotics, especially psychobiotic strains, show the most consistent benefits in reducing depressive and anxiety symptoms, while evidence for prebiotics and dietary interventions remains limited. Current studies are constrained by methodological heterogeneity, small sample sizes, and short intervention durations.

Conclusions. Overall, accumulating data support the gut microbiota as a significant contributor to the development and modulation of depressive and anxiety disorders. While definitive clinical recommendations cannot yet be made, microbiota modulation represents a promising avenue for future integrative treatment approaches and warrants further rigorous investigation.

KEYWORDS

Gut Microbiota, Intestinal Microbiome, Microbiome Composition, Gut–Brain Axis, Microbiota–Gut–Brain Axis, Depression, Major Depressive Disorder, Anxiety, Anxiety Disorders, Short-Chain Fatty Acids, Microbial Metabolites, Probiotics, Prebiotics, Psychobiotics

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1.Introduction

1.1. Significance of the Problem

Depressive and anxiety disorders are among the most common health problems worldwide. It is therefore no surprise that they rank among the top causes of reduced quality of life and disability. According to data from the World Health Organization (WHO), over 332 million people worldwide suffer from depression. Consequently, this condition is considered as one of the most significant challenges facing modern medicine. Anxiety disorders affect globally a similarly large number of people. The problem is further compounded by the fact that these disorders often co-occur (in over 50% of cases), which complicates treatment and reduces the likelihood of successful outcomes. [2]

Both depressive and anxiety disorders are on the rise, drawing particular attention in developed countries. Potential factors contributing to this increase include chronic stress, lifestyle changes, and the widespread use of social media. It is important to remember that these conditions have a significant long-term impact on functioning and well-being, which is highly relevant from both a public health and healthcare systems perspective.

The challenges associated with depression and anxiety disorders pose a substantial burden not only on individuals but also on society. It is often overlooked that the costs related to these conditions include not only hospitalization, specialist care, and pharmacotherapy, but also broader social costs such as long-term sick leave, reduced productivity, and an increased risk of suicide attempts. According to a WHO report, suicide is the third leading cause of death among humans aged 15–29.

Unfortunately, although currently available pharmacological treatments help alleviate symptoms and restore functioning to a pre-illness level for some patients, many others do not experience sufficient relief. For all the reasons outlined above, it is not surprising that the medical community is increasingly interested in new therapies that could reduce the incidence of these disorders. In recent years, there has been a noticeable increase in interest in the role of the gut–brain axis—a promising area of research that may lead to the development of new therapeutic approaches capable of helping many patients.

1.2. The Gut–Brain Axis – More Precisely, the Microbiome–Gut–Brain Axis

The gastrointestinal tract is composed not only of human cells but also of a wide variety of bacteria, viruses, fungi, protozoa, and other microorganisms. Most of these microorganisms are in the large intestine. All of them play a crucial role in maintaining the proper functioning and balance of the human gut. Nevertheless, bacteria are of paramount importance. The microbiota plays an essential role in regulating the immune system, breaking down dietary fibre, and participating in the production of vitamins.

Recent research suggests that the bacterial population of the gastrointestinal tract is approximately 3.8×10^{13}, compared with the total number of human cells, which amounts to roughly 3.0×10^{13}. These findings underscore the importance of the gut microbiome. Moreover, the combined genetic material of these bacterial cells greatly surpasses the quantity of human DNA in the body. In fact, for each human gene, there are more than 100 bacterial genes. Considering the vast genetic capabilities of the microbiota, it is not surprising that it appears to influence nearly every physiological process in the human body, including those occurring in the gut and the brain. [1,23]

Consequently, a hypothesis emerged suggesting that the gut microbiota exerts a significant influence on the brain and its functioning. This concept is referred to as the microbiome–gut–brain axis.

1.3. Purpose and Scope of the Review

The purpose of this review is to present a summary of the current state of knowledge regarding the correlation between the gut–brain axis and depressive and anxiety disorders. This review focuses on changes in the composition of the microbiota in individuals with anxiety disorders or depression compared with control groups. Furthermore, it presents possible biological mechanisms influencing the physiology of emotional states.

This paper provides a review of clinical and experimental studies that have analysed the impact of changes in the microbiota and metabolites produced by gut bacteria on the functioning of the gut–brain axis. Dietary modifications, including the use of probiotics and prebiotics, are also discussed as a potential therapeutic approach in the treatment of depressive and anxiety disorders.

The review aims to identify current trends and hypotheses regarding the influence of the gut microbiota on depression and anxiety disorders.

2. Literature Review Methodology

2.1. Databases

The medical literature used for this work was obtained from scientific databases in the fields of medicine and biomedical sciences. The primary source was PubMed, which contains peer-reviewed and widely respected scientific papers in the fields of psychiatry, microbiology, and public health. Additional materials were sourced from SpringerLink and Elsevier. The papers included in this review consist of clinical trials, reviews, meta-analyses, and observational studies focusing on the gut microbiota, the gut–brain axis, and depressive and anxiety disorders.

2.2. Inclusion Criteria

Considered studies include publications from 2015 to 2025, published in English. Only peer-reviewed studies conducted on humans were included. Additionally, significant preclinical studies exploring the mechanisms of microbiota action, as well as publications examining the relationship between the gut microbiota and depressive and anxiety disorders, were considered.

3. Gut Microbiota in Depressive and Anxiety Disorders – A Review of the Data

3.1. General Characteristics of Microbiota Changes

Depressive and anxiety disorders have been increasingly associated with disturbances in the homeostasis of the entire body, including the gut microbiota. A growing number of studies have identified dysbiosis as one of the possible factors contributing to the development of mental illnesses such as those discussed in this review. Changes in microbiota composition have been described as alterations in the proportions of important taxa, variations in the ratios of specific bacterial groups, and fluctuations in the production of key metabolites (short-chain fatty acids, SCFAs). Studies examining the ratios of individual components of the gut flora reveal recurring patterns in depressive and anxiety disorders, which may indicate a correlation between these conditions and microbiota alterations. However, it should be noted that research findings remain inconsistent. [3,4]

Numerous studies comparing the microbiome of patients with depressive or anxiety disorders have reported reduced diversity in gut microbial composition. A decrease in microbial diversity is considered one of the factors that may disrupt the homeostasis of the entire organism. [4]

Conversely, some articles report no significant differences in alpha diversity between affected patients and healthy controls. These discrepancies likely stem from population variability, differences in dietary habits, the use of psychotropic medications, and variations in methodological approaches. Despite these inconsistencies, the hypothesis of altered gut microbiota composition in mental disorders is frequently cited in scientific literature. [5]

3.2. Taxonomic Changes in Depression

Numerous studies demonstrate recurring changes in the gut microbiota of patients with depressive disorders. The most frequently observed alterations include an increase in pro-inflammatory bacteria and a decrease in bacteria responsible for synthesizing short-chain fatty acids (SCFAs). Increased levels of *Actinobacteria*, *Proteobacteria*, *Rikenellaceae*, *Porphyromonadaceae*, and *Bifidobacteriaceae* have been reported in individuals with depression. Other studies also indicate an increase in *Desulfovibrio*. This genus appears to be particularly strongly associated with elevated inflammatory activity. [3,6]

A decrease in *Faecalibacterium*, *Butyricicoccus*, *Coprococcus*, and *Fusicatenibacter* has been observed in the gut microbiota of individuals with depression. These bacteria are known contributors to butyrate production. Another review similarly reports reductions in the *Ruminococcaceae* family as well as the genera *Faecalibacterium* and *Roseburia*.[4,5]

Additionally, the severity of depressive symptoms has been shown to correlate with specific microbiota changes. An increase in *Bacteroides* and a decrease in *Eubacterium* and *Ruminococcus* significantly increase the likelihood of patients developing more severe forms of depression. [7]

3.3. Taxonomic Changes in Anxiety Disorders

In recent years, a growing number of studies have focused on differences in the gut microbiota between individuals with anxiety disorders and healthy controls. Although the number of studies in this area is still considerably lower than in the context of depression, scientific interest in this relationship continues to increase. Analyses of the gut microbiota in humans with anxiety disorders, similarly to those in depression, have identified reduced numbers of SCFA-producing bacteria and decreased microbial diversity. Another study reported a significant decrease in bacterial groups such as *Firmicutes*, *Lachnospira*, *Faecalibacterium*, *Sutterella*, and *Butyricicoccus*. Most of these taxa are closely associated with SCFA production and anti-inflammatory activity. [6,8]

Interestingly, an increase in potentially pro-inflammatory bacteria, including *E. coli*, *Escherichia–Shigella*, *Fusobacterium*, and *Ruminococcus gnavus*, has been observed. Some researchers have also reported a significant increase in the phylum *Bacteroidetes* and the family *Enterobacteriaceae*. Reduced concentrations of SCFAs negatively affect immune function and intestinal integrity. Therefore, it can be assumed that a decreased abundance of SCFA-producing bacteria may adversely impact the functioning of the entire organism. Likewise, an increase in pro-inflammatory bacteria may promote heightened susceptibility to inflammation, disruption of the intestinal barrier, and translocation of microbial products. All of which can interfere with the functioning of the gut–brain axis. [6,7]

While these findings are promising, the limitations of the existing studies must be acknowledged. Most available studies are cross-sectional, making it impossible to determine whether microbiota alterations are a cause or consequence of anxiety disorders. Additionally, study participants often came from diverse populations, consumed different diets, and led varied lifestyles. Moreover, research directly linking anxiety disorders to dietary patterns is still in its early stages, and far fewer studies exist in comparison with the extensive literature linking depression to microbiota changes.

4. Mechanisms of the Potential Impact of Microbiota on Depression and Anxiety

4.1. Microbiota Metabolites (SCFAs, Neurotransmitters)

A growing number of studies have identified short-chain fatty acids (SCFAs) as key metabolites influencing the gut–brain axis. These compounds—primarily acetate, butyrate, and propionate—are produced through the fermentation of dietary fiber by specific intestinal bacteria. SCFAs play multiple roles, including modulating inflammation and influencing the activity of immune and neural cells, which may be relevant to mood regulation and cognitive functioning. As a result, it has been suggested that alterations in SCFA and amino acid metabolism may represent a missing link between gut dysbiosis and depressive and anxiety disorders. Importantly, metabolites produced by the gut microbiota may indirectly affect neuroendocrine and neurochemical pathways in the brain, as well as epigenetic mechanisms, thereby amplifying their impact. [9]

Conclusion: intestinal dysbiosis → disrupted production/metabolism of SCFAs and other metabolites → potential impact on brain function and increased risk of mood disorders.

4.2. The Vagus Nerve Axis

Another important gut–brain communication pathway is the vagus nerve. It serves as a route for transmitting mechanical and chemical signals generated in the intestine. Compounds produced by the microbiota can activate intestinal and neuroendocrine cells, leading to the initiation of neural signals that are subsequently transmitted through vagal nerve fibers. [11]

Conclusion: microbiota → signaling within the gut → activation of the vagus nerve → effects on the nervous system/brain, including possible changes in mood, stress regulation, and emotional processing.

4.3. Immune System Modulation and Inflammation

Another factor believed to link the gut microbiota with depression and anxiety disorders is inflammation. A review of the literature indicates that gut dysbiosis leads to the activation of pro-inflammatory pathways, including the production of cytokines such as IL-6, IL-1β, and TNF-α. Through the gut–brain axis, inflammatory processes in the gut can translate into changes in brain function. As mentioned earlier, short-chain fatty acids have been shown to reduce inflammatory responses and exert neuroprotective effects. [9,12]

Furthermore, dysbiosis contributes to the weakening of the intestinal barrier, which facilitates the translocation of bacterial endotoxins into the bloodstream. This, in turn, affects the functioning of the entire organism, including the central nervous system. [11]

Conclusion: the microbiota influences immune function — a healthy microbiota promotes an anti-inflammatory state, while dysbiosis supports neuroinflammation, which may predispose individuals to depression and anxiety disorders.

4.4. The HPA Axis and Stress Regulation

Studies have shown that the gut microbiota is one of the factors involved in regulating the activity of the hypothalamic–pituitary–adrenal (HPA) axis. This pathway is responsible for the body's response to stress. Evidence indicates that in individuals with depression and disrupted gut microbiota, the HPA axis is overactive, which consequently leads to elevated cortisol levels. This hormone contributes to an altered stress response and increased susceptibility to mood fluctuations. Therapeutic interventions aimed at restoring a healthy microbiota may help regulate the activity of the HPA axis. This represents a potential therapeutic target. [11,13,14]

Conclusion: microbiota ↔ HPA axis regulation / stress response → alterations in this system may influence the risk of developing depression and anxiety disorders.

4.5. Intestinal Barrier and Blood–Brain Barrier

Studies have demonstrated the positive impact of a healthy gut microbiota on maintaining the integrity of the intestinal barrier. Dysbiosis, in contrast, leads to weakened intercellular junctions, resulting in increased intestinal permeability and the translocation of endotoxins into the bloodstream. These substances, along with other bacterial products and cytokines, can cross the blood–brain barrier, contributing to neuroinflammation. Disruptions in brain homeostasis may lead to symptoms of depression and anxiety. [12,15]

Conclusion: healthy microbiota → stable intestinal barrier and blood–brain barrier → protection against neuroinflammation;

dysbiosis → increased intestinal permeability and impaired BBB integrity → potential impact on the development of depression and anxiety disorders.

5. Microbiota-Targeted Interventions as Potential Therapeutic Methods

Data from a growing number of studies suggest that improving the composition of the gut microbiota may serve as a complementary or adjunctive therapeutic approach for depressive and anxiety disorders. The interventions most frequently considered include probiotics, prebiotics, postbiotics, dietary modifications, and fecal microbiota transplantation. Although these findings offer promising prospects for incorporating such methods into clinical practice, their potential applications still require more extensive and rigorous research.

5.1. Probiotics

Overall Efficacy

A meta-analysis of 34 studies indicates that probiotics have only a modest effect on reducing depressive symptoms. Another analysis focusing on patients diagnosed with depressive or anxiety disorders reported a clinically significant reduction in the severity of depressive symptoms and a moderate reduction in anxiety symptoms. However, the therapeutic effects of probiotics depend strongly on the specific strains used, as different strains exert different biological actions. [16,17]

Strains Studied in Depression

Strains such as *Lactobacillus acidophilus*, *Lactobacillus paracasei*, *Lactobacillus casei*, *Lactobacillus plantarum*, *Lactobacillus salivarius*, *Bifidobacterium bifidum*, *Bifidobacterium lactis*, *Bifidobacterium breve*, and *Bifidobacterium longum* have been evaluated in patients with depression and have shown potential for reducing symptom severity.[18,22]

In one clinical trial involving patients with major depressive disorder (MDD), supplementation with *Lactobacillus helveticus* and *Bifidobacterium longum* for eight weeks resulted in a significant reduction in BDI scores compared with placebo. [17,22]

Strains Studied in Anxiety Disorders

Although the number of studies is smaller than in the case of depression, meta-analyses indicate that probiotics may exert a moderate anxiolytic effect in individuals with anxiety disorders or anxiety associated with other medical conditions. Reviews show that strains belonging to the genera *Lactobacillus* and *Bifidobacterium* are the most commonly used in psychobiotic research and form the dominant group of microorganisms assessed in these interventions. [17,19]

5.2. Prebiotics and Postbiotics

According to a 2023 meta-analysis of randomized controlled trials, the effect of prebiotics on depressive symptoms was small and statistically insignificant (SMD: –0.28; 95% CI: –0.61, 0.04). The same analysis emphasized, however, that although prebiotics generally show weaker effects than probiotics, some studies have reported beneficial trends in anxiety reduction and mood improvement. This suggests their potential value, but confirmation of these effects requires further, more rigorous clinical trials. [17,21]

Reviews addressing the concept of *psychobiotics* note that bacterial metabolites—referred to as postbiotics—such as short-chain fatty acids (SCFAs), neurotransmitters, and other bioactive compounds, may also play a significant role. These substances can influence gut–brain axis functioning and may mediate some of the effects observed in microbiota-centered studies.[19,21]

Current literature concludes that prebiotics exhibit weaker and less predictable therapeutic effects than probiotics. This does not negate their potential but highlights the need for additional high-quality research investigating their impact on depressive and anxiety disorders.

5.3. Diet and Dietary Modifications

Although the number of randomized controlled trials directly assessing the impact of diet on depression and anxiety through modulation of the gut microbiota is limited, a growing body of literature indicates that dietary patterns rich in fiber, vegetables, healthy fats, and fermented foods may serve as a complementary strategy for supporting mental health. Reviews on psychobiotics emphasize that diets promoting the growth of beneficial gut bacteria—particularly those producing short-chain fatty acids (SCFAs)—may positively affect gut–brain axis functioning and the regulation of neuroimmune processes. For this reason, dietary patterns that enhance microbiota diversity are considered an important complement to probiotic and prebiotic interventions. [19]

The most frequently highlighted benefits of such dietary strategies include increased microbiota diversity, enhanced growth of beneficial bacterial species, the provision of essential substrates for SCFA production—which may support neuroprotection and immune system regulation—as well as potential synergistic effects with probiotics and prebiotics that may further strengthen therapeutic outcomes.

5.4. Fecal Microbiota Transplantation (FMT) – State of the Art

In the literature on mood disorders and the gut microbiota, the topic of fecal microbiota transplantation (FMT) is far less developed than that of probiotics. There is a notable lack of well-designed randomized controlled trials assessing FMT in the treatment of depression or anxiety disorders. A review of psychobiotics indicates that although FMT has considerable theoretical potential, the current evidence base is too limited to recommend it as a standard psychiatric treatment. [19,20]

5.5. Limitations of Intervention Studies

An analysis of the available literature highlights several important limitations that should be taken into account when interpreting findings from studies examining microbiota-targeted interventions for depression and anxiety. The primary issue concerns the significant heterogeneity of probiotic strains, their doses, and research protocols. Individual studies employ different single-strain or multi-strain preparations administered over varying durations, which greatly complicates result comparison. A 2024 meta-analysis further emphasizes that probiotic effects are strictly strain-specific, making it difficult to draw generalized conclusions.

Additionally, many studies include small participant groups or lack sufficient numbers of high-quality randomized clinical trials. This reduces statistical power and limits confidence regarding both the effectiveness and safety of the interventions. The typically short duration of most studies—often only a few weeks—poses another challenge, preventing reliable assessment of long-term effects or the persistence of benefits after supplementation ends.

The lack of standardized study populations also remains a significant limitation. Differences in diagnostic criteria, degrees of symptom severity, comorbid somatic conditions, as well as variations in diet and lifestyle, can substantially influence outcomes and reduce generalizability. Finally, many studies rely heavily on self-reported mental health assessment tools, which are susceptible to placebo effects, participant expectations, and subjective measurement variability. This naturally complicates the unambiguous interpretation of the observed findings.

6. Summary and Conclusions

The gut microbiota plays an increasingly prominent role in regulating neurobiological, immunological, and metabolic processes that influence human mental functioning. A review of the available literature indicates that depressive and anxiety disorders are associated with characteristic alterations in microbiota composition and its metabolites, as demonstrated by both clinical studies and numerous animal models. Publications analyzing the gut–brain axis highlight the importance of mechanisms such as short-chain fatty acid (SCFA) production, neurotransmitter modulation (including serotonin and GABA), interactions with the vagus nerve, immune system regulation, and the effects on the integrity of the intestinal barrier and the blood–brain barrier.

Current data suggest that microbiota-targeted interventions—including probiotics, prebiotics, postbiotics, dietary modifications, and fecal microbiota transplantation—represent a promising therapeutic avenue for the treatment and support of individuals with depressive and anxiety disorders. The strongest and most consistent evidence concerns probiotics, particularly those classified as psychobiotics, which have been shown in multiple studies to exert beneficial effects on mood symptoms, stress levels, and inflammatory markers. Prebiotics, by contrast, yield less conclusive results: meta-analyses report small and statistically insignificant effects on depressive symptoms, although some studies note favorable trends in anxiety reduction and stress regulation. Diets rich in fiber, vegetables, whole grains, healthy fats, and fermented foods—known to promote greater microbiota diversity and SCFA production—appear to be a valuable complementary approach in interventions targeting the gut microbiota.

Despite the growing body of research, the interpretation of findings remains challenging due to significant methodological limitations. These include heterogeneity in probiotic strains, varying doses and supplementation protocols, small sample sizes, short intervention durations, substantial variability among study populations, and the widespread reliance on subjective mental health assessment tools. Consequently, more robust and well-designed clinical trials are needed, incorporating standardized formulations, longer follow-up periods, dietary controls, and objective biological marker measurements.

In conclusion, the gut microbiota constitutes an important and rapidly evolving field within psychiatric research, offering new opportunities for understanding the pathophysiology of depressive and anxiety disorders as well as potential therapeutic strategies. Although current evidence is insufficient to establish definitive clinical recommendations, findings increasingly suggest that microbiota modulation—through probiotics, dietary interventions, or other approaches—may become an important component of future integrated treatment strategies for mood disorders.

Disclosure

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