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Gut Microbiota and Mental Health: the Role of Physical Activity, Stress Response, and Lifestyle Interventions

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Abstract

Gut microbiota has increasingly been recognized as an important regulator of both physiological processes and mental health. A growing body of evidence suggests that alterations in gut microbial composition, commonly referred to as dysbiosis, are associated with the development of depression, anxiety disorders, and disturbances in stress response. The microbiota–gut–brain axis represents a complex and multidimensional communication network involving neural, immune, endocrine, and metabolic pathways.

Lifestyle-related factors, particularly physical activity and dietary patterns, appear to significantly influence gut microbiota composition and, consequently, mental health outcomes. Regular exercise has been associated with increased microbial diversity and reduced systemic inflammation, while diets rich in fiber and bioactive compounds may support beneficial microbial activity.

Materials and methods: This narrative review was conducted using PubMed, Google Scholar, and UpToDate databases, as well as peer-reviewed articles from major scientific journals. Keywords included gut microbiota, depression, anxiety, stress response, gut–brain axis, physical activity, and lifestyle interventions. Articles published between 2010 and 2025 were considered.

Results: Current evidence indicates a meaningful association between gut microbiota and mental health, mediated through inflammatory pathways, neurotransmitter modulation, and regulation of the hypothalamic–pituitary–adrenal axis. However, findings remain heterogeneous, and causal relationships have not yet been fully established. These observations highlight the potential of microbiota-targeted lifestyle interventions as supportive strategies in mental health management.

Keywords: gut microbiota, depression, anxiety, stress, gut–brain axis, physical activity, lifestyle, inflammation

Introduction

Mental health disorders, particularly depression and anxiety, continue to represent a major global health burden, significantly affecting quality of life and daily functioning [12]. Their impact extends beyond individual well-being, influencing social relationships, occupational functioning, and healthcare systems worldwide. Despite advances in pharmacological and psychotherapeutic approaches, a substantial proportion of patients still do not achieve full remission or experience only partial improvement. This has led to growing interest in additional biological mechanisms that may contribute not only to the development, but also to the persistence and recurrence of these conditions.

In this context, gut microbiota has emerged as an important regulator of host physiology. The human gastrointestinal tract harbors a highly diverse microbial ecosystem that extends its influence beyond digestion. Through the microbiota–gut–brain axis, these microorganisms communicate bidirectionally with the central nervous system via neural, immune, endocrine, and metabolic pathways [1–4]. This interaction is increasingly recognized as dynamic and multidirectional, rather than linear, suggesting that changes in gut microbial composition may have systemic consequences.

Accumulating evidence suggests that disturbances in microbial composition may be involved in the pathophysiology of psychiatric disorders [13,26,27]. These effects are likely mediated by immune activation, altered neurotransmitter production, and dysregulation of stress-response systems [14,15,17]. In particular, low-grade systemic inflammation and altered signaling within the hypothalamic–pituitary–adrenal axis have been repeatedly associated with mood disorders, highlighting the relevance of gut-derived mechanisms. At the same time, it is important to acknowledge that these relationships are complex and not yet fully understood, and that microbiota should be considered as one component within a broader biopsychosocial framework.

At the same time, lifestyle-related factors such as diet and physical activity appear to play a meaningful role in shaping both gut microbiota and mental health outcomes [6,21,25]. Dietary

patterns rich in fiber, plant-based foods, and bioactive compounds have been associated with increased microbial diversity and beneficial metabolite production, whereas highly processed diets may contribute to dysbiosis and inflammatory processes [21,22,25]. Similarly, regular physical activity has been linked to improved microbial composition, reduced inflammation, and enhanced psychological well-being [6,8,11,23,24]. These observations make the topic particularly relevant from both preventive and therapeutic perspectives.

Importantly, current research does not support a single mechanistic pathway linking gut microbiota and mental health. Instead, available evidence suggests the involvement of multiple interacting processes, including immune modulation, metabolic signaling, neurotransmitter synthesis, and stress regulation. This complexity underscores the need for cautious interpretation of existing findings, as well as for further well-designed studies.

Aim of this review: The aim of this review was to critically evaluate current evidence on the role of gut microbiota in mental health, with particular emphasis on depression, anxiety disorders, and stress response, and to assess the impact of physical activity and lifestyle interventions on the gut–brain axis.

Gut–brain axis: biological background

The gut–brain axis represents a highly integrated and bidirectional communication system linking the gastrointestinal tract and the central nervous system [1–5]. This interaction is mediated through neural pathways, particularly the vagus nerve, as well as endocrine, immune, and metabolic mechanisms. Increasingly, this system is understood as a dynamic network rather than a single pathway, allowing continuous communication between gut microbiota and brain function.

The hypothalamic–pituitary–adrenal (HPA) axis plays a central role in stress regulation. Chronic activation of this system leads to sustained cortisol release, which may disrupt gut microbiota composition, increase intestinal permeability, and promote systemic inflammation [17]. Importantly, gut microbiota can also modulate HPA axis activity, suggesting a bidirectional relationship [7].

Immune signaling constitutes another critical pathway. Gut microbiota influences cytokine production, and elevated levels of pro-inflammatory mediators such as IL-6 and TNF-α have

been associated with depression and anxiety [10,14]. These inflammatory processes may directly or indirectly affect brain function and behavior.

Additionally, gut microorganisms contribute to the synthesis and modulation of neurotransmitters, including serotonin, dopamine, and gamma-aminobutyric acid (GABA) [15]. Short-chain fatty acids, particularly butyrate, play a role in maintaining intestinal barrier integrity and exert anti-inflammatory and neuroprotective effects [18]. These metabolites may also influence neural signaling and contribute to the regulation of mood-related pathways.

Gut microbiota and depression

Depression is increasingly recognized as a multifactorial disorder involving neurochemical imbalance, immune activation, and metabolic disturbances. Within this broader framework, gut microbiota has been identified as a potentially important contributing factor [10,13,28]. This perspective reflects a shift toward more integrative models of mental health, in which peripheral biological systems may influence central nervous system function.

Several studies have reported that individuals with depression exhibit reduced microbial diversity and alterations in bacterial composition [26,28]. In particular, decreased levels of short-chain fatty acid-producing bacteria have been observed, which may contribute to inflammatory processes and impaired gut barrier function [18]. These microbial changes may also affect metabolic and neurochemical pathways involved in mood regulation.

Chronic low-grade inflammation is considered a key mechanism linking gut microbiota to depressive symptoms [10,14]. Elevated levels of pro-inflammatory cytokines have been consistently associated with altered mood and behavioral changes. In parallel, gut microbiota may influence serotonergic signaling, further affecting emotional regulation [15]. These findings support the hypothesis that immune and neurochemical pathways act together in the development of depressive symptoms.

Experimental studies provide additional support for this association. Transfer of microbiota from individuals with depression to germ-free animals has been shown to induce depressive-like behaviors, suggesting a potential causal component, although direct translation to humans remains limited [19,20]. While these findings are promising, they should be interpreted with caution due to differences between experimental models and clinical conditions.

Gut microbiota and anxiety disorders

The relationship between gut microbiota and anxiety disorders is less consistent but remains an area of active investigation. Alterations in microbial composition may influence anxiety through modulation of neurotransmitter systems, particularly GABAergic pathways [15,26]. This interaction highlights the potential role of gut-derived signals in the regulation of emotional and stress-related responses.

Preclinical studies indicate that certain probiotic strains may reduce anxiety-like behaviors; however, findings from human trials remain heterogeneous and sometimes inconclusive [9,16]. These discrepancies may reflect differences in study design, population characteristics, intervention protocols, and variability in microbiota assessment methods. As a result, direct clinical translation remains challenging.

The interaction between gut microbiota and the HPA axis appears particularly relevant. Dysregulation of stress-response mechanisms may increase vulnerability to anxiety disorders, highlighting the importance of microbiota–stress interactions [7,17]. In this context, gut microbiota may contribute to both the initiation and modulation of anxiety-related responses.

Gut microbiota and stress response

The stress response is primarily regulated by the hypothalamic–pituitary–adrenal axis, which controls cortisol secretion [17]. Chronic stress has been shown to alter gut microbiota composition, increase intestinal permeability, and promote systemic inflammation [14]. These changes may disrupt gut homeostasis and contribute to further dysregulation of physiological stress mechanisms.

Conversely, gut microbiota may influence stress reactivity by modulating HPA axis activity, suggesting a bidirectional relationship between microbial composition and stress response [2,7]. This interaction indicates that gut microbiota may play a role not only in stress-related pathology, but also in the regulation of stress resilience.

Emerging evidence suggests that greater microbial diversity may be associated with improved stress resilience; however, causal mechanisms remain to be clarified [29]. These findings should be interpreted with caution, as most available studies are observational and do not establish direct cause–effect relationships.

Role of physical activity

Physical activity has emerged as an important modulator of both gut microbiota and mental health. Regular exercise is associated with increased microbial diversity and a higher abundance of beneficial bacterial strains [6,23,24]. These changes are considered beneficial for overall gut health and may contribute to improved physiological functioning.

In addition to microbiota-related effects, physical activity contributes to reduced systemic inflammation, improved immune function, and enhanced neuroplasticity. These processes are closely linked to improved mood and reduced symptoms of depression and anxiety [8,11]. Exercise may also influence the production of neuroactive compounds, further supporting its role in mental health regulation.

Recent studies suggest that exercise-induced changes in gut microbiota may contribute to improved stress resilience and cognitive function. Nevertheless, further research is required to better understand these mechanisms and their clinical relevance [30]. Current evidence, while promising, remains limited by variability in study design and population characteristics.

Lifestyle interventions

Dietary patterns play a central role in shaping gut microbiota composition. Diets rich in fiber, fruits, vegetables, and polyphenols promote the growth of beneficial bacterial species and increase short-chain fatty acid production [21,25]. These dietary components support microbial diversity and contribute to improved metabolic and immune regulation.

In contrast, diets high in processed foods and saturated fats are associated with dysbiosis and increased inflammatory activity [22]. Such dietary patterns may negatively affect both gut health and mental well-being, further highlighting the importance of nutritional factors in the gut–brain axis.

Probiotic and prebiotic interventions have been explored as potential strategies to improve mental health outcomes; however, current findings remain inconsistent [9,16]. Differences in study design, bacterial strains, and intervention duration may contribute to variability in results. As a result, clear clinical recommendations are still limited.

Recent randomized controlled trials suggest that microbiota-targeted dietary interventions may have beneficial effects on depressive symptoms, although further high-quality research is

needed before definitive clinical recommendations can be established [31]. Overall, lifestyle interventions appear promising, but their effectiveness likely depends on multiple interacting factors.

Mechanisms linking gut microbiota and mental health

The relationship between gut microbiota and mental health involves multiple interconnected pathways, including immune modulation, neurotransmitter production, metabolic signaling, and inflammation [1,10,14]. Rather than acting through a single mechanism, these processes interact dynamically, forming a complex network that links peripheral physiological changes with central nervous system function.

Microbial metabolites, particularly short-chain fatty acids, influence immune responses, intestinal barrier integrity, and brain function. These compounds may modulate inflammatory processes, support gut homeostasis, and contribute to neuroprotective mechanisms [18]. In addition, gut microbiota plays a role in the synthesis and regulation of neurotransmitters, which may directly affect mood, cognition, and emotional regulation [15].

At the same time, cytokine-mediated inflammation appears to play a central role in the development and persistence of psychiatric symptoms. Increased levels of pro-inflammatory mediators may influence brain function, alter neurotransmission, and contribute to behavioral changes associated with depression and anxiety [10,14]. These pathways are closely linked with stress-related mechanisms, including HPA axis dysregulation.

Overall, these mechanisms do not operate independently but rather interact within a broader physiological network. This complexity highlights the importance of considering gut microbiota within an integrative framework of mental health rather than as a single causal factor.

Limitations of current evidence

Despite growing interest in this field, current evidence remains limited by methodological heterogeneity, relatively small sample sizes, and a predominance of observational studies. Many findings do not establish causality, and inconsistencies across studies remain common. These limitations make it difficult to draw definitive conclusions regarding the role of gut microbiota in mental health.

Furthermore, variability in microbiota assessment techniques and the lack of standardized research protocols complicate comparisons between studies. Differences in sequencing methods, population characteristics, and analytical approaches may contribute to inconsistent results. This methodological diversity represents a significant challenge for the interpretation and generalization of findings.

Another important limitation is the complex and multifactorial nature of mental health disorders, which are influenced by genetic, environmental, and psychosocial factors. As a result, isolating the specific contribution of gut microbiota remains challenging. Future research should focus on well-designed, large-scale randomized controlled trials to clarify these relationships and strengthen the evidence base.

Conclusion

Gut microbiota plays an important role in mental health through complex interactions within the gut–brain axis. Dysbiosis has been associated with depression, anxiety disorders, and altered stress response, suggesting that microbial balance may influence both physiological and psychological processes.

Physical activity and lifestyle interventions represent promising, low-risk strategies for modulating gut microbiota and improving mental health outcomes. These approaches may support immune regulation, reduce inflammation, and contribute to improved stress resilience and emotional well-being.

However, further research is required to establish causal relationships and develop evidence-based clinical recommendations. In particular, well-designed randomized controlled trials are needed to better understand the mechanisms involved and to determine the effectiveness of microbiota-targeted interventions.

Importantly, integrating lifestyle-based approaches into mental health care may support more comprehensive and individualized treatment strategies. These findings may also have broader implications for public health, highlighting the potential role of lifestyle modification in mental health prevention and long-term management.

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