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Probiotics, Gut-brain axis, and stress: A review of nutritional therapeutics

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Abstract
The intricate connection between the gut and the brain, known as the gut-brain axis, has garnered increasing attention in recent years, particularly regarding its role in mental health and stress regulation. Emerging evidence highlights the influence of gut microbiota on neural, endocrine, and immune pathways, suggesting that modulation of the gut environment can have profound effects on psychological well-being. Probiotics—live microorganisms that confer health benefits to the host—have shown promising potential in supporting gut health and, consequently, mental health. This review explores the current understanding of the gut-brain axis and the role of probiotics as a nutritional therapeutic in stress management. Key mechanisms include the production of neuroactive compounds such as serotonin and gamma-aminobutyric acid (GABA), modulation of systemic inflammation, and regulation of the hypothalamic-pituitary-adrenal (HPA) axis. While preclinical and clinical studies indicate that specific probiotic strains may alleviate stress-related symptoms and improve mood, further research is required to standardize probiotic interventions and clarify strain-specific effects. This review emphasizes the therapeutic promise of probiotics in stress-related disorders and underscores the need for integrative approaches in nutritional psychiatry.

Keywords: Probiotics, gut-brain axis, stress, microbiota, nutritional therapeutics, Psychobiotics

1. Introduction
The intricate connection between the gut and brain, known as the gut-brain axis, has emerged as a crucial area of research in understanding the physiological and psychological aspects of health (Liang *et al*., 2018) [11]. Recent studies highlight the pivotal role of gut microbiota in modulating brain function and behavior, particularly in response to stress (Molina-Torres *et al*., 2019) [16]. Probiotics—live microorganisms that confer health benefits when consumed in adequate amounts—have gained attention as potential nutritional therapeutics that can influence the gut-brain axis (Dahiya and Nigam, 2022) [5]. By modulating gut microbiota composition, enhancing intestinal barrier function, and regulating inflammatory and neurochemical pathways, probiotics may help alleviate stress-related symptoms and support mental well-being (Meher *et al*., 2024) [13]. This review explores the current scientific evidence on the relationship between probiotics, the gut-brain axis, and stress, aiming to provide insights into their therapeutic potential and mechanisms of action.

2. The Gut-Brain Axis: An Overview
The gut-brain axis (GBA) is a complex bidirectional communication network that links the central nervous system (CNS) with the enteric nervous system (ENS) of the gastrointestinal tract (Carabotti *et al*., 2015) [4]. This intricate system involves neural, hormonal, and immunological signaling pathways, allowing the brain and gut to influence each other's function and state (Dantzer, 2018) [7]. Recent research highlights the critical role of gut microbiota in modulating this axis, affecting mood, cognition, and behavior through the production of neurotransmitters and other bioactive compounds (Dezfouli *et al*., 2025) [8]. Understanding the gut-brain axis has opened new avenues in neuroscience, gastroenterology, and mental health, offering promising insights into the treatment of conditions such as depression, anxiety, irritable bowel syndrome (IBS), and neurodegenerative diseases (Skonieczna-Żydecka *et al*., 2018) [19].
The GBA comprises:

- The central nervous system (CNS)
- The enteric nervous system (ENS)
- The autonomic nervous system (ANS)

- The hypothalamic-pituitary-adrenal (HPA) axis
- The immune system

Communication across these systems is mediated through neurotransmitters, cytokines, and microbial metabolites such as short-chain fatty acids (SCFAs). Disruptions in this axis have been associated with anxiety, depression, and irritable bowel syndrome (IBS) (Dalile *et al*., 2019) [6].

3. Probiotics and Their Mechanism of Action

Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host by modulating the gut microbiota and enhancing various physiological functions (Sánchez *et al*., 2017) [18]. These beneficial bacteria, primarily from the genera *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces*, exert their effects through multiple mechanisms of action (Marteau and Shanahan, 2003) [12], including competitive exclusion of pathogenic microbes, enhancement of intestinal barrier integrity, modulation of the immune response, and production of bioactive compounds such as short-chain fatty acids and antimicrobial peptides. By influencing the gut environment and interacting with host cells, probiotics play a crucial role in maintaining gut homeostasis and supporting overall health, particularly in gastrointestinal, immune, and metabolic functions (Sánchez *et al*., 2017) [18].

Probiotics exert their effects through multiple mechanisms:

- Enhancement of gut barrier integrity
- Modulation of immune responses
- Production of neuroactive compounds (e.g., GABA, serotonin)
- Inhibition of pathogenic bacteria

Certain strains such as *Lactobacillus rhamnosus*, *Bifidobacterium longum*, and *Lactobacillus helveticus* have shown anxiolytic and antidepressant effects in both human and animal studies.

4. Stress and the Gut Microbiota

Stress and the gut microbiota share a dynamic, bidirectional relationship that plays a critical role in maintaining overall health (Molina-Torres *et al*., 2019) [16]. The gut microbiota—a diverse community of microorganisms residing in the gastrointestinal tract—interacts closely with the central nervous system through the gut-brain axis, a complex communication network involving neural, hormonal, and immune pathways (Wang and Wang, 2016) [24]. Stress, whether acute or chronic, can disrupt this balance by altering gut motility, increasing intestinal permeability, and modifying microbial composition, often leading to dysbiosis. This microbial imbalance, in turn, can exacerbate stress-related symptoms and contribute to a range of physiological and psychological disorders. Understanding this intricate interplay opens new avenues for managing stress through dietary and probiotic interventions that support a healthy gut ecosystem (Verma *et al*., 2024) [23].

Stress can lead to:

- Alterations in gut microbiota composition (dysbiosis)
- Increased intestinal permeability
- Enhanced systemic inflammation
- Activation of the HPA axis

These changes can further exacerbate psychological stress, creating a vicious cycle. Nutritional strategies that restore microbiota balance could be crucial in breaking this cycle.

5. Probiotics as Nutritional Therapeutics for Stress

Probiotics, defined as live microorganisms that confer health benefits to the host when administered in adequate amounts, have emerged as promising nutritional therapeutics for managing stress and promoting mental well-being (Tegegne and Kebede, 2022) [21]. Recent research highlights the crucial role of the gut-brain axis—a bidirectional communication network between the gastrointestinal tract and the central nervous system—in regulating mood and stress responses (Arneth, 2018) [1]. By modulating gut microbiota composition, enhancing intestinal barrier function, and influencing neurochemical production, probiotics may help reduce stress-related symptoms and improve psychological resilience (Zhang *et al*., 2023) [25]. This growing body of evidence supports the integration of probiotics into dietary strategies aimed at mitigating the negative effects of stress on both mental and physical health (Meher *et al*., 2024) [13].

5.1 Preclinical Evidence

Rodent models have demonstrated that probiotics can:

- Decrease stress-induced corticosterone levels
- Improve behavior in anxiety-like tasks
- Restore gut microbial balance after stress exposure

5.2 Clinical Evidence

Human studies, although limited, suggest:

- Reduction in perceived stress levels
- Improved mood and cognitive performance
- Decreased inflammation and cortisol levels

Randomized controlled trials (RCTs) have reported benefits of multi-strain probiotic formulations in reducing psychological distress.

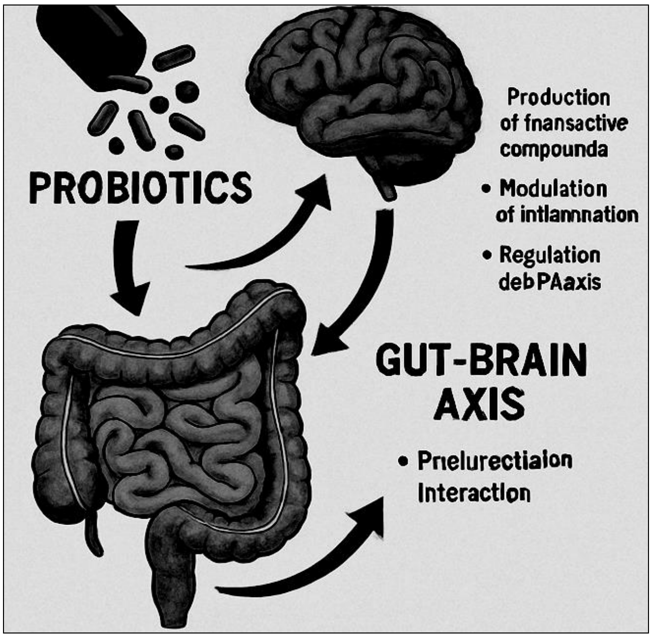

Fig 1: Probiotics and gut-brain axis

Table 1: Summary of Probiotic Strains and Interventions Targeting the Gut-Brain Axis (GBA) and Stress-Related Outcomes

Probiotic Strain / Intervention	Mechanism of Action	Effect on Stress / GBA	Reference
Lactobacillus rhamnosus (JB-1)	Modulates GABA receptor expression via vagus nerve	Reduces anxiety- and depression-related behavior in mice	(Bravo *et al*., 2011) [3]
Bifidobacterium longum NCC3001	Alters vagal pathways and gut-brain signaling	Reduces anxiety-like behavior in IBS patients	(Bercik *et al*., 2011) [2]
Lactobacillus helveticus R0052 & *Bifidobacterium longum* R0175	Regulates HPA axis activity, lowers cortisol levels	Reduces psychological stress and improves mood in humans	(Messaoudi *et al*., 2011) [14]
Multi-strain probiotic (8 species)	Improves gut barrier function and modulates cytokine levels	Lowers psychological distress in healthy volunteers	(Kato-Kataoka *et al*., 2016) [10]
Bifidobacterium bifidum, *L. casei*, etc. (fermented milk)	Reduces systemic inflammation and improves microbiota composition	Alleviates stress and improves quality of life in students	(Takada *et al*., 2016) [20]
Lactobacillus plantarum P8	Reduces pro-inflammatory cytokines (e.g., IL-6, TNF-α)	Improves cognitive function and reduces anxiety	(Mohammadi *et al*., 2016) [15]
Psychobiotic diet (high in prebiotics and fermented foods)	Promotes beneficial microbiota and SCFA production	Enhances resilience to stress, improves well-being	(Johnstone *et al*., 2021) [9]
Lactobacillus reuteri	Increases oxytocin, modulates vagal tone	Improves social behavior and reduces stress in animal models	(Varian *et al*., 2016) [22]
Synbiotic (probiotic + prebiotic)	Synergistic effect on microbial balance and gut-brain communication	Enhances mood and cognitive flexibility	(Papalini *et al*., 2019) [17]

6. Conclusion

In conclusion, the intricate interplay between probiotics, the gut-brain axis, and stress underscores the promising role of nutritional therapeutics in mental health management. Emerging evidence highlights how specific probiotic strains can modulate gut microbiota composition, enhance intestinal barrier function, and influence neurochemical signaling pathways that regulate stress responses. These findings suggest that probiotics may serve as a complementary approach to conventional stress management strategies, offering potential benefits in alleviating symptoms of anxiety, depression, and other stress-related disorders. However, further clinical research is needed to identify strain-specific effects, optimal dosages, and long-term outcomes to fully establish probiotics as a reliable intervention within the realm of nutritional psychiatry.

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