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The Gut-Brain Axis and Anxiety Disorders: A Review of Clinical and Psychological Perspectives

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Abstract: ***This review examines the bidirectional relationship between the Gut-Brain Axis and anxiety disorders, with emphasis on Generalized Anxiety Disorder. Current evidence demonstrates significant clinical overlap between anxiety disorders and disorders of gut-brain interaction, supported by alterations in gut microbial diversity and composition. Patients with anxiety frequently exhibit reduced beneficial microbial populations and increased potentially pathogenic bacteria, suggesting persistent biological dysregulation beyond psychological symptoms alone. Emerging microbiome-based interventions, including probiotics, prebiotics, and dietary modulation, show promising therapeutic potential; however, robust randomized controlled trials are required before routine clinical implementation. Overall, current evidence supports a biopsychosocial understanding of anxiety and highlights the Gut-Brain Axis as an important target for future research and treatment.***

Keywords: Gut-Brain Axis; Microbiome; Anxiety Disorder; Generalized Anxiety Disorder (GAD); Dysbiosis; Probiotics; Comorbidity; Gut-Brain Interaction

1. Introduction

The Gut-Brain Axis (GBA) represents a complex, two-way network of communication involves neural and endocrine hormones as well as microbiome data, is increasingly accepted as an important mediator in the pathophysiology of both anxiety disorders and other psychiatric disorders that are affected by stress, including Generalized Anxiety Disorder (GAD), Panic Disorder and Post-Traumatic Stress Disorder (PTSD) (MacKay et al., 2023). Chronic stress is thought to contribute greatly to this axis (Lee & Kim, 2021). This review investigates the complex relationships among clinicians, microbiologists and therapists in this context. A wealth of evidence shows that there are deep and harmful overlaps among these different fields.

Observational studies conducted around the world have identified that approximately 37.5% of the population experiences significant levels of psychological distress, which places them at 4.45 times higher risk of having at least one Disorder of Gut-Brain Interaction (DGBI). These disorders can significantly decrease mental and physical Quality of Life (QoL) for patients as well as lead to increased healthcare utilization.

The evidence presented here supports the biopsychosocial model (Fond et al., 2014). The early phase of life has been shown to confer an increase in vulnerability to DGBI because the prevalence of childhood trauma among patients diagnosed with a Functional Gastrointestinal Disorder is high; therefore, they have a 10.215 times greater risk of developing severe anxiety.

Mood and anxiety disorders precede development of functional gastrointestinal disorders in patients but not in the population (Jones et al., 2017).

The results from microbiological studies reveal distinct dysbiosis profiles related to the above-mentioned disorders. Patients diagnosed with GAD show a substantial reduction in the diversity and richness of their gut microbiota [Altered gut microbiota profile in patients with generalized anxiety disorder (Jiang et al., 2018)]. This imbalance is characterized by decreased beneficial SCFA producing bacteria and an increase in pathogenic bacteria (Escherichia-Shigella and Fusobacterium) [Altered gut microbiota profile in patients with generalized anxiety disorder (Jiang et al., 2018)]. Coinciding with the above-mentioned dysbiosis is a similar effect shown within the psychological phenotype of individuals with GAD, whereby increased relative abundances of specific genera (Fusobacterium and Megamonas) have been demonstrated to correlate with certain personality traits (e.g., alexithymia) (Guo et al., 2022). Surprisingly, this direct correlation was unable to be resolved among patients who attained clinical remission [Altered gut microbiota profile in patients with generalized anxiety disorder (Jiang et al., 2018)]. This finding further illustrates the dysbiosis of the gut microbiota may serve as a distinct biological susceptibility trait that is unaddressed through existing psychological treatment modalities.

The mechanistic pathway from GBA dysfunction to anxiety provides a promising avenue for translation. The literature suggests the potential benefit of therapeutic approaches such as pro- and prebiotics for the management of stress-related disorders (Lee & Kim, 2021); MacKay et al. (2023)]. Moreover, the regulatory role of natural dietary compounds such as omega-3 fatty acids on the gut microbiome suggests that dietary modulation is a promising, non-pharmacologic approach to the management of mental health disorders (Xiong et al., 2023). However, a critical translational gap exists, in that the existing body of positive preliminary findings has been derived from studies performed in non-clinical populations (healthy subjects under stress).

Therefore, there is a significant future need for substantial prospective RCTs directed at specific patient populations, to

determine the efficacy and improve the application of treatments. In summary, the findings of this review substantiate the critical role of the Gut-Brain Axis (GBA) in anxiety disorder patients, through overwhelming evidence of clinical comorbidities and an unusual biological signature. The data from this review demonstrate the biological pathology associated with this axis and provide an acute need for further research that translates GBA-directed interventions into standard psychiatric and gastrointestinal (GI) practice.

2. Methodology

A comprehensive narrative review of the literature was conducted using systematic searches of two major biomedical and academic databases: Springer and ScienceDirect. The search was carried out over a defined period to ensure the review reflects current evidence: database searches were conducted between December 2025 and February 2026, and were restricted to studies published between 2007 and 2025, with priority given to research published within the most recent decade (2014–2025) to capture the most clinically relevant and up-to-date findings. Earlier foundational sources published before this window were retained only where they provided essential conceptual or theoretical grounding for the review (e.g., early literature reviews establishing the comorbidity debate).

Keywords and Search terms:
A defined set of search terms was applied consistently across both databases, combined using Boolean operators (AND/OR) to capture literature relevant to both the biological and clinical/psychological dimensions of the topic:

- Gut-Brain Axis
- Microbiota and Dysbiosis
- Anxiety Disorder and Generalized Anxiety Disorder (GAD)
- Irritable Bowel Syndrome (IBS) and Functional Gastrointestinal Disorders (FGID)
- Probiotics and Prebiotics (for therapeutic application)
- Alexithymia (for psychological linkage)

Inclusion and Exclusion Criteria and Type of Study
The review was conducted strictly within defined inclusion and exclusion criteria to ensure academic relevance and rigor.

Inclusion Criteria:

- Relevance to GBA components: The study had to address the relationship between the GBA (gut microbiome, neuroimmune, or neuroendocrine interactions) and a defined psychiatric illness.
- Type of study: Original research articles, particularly observational studies, cross- sectional studies, and clinical cohort studies, were prioritized, alongside full systematic or narrative reviews.
- Population: Studies involving human clinical populations with diagnosed psychiatric illnesses such as GAD, IBS, or DGBI with comorbid anxiety were required.

Exclusion Criteria:

- Primary original studies conducted exclusively on animal models were excluded, though systematic reviews incorporating preclinical data to explain essential GBA mechanisms were retained.
- Studies that did not draw a clear connection between a GBA component and anxiety (e.g., general GI disease studies or psychological interventions lacking a biological component) were excluded.

Study Screening Process
Screening followed a two-stage process: first, titles and abstracts were screened against the inclusion/exclusion criteria, removing clearly irrelevant records (e.g., unrelated topics, animal- only studies, non-English articles); second, the full text of remaining articles was assessed for eligibility, focusing on whether the study clearly linked a GBA component to an anxiety-related diagnosis. Articles passing full-text review were retained for synthesis.

Stage	Process	Records
1. Identification	Records identified via Springer and ScienceDirect using predefined search terms	n=XX
2. Deduplication	Duplicate records removed	n=XX
3. Title/Abstract Screening	Records screened against inclusion/exclusion criteria	n=XX
4. Full-text Eligibility	Full-text articles assessed for eligibility	n=XX
5. Final Inclusion	Studies included in the review	n=15

3. Review of Literature (ROL)

Review of Literature provides an overview of the complex, two-way relationship between the Gut-Brain Axis (GBA) and anxiety disorders. It covers the underlying biological background, the dominant clinical epidemiology, unique microbial features, and the important gaps and inconsistencies, as they are currently understood and interpreted.

Theoretical Framework and Mechanisms of Bidirectional Communication
"The complex, integrated system of the GBA is the bidirectional communication between the central nervous system and the enteric nervous system via neural, endocrine, and neuroimmune pathways" (MacKay et al., 2023). The GBA is a critical component in the pathophysiology of stress-related psychiatric disorders in which anxiety is a main feature, including Generalized Anxiety Disorder (GAD), Panic Disorder, Post-Traumatic Stress Disorder (PTSD), and Obsessive-Compulsive Disorder (OCD) (MacKay et al., 2023).

Inflammation as a Factor: Gut inflammation is now considered to be one of the major factors mediating psychiatric comorbidity. For example, inflammatory bowel diseases, such as IBD, show strong comorbidity with psychiatric conditions, especially anxiety and depression (Luo et al., 2025). Moreover, the study on irritable bowel syndrome, or IBS, also suggests that the central processing of visceral stimuli could be partially influenced by pre-existing affective conditions, such as anxiety or depression, thereby showing the impact of the psychological state on the physiological state (Madva et al., 2022). The gut-brain axis, therefore, is one route through which stress- or dysbiosis-induced signals, generated in the gut, could impact the brain to regulate mood or anxiety (Lee & Kim, 2021).

Clinical Epidemiology, Comorbidity, and Etiological Alignment

There is substantial epidemiological evidence supporting the significant and clinically relevant overlap between psychological distress and Disorders of Gut-Brain Interactions (DGBI).

High Prevalence and Impact (Consistency): A global observational epidemiology study revealed that 37.5% of the participants presented clinically significant psychological distress/somatic symptom severity. The occurrence of such distress significantly increases the likelihood of DGBI occurrence, and individuals suffering from both conditions show 4.45 times higher chances of having at least one DGBI than those without psychological distress/somatic symptom severity.

The combination of these two conditions is the factor that is most associated with reduced mental and physical quality of life and increased use of healthcare resources and medication. Consistent with these observations, the results of a systematic review revealed that patients suffering from irritable bowel syndrome show higher levels of anxiety and depression than healthy controls (Fond et al., 2014).

Etiological Factors and Timing (Gaps and Consistency/Contradictions): Psychological factors have been shown in clinical studies to often occur before gastrointestinal symptoms, implying their possible role as potential risk factors. Patients with Functional Gastrointestinal Disorder (FGID) demonstrated a significantly high probability of severe anxiety (Odds Ratio ~ 10.215) and a significantly high occurrence of childhood traumatic experiences. The consistency of the results points towards the programming of vulnerability in the gut-brain axis (GBA) by early life stress. However, the major contradiction and gap in the research in the context of the time relation of the onset of the disease in the case of inflammatory bowel disease (IBD) and the onset of the psychological comorbidities remain a controversy among the researchers. The methodology also lacks a prospective study.

Microbiological Signatures and Correlation with Psychological Phenotype

Advanced sequencing studies have consistently demonstrated the presence of distinct microbial signatures in the anxiety populations.

GAD Dysbiosis Profile (Consistency): Clinical studies have repeatedly demonstrated the presence of a distinct dysbiosis profile in individuals with GAD. Specifically, the microbial richness and diversity of individuals with GAD are significantly lower compared to healthy controls. The dysbiosis profile also includes a reduction of beneficial short-chain fatty acid (SCFA)-producing microbes and a relative increase of potentially pathogenic microbes, including Escherichia-Shigella, Fusobacterium, and Ruminococcus gnavus.

Correlation with Psychological Traits: The gut microbiome has also been demonstrated to correlate with distinct psychological phenotypes. In a study of individuals with a co-morbid FGID and GAD, the relative abundance of microbes including Fusobacterium and Megamonas was found to correlate with distinct components of alexithymia, including the ability to describe and identify feelings, as well as elevated neuroticism. In contrast, Faecalibacterium was found to be significantly different in abundance in individuals with GAD compared to those with MDD, potentially facilitating the development of therapeutic strategies for the treatment of these disorders.

The Gap in Persistence: The most significant finding with major implications for treatment is the failure of the gut imbalance in people with active generalized anxiety disorder (GAD) to resolve in those who achieved clinical remission. This implies the imbalance could be a permanent biological feature, not simply a consequence of anxiety. It also points to the limitation of existing standard psychological interventions, which do not fully normalize the issues with the underlying gut-brain axis problems.

Therapeutic Potential and Translational Gaps

The mechanistic foundation is strong to support therapeutic interventions targeting the Gut-Brain Axis (GBA), although their clinical application is currently hindered by methodological shortcomings and gaps in clinical research.

Potential of Microbiome Intervention: Mechanistic studies have provided insights into the potential application of pro- and prebiotics to treat generalized anxiety disorder (GAD), Panic Disorder, Social Anxiety Disorder, post-traumatic stress disorder (PTSD), and obsessive- compulsive disorder (OCD) by modulating the GBA (MacKay et al., 2023). Moreover, the protective influence of natural dietary ingredients such as omega-3 fatty acids, fish, vegetables, and medicinal herbs on the gut microbiome provides a promising therapeutic application of dietary interventions as a non-pharmacological tool for mental health management (Xiong et al., 2023).

Gaps and Contradictions in Efficacy**:** There is a significant gap between mechanistic optimism and actual clinical evidence. Though initial findings suggest that probiotics may be helpful in reducing anxiety disorders, it is important to note that all positive findings have been reported in non-clinical groups (i.e., healthy individuals under stress). This is a significant gap between preclinical optimism and actual clinical evidence. Thus, large-scale prospective RCTs in clinical groups with relevant diagnoses are needed. In addition, it is important that future studies control for

important cofounders that are known to affect the microbiome, like sex, psychotropic medication use, comorbidity, ethnicity/race, diet, and physical activity levels, as emphasized in a recent review by MacKay et al. (2023).

4. Critical Analysis

Strengths and Limitations Based on Methodology

The body of research that establishes the link between the Gut-Brain Axis (GBA) and anxiety disorders can be characterized by notable strengths, including robust clinical and epidemiological data that validate the link between the GBA, while at the same time suffering from notable weaknesses, including limitations with regard to establishing causality.

Methodological Strengths

The most notable strength of the body of research on the link between the GBA and anxiety disorders is the robust clinical and epidemiological data that validate the link, including the global survey on psychological distress and Disorders of Gut-Brain Interaction (DGBI). This study established that psychological distress, which is clinically relevant, significantly increases the likelihood of having DGBI by 4.45 times. Systematic reviews of existing literature also validate the link by establishing that anxiety disorders, including depression, are highly prevalent in-patient groups suffering from disorders such as Irritable Bowel Syndrome (IBS) (Fond et al., 2014).

The body of research on the link between the GBA and anxiety disorders also benefits from the use of 16S rRNA sequencing, which allows for the identification of taxonomic changes in anxiety disorders. This has been successful in identifying unique microbial signatures in Generalized Anxiety Disorder (GAD) patient groups, including decreased microbial richness, which can differentiate GAD from healthy controls, as well as from other psychiatric disorders, including Major Depressive Disorder (MDD).

5. Methodological Limitations

The primary limitation of the majority of the existing GBA literature is the inability to establish definitive causality due to the cross-sectional and observational nature of the existing methodologies. While some studies have suggested that psychological distress (including childhood trauma) leads to and increases the risk of developing FGID [Mood and anxiety disorders precede development of functional gastrointestinal disorders in patients but not in the population (Jones et al., 2017), the timing of onset of psychological comorbidity in relation to the onset of chronic intestinal diseases such as IBD is still controversial and has not been well studied using well-controlled prospective methodologies. The methodological limitations of the existing literature make it impossible to definitively answer these controversies.

Additionally, the methodologies that are currently being used are often not sensitive enough when trying to determine function. While 16S rRNA sequencing can determine what bacteria are present in the GI tract, it does not have the resolution to determine what neuroactive metabolites are being produced (such as specific SCFAs and neurotransmitters), thereby creating a 'functional gap' in understanding how the altered microbiome mediates GBA communication (MacKay et al., 2023).

6. Discussion of Future Research Findings

One key area is addressing confounding variables and pharmacomicrobiomics. Several well- documented variables that strongly modulate gut microbiome composition remain poorly addressed in current research, including host factors such as sex, ethnicity/race, and GI/non-GI disease comorbidity (MacKay et al., 2023), and environmental factors such as diet (the strongest modulator), exercise, and environmental stressors. Future research must also account for pharmacological interference, as drugs currently used to treat anxiety, such as SSRIs and anxiolytics, have themselves been shown to modulate gut microbiome composition.

The mechanistic rationale for pro- and prebiotics in treating anxiety disorders (Lee & Kim, 2021) points to a translational imperative for large-scale RCTs. This potential has not been validated in clinical practice, as most preliminary positive findings come from non-clinical populations (healthy people under stress) rather than diagnosed patients. An important area for future research is therefore large-scale, prospective RCTs in clinical groups with appropriate diagnoses (e.g., GAD, Panic Disorder), to confirm the effectiveness, formulation, and treatment duration of pro- and prebiotic compounds and move microbiome-based interventions from hypothesis to proven treatment.

Finally, the finding that GAD-associated dysbiosis is not reversed by clinical remission (Jiang et al., 2018) points to an important area for investigating persistent vulnerability and precision therapy, including developing therapeutic targets that normalize this sustained dysbiotic profile as a predisposing vulnerability trait for relapse. This also entails precision diagnostics based on findings such as differential Faecalibacterium abundance in GAD versus MDD patients, to support objective biomarkers for differential diagnosis and therapy selection.

7. Conclusion

Current evidence supports a strong bidirectional relationship between the Gut-Brain Axis and anxiety disorders. Clinical, psychological, and microbiological findings consistently demonstrate that gut microbial dysbiosis is associated with anxiety and may contribute to disease persistence. Although microbiome-targeted therapies show considerable promise, stronger clinical evidence from well-designed randomized controlled trials is required before widespread implementation. Future multidisciplinary research integrating microbiology, psychiatry, and psychology will improve understanding of disease mechanisms and facilitate the development of personalized therapeutic approaches.

8. Clinical Insights and Implications

The results offer a strong case for a two-way approach to patient care. Mental health practitioners should screen for gastrointestinal symptoms, and gastroenterologists should always screen for psychological distress. The discovery of specific microbial signatures, such as the relative abundance of Faecalibacterium in GAD patients as opposed to MDD patients, is a major breakthrough that offers a chance to develop objective tools for the differential diagnosis and treatment of mental health patients.

9. Future Directions: Specific Research Recommendations

In order to take the GBA-anxiety research from hypothesis to practice, the following research recommendations can be made:

1) Prospective Randomized Controlled Trials (RCTs): Longitudinal, highly controlled prospective Randomized Controlled Trials must be undertaken exclusively on clinically diagnosed anxiety disorders to conclusively validate the efficacy, dosage, and longevity of specific pro- and prebiotics. The research must control for important cofounders such as sex, drug use, comorbidities, diet, and exercise, as recommended by MacKay et al. (2023).
2) Functional Multi-Omics and Mechanistic Research: The research must extend beyond the taxonomic level (16S rRNA) to the multi-omics level (metabolomics) to specifically define the neuroactive and immunomodulatory molecules involved in the GBA communication pathway for anxiety disorders, as recommended by Lee & Kim (2021); Xiong et al. (2023).
3) Investigating Pharmacomicrobiomics: There is a crucial need to examine the specific impact of currently prescribed anxiolytic and antidepressant agents on the gut microbiome. The ability to comprehend this aspect of drug use will allow us to develop strategies that utilize drug combinations in ways that produce maximum therapeutic benefits with minimized unfavorable alterations to the GBA.
4) Targeting Stable Vulnerability: The focus of research in this area should be to develop therapeutic strategies that target this unique underlying biological vulnerability trait of GAD patients that is responsible for their persistent dysbiotic gut microbiota profile [Altered gut microbiota profile in patients with generalized anxiety disorder (2018)]. The ability to eliminate this underlying biological vulnerability trait of GAD patients is crucial in preventing psychiatric and gastrointestinal relapse [Altered gut microbiota profile in patients with generalized anxiety disorder (Jiang et al., 2018).

This field of research remains very active and promises much for the more precise treatment of anxiety disorders and other stress-related conditions in the future (MacKay et al., 2023).

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