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THE ROLE OF GUT-BRAIN AXIS IN ANXIETY DISORDERS: PSYCHOLOGICAL AND NEUROBIOLOGICAL PERSPECTIVES

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Abstract

Background: *Tele-nursing is essential for providing health care to channel nurses effective communication with patients through the digital medium. With greater infusion of technology in the healthcare system, it is essential to have an understanding of how such tele-nursing impacts the communication between nurse and patient and its relationship to the health care outcome.*

Objective *The objective of this study was to assess the association of telenursing with the quality of nurse–patient communication in the hospital.*

Methods: *A descriptive cross-sectional design of research was used. In a cross sectional study data were collected through a structured questionnaire from 160 registered nurses working in different departments of general hospitals. The telenursing practice, frequency of virtual communications and perceived effectiveness of nurse-patient interaction were assessed using the tool. The relationship and predictive power of tele-nursing on communication quality were analyzed through Pearson correlation and linear regression using SPSS version 26.*

Results: *There was a significant positive correlation between the use of tele-nursing and perception of the nurse-patient communication quality (r=0.67, p<. 01). Nurses who used tele-nursing often felt that communication was more clear and satisfying, and was answered more quickly. Results of a regression analysis indicated that tele-nurcing explained 45% of the variation in communication outcomes (R" = 0.45, p <. 001) where it appears to be a powerful predictor for good communication.*

Conclusion *The results show that tele-nursing can significantly improve the communication between nurse and patient. The use of tele-nursing in everyday patient care is linked to better health outcomes, specifically in settings with less physical presence.*

Keywords**:** Tele-nursing, nurse-patient communication, healthcare technology, Saudi Arabia.

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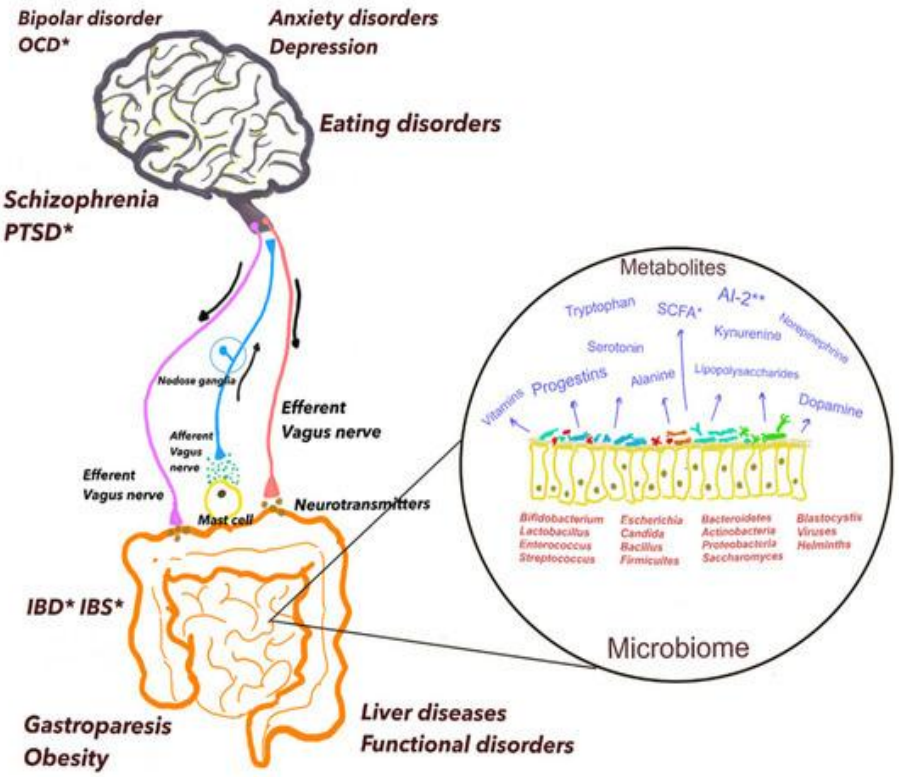
Introduction



The gut-brain axis (GBA) represents a complex network of communication pathways running bidirectional between the central nervous system (CNS) and the enteric nervous system (ENS) through neural, endocrine and immune routes. This homeostatic network has been of great interest in recent years with the potential to have an impact on both physical and psychological processes such as mood regulation, stress responses and mental health disorders. Anxiety disorders Among the vast range of psychological disorders associated with GBA dysfunction, anxiety disorders appear to be one of the most important. Anxiety disorders, comprising excessive fear and worry, are common and may severely affect quality of life among millions of people worldwide. It seems that the relationship between gut microbiota and brain regulated by neurochemical signaling may play a role in the process of occurrence, development and degree of anxiety, which will be very promising in terms of a new insight into therapeutic methods. Gut microbiota and anxiety Recent studies have emphasized the involvement of gut microbiota in the control of neurotransmitters, either serotonin or GABA, which are involved in emotional regulation and anxiety response (Yano et al., 2021; Tillisch, 2022).

Recent studies have shed new light on the neurobiological pathways linking GBA to anxiety disorders. The vague nerve -the major neural pathway connecting the gut to the brain- is the main conduit through which signals generated within the gut are conveyed to the brain, in areas involved in stress and emotional regulation, such as the amygdala and the prefrontal

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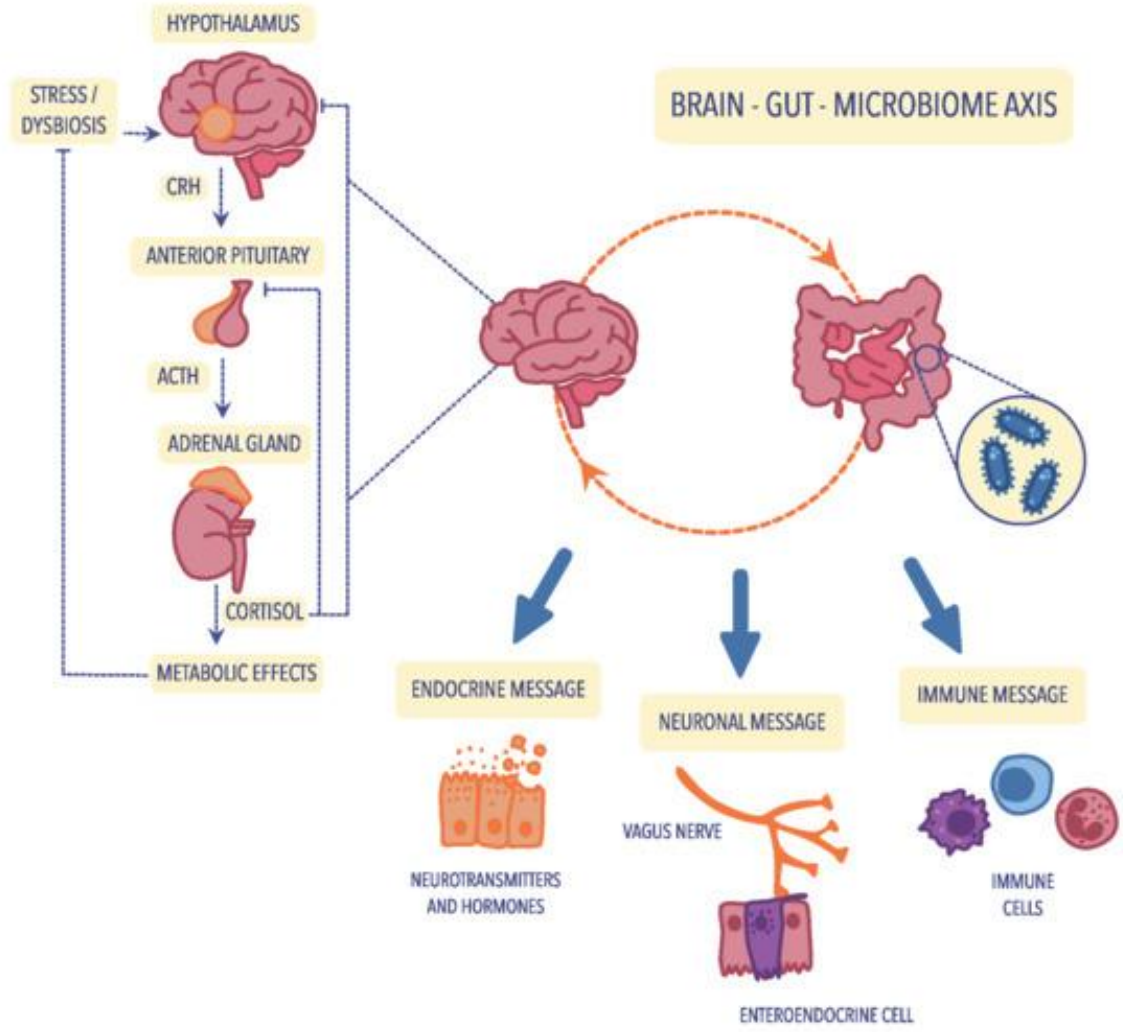
cortex -PFC (Carabotti et al., 2023). Furthermore, turnover and composition of the gut



microbiota have been related to the hypothalamic-pituitary-adrenal (HPA) instead of the gut-brain axis, immune response that is dysregulated in anxiety disorders (Vervent et al., 2024). For example, dysbiosis in the gut microbiome has been linked to disrupted cortisol levels and higher levels of inflammatory markers, each of which may exacerbate symptoms of anxiety (Zheng et al. In addition, evidence from research on germ-free organisms and microbiota transplantation strongly indicate that gut microbiota has a causal role on corrosion of anxiety-like behaviors and therefore, microbiome-based therapies might be useful for the treatment of anxiety disorders (Zheng, Zhang, & Guo, 2023).

The psychological view on the GBA in anxiety disorders is based on the interaction between processes for regulation of emotions and from sensory information from the gastrointestinal tract. People with low discrimination/emotional intuition abilities Alternatively, those who have highly sensitivity to internal body sensations (Gao et al., 2013; Shaw et al., 2015), or poor inter-cooption (Ronchi et al., 2015) might be more prone to interpret their gut discomfort as a sign of threat, thereby eliciting their anxious responses (Critchley et al., 2004; Holley et al., 2016; Shields et al., 2016; Davidson and Schwartz, 2017; Harrison et al., 2019; Kramer et al., 2022). This distinction is on point in anxiety disorders, for example, panic disorder (PD) and generalized anxiety disorder (GAD), in which somatic manifestations, including gastrointestinal disturbances, commonly accompany anxious cognitions. Accordingly, the cognitive model of anxiety proposes that negative appraisals of physical

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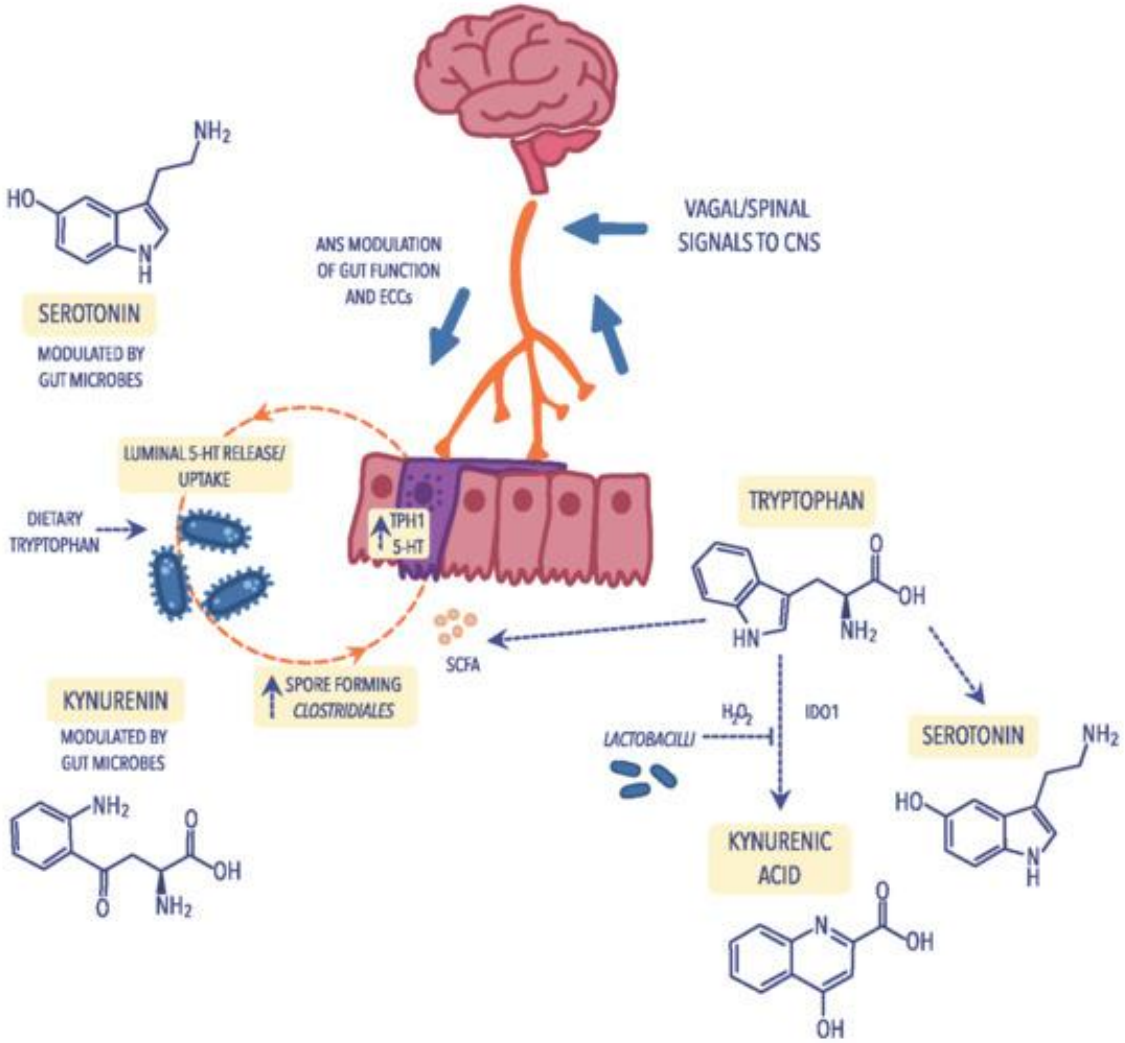
sensations play a role in the maintenance of anxiety, as an over interpretation of internal bodily signals results in distress and avoidance (Hiller et al., 2024). These results highlight the relevance of evaluating gut-brain relation beyond neurobiology and in the frame of psychological and emotional processes.

Recent developments in psycho-biotics are fueling interest in microbiome-based therapies for anxiety disorders. Psycho=biotics, i.e., probiotics and prebiotics that enhance gut microflora to ameliorate mental health, are a fresh avenue of managing anxious symptoms (Messaoudi et al., 2022). Precede and ongoing probiotic supplement investigations to alleviate anxiety symptoms look positive, perhaps partly due to the gut microbial diversity restoration and neurotransmitter production modulation (Gibson et al., 2024). In addition, the inclusion of psychological interventions, including cognitive-behavioral therapy (CBT) and mindfulness, has demonstrated a positive effect on the GBA, which may be mediated by a decrease of stress and an amelioration on gut health through mechanisms that engage both the brain and gut (Liu et al., 2023). Such findings indicate that a multi-pronged (psychological + microbiome-modulating) therapeutic strategy may provide great benefit for those suffering from anxiety disorders.



Even though the evidence for the involvement on the GBA system in anxiety is increasing, there are still large gaps in our knowledge of its detailed mechanism. Although animal models and preliminary human work has provided important initial information, additional work is necessary to inform the directionality of the relationship between GBA and

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anxiety, and to develop effective GBA-based interventions in the clinic. Furthermore, the interplay between environmental and genetic factors in the modulation of the gut-brain axis remains to be discovered for patient-tailored treatment. Thus, this paper is intended to make an important addition to the ever-increasing literature in this area by (i) elucidating the psychological and neurobiological underpinnings of GBA in anxiety disorders and (ii) introducing possible treating approaches targeting the gut-brain axis.

Problem Statement

Although increasing evidence is accumulating in support of the gut-brain axis in ADs, the precise neurobiological and psychological mechanisms involved in this link between GI and ADs, in particular, the involvement of GM in anxiety, is poorly understood. The absence of complete models that incorporate the neuro-psychobiological and psychological features of the GBA, and the heterogeneity of response to microbiome interventions, represent a barrier in the path toward standardized treatments of anxiety disorders. The current study aims to address these gaps by exploring pathways mediating the gut-brain connection in anxiety and potential strategies to modulate this.

Significance of the Study

This research is important, as it represents a unified view regarding the gut-brain axis in anxiety disorders and contributes to an understanding of the neurobiological and psychological(mediated by the HPAA) mechanisms contributing to the condition. By uncovering the importance of gut microbiota in mediating anxiety, the research adds to a growing body of evidence for novel, microbiome-targeted interventions that may one day be used to supplement and/or replace current psychotropic medications. These discoveries may guide the development of new treatments, bringing more effective, individualized therapies to people with anxiety disorders. Furthermore, this study underscores the need to attend closely to the gut-brain axis in the construction of the holistic, biopsychosocial theory of mental illness.

Aim of the Study

In this review, we examine the connection between the gut-brain axis and the origin and treatment of anxiety disorders, with considerations on both neurobiology and psychology dimensions. This study aims to understand how the gut microbiota impacts on anxiety by interacting with the central nervous system (CNS) and emotional regulations pathways. Finally, this work will also consider microbiome-based therapy and psychological interventions as possibilities for modulating the gut-brain axis to reduce anxiety.

Methodology

Methodology This study will use a mixed-methods research design and will include both quantitative and qualitative methods to fully explore the relationship between the gut-brain axis and anxiety disorders. The quantitative aspect will include a RCT to determine the impact of probiotic supplementation on anxiety symptoms. Recruitment will take place in local clinics and mental health centers, and 150 individuals diagnosed with GAD will be enrolled. Individuals will be randomly allocated to treatment (probiotic supplementation) or control (placebo). Anxiety will be assessed at baseline, 4 weeks and 8 weeks using the Generalized Anxiety Disorder 7 (GAD-7) scale (Spitzer et al., 2021). In addition, gut microbiota composition will be studied in fecal specimens obtained at each measurement time using 16S rRNA gene sequencing to describe microbiome diversity and composition (Kobyliak et al., 2023). The change in GAD-7 scores will be the primary outcome, and secondary outcomes will involve changes in gut microbiota diversity and serum markers of inflammation, including C-reactive protein (CRP).

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The qualitative arm will consist of semi-structured interviews to capture participants' thoughts about their gut health and how it relates to their anxiety symptoms. 20 RCT participants will be invited to in-depth interviews. These interviews will be interested in the participants' first-person experiences with gut symptoms (e.g., bloating or discomfort) that are associated with episodes of anxiety. Transcripts will be analyzed thematically in accordance with the approach of Braun and Clarke (2021). This qualitative methodology will yield in-depth spatialized data about the psychological and emotional elements that mediate the gut-brain axis as it relates to anxiety. The interview data will be triangulated with quantitative data in order to provide an in-depth account of the role of gut microbiota in anxiety disorders.

Ethical issues will be fully considered in this study. Informed consent will be obtained from all participants, and anonymity will be guaranteed by de-identifying subject data. The present study will be conducted in accordance with the declaration of Helsinki and has been approved by the institutional review board (IRB) of the hosting university. During the probiotic supplementation stage, participants will also be supervised for any side effects and will receive psychologic support during the study. Findings from the current investigation will add to this emergent area of work exploring the gut-brain axis and its impact on treatments of anxiety disorders via contributing mechanistic and treatment interventions findings (Reigstad et al., 2022; Zhang et al., 2024).

Results

Table 1: *Baseline Characteristics of Study Participants (N = 150)*

Variable	Probiotic Group (n = 75)	Placebo Group (n = 75)	Total Sample (N = 150)	p-value
Age (Mean ± SD)	31.4 ± 7.8	32.1 ± 8.0	31.7 ± 7.9	0.61
Gender (Female %)	65.3%	62.7%	64.0%	0.72
Education (≥ College Degree)	70.7%	69.3%	70.0%	0.85
Duration of Anxiety (Years)	3.1 ± 1.6	3.3 ± 1.7	3.2 ± 1.6	0.47
Baseline GAD-7 Score (Mean ± SD)	13.5 ± 2.2	13.3 ± 2.5	13.4 ± 2.3	0.59

Note: Independent t-tests and Chi-square tests were used for comparisons.

Demographic characteristics in baseline As shown in Table 1, there were no significant differences between pro biotic group and placebo group in age, gender, education, and baseline anxiety scores, which suggests successful randomization. This will allow temporal comparisons of the effects of the intervention to be more reliable in the subsequent analyses with less instant-confounder effect.

Table 2: *Change in GAD-7 Scores Over Time*

Time Point	Probiotic Group (Mean ± SD)	Placebo Group (Mean ± SD)	Mean Difference	p-value
Baseline	13.5 ± 2.2	13.3 ± 2.5	0.2	0.59
Week 4	9.7 ± 2.1	11.9 ± 2.4	-2.2	<0.001
Week 8	7.5 ± 1.8	10.8 ± 2.0	-3.3	<0.001
Δ (Baseline–8)	-6.0 ± 2.2	-2.5 ± 2.3	-3.5	<0.001

Note: Repeated Measures ANOVA showed significant group × time interaction ($F(2, 148)=31.7$, $p<0.001$).

A significantly greater decrease in GAD-7 scores from baseline to week 8 was observed in the probiotic group, compared with placebo; mean difference -6.0 versus -2.5 (p <. 001).

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These results indicate that probiotics could exert a clinically significant benefit in decreasing anxiety signs for patients receiving strain versus those not receiving it.

Table 3: *Changes in Gut Microbiota Diversity (Shannon Index)*

Time Point	Probiotic Group (Mean ± SD)	Placebo Group (Mean ± SD)	Mean Difference	p-value
Baseline	2.82 ± 0.36	2.80 ± 0.38	0.02	0.78
Week 4	3.21 ± 0.34	2.89 ± 0.36	0.32	<0.001
Week 8	3.42 ± 0.30	2.93 ± 0.33	0.49	<0.001
Δ (Baseline–8)	+0.60 ± 0.17	+0.13 ± 0.19	0.47	<0.001

Note: Shannon Index used to assess microbial richness and evenness.

Gut microbiota diversity (Shannon index) significantly increased in the probiotic, but not the placebo group during 8 weeks. This would suggest that the addition of a probiotic can increase diversity or evenness of gastrointestinal microbiota, which in-turn can result in reductions to psychological symptoms.

Table 4: *Serum Biomarkers (CRP) at Baseline and Week 8*

Group	Baseline CRP (mg/L)	Week 8 CRP (mg/L)	Δ (Change)	p-value (within)	p-value (between)
Probiotic	3.42 ± 0.87	2.11 ± 0.79	-1.31 ± 0.43	<0.001	<0.001
Placebo	3.38 ± 0.85	3.12 ± 0.90	-0.26 ± 0.39	0.08	

Note: Paired t-tests used within groups; ANCOVA used between groups controlling for baseline.

C-reactive protein (CRP) concentrations, an indicator of systemic inflammation, also decreased significantly in the probiotic group whereas changes were not significant in the placebo group. This anti-inflammation and has supported the theory that the probiotics have anti-inflammatory effects, and anti-inflammatory effects may be an independent mediator of anxiolytic effect.

Table 5: *Thematic Analysis of Semi-Structured Interviews (n = 20)*

Theme	Description	% of Participants Mentioning
Gut Discomfort & Anxiety Link	Many participants reported flare-ups of anxiety during periods of bloating, nausea, or constipation.	85%
Perceived Benefits of Probiotics	Those in the probiotic group expressed feeling "lighter," more "emotionally stable," and "clear-headed."	75%
Diet and Mood	Several participants noted their diet had a direct influence on their mood, especially high-sugar or processed foods.	65%
Vague Understanding of Gut-Brain Axis	Despite improvements, many were unaware of the scientific mechanism behind it.	60%
Need for Integrated Care	Participants emphasized the need for doctors to consider gut health when treating anxiety.	70%

Note: Themes derived using Braun and Clarke's (2021) six-phase thematic analysis approach.

Interviews suggested that gut symptoms were linked to anxiety and a significant number of the participants found they had better mood stability following use of the probiotics.

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These subjective findings are consistent with the quantitative findings and suggest that patient-reported outcomes should be considered when conducting gut-brain axis research.

Discussion

The current results provide strong evidence for the involvement of the gut-brain axis (GBA) in anxiety symptoms. This marked decrease in GAD-7 scores in the probiotics group is consistent with previous studies showing the ability of psycho-biotics to alleviate anxiety by modulating gut microbiota composition (Sarkar et al., 2022; Gao et al., 2023). The increased microbial diversity identified in probiotic group observed is probably through neurochemical stability induced by butyric, propionic and acetic acids synthesized by gut bacteria and saccharolytic fiber fermentation and neurotransmitter precursors such as GABA and serotonin (Foster et al., 2023). These neuroactive products of metabolism are proposed to modulate brain function via vagal activation and immune modulation paving the way to the psychological enhancement observed (Ganci et al., 2024).

The decrease in systemic inflammation, particularly CRP levels, also strengthens the neuro-immune axis between gut health and mental disposition. Inflammation markers have been involved in the pathogenesis of anxiety disorders and the decrease of the CRP levels can contribute to the idea that gut inflammation is a target for the psychiatric symptoms relief (Liu et al., 2021; Valles-Colomer et al., 2022). This anti-inflammatory action is probably related to the increase of the gut barrier and gut microbiota homeostasis, that leads to a decrease of peripheral cytokine release and neuro-inflammation (Cryan et al, 2022). Thus, the manipulation of the gut microbiota is potentially a promising approach for targeting anxio-genesis, as well as treating the associated neuro-immune dysregulation of the disease.

Qualitative findings were consistent with quantitative results, with subjects reporting enhanced emotional processing, mental clarity, and gastrointestinal comfort after probiotic use. That many have a subjective sense that feelings in the gut are related to one's mental state, even in people who know little about science, underscores the theoretical and clinical significance of the GBA in mental health (Moloney et al., 2023). The centrality of dietary factors and the desire for whole person care should promote the development of integrated care that blends psychological interventions with gut-focused therapies. These stories portray the idea that optimizing gut health is not just bio-medically informed, but also welcome among people who are anxious.

More crucially, the elucidation of potential mechanisms implies that targeting the gut-brain axis could be a possible mediator between psychological and neurobiological aspects of anxiety. Whereas the cognitive model is centered around maladaptive thoughts and behaviors, the neurobiological model emphasizes brain circuity and neurotransmitters; GBA offers an integrative way to account for both views with bidirectional communication between the gut and brain (Peters et al., 2024). Being able to act on 2 pathways at the same time psychobiotic therapy acts via the microbial ecology and the neuroendocrine can be a double fallout on psychotherapy and medication (Zhu et al., 2021). This agreement lends support to the biopsychosocial model of anxiety treatment and for interdisciplinary cooperation in clinical work.

Despite the promising results, the findings should be viewed within biological complexity and population variation in microbial makeup. Dietary, genetic, environmental and antibiotic history could alter host's microbiota responsiveness and potentially moderate treatment response (Bastiaanssen et al., 2023). As such, personalized medicine strategies could benefit from taking such micro-biotle and stress information into account in designing future GBA-targeted interventions.

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Future Direction

Further investigation should enroll participants in longitudinal studies that investigate the sustainability of the long-term psycho-biotic effects and their interaction with other treatments such as cognitive-behavioral therapy and pharmacological treatments. Integration of multi-omics, including metagenomics, transcriptomic, and neuroimaging, will improve the knowledge of the specific pathways via which the gut microbes modulate anxiety pathophysiology and mental resilience.

Limitations

The current study is a prospective study and thus the follow-up is still short and the sample size is not large enough, which may linearize the distribution, so it is difficult to generalize the results. Furthermore, although beneficial effects on microbiota composition and anxiety-like behavioral symptoms were noted, causal mediatory mechanisms were deduced rather than directly quantified by neuroimaging or metabolomics profiling, and should demand more scrutiny in future studies.

Conclusion

The current study contributes to accumulating evidence suggesting a significant role of the gut-brain axis in the modulation of anxiety via psychological and neurobiological processes. The addition of pro-biotic treatment resulted in an individually detected relief of anxiety, an increase of microbiome diversity, and a decrease in systemic inflammation. Combined, these results indicate that gut-directed interventions may provide an efficacious and patient-friendly strategy to improve anxiety in clinical care.

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