



## Current insights on the intersection between the gut microbiome and psychiatric disorders

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### Abstract

**Background:** Over recent years, growing evidence points to gut dysbiosis as a potential factor in the development of several neuropsychiatric illnesses. However, the significant discrepancies between studies has made it necessary to compile new information, elucidating the mechanisms behind gut-brain connection.

**Objectives:** This review attempts to incorporate the most recent data and noteworthy findings by focusing on research conducted within the past five years, ultimately offering insights into the complex interaction between gut microbiota and mental health.

**Findings of the review:** There is evidence linking psychiatric disorders to dysbiosis. Studies on anorexia nervosa have shown an increase in inflammatory taxa and a decrease in helpful bacteria like *Bifidobacterium*.

Probiotics such as *Bifidobacterium breve* and *Lactobacillus plantarum* have demonstrated promise in reducing depressive symptoms. Moreover, they have been shown to lower oxidative stress biomarkers in schizophrenia and anxiety, although the effects on symptom severity are still unclear. Changes in *Blautia* and *Streptococcus* have been linked to sleep disruptions, suggesting a complex relationship between gut health and sleep regulation. Furthermore, it has been demonstrated that microbial metabolites affect the synthesis of neurotransmitters.

**Conclusions:** Gut microbiomes play a crucial role in the pathophysiology of several psychiatric illnesses. New approaches may be made possible by therapeutic therapies that target the gut microbiota. Nevertheless, there are still important study gaps which call for well-designed clinical trials.

**Keywords:** Gut-brain axis- gut microbiota- psychiatric disorders- dysbiosis

### Introduction

Over recent years, the intricate gut microbiota relationship has attracted a lot of attention globally. Trillions of gut microbiotas inhabit the human gastrointestinal system and are essential for many physiological processes, such as metabolism, immune regulation, and digestion. Especially noteworthy is the gut-brain axis (GBA), a sophisticated communication network that links the gastrointestinal tract with the nervous system immunologically, hormonally, and metabolically [1, 3]. This approach has completely changed our concepts of how gut microbes may affect mood, behavior, brain function, and the emergence of psychiatric disorders.

Growing evidence points to gut dysbiosis as a potential factor in the development and course of several neuropsychiatric illnesses [2, 4, 6]. Antipsychotic drugs are the mainstay of current therapy; however, they frequently fall short in addressing the severity and heterogeneity of symptoms in many patients [1]. This restriction emphasizes how urgently novel therapeutic approaches are needed.

The gut microbial makeup of people with psychiatric disorders and healthy controls differs significantly, according to comparative studies, and several bacterial genera are associated with the severity of symptoms [1, 7]. Furthermore, extracellular vesicles and microbial metabolites have been identified as putative gut-brain interaction mediators that impact neurotransmitter production, neuroinflammation, and host behavior [4, 8].

These results point to a mechanistic connection that is both therapeutically exploitable and physiologically reasonable.

Despite the increase of pertinent research, there are still significant discrepancies between studies, in part because of differences in study design, confounding variables such as nutrition and medication use, and the complexity of psychiatric diseases [3, 6, 7]. This circumstance has made it necessary to compile new information, elucidate the mechanisms behind gut-brain connection, and evaluate the therapeutic utility of therapies that target microbiomes.

Even though many works in this area were published before 2020, metagenomic, metabolomic, and bioinformatics revolution have produced new discoveries and conceptual framework [3, 5, 9, 10]. By concentrating on the studies during the last five years, this review is guaranteed to include the most up-to-date approaches, theoretical models, and therapeutically significant discoveries. We aim to shed insight on the intricate relationship between gut microbiota and mental health. A more individualized, integrated approach to psychiatric therapy may result from the findings, which may provide physicians and mental health professionals with up-to-date information on supplementary treatment approaches. In the end, combining psychiatry and microbiology may change how mental health conditions are perceived and treated.

### Gut microbiota and Psychiatric Disorders

The interplay between gut microbiota and psychiatric health has become a hot area of research. Our review deliberately

concerns the recent literature (2020- 2025) with a special emphasis on anorexia nervosa, depression, anxiety, schizophrenia, and sleeping disorders.

### 1. Anorexia Nervosa

Anorexia nervosa (AN) is a psychiatric disorder characterized by a distorted body image, severe dietary restriction, and an overwhelming dread of gaining weight. Recent studies have started to reveal an intriguing connection between AN and gut microbiota, indicating that alterations in gut flora may affect mood, appetite, behavior, and physical health. Moreover, the gut microbiome of people with AN differs significantly from that of healthy people, according to several studies.

Yuan *et al.* discovered significant variations in the kinds and variety of bacteria, with an increase in inflammatory bacteria and a decrease in beneficial bacteria. These alterations may account for some of the patients' psychological symptoms as well as their gastrointestinal distress [11]. Considering this, scientists have begun investigating the possibility that altering the gut microbiota could aid in the treatment of AN. Wilson *et al.* reported a pilot project about fecal microbiome transfer (FMT) in which they transfer gut bacteria from healthy donors to give AN patient to improve the microbial balance and aid with their psychiatric recovery [12].

The administration of probiotics is another promising therapeutic strategy. Gröbner *et al.* designed a study to investigate the possible beneficial effects of AN-specific probiotic supplements in teens in changing the gut flora [13]. Similar research has been carried out by different scientists to explore the potential effects of diet on health. One such study is MiGBAN study that examines whether supplementing polyunsaturated fatty acids (PUFAs) can improve gut health and cognitive and emotional well-being [14].

Another intriguing pathway involves the function of short-chain fatty acids (SCFAs), which are microscopic molecules generated by gut microbes and appear to have significant impacts on mood, stress, and even eating habits. Additionally, increasing SCFA levels may help control these reactions in patients [15]. This is corroborated by Xu *et al.* who proved that blood levels of SCFA are aberrant in both active and recovering anorexics, indicating long-term impacts on the body's metabolism [16].

Certain probiotics, such as *Lactobacillus reuteri* have also demonstrated promising results - not only in improving their nutritional status in children and adolescents with AN but also reported relief from constipation, a prevalent yet neglected symptom in these patients [17].

Research on animals is deepening our understanding even further. It was shown that alterations in gut flora and brain architecture could be seen following refeeding in a rat model. This implies that in the process of recovering from anorexia, gut healing may coexist with brain restoration [18]. When viewed together, these results present an intriguing picture: addressing the gut microbiota may be a potent supplement to establish anorexia nervosa therapy. With the advancement of science, it's becoming more evident that healing may entail not just therapy and nourishment but also

fostering the microscopic ecosystems that reside inside the human body.

### 2. Depression

Research has established a strong connection between gut microbiota and depression. A study conducted by Park *et al.* showed that orange juice rich in flavonoids might raise *Lachnospiraceae* and *Bifidobacterium* in young adults with depressive symptoms [19]. The robustness of these findings was, however, constrained by the small sample size and absence of dietary control. Similarly, probiotics were associated with decreased intestinal inflammation as shown in the study of Otaka *et al.*, but causal interpretations were hampered by the lack of a placebo group [20].

Chen *et al.* presented an observational data linking gut microbiome dysbiosis to the severity of depression in women [21]. Close to this context, Schaub *et al.* identified a microbial marker that differentiates depressed individuals from healthy controls, however, these results could not be generalized due to inadequate sample size and a paucity of stool metabolite data [22]. Although their results were only correlational, Radjabzadeh *et al.* further discovered neurotransmitter-related bacterial taxa linked to depression, supporting the link between the microbiota and depression [23]. Tian *et al.* studied the possible advantages of *Bifidobacterium breve* on depression; nevertheless, the reliability of findings was constrained by the small sample size [24]. Park *et al.* similarly found microbiome dysbiosis in Korean people with depression, but their findings were less useful without evaluating therapies [25].

### 3. Anxiety & schizophrenia

Recent studies have started to investigate the connection between anxiety and schizophrenia and the gut microbiota. Research shows that anxiety patients and healthy controls have quite different gut microbiota compositions overall. For example, whereas *Parasutterella* is more common in healthy people,

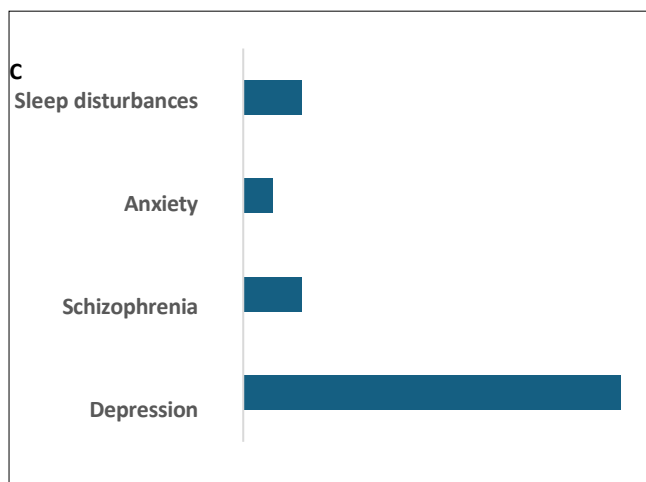
genera like *Gordonibacter* and *Anaeromassilibacillus* are more common in SAD patients. On the other hand, *Anaeromassilibacillus* is more prevalent in anxiety patients at the species level [26]. Furthermore, studies using mice given gut microbiota from anxiety patients showed a particular rise in social fear without changing other behaviors, pointing to a biological basis for the association between gut microbiota and social anxiety [27]. Probiotic supplementation had a marginally beneficial effect on verbal memory and had a positive effect on intestinal permeability and inflammation markers, but it did not significantly reduce psychiatric symptoms [28]. Zhou *et al.* found that nine taxa are positively linked to schizophrenia risk, including Firmicutes, Clostridia, *Alloprevotella* and *Hungatella*. In contrast, six taxa provide protective effects against schizophrenia, including *Rhodospirillaceae*, *Veillonellaceae*, *Coprobacter* and *Gordonibacter*. The study further supports the causal effects of Clostridia, *Rhodospirillaceae*, and *Desulfovibrio* on schizophrenia [29]. Regarding schizophrenia, probiotic supplements improved cognitive function in patients according to Mohammadi *et al.*'s findings. However, they concluded that this difference was not statistically significant, which suggests that it may not

have been powerful enough to indicate that the probiotic affected those symptoms [30].

#### 4. Sleeping disorder

Recent research highlights that gut bacteria plays a critical role in sleep disturbances, and cognitive decline. Certain gut microbiome patterns could act as biomarkers for various disorders, enabling prompt diagnosis and focused treatment [31]. Patients with post-stroke sleep difficulties have a different gut microbiota profile, characterized by a decrease in *Blautia* and *Paeniclostridium* and an increase in *Streptococcus* and *Granulicatella* [31].

Notwithstanding these results, there is still a dearth of research in the last three psychiatric disorders, suggesting that more work is necessary to completely comprehend the connections between changes in the gut microbiota and these illnesses.



#### Clinical trials on Microbiome and Psychiatric Disorders

Despite increased interest in the gut-brain axis, clinical research, especially randomized controlled trials (RCTs), is still scarce for many neuropsychiatric disorders, as seen in Figure (1), depression is the subject of about 72% of published RCTs, making up the vast bulk of these studies. On the other hand, anxiety has only been the subject of 6% of studies, but schizophrenia and sleep disorders account for 11% apiece. This unequal distribution draws attention to a

serious research gap and underscores the need for more thorough research into the involvement of gut microbiota in a wider spectrum of neurological and psychiatric disorders. Research on the association between gut microbiota and psychiatric disorders is a hot area of research with important therapeutic implications. Numerous probiotic therapies have been investigated in recent clinical studies, with both encouraging outcomes and significant difficulties identified. One important conclusion from several research is that certain probiotics may have an impact on depression symptoms. For instance, *Clostridium butyricum*, showed antidepressant-like benefits, pointing to a mechanism by which gut health may mitigate mood disorders [32]. Nevertheless, not all clinical trials yielded commensurate results; for example, the administration of *Lactobacillus plantarum* resulted in decreased depression scores without appreciable changes in biomarkers, suggesting that symptom relief may not always be correlated with detectable biological changes [33]. This brings up significant issues regarding the underlying mechanisms of action and the microbiome's function in mood regulation.

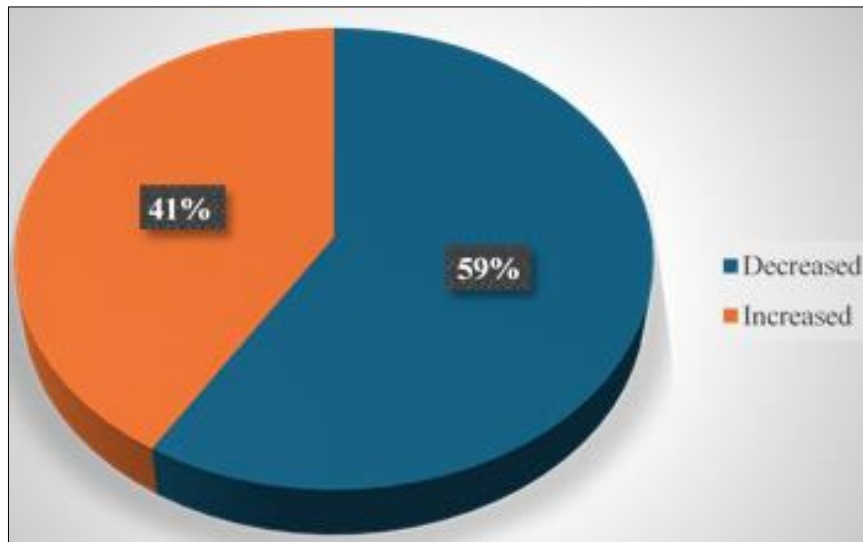
Additionally, the results of multi-strain probiotic experiments highlight the intricacy of gut-brain interactions. Despite changes in microbiota composition, some studies found no meaningful results, while others indicated increased microbial diversity and decreased depression severity [34, 35]. This disparity highlights the need for more research on the potential varied effects of probiotic strains and combinations on mental health.

Studies on schizophrenia have shown that probiotic administration improves metabolic indicators and cognitive performance but does not lessen the intensity of symptoms [30]. This implies that although gut therapies might improve some parts of cognition, they might not be able to address every aspect of complex psychiatric illnesses.

Furthermore, the broad-spectrum impacts noted in the Lee *et al.* study suggest that gut microbiome therapies may help with a variety of psychiatric illnesses, including anxiety and sleep problems, demonstrating the potential for integrated treatment modalities [36]. Recent clinical trials are compiled in Table (1), which highlights the variety of methods and results in this exciting field of research.

**Table 1:** Clinical trials on gut microbiome and psychiatric disorders: Interventions and effects

Disorder	Participants	Intervention	Effect	Study Ref.
	85	<i>Clostridium butyricum</i>	Decreased depression scores	Liu <i>et al</i> [32].
	32	<i>Lactobacillus plantarum</i>	Decreased depression scores	Lin <i>et al</i> [33].
	11	<i>L. plantarum</i>	Decreased depression scores	Chen <i>et al</i> [34].
Depression,	82	<i>Bifidobacterium bifidum</i> , <i>B. lactis</i> , <i>B. lactis</i> , <i>L. acidophilus</i> , <i>L. casei</i> , <i>L. paracasei</i> , <i>L. plantarum</i> , <i>L. salivarius</i> and <i>L. lactis</i>	<ul style="list-style-type: none"> <li>• Decreased depression and anxiety severity.</li> <li>• Improved sleep quality</li> </ul>	Reininghaus <i>et al</i> [35].
	47	<i>Streptococcus thermophilus</i> , <i>Bifidobacterium breve</i> , <i>B. lactis</i> , <i>Lactobacillus acidophilus</i> , <i>L. plantarum</i> , <i>L. paracasei</i> , and <i>L. helveticus</i>	Increased microbial $\beta$ -diversity ( <i>Ruminococcus gausvreauii</i> & <i>Coprococcus</i> ), but no significant clinical difference	Schaub <i>et al</i> [22].
Depression Anxiety, and sleep disorder	156	<i>Lactobacillus Reuteri</i> <i>Bifidobacterium adolescentis</i>	Decreased depression scores	Lee <i>et al</i> [36].
Schizophrenia	70	<i>Lactobacillus acidophilus</i> , <i>L. rhamnosus</i> , <i>L. reuteri</i> , <i>L. paracasei</i> , <i>B. longum</i> , and <i>Bacillus coagulans</i>	No significant clinical difference	Mohammadi <i>et al</i> [30].



**Fig 2:** Relative abundance of gut microbiome in psychiatric disorders

**Table 2:** The Role of Gut Microbiota in Neurological Disorders: Bacterial Imbalances and Their Impact

Disorder	Bacteria Involved	Predicted association	Study Ref.
Sleep Disorders	<i>Blautia Streptococcus</i>	Key microbiome signature for sleep disorders.	Xie H <i>et al</i> [31].
		Significant predictor for post- stroke sleep disorders.	
Anorexia Nervosa	<i>Clostridium Coccoides, Clostridium leptum, Bacteroides fragilis</i>	Associated with lower levels of short-chain fatty acids.)	Yuan R <i>et al</i> [11].
Depression	<i>Ruminococcus gauvreauii</i>	Found to correlate with mood improvement.	Schaub A <i>et al</i> [22].
	<i>Bifidobacterium breve</i>	Associated with improved depressive symptoms.	Tian P <i>et al</i> [24].
	<i>Faecalibacterium prausnitzii</i>		Liu QF <i>et al</i> [37].

**1. Gut Microbiome in psychiatric disorders**

Gut microbiome changes in individuals with psychiatric illnesses have been the subject of an increasing number of clinical investigations, which have shown patterns of microbial dysbiosis that could be involved in the pathophysiology of the disease.

Changes in gut microbiota have been found to be proportionately distributed in psychiatric disorders (Figure 2). Some microbiomes have been connected to altered neurotransmitter production and pro-inflammatory activity. The

connection between the gut microbiota and the pathogenesis of psychiatric illnesses is further supported by these changes in microbial composition. Most reported bacterial taxa showed a decline in relative abundance, as seen in Table (2).

**2. Microbiome, neurotransmitters, and psychiatric Outcome**

Numerous therapeutic approaches have investigated the gut-brain axis by focusing on neurotransmitters and microbial

metabolites. Some probiotic trials showed microbiota-mediated neuromodulatory effects, whereas others did not produce any discernible improvements in mood, cognition, or stress biomarkers. For example, BLa80 supplementation was linked to increased Gamma-aminobutyric acid (GABA) synthesis and better sleep, most likely as a result of Firmicutes and Bacteroidetes population adjustment. Likewise, some treatments, such as 5-hydroxytryptamine and particular probiotic strains, improved subjective sleep or depression symptoms by raising serotonin levels. Additionally, gut-derived compounds such as SCFAs and indole derivatives have been identified as important mediators that connect neurotransmitter pathways to microbial activity. According to the compiled data, certain microbial strains, neurotransmitter production, and metabolic pathways may all play a role in the indirect modulation of psychiatric symptoms by microbial interventions. Table (3) illustrates the important randomized controlled studies examining the relationships between neurotransmitters, microbiota, and psychiatric outcomes.

**Table 3:** Microbiota-neurotransmitter-psychiatric outcome links in clinical studies

Study Focus	Effect on microbiota	Impact on neurotransmitter	Psychiatric outcome	Study Ref.
<i>Bifidobacterium animalis</i> (BLa80)	<i>Proteobacteria:</i> (IA), <i>Bacteroidetes:</i> (DA)	GABA: Increase	Improved sleep quality	Liu <i>et al</i> [38].
5-hydroxytryptamine	Increase SCFA producers Increase microbiome diversity	5-hydroxytryptophan: Increase	Improved sleep quality	Sutanto <i>et al</i> [39].
Danzhi-xiaoyao-San*	<i>B. coprophilus</i> (IA), <i>Ruminococcus gnavus:</i> (DA)	Lysophosphatidic acid: increase	Improved depressive symptoms	Zhu <i>et al</i> [40].

Lacticaseibacillus paracasei	<i>Bacteroidetes:</i> (IA) <i>Firmicutes/Bacteroidetes ratio:</i> (DA)	SCFA: Increase	Improved sleep quality	Li <i>et al</i> <sup>[41]</sup> .
<i>Bifidobacterium breve</i>	Increase SCFAs	GABA: Increase	Improved sleep quality	Li <i>et al</i> <sup>[42]</sup> .
<i>Bifidobacterium breve</i>	Increase Microbial diversity	Serotonin turnover: Decrease	Improved depressive symptoms	Tian <i>et al</i> <sup>[24]</sup> .
Dairy based product	<i>Bifidobacterium:</i> (IA)	Salivary cortisol: Decrease	Improved depressive symptoms	Schaafsma <i>et al</i> <sup>[43]</sup> .

**3. Critical Analysis and Future Directions**

The reviewed studies demonstrate the important role that microbiomes play in mental illnesses, providing both observational and therapeutic insights. Nevertheless, there are still a few significant restrictions. Firstly, small sample sizes and a lack of placebo controls makes it difficult to establish causality in many studies, especially those looking into probiotics <sup>[23]</sup>. Furthermore, although gut microbiota is shown to have an impact on animal models, it is difficult to extrapolate these results to human populations <sup>[32]</sup>. Additionally, even though observational studies have linked microbial markers to several psychiatric conditions, they frequently fall short of establishing clear causal links. Finally, the short duration of many interventional studies limits their ability to identify long-term effects <sup>[21, 23]</sup>.

**Conclusion**

The review's findings highlight the significant role that gut microbiota plays in the pathophysiology of several psychiatric illnesses. The severity of symptoms in conditions like anorexia nervosa, depression, anxiety, and sleep disturbances has been repeatedly associated with changes in particular bacterial taxa. Probiotics have clear therapeutic promise in lowering psychiatric disorders symptoms, indicating that gut microbiome modification may be a useful supplement to conventional therapies. Even with these encouraging results, small sample sizes, absence of placebo controls in some trials, short study durations, and variability in research designs represent a limitation that undermine the statistical power and generalizability of the results. Future studies should concentrate on better-designed randomized controlled trials with larger and diverse cohorts to overcome these problems.

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**Conflict of interest**

Authors declared that there is no conflict of interest

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