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Dysbiosis and Schizophrenia: A Review of Current Evidence on the Gut–Brain Axis and Probiotic Interventions

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Abstract

Introdution:

Schizophrenia is a complex mental disorder influenced by both genetic and environmental factors. Recent research has highlighted the potential role of the gut microbiota in mental health, including schizophrenia. Disruptions in gut microbiota composition, known as dysbiosis, may affect the central nervous system through immune modulation, neuroinflammation, neurotransmitter imbalance, and increased intestinal permeability. Notably, studies have shown associations between dysbiosis and the severity of psychotic symptoms as well as treatment response. Some evidence also suggests that probiotics may help alleviate certain psychiatric symptoms, including those seen in schizophrenia. Although further research is needed, probiotics are being investigated as a promising adjunctive therapy.

Aim of the study:

A literature review was conducted using PubMed and Google Scholar, covering studies from 2018 to 2025. Keywords included: "gut", "microbiome", "microbiota", "gut-brain axis", "dysbiosis", "schizophrenia", "antipsychotic drugs", "prebiotics", and "psychobiotics".

Materials and Methods:

A literature review was performed using PubMed, Google Scholar from 2018 to 2025, was conducted using keyword such as "gut", "microbiome", "microbiota", "gut-brain axis", "dysbiosis", "schizophrenia", "antipsychotic drugs", "prebiotics", and "psychobiotics".

Summary

The gut microbiota significantly influences mental health, and its disturbances may contribute to schizophrenia. Patients with schizophrenia often exhibit reduced microbial diversity and specific changes in microbiota composition, which may correlate with symptom severity. Antipsychotic medications also impact the microbiota. Prebiotics and probiotics appear to offer promising support to standard treatment, opening new avenues for therapeutic strategies.

Keywords:

gut, microbiome, microbiota, dysbiosis, schizophrenia, antipsychotic drugs, prebiotics, psychobiotics

Introdution

Schizophrenia is a complex psychiatric disorder with a multifactorial etiology, in which both genetic predispositions and environmental influences play a crucial role. In recent years, growing attention has been directed toward the role of the gut microbiota in modulating central nervous system function, leading to the development of the gut–brain axis concept. Imbalances in the gut microbial ecosystem, known as dysbiosis, have been implicated in the pathogenesis of various neuropsychiatric conditions, including schizophrenia.

The gut microbiota, a dynamic community of microorganisms residing in the human body, is shaped by mutual microbial interactions as well as the physiological environment of the host. [1]

Alterations in microbiota composition may influence brain function through mechanisms involving immune regulation, neuroinflammation, neurotransmitter modulation, and increased intestinal permeability. A growing body of evidence suggests that these pathways may contribute to the development and progression of schizophrenia by disrupting neural homeostasis and potentially increasing vulnerability to psychotic symptoms. [2]

Recent studies have demonstrated that individuals with distinct gut microbiota profiles may exhibit differential responses to antipsychotic treatment, underscoring the potential relevance of the gut microbiota in the personalization of schizophrenia therapy. [3]

Moreover, interventions aimed at modulating the gut microbiome—such as the administration of prebiotics and probiotics—are being explored for their potential to alleviate schizophrenia symptoms and enhance treatment outcomes. [4]

Schizophrenia

Schizophrenia is a chronic, severe mental disorder characterized by delusions, hallucinations, disorganized thinking, and deficits in cognitive and emotional functions. According to DSM-5 criteria, the symptoms must persist for at least six months, including at least one month of active disease phase. The prevalence of schizophrenia is estimated to be around 0.5–1% of the general population, with the disease more commonly developing in men aged 21–25 years and in women between 25 and 30 years of age. [2,5]

Schizophrenia symptoms can be divided into three main categories. Positive symptoms include delusions, hallucinations, and disorganized thinking (which are characterized by a loss of contact with reality, disorganized speech, and agitated behavior). Negative symptoms include anhedonia, emotional flattening, lack of motivation, and social withdrawal. Cognitive symptoms involve deficits in attention, working memory, and executive functions [2,6]

The severity of clinical symptoms is assessed using the PANSS (Positive and Negative Syndrome Scale), which allows for monitoring the progression of the disease and the effectiveness of pharmacological treatment. [5]

Current treatment for schizophrenia includes psychotherapy and pharmacotherapy using antipsychotic drugs, which may cause numerous side effects. Given the individual differences in gut microbiota composition and the varied response of patients to treatment, targeted modulation of the microbiome through modern prebiotics may offer an effective and natural therapeutic alternative in the treatment of schizophrenia. [7]

The Role of Microbiota in Mental Health

Microbiota refers to the collection of microorganisms that inhabit the human body, with the intestinal microbiota being of the greatest significance for human health. It is primarily composed of bacteria from the Firmicutes (e.g., *Lactobacillus*, *Clostridium*, *Enterococcus*)

and Bacteroidetes (e.g., *Bacteroides*) phyla, along with smaller amounts of Actinobacteria, Proteobacteria, and others. [8]

The composition of the microbiota depends on various factors, including genetic predispositions, age, diet, physical activity, environmental conditions, stress, infections, diseases, and the use of antibiotics. It is estimated that intestinal microorganisms constitute as much as 90% of the total human microbiota, with a total mass of 1–2 kg. Their composition and abundance are strictly dependent on factors such as pH, oxygen availability, nutrients, and intestinal peristalsis. [1,9]

The microbiota plays a crucial role in the functioning of the body – it supports digestion, synthesizes vitamins (e.g., B and K), regulates the immune system, and serves as a barrier against pathogens. Dysbiosis, or disturbances in its composition, can lead to metabolic, autoimmune, and neurological diseases. Microorganisms also support gastric mucus secretion, enzymatic activity, and immune system development. Additionally, the microbiota affects epithelial cell proliferation, insulin resistance, and regulation of the central nervous system's homeostasis.[1, 2, 8]

The gut flora also plays a significant role in brain function and maturation, suggesting its impact on mood. [10] The intestinal microbiota influences brain function through neurotransmitter production, modulation of the immune system, and maintenance of the intestinal barrier integrity. A key role in this communication is played by the vagus nerve, which serves as the main pathway connecting the gut and the brain. [11]

An increasing number of studies indicate a link between microbiota and mental disorders, including schizophrenia. Patients with schizophrenia show significant differences in their microbiota composition, which may influence the immune system and neurotransmission. [2]

Recent studies suggest that dynamic changes in the composition of the gut microbiome can affect the host's metabolism, potentially leading to epigenetic changes and, consequently, modifications in the expression of genes associated with the development of psychosis. [7]

The Relationship Between Gut Dysbiosis and Schizophrenia

In the context of schizophrenia, studies suggest that patients with this disorder exhibit decreased diversity of gut microbiota and specific alterations in its composition compared to healthy individuals. [12] An increasing number of studies confirm the influence of gut microbiota on stress-related behaviors, including anxiety and depression levels, as well as the development of neuropsychiatric disorders. [13] Furthermore, some studies indicate a link

between gut dysbiosis and the severity of psychotic symptoms and cognitive dysfunction in patients experiencing their first episode of psychosis. [14]

Gut microbiota plays a crucial role in regulating the secretion of neuroactive substances by the central nervous system, including neurotransmitters such as serotonin, dopamine, and melatonin. These substances are involved in mood regulation and cognitive functions. Therefore, the gut microbiota may play a significant role in the treatment of mood disorders. [10]

Additionally, intestinal epithelial cells have sensory functions, enabling rapid signal transmission to the brain via the vagus nerve. This process occurs swiftly due to the synthesis and release of neurotransmitters, forming an essential element of gut–brain communication. [15] A meta-analysis of gut microbiota composition in mental disorders conducted by McGuinness et al. indicates no significant differences in α-diversity of gut bacteria compared to the control group. However, in disorders such as major depression, schizophrenia, and bipolar disorder, differences in microbiota composition (β-diversity) were observed. These changes may reflect the potential influence of microbiota on the development and course of these disorders, suggesting an association between gut dysbiosis and the pathophysiology of psychiatric conditions. [1]

One of the first studies by Schwartz analyzed the gut microbiome of patients with first-episode psychosis, revealing significant differences in microbiota composition compared to healthy controls. Patients exhibited increased abundance of *Lactobacillaceae, Halothiobacillaceae, Brucellaceae, and Micrococcineae*, with a simultaneous decrease in *Veillonellaceae*. These changes correlated with the severity of psychotic symptoms and patient functioning during hospitalization. [12] Notably, patients with the most significant microbiota deviations had a lower remission rate after one year (28%) compared to those with a more stable microbial profile (70%). A predictive model based on five bacterial families confirmed the significance of these differences, independent of BMI, physical activity, or duration of antipsychotic treatment. These results suggest a potential link between the microbiome and the course of schizophrenia and treatment response. [12]

The study by Ma et al. showed significant differences in gut microbiome composition in patients with psychosis compared to healthy controls. Individuals with psychosis presented elevated levels of *Christensenellaceae, Enterobacteriaceae*, and *Victivallaceae*, along with a decrease in *Pasteurellaceae, Turicibacteraceae, Peptostreptococcaceae, Veillonellaceae*, and *Succinivibrionaceae.* [14]

Zhu et al. found that the beta diversity of gut microbiota in first-episode psychosis patients differed from that in schizophrenia patients and healthy controls. Notably, an excess of *Haemophilus* correlated with more severe negative symptoms, agitation, cognitive deficits, and depression in schizophrenia patients. In contrast, an abundance of *Coprococcus* was inversely related to negative symptoms, suggesting its potential protective role in schizophrenia. [14]

Zheng et al. compared the gut microbiome of schizophrenia patients and healthy individuals, revealing significant intergroup differences. Patients exhibited reduced α-diversity regardless of treatment. *Veillonellaceae* and *Lachnospiraceae* taxa correlated with the severity of schizophrenia symptoms measured by the PANSS scale. Additionally, a microbial panel including *Aerococcaceae, Bifidobacteriaceae, Brucellaceae, Pasteurellaceae*, and *Rikenellaceae* effectively distinguished patients from controls. [15]

Research by Błażej Misiak and colleagues showed increased abundance of *Lactobacillales, Bacilli*, and *Actinobacteriota* in individuals with schizophrenia, as well as significant associations between certain bacterial groups (*Bacteroidia* class, *Actinobacteriota* phylum, *Bacteroidota* phylum, *Coriobacteriales* order, and *Coriobacteria* class) and the severity of negative symptoms, linguistic abilities, and levels of social and occupational functioning. [16]

Zhou et al. identified nine taxa more prevalent in individuals with schizophrenia, including *Desulfovibrio*, *Firmicutes*, *Betaproteobacteria*, and *Prevotellaceae*. An association between *Clostridium difficile* and an increased risk of schizophrenia was also noted. Increased production of short-chain fatty acids (SCFAs) in these patients may contribute to microglial activation and membrane dysfunction, supported by higher choline levels. [17]

Growing evidence indicates a link between intestinal barrier dysfunction ("leaky gut") and the pathophysiology of schizophrenia. Increased gut permeability may lead to microbial lipopolysaccharide translocation, triggering inflammatory responses that may contribute to cognitive impairment. [18] Acute stress transiently affects gut motility and secretion, whereas chronic stress can alter the microbiota, weaken immunity, and disrupt the intestinal barrier. In turn, dysbiosis may lead to excessive activation of the hypothalamic–pituitary–adrenal axis, potentially impairing the balance necessary for optimal brain development. [15]

Ishida et al. found that schizophrenia patients had significantly elevated gut permeability as measured by the lactulose–mannitol test (LMT) compared to healthy controls. These findings support the hypothesis that "leaky gut" may exacerbate inflammatory processes linked to

schizophrenia development, highlighting the role of gut microbiota in the disease's mechanisms. [18]

Tomasik et al. investigated the effects of the probiotic strains *L. rhamnosus* GG and *B. animalis* subsp. *lactis* Bb12 in patients with chronic schizophrenia. They found a significant reduction in von Willebrand factor levels and increases in BDNF, macrophage inflammatory protein-1 beta, monocyte chemoattractant protein-1, and RANTES. These results suggest that probiotic supplementation may support gut barrier function in patients with schizophrenia. [19]

Chronic inflammation plays a key role in the development of schizophrenia. Structural damage to the gut may lead to chronic inflammation driven by gut microbiota. Autopsy studies of schizophrenia patients revealed intestinal inflammation that compromises the structural integrity of the intestinal wall. Elevated levels of soluble CD14, a marker of bacterial translocation, were associated with a threefold increased risk of schizophrenia, suggesting that microbiota components other than lipopolysaccharides may stimulate immune responses. Infection with *Toxoplasma gondii* may induce gut microbiota dysbiosis, serving as a potential risk factor for schizophrenia. Furthermore, bacteriophages, particularly those associated with *Lactobacillus*, may alter microbiota composition and bacterial metabolism, also implicated in schizophrenia. [9]

Early life stressors, such as social isolation, may exert significant influence on the gut microbiome, potentially leading to enduring alterations in its composition. These microbiota changes have been implicated in the disruption of both neural and endocrine system functioning, thereby suggesting a potential role in the pathogenesis of schizophrenia. [20]

Evidence from animal studies demonstrates that stress can induce shifts in the gut microbial community, including a reduction in *Lactobacillus* populations. Furthermore, the microbiome of mice subjected to stress induced by social disruption differed markedly from that of non-stressed control mice, with a notable decrease in *Bacteroides* and *Clostridium species*. [21]

An increasing body of evidence supports a significant link between gut microbiota and the pathophysiology of schizophrenia. Patients with this disorder exhibit reduced microbial diversity, specific alterations in microbiota composition, and impaired intestinal barrier function. These changes are correlated with the severity of psychotic symptoms, cognitive deficits, and treatment response. Dysbiosis may affect the gut–brain axis, immune system activation, and chronic inflammation, all of which may contribute to the onset and progression of the disease. Therefore, gut microbiota disturbances may serve as a relevant biomarker and a promising target for novel therapeutic strategies in schizophrenia.

The Impact of Antipsychotic Drugs on Gut Microbiota

Antipsychotic drugs are divided into two main groups: first-generation (typical) and second-generation (atypical) antipsychotics. First-generation antipsychotics, such as chlorpromazine and haloperidol, are effective in alleviating the positive symptoms of schizophrenia, such as delusions and hallucinations. However, they are associated with numerous side effects, including extrapyramidal symptoms. Second-generation antipsychotics, including clozapine, risperidone, olanzapine, quetiapine, aripiprazole, and brexpiprazole, demonstrate greater efficacy in treating both positive and negative symptoms and carry a lower risk of motor-related side effects compared to first-generation drugs. They are also frequently used in long-acting injectable formulations. Despite these advantages, SGAs can cause weight gain and metabolic disturbances, increasing the risk of diabetes and elevated cholesterol levels, which requires close monitoring during long-term treatment. [22]

Antipsychotic medications are particularly significant due to their antimicrobial properties, which can lead to alterations in gut microbiota composition and gastrointestinal function, including increased intestinal permeability in vivo and effects on bacterial growth in vitro. [23]

Second-generation antipsychotics such as olanzapine, clozapine, and risperidone significantly alter the gut microbiota composition in patients with schizophrenia, often exacerbating dysbiosis and contributing to metabolic side effects. These changes result in metabolic dysfunctions characterized by weight gain, elevated triglyceride and glucose levels, prediabetic abnormalities, and hypertension—ultimately reducing life expectancy by 10–15 years. [18]

Furthermore, patients with schizophrenia treated with antipsychotics exhibited increased abundance of *Peptostreptococcaceae, Veillonellaceae*, as well as the genera *Megasphaera*, *Fusobacterium*, and *SMB53* compared to drug-naive individuals experiencing their first episode of psychosis. Notably, these specific changes correlated with abnormal volume in the right middle frontal gyrus, suggesting a potential link between gut microbiota and brain structure in schizophrenia. [14]

Alterations in the gut microbiota were also observed in first episode of psychosis patients after 24 weeks of risperidone treatment. Before treatment, reduced levels of *Bifidobacterium*, *Escherichia coli*, and *Lactobacillus*, and increased levels of *Clostridium coccoides* were noted. After treatment, *Bifidobacterium* and *E. coli* increased, while *C. coccoides* decreased, suggesting an antipsychotic-induced shift in microbiota composition. [7]

Similarly, patients treated with olanzapine or risperidone showed altered levels of *Akkermansia*, *Sutterella*, and *Lachnospiraceae* compared to healthy controls. [7]

Further studies have demonstrated that gut microbiota plays a crucial role in the mechanism of olanzapine-induced weight gain—one of the most frequent and serious side effects of this drug. Antipsychotics can also contribute to constipation by affecting gastrointestinal motility. A higher relative abundance of *Desulfovibrio* species has been observed in patients with psychiatric disorders experiencing constipation. [17]

Research has shown that schizophrenia patients treated with various classes of antipsychotic drugs display distinct gut microbiota profiles. Individuals treated with atypical antipsychotics had increased levels of *Faecalibacterium prausnitzii*, *Clostridium aldenense*, and *Tetragenococcus halophilus* compared to those receiving typical antipsychotics. Moreover, the microbiota of the typical group was enriched in butyrate-producing bacteria—including *Erysipelotrichaceae*, *Butyricimonas*, *Blautia*, and *Paraprevotella*—compared to the atypical group. Interestingly, although the gut microbiota of the atypical group showed a lower diversity of butyrate producers, it exhibited a significant enrichment in *Faecalibacterium prausnitzii*, a bacterium known for its anti-inflammatory properties. [3]

On the other hand, the microbiota of patients in the typical group, in addition to beneficial microbes, also contained potentially pathogenic taxa such as *Fusobacteriaceae*, *Helicobacteraceae*, and *Klebsiella*, which are associated with dysbiosis and increased systemic inflammation [3]

Psychobiotics in Mental Health

Psychobiotics refer to a broad category encompassing probiotics, prebiotics, and other microbiota-targeted interventions that exert beneficial effects on neurological and brain functions. [19]

Growing evidence suggests that interventions such as probiotics and prebiotics may improve treatment outcomes in individuals with schizophrenia by restoring gut microbiota balance, reducing medication side effects, and enhancing overall health status. However, further studies are necessary to confirm the link between gut dysbiosis and schizophrenia. [15]

Certain bacterial populations inhabiting the gut may promote dysbiosis by acting as endogenous triggers that sustain inflammation associated with neuropsychiatric disorders. [11]

Nagamine et al. demonstrated that a probiotic mixture consisting of *Clostridium butyricum*, *Streptococcus faecalis*, and *Bacillus mesentericus* could alleviate symptoms of schizophrenia.

Similarly, Dickerson et al. found that a combination of *B. animalis* subsp. *lactis* Bb12 and *L. rhamnosus* improved gastrointestinal function in patients with schizophrenia. [24]

Severance et al. assessed the effects of probiotic supplementation on intestinal yeast infections and psychiatric symptoms in individuals with schizophrenia. Results indicated a reduction in *Candida albicans* antibody levels and a decrease in gastrointestinal symptoms in male patients. Notably, a trend toward reduction in positive symptoms was observed in seronegative individuals receiving probiotics. [25]

A 2019 study reported that supplementation with vitamin D3 (50,000 IU biweekly) and a probiotic blend (*L. acidophilus*, *B. bifidum*, *L. reuteri*, *L. fermentum*) led to decreased PANSS scores, suggesting symptom improvement in patients with schizophrenia. Furthermore, Okubo et al. demonstrated that a four-week intervention with *B. breve* A-1 improved anxiety and depression scores and modulated cytokine and chemokine levels. [24]

Meta-analyses have shown that probiotics reduce serum C-reactive protein (CRP) levels across a range of inflammatory conditions, including osteoarthritis, autoimmune diseases, and neurological disorders. Although only a few randomized controlled trials (RCTs) have evaluated the effects of probiotics on inflammatory markers in schizophrenia, initial results are promising. [11]

Notably, a significant reduction in CRP levels was observed after 12–14 weeks of probiotic supplementation compared to control groups, indicating a beneficial effect both in healthy individuals and in those with schizophrenia or neurological disorders.

Current evidence suggests that psychobiotics may, in the near future, serve as a valuable adjunct to antipsychotic and antidepressant therapy—enhancing treatment efficacy while potentially mitigating adverse effects such as weight gain and metabolic disturbances. [25]

Summary

Current evidence suggests that the gut microbiota plays a significant role in the pathophysiology of schizophrenia by modulating the gut–brain axis through immunological, metabolic, and neurochemical mechanisms. Individuals with schizophrenia exhibit alterations in the composition and diversity of gut microbiota, which may contribute to the severity of both psychotic and non-psychotic symptoms. Antipsychotic medications, especially second-generation agents, substantially influence the gut microbiome, potentially exacerbating dysbiosis and inducing adverse effects, including metabolic disturbances. In contrast, psychobiotics—though still underexplored in this patient population—offer a promising

adjunctive therapeutic approach, with potential benefits in symptom alleviation and improved treatment tolerability. Further large-scale, standardized clinical studies are necessary to determine the efficacy and safety of microbiota-targeted interventions in psychiatric care.

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