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# THE CORRELATION BETWEEN GUT MICROBIOTA AND SCHIZOPHRENIA

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**ABSTRACT:** Schizophrenia is a serious psychiatric disorder that affects millions of people globally, and is characterized by positive, negative symptoms, disorganization, neurocognitive deficits and social impairment. Its etiology involves genetic, neurobiological and environmental factors, with emphasis on dopaminergic dysfunction and alterations in neurodevelopment. Diagnosis is based on DSM-5 criteria, and treatment involves the use of antipsychotics and psychosocial interventions. However, challenges such as cognitive deficits persist, requiring new therapeutic approaches. Recent studies indicate that the gut microbiota may play a relevant role in schizophrenia, due to its influence on the gut-brain axis. Patients with the disease show alterations in microbial composition and elevated inflammatory markers, suggesting a possible impact on the regulation of neurotransmitters such as serotonin and GABA. In addition, intestinal dysbiosis can aggravate psychiatric symptoms, reinforcing the need for strategies aimed at restoring the balance of the microbiota. In light of this, research has explored the potential of using prebiotics, probiotics and nutritional interventions as complementary therapies for schizophrenia. These approaches can modulate the microbiota and reduce inflammatory processes, contributing to improvements in the clinical picture. Thus, understanding the relationship between gut microbiota and schizophrenia can open up new perspectives for more effective treatments, highlighting the importance of an integrative approach to managing the disease.

## INTRODUCTION

Schizophrenia is a severe psychiatric disorder with wide epidemiological distribution and significant public health impacts. Globally, schizophrenia affects more than 21 million people and is related to genetic, environmen-

tal and neurobiological factors that affect its manifestation and progression. In Brazil, studies indicate a high rate of hospital admissions associated with the disease, highlighting the need for strategies to increase access to mental health services and reduce barriers to adequate treatment (Correll *et al.*, 2024).

The development of schizophrenia is related to dopaminergic dysfunction, characterized by imbalances in dopamine levels or activity, in addition to neurodevelopmental changes that also play a crucial role. These alterations impact cognition, information processing and the social functionality of patients from the earliest stages of the disease. These findings reinforce the importance of early diagnosis and appropriate therapeutic approaches (Rodrigues *et al*., 2024). The pathophysiology of schizophrenia involves dysfunctions in the dopaminergic and glutamatergic systems, which are directly associated with positive, negative and cognitive symptoms. Increased dopamine in the mesolimbic pathway is related to hallucinations and delusions, while decreased dopamine in the mesocortical pathway is linked to cognitive and emotional deficits (Fernandes *et al.,* 2024).

The symptomatology of schizophrenia is highly heterogeneous and includes five main groups of symptoms: positive ones such as hallucinations and delusions, negative ones such as volition and affective blunting, disorganized incoherent speech and disorganized behavior, neurocognitive deficits impairment in memory, attention and executive functions and social cognitive impairments difficulty in interpreting emotions and interacting socially. These symptoms vary in severity and duration, significantly impacting the functionality of individuals, from difficulties in maintaining relationships to challenges in work and self-care (Striebel, 2024).

The diagnosis of schizophrenia is made through a detailed clinical assessment based on codified criteria, such as those in the DSM--5TR, to ensure greater accuracy and reliability. The condition is characterized by the presence of at least two of the main symptoms over a period of at least one month, including delusions, hallucinations, disorganized speech, disorganized or catatonic behaviour and negative symptoms such as affective blunting and involution. In addition, it must cause significant impairments in functional areas such as work, interpersonal relationships or self-care, and the signs of the disorder must persist for at least six months. Diagnosis usually occurs in early adulthood and is preceded by a prodromal period in which the patient may show subtle changes in behavior, cognitive difficulties and social withdrawal (Jauhar *et al.,* 2022).

The treatment of schizophrenia involves the use of antipsychotics, which act mainly on the dopaminergic and glutamatergic systems to reduce the positive and negative symptoms of the illness. In addition to medication, psychosocial approaches, such as cognitive-behavioral therapy and rehabilitation programs, are essential for improving patients' functionality and quality of life. Despite the advances, there is no specific treatment approved for the cognitive impairment associated with schizophrenia, although research into the microbiota-intestine-brain axis is underway to develop new therapies (Javitt, 2022).

The intestinal microbiota is made up 90% of *Firmicutes*, *Bacteroidetes*, *Proteobacteria* and *Actinobacteria*, the other 10% of viruses, fungi and archaea, which play essential roles in digestion, nutrient absorption and fiber fermentation, as well as producing short-chain fatty acids and B and K vitamins (Flório *et al.*, 2024). Its composition is influenced by factors such as genetics, type of delivery, diet and use of medication. The microbiota participates in communication between the intestine and the central nervous system, impacting mental and metabolic health, as well as strengthening

the intestinal barrier and the immune system, preventing infections and inflammation. Studies indicate its relationship with obesity, diabetes, neuropsychiatric disorders and inflammatory bowel diseases, highlighting the importance of strategies for its balance, such as proper nutrition and conscious use of antibiotics (Oliveira *et al.*, 2024; Lima *et al.*, 2025).

The relationship between the gut microbiota and schizophrenia has been increasingly investigated, revealing important connections between the gut and the brain. According to Damázio and Zugno (2022), patients with schizophrenia have a different microbial composition when compared to healthy individuals, as well as inflammatory and immunological changes that can aggravate the symptoms of the disease. Studies also indicate that factors such as an unbalanced diet and the frequent use of antibiotics, as well as stress, can disrupt this balance, leading to so-called intestinal dysbiosis, which can affect the production of essential neurotransmitters such as serotonin and gamma-aminobutyric acid (GABA), interfering with brain function and possibly contributing to the development or progression of schizophrenia. In addition, there is evidence that interventions such as the use of pre- and probiotics can help modulate the microbiota, reducing inflammatory markers and improving some psychiatric symptoms, which reinforces the importance of intestinal health in the therapeutic approach to this condition (Pina *et al*., 2024).

Thus, this review aims to investigate the relationship between the gut microbiota and schizophrenia, exploring how changes in microbial composition can influence the pathophysiology of the disease. Analyze the impact of the gut-brain axis on schizophrenia, with an emphasis on the interactions between the central nervous system and the microbiota. To evaluate the therapeutic implications of modulating the gut microbiota as a complementary strategy in the treatment of schizophrenia. To explore the role of nutrition in balancing the gut microbiota, considering how diets and dietary interventions can promote a healthy microbiome, influence the gut-brain axis and possibly attenuate the psychiatric symptoms of schizophrenia.

## METHODOLOGY

This literature review was carried out using databases such as PubMed, SciELO and LILACS, using descriptors such as "gut microbiota", "schizophrenia", "gut-brain axis", "gastrointestinal microbiome" and "microbiota and mental health". We included studies published in Portuguese and English between 2021 and 2025, which were available in full and dealt with the influence of the gut microbiota on schizophrenia, with a focus on changes in microbial composition, impact on the gut-brain axis and possible implications for the treatment of the disease. Incomplete studies, reviews without substantial data and texts with restricted access were excluded. After the initial search, the abstracts were carefully read to select articles that directly addressed the central question: "What is the relationship between gut microbiota and schizophrenia?". The search resulted in 35 articles being selected for detailed analysis, while the others were discarded for not meeting the established criteria. The selected texts were analyzed in depth, paying special attention to the objectives, methods and results presented, ensuring a coherent and relevant synthesis. The analysis of the materials involved categorizing the studies and critically interpreting the findings, allowing for the identification of the main trends and conclusions related to the role of the intestinal microbiota in schizophrenia.

## RESULTS AND DISCUSSIONS

### SCHIZOPHRENIA

Schizophrenia is a serious psychiatric disorder that affects around 1% of the world's population and is characterized by positive symptoms such as delusions and hallucinations, negative symptoms such as reduced emotional expression and motivation, and cognitive deficits. Its onset usually occurs in adolescence or early adulthood, with a slight predominance in men. The disease is influenced by genetic, environmental and neurobiological factors, and is more prevalent in urban than rural areas, with a higher risk in cities. In approximately 8% of cases, schizophrenia manifests before the age of 18, and around 18% of patients report initial symptoms at this stage (Correll *et al.*, 2024). This disorder is associated with significant impairments in social and cognitive functions, directly impacting patients' quality of life (Takeda *et al.,* 2024).

Schizophrenia is a mental disorder that significantly affects the Brazilian population, resulting in a high number of hospitalizations. Between 2018 and 2023, more than 415,000 hospitalizations were recorded in the country, with the highest incidence in the Southeast Region, which concentrated 41.4% of cases. The epidemiological profile indicates a higher prevalence among men aged between 30 and 39. In addition, mortality associated with schizophrenia amounted to 1,157 deaths in the period analyzed.These data demonstrate the need for strategies aimed at early diagnosis, access to appropriate treatment and public policies that reduce the barriers to psychiatric care in the country (Rodrigues *et al*., 2024).

The pathophysiology of schizophrenia involves dysfunctions in the dopaminergic and glutamatergic systems, contributing to positive, negative and cognitive symptoms. An excess of dopamine in the mesolimbic pathway is linked to hallucinations and delusions, while a reduction in the mesocortical pathway is associated with cognitive and emotional deficits (Fernandes *et al.,* 2024). In addition, alterations in the hippocampus and prefrontal cortex indicate a disturbance in neurodevelopment, affecting neural connectivity and synaptic function. Studies also indicate that epigenetic factors, such as DNA methylation, can modulate gene expression and increase vulnerability to the disease. Environmental factors, such as early stress and perinatal infections, also play an important role and can influence the progression and severity of symptoms throughout life (Mendes *et al.,* 2024).

The symptomatology of schizophrenia is highly heterogeneous and includes five main groups of symptoms: (positive) such as hallucinations and delusions, (negative) such as avolition and affective dullness, (disorganization) such as incoherent speech and disorganized behavior, (neurocognitive deficits) impairment in memory, attention and executive functions and (social cognitive impairments) difficulty interpreting emotions and interacting socially. These symptoms vary in severity and duration, significantly impacting the functionality of individuals, from difficulties in maintaining relationships to challenges in work and self-care (Striebel, 2024).

The diagnosis of schizophrenia is made through a detailed clinical assessment, based on codified criteria, such as those in the DSM-5, to ensure greater accuracy and reliability. The condition is characterized by the presence of at least two of the main symptoms over a period of at least one month, including delusions, hallucinations, disorganized speech, disorganized or catatonic behaviour and negative symptoms such as affective blunting and avolition (Fariba *at et*., 2024). In addition, the illness must cause significant impairment in functional areas such as work, interpersonal relationships or self-care, and the signs of the disorder must persist for at least six months. Diagnosis usually occurs in early adul-


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thood and is preceded by a prodromal period in which the patient may show subtle changes in behavior, cognitive difficulties and social withdrawal (Jauhar *at et.,* 2022).

The treatment of schizophrenia is based on the use of antipsychotics, which act mainly by blocking dopamine D2 receptors to reduce positive symptoms, such as delusions and hallucinations, and have some effect on negative and cognitive symptoms. In addition to dopamine, evidence suggests the involvement of the glutamatergic system, leading to research into N-methyl-d-aspartate (NMDA) receptor antagonists as potential new therapies (Kruse *at el.*, 2022). The choice of antipsychotic may vary according to the patient's profile, tolerance to side effects and response to treatment, with second-generation antipsychotics being preferred because they present a lower risk of extrapyramidal effects. In addition to medication, psychosocial interventions such as cognitive-behavioral therapy, social and occupational rehabilitation programs and family support are fundamental to improving functionality, reducing relapses and promoting social reintegration (Javitt, 2023). However, there is still no effective treatment approved for the cognitive impairment associated with schizophrenia, one of the main challenges in the rehabilitation of these patients. Recent research explores the relationship of the gut microbiota to develop more targeted therapeutic approaches aimed at minimizing cognitive deficits and improving the quality of life of affected individuals.

## HUMAN MICROBIOTA

The human gut is home to trillions of microorganisms that make up the intestinal microbiota, performing essential functions in digestion, the immune system and the regulation of neurological functions (Chen *et al.*, 2021). This microbial community is dynamic and is influenced by various factors, such as diet, the use of medication, stress and even the type of birth, and its balance can be significantly altered. When this balance is compromised, dysbiosis occurs, a condition associated with a series of inflammatory, metabolic and psychiatric diseases. Studies indicate that this imbalance can generate a state of chronic low-grade inflammation, contributing to the development of pathologies such as obesity, type 2 diabetes and mental disorders (Góralczyk-Bińkowska *et al.*, 2022).

Two of the main bacterial groups in the gut microbiota are the *Firmicutes* and *Bacteroidetes* phyla, which play key roles in the digestion and absorption of nutrients. They participate in the fermentation of dietary fibers, generating essential metabolites such as short-chain fatty acids (SCFAs), which help regulate energy metabolism and maintain the integrity of the intestinal barrier (Zhang *et al*., 2024). The balance between these phyla is an important indicator of intestinal health, as alterations in this ratio favor the growth of potentially pathogenic bacteria, such as those from the *Proteobacteria* phylum, increasing the risk of inflammatory processes and metabolic diseases. In addition, the intestinal microbiota contributes to the synthesis of essential vitamins, such as biotin and vitamin K, which are fundamental for the body's homeostasis (Flório *et al.*, 2024).

Communication between the microbiota and the central nervous system occurs via the so-called gut-brain axis, a complex system involving the vagus nerve, immune modulation and the production of neuroactive metabolites (Philip *et al.*, 2024). Research shows that changes in microbial composition can directly impact brain functions such as cognition, memory and emotional regulation. Dysbiosis, in turn, can trigger systemic inflammation capable of compromising the blood-brain barrier, allowing pro-inflammatory substances to pass into the brain. This phenomenon has been associated with the development of disorders such as depression, anxiety and schizophrenia (Freitas *et al.,* 2024).


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In addition to influencing the immune response and neuroinflammation, the gut microbiota also participates in the production of essential neurotransmitters, such as serotonin, dopamine and GABA, which play crucial roles in the balance of the nervous system. It is estimated that around 90% of the body's serotonin is produced in the gut and its synthesis can be modulated by beneficial bacteria, directly impacting mood and behavior (Ramagem *et al.*, 2024). In view of this, modulating the microbiota, whether through diet or the use of probiotics, has emerged as a promising strategy to help manage psychiatric disorders, reducing inflammation and promoting the balance of neurotransmitters (Andrade *et al.,* 2024).

Therefore, the gut microbiota goes far beyond digestion; it plays a multifunctional role in regulating metabolism, the immune system and the nervous system. With the advancement of research into these interactions, new therapeutic approaches have emerged to balance the microbiome and promote intestinal and systemic health. In this sense, healthy eating habits, combined with the use of prebiotics and probiotics, represent an affordable and effective alternative for preventing various diseases and maintaining general well--being (Hou *et al.*, 2022).

In this way, it is becoming increasingly clear that taking care of the intestinal microbiota is also taking care of health as a whole. Small everyday choices, such as eating a diet rich in fiber, consuming fermented foods and even reducing stress, can have a direct impact on this essential ecosystem. In addition, the use of probiotics and prebiotics is gaining ground as a viable alternative to help restore intestinal balance and consequently improve physical and mental well-being. As science advances, new strategies are emerging to strengthen this gut-brain connection, opening up promising avenues for the prevention and treatment of various diseases (Rosa *et al.,* 2024).

Growing evidence indicates that the intestinal microbiota plays a fundamental role in regulating the nervous system, influencing neuroinflammatory processes and neurotransmitter homeostasis. This means that intestinal dysbiosis can contribute to neurological dysfunctions by affecting the integrity of the blood-brain barrier and stimulating systemic inflammatory responses. This mechanism has been associated not only with neurodegenerative diseases, but also with psychiatric disorders such as schizophrenia. Changes in microbial composition can directly impact the gut-brain axis, modulating neurotransmission and increasing susceptibility to mental disorders. In view of this, it is essential to understand how these biological interactions can influence the pathophysiology of schizophrenia, which will be addressed below (Oliveira *et al*., 2025).

## NUTRITION, MICROBIOTA AND SCHIZOPHRENIA

The D1 and D2 dopamine receptors play different roles in neurotransmission. When activated, the D1 receptor stimulates the Gs protein, activating adenylyl cyclase and increasing levels of cyclic AMP (cAMP), which modulates neuronal excitability. In contrast, the D2 receptor is coupled to the Gi protein, which inhibits adenylyl cyclase, reducing cAMP levels and decreasing the release of neurotransmitters (Zhuang *et al.*, 2021). Recent studies highlight the relevance of dopamine receptors in the pathophysiology of schizophrenia. Alterations in dopaminergic signaling, especially increased activity of D2 receptors in the striatum and decreased function of D1 receptors in the prefrontal cortex, are associated with the positive and negative symptoms of the disease. This dysfunction can lead to an imbalance in glutamatergic neurotransmission, contributing to cognitive and behavioral deficits observed in schizophrenic patients (Gomes *et al.*, 2021).

Recent literature has highlighted the significant interaction between the gut microbiota and the central nervous system in the development and progression of schizophrenia. The gut microbiota influences essential physiological functions such as the metabolism of neurotransmitters, the modulation of the immune system and the maintenance of the integrity of the blood-brain barrier, all aspects involved in the pathophysiology of the disorder (Jaqueline *et al.*, 2021). Alterations in this communication axis can lead to exacerbated neuroinflammatory responses, synaptic dysfunction and increased oxidative stress, processes directly implicated in the origin and maintenance of psychotic symptoms (Borkent *et al.*, 2022).

Individuals with schizophrenia often have intestinal dysbiosis, with alterations in microbial composition and diversity. This condition is associated with a decrease in short-chain fatty acids (SCFAs), which are bacterial metabolites with anti-inflammatory and neuroprotective action (Ju S *et al.,* 2021). The reduction of these metabolites can compromise the intestinal barrier and favor a systemic inflammatory state that negatively affects the brain, contributing to the worsening of psychiatric symptoms and cognitive characteristic of schizophrenia. In addition, studies suggest that dysbiosis can directly modulate dopaminergic and glutamatergic signaling, central neurotransmitters in schizophrenia (Mhanna *et al.*, 2024).

In addition, nutrition plays an essential role in modulating the microbiota and, consequently, the gut-brain axis. A diet rich in fiber, vegetables, fruits and fermented foods favors the production of SCFAs and the maintenance of a healthy microbiota. On the other hand, Western dietary patterns, characterized by excessive consumption of saturated fats and simple sugars, are associated with dysbiosis and aggravation of inflammatory processes. It is worth noting that specific nutritional deficiencies, such as B vitamins and omega-3 fatty acids, often observed in patients with schizophrenia, also contribute to microbial imbalance (Socała *et al*., 2023).

The Western diet, rich in saturated fats and simple sugars, aggravates the inflammatory process by inducing intestinal dysbiosis and altering the gut-brain axis. This dysbiosis reduces the production of short-chain fatty acids (SCFAs), compromising the intestinal barrier and favoring systemic inflammation (Malesza *et al*., 2021). Studies indicate that this condition can influence dopaminergic neurotransmission, promoting an imbalance between D1 and D2 receptors, which negatively impacts cognition and behavior. In addition, exacerbated inflammation potentiates synaptic dysfunction and oxidative stress, factors implicated in psychiatric disorders. The deficiency of essential nutrients, such as B vitamins and omega-3, often associated with this diet, aggravates the condition, making it essential to adopt healthier eating patterns to modulate the gut microbiota and reduce the neuroinflammatory impact (García *et al.,* 2021).

(2023) also point out that nutritional interventions, such as the use of prebiotics, probiotics and specific diets, can improve microbial composition, reduce inflammatory processes and possibly attenuate symptoms of schizophrenia, paving the way for complementary strategies to conventional treatment. These dietary approaches are increasingly being explored as an adjunct to drug treatment, showing promising results in improving cognition and symptoms. These findings reinforce the importance of integrating gut health, eating habits and mental health in the management of schizophrenia.

## CONCLUSION

The relationship between the gut microbiota and schizophrenia highlights a promising field in understanding the pathophysiology of the disease and in the search for new therapeutic approaches. Evidence indicates that gut dysbiosis can negatively influence neurotransmission and inflammation, contributing to the manifestation of schizophrenic symptoms. In addition, interventions such as the use of prebiotics, probiotics and nutritional strategies can modulate the microbiota and potentially improve some aspects of the disease. In view of this, integrating intestinal health into psychiatric treatment could represent a significant advance in patients' quality of life.

Although schizophrenia is a complex disorder with multiple factors involved, the growing understanding of the gut-brain axis opens up possibilities for more personalized complementary therapies. However, more research is needed to validate the effectiveness of these interventions and define clinical guidelines based on robust evidence. Thus, the study of gut microbiota not only broadens the view of schizophrenia, but also reinforces the importance of a multidisciplinary approach in the management of the disease, considering both neurobiological and metabolic and immunological aspects.

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