

# Literature review on the relationship between gut microbiota and mental health: the gut-brain axis

## Revisão bibliográfica sobre a relação entre microbiota intestinal e saúde mental: o eixo intestino-cérebro

## Revisión literaria sobre la relación entre la microbiota intestinal y la salud mental: el eje intestino-cerebro

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# REVISA

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### RESUMO

**Objetivo:** Analisar a relação entre a microbiota intestinal e a saúde mental, com ênfase nos mecanismos envolvidos no eixo intestino-cérebro. **Métodos:** Trata-se de uma revisão integrativa da literatura, realizada nas bases PubMed, SciELO e Biblioteca Virtual em Saúde. Foram utilizados descritores DeCS/MeSH relacionados à microbiota intestinal e saúde mental, combinados por operadores booleanos. Foram incluídos artigos publicados nos últimos 5 anos, em inglês e português, com acesso ao texto completo. Ao final, 10 estudos compuseram a amostra. **Resultados:** Os achados indicam associação entre alterações na microbiota intestinal e transtornos mentais, especialmente ansiedade e depressão. Mecanismos propostos incluem modulação imunológica, produção de metabólitos e neurotransmissores, além da comunicação por vias neurais, endócrinas e inflamatórias. Intervenções como probióticos, dieta e regulação do sono demonstram potencial benefício, embora com resultados heterogêneos. **Conclusão:** A microbiota intestinal exerce papel relevante na saúde mental, porém a relação observada é predominantemente associativa. Evidências clínicas ainda são limitadas, reforçando a necessidade de estudos mais robustos para melhor compreensão dos mecanismos e aplicação terapêutica

**Descritores:** Saúde mental; Microbiota intestinal; Eixo intestino-cérebro..

### ABSTRACT

**Objective:** To analyze the relationship between the gut microbiota and mental health, with emphasis on the mechanisms involved in the gut-brain axis. **Methods:** This is an integrative literature review, conducted in the PubMed, SciELO, and Virtual Health Library databases. DeCS/MeSH descriptors related to gut microbiota and mental health were used, combined with Boolean operators. Articles published in the last 5 years, in English and Portuguese, with access to the full text, were included. In the end, 10 studies comprised the sample. **Results:** The findings indicate an association between alterations in the gut microbiota and mental disorders, especially anxiety and depression. Proposed mechanisms include immune modulation, production of metabolites and neurotransmitters, as well as communication through neural, endocrine, and inflammatory pathways. Interventions such as probiotics, diet, and sleep regulation demonstrate potential benefit, although with heterogeneous results. **Conclusion:** The gut microbiota plays a relevant role in mental health, but the observed relationship is predominantly associative. Clinical evidence remains limited, reinforcing the need for more robust studies to better understand the mechanisms and therapeutic application.

**Descriptors:** Handgrip strength; Muscle strength; Ventilation weaning; Mechanical ventilation.

### RESUMEN

**Objetivo:** Analizar la relación entre la microbiota intestinal y la salud mental, con énfasis en los mecanismos involucrados en el eje intestino-cerebro. **Métodos:** Se realizó una revisión bibliográfica integradora en las bases de datos PubMed, SciELO y Virtual Health Library. Se utilizaron descriptores DeCS/MeSH relacionados con la microbiota intestinal y la salud mental, combinados con operadores booleanos. Se incluyeron artículos publicados en los últimos 5 años, en inglés y portugués, con acceso al texto completo. Finalmente, la muestra estuvo conformada por 10 estudios. **Resultados:** Los hallazgos indican una asociación entre alteraciones en la microbiota intestinal y trastornos mentales, especialmente ansiedad y depresión. Los mecanismos propuestos incluyen la modulación inmunitaria, la producción de metabolitos y neurotransmissores, así como la comunicación a través de vías neuronales, endocrinas e inflamatorias. Intervenciones como probióticos, dieta y regulación del sueño demuestran un beneficio potencial, aunque con resultados heterogéneos. **Conclusión:** La microbiota intestinal juega un papel relevante en la salud mental, pero la relación observada es predominantemente asociativa. La evidencia clínica sigue siendo limitada, lo que refuerza la necesidad de realizar estudios más sólidos para comprender mejor los mecanismos y la aplicación terapéutica.

**Descriptores:** Salud mental; Microbiota intestinal; Eje intestino-cerebro.

REVISÃO

## Introduction

The gastrointestinal system is an essential structure of the human body, responsible for several functions, most notably the digestion of food and the absorption of nutrients <sup>1</sup>. However, this system has several other functions, such as immune regulation and the maintenance of metabolic balance. In recent years, significant advances in science have revealed the intrinsic relationship between the gut and the brain, a system known as the gut-brain axis. Growing studies suggest that the gut microbiota plays a fundamental role in this axis, influencing not only physical health but also mental well-being <sup>2</sup>.

The gut microbiota consists of millions of microorganisms that inhabit the gastrointestinal tract in balance, belonging to approximately 1,000 to 5,000 distinct species <sup>3</sup>. This microbiota is essential for the gastrointestinal system to perform its functions, contributing to homeostasis and processes such as digestion, absorption, immune regulation, vitamin secretion, protection against pathogens, among others. Furthermore, the microbiota also produces metabolites, such as short-chain fatty acids and neurotransmitters, which directly influence brain function <sup>4</sup>.

The gut microbiota interacts with the central nervous system (CNS) through various pathways, directly influencing mental health. The brain-gut-microbiota axis encompasses the enteric nervous system (ENS), the vagus nerves, and the spinal nerves, which together form a complex communication network between the gastrointestinal tract and the CNS. The ENS is known as the second brain of the human body and acts in the regulation of the microbiome, neurotransmitters, immune signaling, among others, thus establishing a bidirectional connection with the CNS <sup>5</sup>. The vagus nerve is responsible for gastrointestinal functions such as motility, hormone secretion, and metabolic homeostasis, but it is also involved in inflammatory mechanisms between the gut and the brain <sup>6</sup>.

The gut-brain axis was first described in 1980, following the discovery of hormonal signaling from the gastrointestinal system to neurons and brain cells. Since then, further studies on this communication have been conducted, including the role of the microbiota in this axis <sup>7</sup>. Currently, the brain-gut-microbiota axis performs several functions in the body, also being responsible for maintaining the individual's health. When an imbalance occurs in this axis, mental illnesses such as depression and anxiety can manifest, highlighting its relevance. In other words, through this axis, the gut not only digests and absorbs nutrients, but also influences mood, cognition, and behavior <sup>5,1</sup>.

## Objetivo

Given that alterations in the composition of the gut microbiota, known as dysbiosis, are related to a number of psychiatric and neurological disorders, the aim of this article is to conduct a review of the brain-gut-microbiota axis, addressing its mechanisms and exploring its impacts on mental health.

## Methods

This study is characterized as an integrative literature review. The search was conducted in the PubMed, SciELO, and Virtual Health Library databases. The search strategy utilized the English descriptors "gut microbiota" AND "mental health," combined using the Boolean operator AND, to increase sensitivity. Controlled descriptors from the MeSH (Medical Subject Headings) and DeCS (Descriptors in Health Sciences) vocabularies were also used, combined with free terms, to increase the sensitivity and specificity of the search.

The main descriptors used were: "gut microbiota", "microbiome", "gastrointestinal microbiome", "mental health", "psychiatric disorders", "depression", and "anxiety", combined using the Boolean operators AND and OR. The search strategy was structured as follows: ("gut microbiota" OR "microbiome" OR "gastrointestinal microbiome") AND ("mental health" OR "psychiatric disorders" OR "depression" OR "anxiety").

The inclusion criteria were: articles published in the last 5 years, available in English or Portuguese, with free access to the full text, and directly addressing the relationship between gut microbiota and mental health. Exclusion criteria included: duplicate studies, publications prior to the defined time frame, articles with restricted access, as well as abstracts, editorials, theses, dissertations, and studies that were not thematically relevant to the objective of the review.

The study selection process took place in stages. Initially, the titles and abstracts of the identified articles were read, followed by a full reading of the potentially eligible studies. The final sample consisted of 10 articles, selected according to the previously established criteria.

For data extraction and organization, aspects such as main findings and conclusions were considered. Data analysis was conducted in a descriptive and comparative manner, allowing the identification of gaps in the literature regarding the relationship between gut microbiota and mental health.

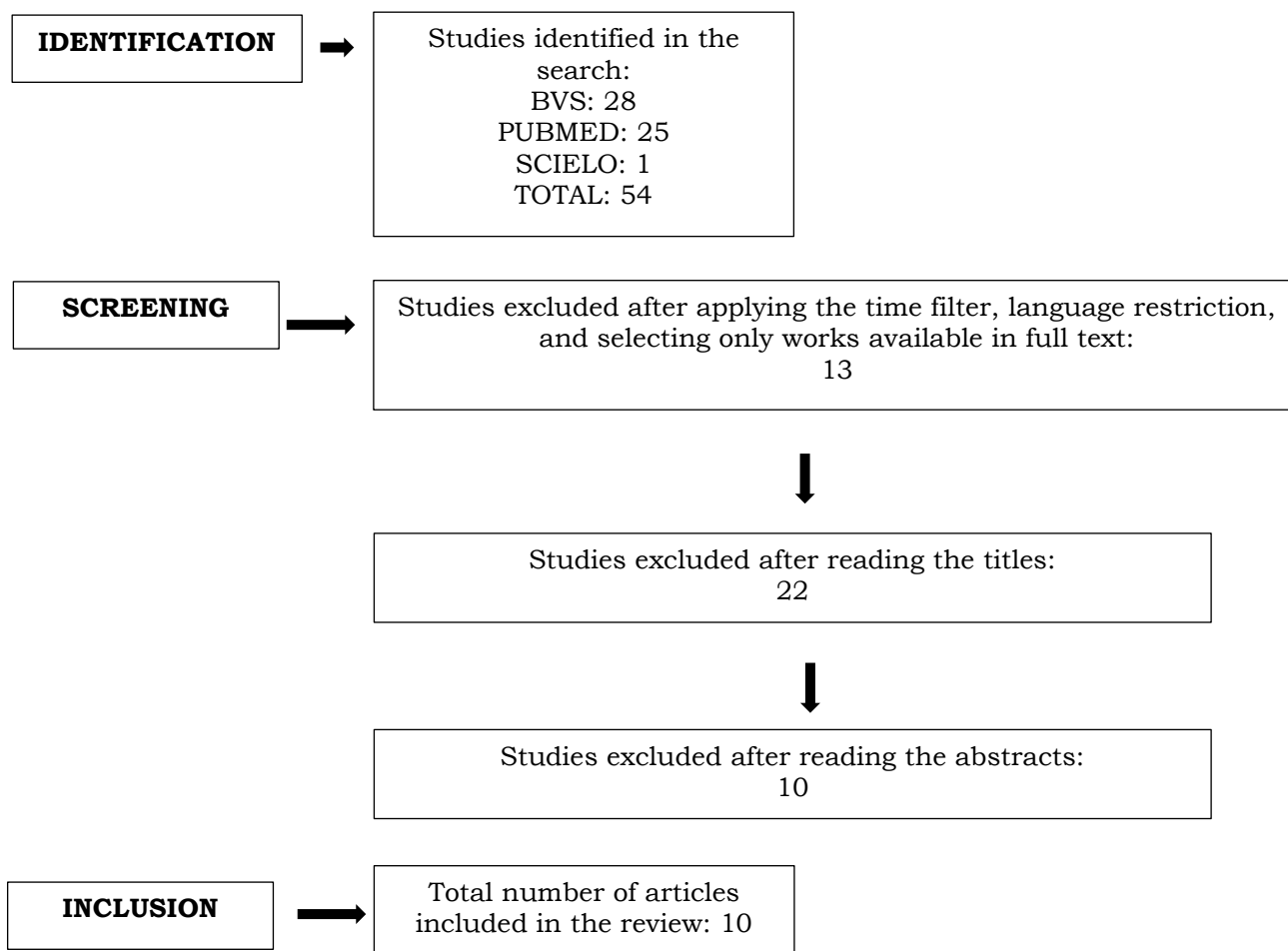
## Results

The study selection process occurred in stages. Initially, the titles and abstracts of the identified articles were read, followed by a full reading of the potentially eligible studies. The final sample consisted of 10 articles, selected according to the previously established criteria.

Initially, the research retrieved 54 articles, 28 from BVS, 25 from PubMed, and 1 from SciELO. After applying the eligibility criteria, including time frame, language, and availability of free full text, 13 studies were excluded, leaving 41 texts for the screening stage.

In the screening phase, the 41 studies were initially evaluated by reading the titles, resulting in the exclusion of 22 articles for not aligning with the research objective. Subsequently, the remaining 18 studies were subjected to reading of the abstracts, with 10 articles being excluded for not meeting the thematic relevance criteria. At the end of the selection process, 10 studies were included in the final sample of this review, as described in Figure 1.

**Figure 1. Flowchart of the article selection process for this review.**



Source: Authors, 2025

Overall, the findings indicate a consistent association between alterations in the gut microbiota and outcomes related to mental health, especially with regard to disorders such as anxiety and depression. Furthermore, the studies analyzed highlight that interventions aimed at modulating the microbiota, such as the use of probiotics, dietary changes, and sleep regulation, have a potentially positive impact on mental health, although with variations in the results and magnitude of the effects observed.

## Discussion

Research has identified that the gut microbiota influences the brain-gut axis, having a considerable impact on people's well-being and mental health. Studies show that when the brain-gut-microbiota axis becomes unbalanced, it is directly related to mood and behavioral changes, and also influences the development of psychiatric illnesses such as depression and anxiety <sup>8</sup>.

In general, there is a consensus in recent literature that there is a significant relationship between the gut microbiota and mental health, especially with regard to disorders such as anxiety and depression. However, this consensus should be interpreted with caution, since most of the available evidence comes from observational studies,

which limits the inference of causality and leaves room for confounding factors that are still poorly explored.

The gut microbiota produces metabolites such as short-chain fatty acids, which regulate systemic inflammation and influence the integrity of the blood-brain barrier. In addition, some bacteria produce neurotransmitters, such as gamma-aminobutyric acid (GABA), serotonin, and dopamine, which can directly modulate mood and cognition. The microbiota also affects immune regulation and can interact with the ENS (enteric nervous system) and the vagus nerve <sup>9, 10</sup>. Although these mechanisms are well described, the translation of these biological processes into clinical outcomes is not yet fully explained, especially in humans, which reveals a gap between experimental research and clinical application.

Despite these biologically plausible mechanisms, it is important to consider that most of the evidence still derives from preclinical or observational studies, which limits a complete understanding of how these processes translate into consistent clinical effects in humans. Furthermore, it is important to recognize that these processes do not occur in isolation, but rather within a complex network involving interactions between neural, immunological, and endocrine systems, making it difficult to determine the relative weight of each pathway in different clinical contexts.

The brain-gut axis is a bidirectional system between the central nervous system (CNS) and the autonomic nervous system (ENS). This system is interconnected by a neural network that connects emotions, cognition, and memory to the gut. In a state of homeostasis, this axis remains in balance and does not affect mental health in any way <sup>11, 12</sup>. However, when the axis is dysregulated, homeostasis is disrupted. The axis, through its neural connections, allows the brain to modulate various cellular activities, including those of intestinal cells, which are under the influence of the gut microbiota. In other words, the microbiota directly affects the axis, being an important component in regulating brain-gut communication, forming the brain-gut-microbiota axis <sup>13</sup>.

Furthermore, more recent studies reinforce that this communication does not occur in isolation, but involves multiple interdependent systems, including inflammatory and hormonal responses, which makes the gut-brain axis a highly complex system that is not yet fully understood <sup>11,12</sup>. This complexity not only expands the possibilities for investigation, but also poses challenges for the development of more targeted therapeutic interventions.

The gut microbiota can communicate with the brain through three pathways: neural pathways via the vagus nerve and the enteric nervous system (ENS), immunological pathways, and endocrine pathways. The vagus nerve modulates intestinal motility, permeability, hormone secretion, and peristalsis through efferent fibers. In addition, it sends stimuli related to hunger, satiety, inflammation, and metabolism through afferent fibers. Other receptors on vagus nerve fibers, such as serotonin receptors, also play a role in sending messages to the brain <sup>13, 14</sup>. However, the relevance of each of these pathways is not yet fully explained, which makes it difficult to understand which mechanism predominates in different clinical contexts.

The production of various metabolites occurs, mainly neurotransmitters such as serotonin, GABA, catecholamines, dopamine, norepinephrine, among others. Thus, metabolites produced by the bacteria of the gut microbiota can affect the CNS through actions on the ENS or vagus nerve. Serotonin is a neurotransmitter that is directly related to feelings of happiness and mood regulation, which is produced in the gut microbiota, functioning as a preventative measure against depression and anxiety <sup>11</sup>. However, caution is needed when interpreting this finding, since most of the serotonin produced in

the gut does not directly cross the blood-brain barrier, suggesting that its effects on the brain occur indirectly. Furthermore, the gut microbiota also acts through immune mechanisms via intestinal immune cells, such as dendritic cells and cytokines, and also through endocrine mechanisms via the secretion and release of hormones<sup>13</sup>.

However, it is important to highlight that, although intestinal serotonin production is relevant, its effects on the brain are indirect, indicating that other mediators, such as neural and immunological pathways, play a fundamental role in this communication. Considering this intrinsic relationship between the gut-microbiota axis and mental health and brain function, studies show that imbalances in gut health predispose individuals to mental illnesses such as depression, anxiety, and bipolar disorder<sup>9,15</sup>. This influence occurs through the mechanisms described.

Furthermore, recent studies have shown that some other conditions can be prevented or treated by maintaining a balanced and healthy gut microbiome. Disorders such as schizophrenia, OCD (Obsessive-Compulsive Disorder), and autism have their symptoms alleviated by maintaining gut health<sup>15</sup>. Despite this, these associations still show high variability between studies, which contributes to the variation in results and limits the generalizability of the findings<sup>16</sup>.

With this in mind, some studies indicate that probiotics, which are medicines made from live microorganisms, can reduce the effects of stress and improve emotional regulation. In this way, they reduce anxiety, stress, and depressive symptoms<sup>16, 17</sup>. However, the results are still inconsistent, with significant variations between strains used, doses, and intervention time, making it difficult to generalize the findings. Furthermore, the circadian rhythm can also interfere with the functionality of the brain-gut-microbiota axis, affecting individuals' mental health both through effects on the nervous system and on mood due to sleep deprivation<sup>16, 18</sup>. Maintaining a good sleep and rest routine also contributes to intestinal and mental health. Dietary factors and lifestyle habits have the potential to interfere with intestinal health, and consequently with mental health as well.

However, there is still no clear standardization regarding the use of probiotics in clinical practice, especially with regard to the strains used, dosages, intervention time and patient profile, which limits its broader therapeutic application. Another important point is the scarcity of robust randomized clinical trials, which reinforces the need for more controlled studies to confirm the effectiveness of these interventions.<sup>14, 17</sup>

Maintaining a good sleep and rest routine also contributes to intestinal and mental health. Dietary factors and lifestyle habits have the potential to interfere with intestinal health, and consequently with mental health as well.

Finally, a healthy routine contributes to maintaining intestinal health, and consequently also corroborates a balanced mental health. Imbalances in intestinal health and homeostasis can cause numerous problems in the human body, including mental disorders. Therefore, a healthy gut contributes to a healthy and disease-free mind. Thus, although current findings are promising, there are still important limitations that prevent definitive conclusions, and further research is essential for a better understanding of this relationship.

## Conclusion

Understanding the gut-brain axis and its relationship with the gut microbiota opens new perspectives for addressing mental disorders. This axis represents an

integrated communication network between neural, immunological, and endocrine mechanisms, the complexity of which is not yet fully understood. This article showed that the microbiota plays a relevant role in regulating mood and cognition, whether through the production of neurotransmitters or through inflammatory modulation. However, despite the biological plausibility, the causal relationship between gut microbiota and mental disorders is not yet well established in humans.

The bidirectional interaction between the central nervous system and the gastrointestinal tract highlights the influence of environmental, dietary, and lifestyle factors on mental health. Interventions such as probiotics, diet, and sleep have therapeutic potential, but still lack standardization and robust clinical evidence. Thus, current findings point to a complex and multifactorial relationship, reinforcing the need for more rigorous studies on the subject.

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