WÓJCIK, Zofia Martyna, KAMIŃSKA-OMASTA, Katarzyna, OMASTA, Bartosz, KRUPA, Olga, PIETRUKANIEC, Paulina Dorota, ROMAŃCZUK, Kuba Borys, FURTAK, Kinga, STOLARCZYK, Szymon Przemysław, CZERSKA, Magdalena Agata and RYBAK, Daria. Gut Microbiota and Its Impact on Brain Function and Mental Health. Quality in Sport. 2025;38:58196. eISSN 2450-3118.

https://doi.org/10.12775/QS.2025.38.58196 https://apcz.umk.pl/QS/article/view/58196

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.

Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).

Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.

Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

© The Authors 2025;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (http://creativecommons.org/licenses/by-nc-sa/4.0/) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 24.01.2025. Revised: 10.02.2025. Accepted: 10.02.2025 Published: 10.02.2025.

Gut Microbiota and Its Impact on Brain Function and Mental Health - a review of the literature

Authors

Zofia Martyna Wójcik

Kazimierz Pulaski University of Technology and Humanitis in Radom, Jacka Malczewskiego 29 Street, 26-600 Radom, Poland https://orcid.org/0009-0005-2940-9971 zosiawojcik2000@gmail.com

Katarzyna Kamińska-Omasta

Dr. Tytus Chałubiński Radom Specialist Hospital, Adolfa Tochtermana 1 Street, 26-610 Radom, Poland

https://orcid.org/0009-0002-5369-0044 kasia22799@gmail.com

Bartosz Omasta

Dr. Tytus Chałubiński Radom Specialist Hospital, Adolfa Tochtermana 1 Street, 26-610 Radom, Poland https://orcid.org/0009-0001-6685-4899 bomasta9559@gmail.com

Olga Krupa

Masovian Specialist Hospital, 5 Juliana Aleksandrowicza Street, 26- 617 Radom, Poland https://orcid.org/0009-0008-4171-0187 olgaczarnota@interia.pl

Paulina Dorota Pietrukaniec

Kazimierz Pulaski University of Technology and Humanitis in Radom, Jacka Malczewskiego 29 Street, 26-600 Radom, Poland https://orcid.org/0009-0009-7907-6350 paulinapietrukaniec@gmail.com

Kuba Borys Romańczuk

Independent Public Multi-specialist Healthcare Facility in Stargard 27 Wojska Polskiego street, 73-110 Stargard, Poland https://orcid.org/0009-0007-8446-8338 borysromanoff@gmail.com

Kinga Furtak

Fryderyk Chopin University Clinical Hospital in Rzeszów, 35-055 Rzeszów, Poland https://orcid.org/0009-0008-8356-734X furtak.kinga@onet.pl

Szymon Przemysław Stolarczyk,

Pomeranian Medical University 1 Rybacka Street, 70-204 Szczecin, Poland https://orcid.org/0009-0002-9507-8822 szymon.stolarczyk99@gmail.com

Magdalena Agata Czerska,

Independent Public Complex of Health Care Facilities in Kozienice, Wladyslaw Sikorski 10 Street, 26-900 Kozienice, Poland https://orcid.org/0009-0008-9509-3989 mczerska@interia.eu

Daria Rybak,

Masovian Specialist Hospital, 5 Juliana Aleksandrowicza Street, 26-617 Radom, Poland https://orcid.org/0009-0004-0419-9210 rybakdaria5@gmail.com

Affiliations:

1. Masovian Specialist Hospital, 5 Juliana Aleksandrowicza Street, 26-617 Radom, Poland

2. Dr. Tytus Chałubiński Radom Specialist Hospital, Adolfa Tochtermana 1 Street, 26-610 Radom, Poland

3. Independent Public Multi-specialist Healthcare Facility in Stargard 27 Wojska Polskiego street, 73-110 Stargard, Poland

4. Independent Public Complex of Health Care Facilities in Kozienice, Wladyslaw Sikorski 10 Street, 26-900 Kozienice, PL

5. Kazimierz Pulaski University of Technology and Humanitis in Radom, Jacka Malczewskiego 29 Street, 26-600 Radom, Poland

6. Pomeranian Medical University 1 Rybacka Street, 70-204 Szczecin, Poland

7. Fryderyk Chopin University Clinical Hospital in Rzeszów, 35-055 Rzeszów, Poland

Abstract: Introduction

The intestinal microbiota is a dynamic ecosystem essential for maintaining human homeostasis. It comprises billions of microorganisms, including bacteria, viruses, fungi, and archaea, which closely interact with their host. Research shows microbiota not only supports metabolic and immune functions but also influences the central nervous system (CNS) through the gut-brain axis, a bidirectional communication pathway.

The gut-brain axis regulates neurotransmitter production (e.g., serotonin, GABA), modulates immune responses, and interacts via bacterial metabolites. Dysbiosis, or imbalance in the microbiota, has been linked to neuropsychiatric disorders such as depression, anxiety, and autism. Maintaining microbial balance is thus critical for mental health.

This paper reviews literature on the role of gut microbiota in mental health, focusing on mechanisms of the gut-brain axis, dietary influences, and therapeutic potential. These insights are especially relevant for developing personalized medicine targeting the microbiota to address mental disorders.

Aim of the study

To assess the role of gut microbiota in mental health and its influence on diseases like Alzheimer's and Autism.

Materials and Methods

A literature review was performed using PubMed, Oxford Academic, and MDPI databases under key topics: gut microbiota mechanisms, gut-brain axis in neurodegeneration, developmental disorders, and its role in inflammation and neural pathways.

Keywords

Gut microbiota, Gut-brain axis, Mental health, Alzheimer's disease, Autism, Neurodegeneration, Inflammation, Dysbiosis, Probiotics, Prebiotics, SCFAs, Vagus nerve, Serotonin, Behavioral disorders, Microbiome, Neuroinflammation.

Summary

The gut microbiota plays a crucial role in maintaining mental health and has been implicated in various neurodegenerative and neurodevelopmental disorders, such as Alzheimer's disease and Autism Spectrum Disorder. Through the gut-brain axis, microbiota influences brain function via mechanisms involving microbial metabolites, inflammation, and modulation of the immune system. Dysbiosis, or an imbalance in the gut microbiota, has been linked to increased permeability of the gut and altered communication between the gut and the brain. Recent studies highlight the potential therapeutic effects of targeting gut microbiota with probiotics, prebiotics, and dietary interventions to improve mental health outcomes and mitigate disease progression. Further research is necessary to fully understand the complex interplay between gut microbiota and brain health.

Introduction

The human intestinal microbiota is extremely complex and includes more than 1,000 species of bacteria that co-create a unique ecosystem. The most important groups of bacteria are:

Firmicutes: These bacteria, including the genera Lactobacillus and Faecalibacterium, play a key role in the production of short-chain fatty acids (SCFAs), such as butyrate, which supports the integrity of the intestinal barrier and has anti-inflammatory functions. Firmicutes bacteria have many genes responsible for the fermentation of dietary fiber. They can also interact with the intestinal mucosa to help maintain balance in the body [1].

Bacteroidetes: anaerobic bacteria, found mainly in the large intestine, where they play a role in the digestion of complex carbohydrates such as plant polysaccharides through the production of fiber-degrading enzymes. Bacteroidetes have the ability to dynamically adapt to changes in the host's diet, and are a key indicator of patient diet-health interactions. [2] **Actinobacteria**: They play an important role in the intestinal microbiota mainly of the large intestine. The best-known genus among Actinobacteria is Bifidobacterium, which play a key role in fiber digestion. The bacteria produce short-chain fatty acids, such as butyrate, which nourishes the intestinal epithelium and has anti-inflammatory effects. Their existence in the intestines reduces the risk of inflammatory bowel disease or obesity, so an imbalance of these bacteria can lead to dysbiosis. [3]

Proteobacteria: This is a diverse group of bacteria, including both commensal and potentially pathogenic organisms. Among the Proteobacteria we distinguish bacteria such as E.coli, which can perform metabolic functions, however, under favorable conditions can cause

diseases. Bacteria in this group play a role in the metabolism of nitrogen and carbon, in addition, some species help in the fermentation of nutrients and in the production of metabolites significant to the host. Some *Proteobacteria* can be beneficial in maintaining intestinal homeostasis, however, their excessive proliferation, can often promote gastrointestinal infections and diseases. [4]

Gut-brain axis

The gut-brain axis, also known as the microbiota-gut-brain, is a complex communication system that integrates the functions of the nervous system, endocrine system, immune system and gut microbiota. It is a bi-directional pathway that enables the exchange of information between the gut and the brain, influencing many processes in the body, including behavior, mood, as well as metabolic and immune functions."[5]

HPA pathway- Hypothalamus- Pituitary- Adrenal glands

A key component of the gut-brain axis is the hypothalamic-pituitary-adrenal (HPA) axis, which is responsible for the body's response to stress. Under stress, the gut microbiome and other factors, such as dysbiosis, can activate the HPA pathway, leading to the secretion of corticoliberin (CRH) by the hypothalamus, which stimulates the secretion of adrenocorticotropic hormone (ACTH) from the anterior lobe of the pituitary. ACTH stimulates the adrenal glands to produce cortisol, a stress hormone that affects intestinal immune function, including the inflammatory response and the integrity of the intestinal barrier. In addition, in the context of the gut-brain axis, the HPA pathway plays a role in regulating the body's response to changes in the gut microbiota and its impact on gut and brain function. [6,7]

Neuroendocrine and neuronal communication pathways

The gut-brain axis is also regulated by neuroendocrine communication pathways, including neurotransmitters produced by the gut microbiota, such as serotonin, GABA, dopamine and acetylcholine. These substances affect brain function and the nervous system in the gut. For example, *Lactobacillus* and *Bifidobacterium* produce GABA, which is the main inhibitory neurotransmitter in the nervous system, while *Escherichia coli* and *Candida* synthesize serotonin, which regulates mood and cognitive processes. The activity of these neurotransmitters affects behavior, anxiety, depression, and cognitive function. [8]

The role of the enteric nervous system (ENS)

The enteric nervous system, also known as the "second brain," plays a key role in the gutbrain axis. It consists of a vast network of neurons, including Meissner's plexus (in the submucosa) and Auerbach's plexus (between the muscular layers of the intestines), which are responsible for regulating intestinal movements, secretion of digestive juices and intestinal barrier function. This system is independent, but is in constant communication with the central nervous system, including via the vagus nerve (vagus), which transmits impulses from the gut to the brain. Studies show that 90% of signals in the gut-brain axis are sent from the gut to the brain (centripetal response), suggesting that the gut may influence brain processes to a greater extent than previously thought. [9]

Metabolism of tryptophan and serotonin

The gut microbiota influences the metabolism of tryptophan, which is a precursor amino acid for the production of serotonin, a neurotransmitter called the "happy hormone." Most serotonin (about 95%) is produced in the gut, and only a small amount in the brain.

Gut microbes, including *Bifidobacterium infantis*, can affect tryptophan levels and its conversion to serotonin, which is important in regulating mood and behavior. Serotonin deficiency in the central nervous system is associated with disorders such as depression and anxiety. Serotonin, produced in the gut, also influences gastrointestinal function, regulating intestinal peristalsis, enzyme secretion and interactions with immune cells. [10,11]

Importance of microbiota research for mental health

Research on the gut microbiota is becoming increasingly important in the context of mental health, as it uncovers unexpected links between the microbes that inhabit our gut and brain function. A growing body of evidence suggests that the composition of the microbiota may influence our mood, emotions and predisposition to various mental disorders such as depression, anxiety and stress. Understanding the role of the microbiota in regulating neurochemical processes and its impact on inflammatory responses that can affect our psyche opens up new possibilities for treatment and prevention. Research in this area may contribute to the development of innovative therapies that incorporate the microbiome as an important component in the treatment of mental disorders, offering patients a more holistic approach to health in which diet, lifestyle and gut microflora play a key role. [12,13]

Neuroimmune and neurohormonal communication between the gut and the brain. Neuroimmune communication-is a process in which the immune system such as macrophages, dendritic cells or lymphocytes interact with the nervous system in transmitting signals to the brain that can affect the functioning of the body, for example, in situations of stress to the body (including surgery), inflammatory reactions or the development of neurodegenerative disorders. [14]

In the context of neuroimmune communication, its main mechanisms are: the vagus nerve pathway, cytokines, chemokines and inflammatory mediators

Nerve pathway: Vagus nerve

It conducts signals from the gut to medulla oblongata, from where the information then travels to higher brain structures (i.e., hypothalamus, amygdala).

It is a two-way communication: Signals from the brain can influence gut motility and impulses from the gut can modulate behavior, emotional and stress responses in the brain. [14,15] Cytokines and chemokines:

In response to inflammation, the activity of cells of the intestinal immune system leads to the release of cytokines and chemokines, they have the ability to cross the blood-brain barrier and can affect the central nervous system [16].

Pro-inflammatory cytokines can modify changes in mood (such as anxiety and depression) and cognition. Chronic inflammation, resulting from dysbiosis of the gut microbiome, can even lead to **the development of neurodegenerative diseases.** [17]

Gut microbiome:

It is a key element in neuroimmune communication, as gut microbes produce numerous biochemicals and metabolites that can affect brain function.

Neurohormonal communication between the gut and the brain:

This type of communication refers to the interaction of hormones and neurotransmitters produced in the gut and acting on the central nervous system.

Serotonin- 5-hydroxytryptamine (5-HT)

As a result of serotonin activity in the gut, signals are produced that affect the CNS, and information is transmitted from the brain to the digestive system.

Serotonin acts as a neurotransmitter in both the central and peripheral nervous systems, acting on various types of serotonin receptors including HTR1-HTR4.

It plays a key role in regulating intestinal motor functions, due to the fact that there are serotonin receptors in smooth muscle cells, and their stimulation affects intestinal contractions and motility. Too little serotonin can lead to digestive disorders (constipation), while excess serotonin can cause diarrhea. [19]

Serotonin in the gut-brain axis affects the regulation of mucus secretion, motility and blood flow, thereby regulating intestinal homeostasis. On the other hand, the presence of serotonin in the central nervous system affects emotions, mood, cognitive functions, including the ability to feel pain and respond to stress. [20]

5-HT can affect the central nervous system both directly and indirectly. The hormone secreted in the gut can enter the bloodstream and then enter the brain through the blood-brain barrier. In the brain, serotonin acts on receptors that are located in many areas of the brain (including the frontal cortex, hippocampus and amygdala). Activation of these receptors is associated with the regulation of mood anxiety, memory processes, as well as effects on emotional and social reactions. [21]

Stressors, both physical and emotional, can alter serotonin levels in the gut and brain, resulting in imbalances of this amine in the nervous system.

An example is the phenomenon in which changes in the gut microbiome can affect serotonin levels in the gut, which in turn affects serotonin levels in the brain, with potentially important implications for mental health and cognitive function. [22,23]

GABA- gamma- aminobutyric acid

It is the main inhibitory neurotransmitter in the central nervous system and plays a key role in the regulation of many neurophysiological processes (neuronal excitability, muscle relaxation, as well as regulation of emotional state and stress.

GABA is synthesized in the gut, especially in neuroendocrine cells such as enterochromaffin cells, and in enterocytes. The synthesis process is regulated by the activity of the intestinal microbiota.

GABA plays a role in regulating intestinal motility and immune function within the gut. [24] Research suggests that gut bacteria can affect the secretion of GABA, which consequently affects central nervous system activity and emotions.

Communication between the gut and the brain occurs on several levels: GABA affects the activity of sensory neurons in the gut, which transmit information to the brain via the vagus nerve. Gamma-aminobutyric acid, as an inhibitory neurotransmitter, can modulate signals sent from the gut to the brain, affecting pain sensation, inflammation and other gut processes.

GABA in the gut can affect gut microflora, which in turn can affect neurotransmitter synthesis in the brain.

Stress or mental disorders such as depression or anxiety cause changes in GABA concentrations in both the gut and brain. [25]

Reduced levels of GABA in the central nervous system can lead to mood disorders, excessive reactivity to stress, and increased inflammation, which is associated with activation of the HPA axis (hypothalamic-pituitary-adrenal axis).

Certain strains of intestinal bacteria, e.g. Lactobacillus and Bifidobacterium, can synthesize GABA, which affects the activity of the GABAergic neuronal system. It has been shown that these bacteria can affect changes in GABA levels the brain, thereby affecting behavior, anxiety and depression. [26]

GABA imbalances in the gut-brain axis have been linked to a number of psychological pathology conditions, including anxiety, depression, as well as obsessive-compulsive disorder and autism. Changes in GABA levels the brain may be the result of gut microflora disorders, which affects the functioning of the gut-brain axis. Studies suggest that modulation of the GABAergic system in the brain may have beneficial effects on treating mood disorders, including lowering anxiety and depression, indicating an important role for this substance in gut-brain communication. [27]

Dopamine (DA)

It is a key neurotransmitter in the reward and motivation system and emotion regulation. The gut microbiome has the ability to influence the metabolism of dopamine precursors and modulate its levels in the central nervous system.

Some gut bacteria, such as Escherichia coli, can synthesize dopamine or its precursors, such as tyrosine and L-DOPA. [28]

Dopamine deficiency is closely associated with reduced motivation and impaired reward systems, key features of depression. Intestinal dysbiosis can lead to reduced dopamine levels in the mesolimbic system and prefrontal cortex, further exacerbating depressive symptoms. [29]

The microbiota affects the expression of dopamine receptors in the brain, particularly in areas associated with motivation and mood, such as the striatum and hippocampus.

Microbiota-induced dopaminergic dysfunction can lead to dysregulation of the reward system, exacerbating not only depression but also other disorders such as addiction and ADHD. [30,31]

Stress affects the gut microbiota, which consequently disrupts dopaminergic pathways through activation of the HPA axis.

Persistent HPA axis acitvity may inhibit dopamine production, contributing to the severity of depression [32,33].

Norepinephrine (NA)

The gut microbiota can modulate its synthesis and influence its function the nervous and endocrine systems.

Bifidobacterium and Lactobacillus, produce norepinephrine precursors or modulate norepinephrine levels by affecting the hypothalamic-pituitary-adrenal (HPA) axis, which is responsible for stress responses. [34]

Abnormalities in norepinephrine signaling are associated with the anhedonia, loss of energy and impaired concentration characteristic of depression.

Norepinephrine affects synaptic plasticity and the regulation of neurogenesis in the hippocampus, a key brain structure involved in mood.

Chronic inflammation induced by the microbiota may further impair norepinephrine synthesis and increase the risk of mood disorders [35,36].

Effect of gut microbiota on various psychiatric disorders:

The gut microbiota plays an important role in the pathogenesis and course of various psychiatric disorders, such as depression, anxiety, schizophrenia, autism and bipolar disorder,

Through mechanisms of the gut-brain axis. Bacterial metabolites such as short-chain fatty acids (SCFAs), neurotransmitters (e.g., serotonin, GABA, dopamine), and pro- and anti-inflammatory cytokines that modulate the nervous system are crucial. [39]

Gut dysbiosis can lead to chronic inflammation and increased permeability of the intestinal barrier and blood-brain barrier, which exacerbates neuroinflammatory mechanisms in the brain and contributes to symptoms such as anhedonia, excessive anxiety and cognitive deficits. In addition, the composition of the microbiota influences the functioning of the hypothalamic-pituitary-adrenal (HPA) axis, regulating the stress response, which is important in the context of depression and anxiety disorders.

A growing body of evidence suggests that modulation of the gut microbiota, such as through probiotics, prebiotics or diet, may be a potential therapeutic strategy for treating psychiatric disorders. [37,38]

Link between gut microbiota and depression:

Studies indicate a significant link between the gut microbiota and the pathogenesis of depression, gut dysbiosis playing a key role in the mechanism of depression.

A reduction in the diversity of the microbiota and a preponderance of pro-inflammatory bacteria are very common in people with depression.

Disturbances in the microbiota can lead to the overproduction of pro-inflammatory cytokines, which, through neuroinflammatory mechanisms, reduce the synthesis of neurotransmitters such as dopamine and serotonin that are key to mood regulation. [40,41]

Link between gut microbiota and anxiety states

The gut microbiota plays a key role in the pathophysiology of anxiety by influencing the neurobiological and immunological mechanisms of the gut-brain axis. Abnormalities in the composition of the microbiota, such as reduced diversity of gut bacteria, can lead to dysregulation of neurotransmitters, including GABA, serotonin and glutamate, which play a key role in the modulation of anxiety. *Lactobacillus* and *Bifidobacteria*, in particular, are associated with GABA production, and their deficiency can exacerbate anxiety reactions by imbalancing the inhibitory and excitatory systems in the brain.

Increased permeability of the intestinal barrier, resulting from dysbiosis, allows lipopolysaccharides (LPS) to be translocated into the bloodstream, causing chronic low-grade inflammation. This in turn affects the activation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to overproduction of cortisol and exacerbating anxiety symptoms. Studies indicate that chronic inflammation and overactivation of the HPA axis are common mechanisms for both anxiety and depressive disorders. [42, 43]

In addition, the microbiota influences the production of short-chain fatty acids (SCFAs), such as butyrate, which have anti-inflammatory and neuroprotective effects. SCFA deficiency can lead to a weakened blood-brain barrier, increasing vulnerability to environmental stressors and exacerbating anxiety symptoms.

Interventions aimed at modulating the microbiota, such as the use of probiotics, prebiotics, and a diet rich in fiber and polyphenols, are attracting increasing interest. Studies suggest that

probiotics, referred to as "psychobiotics," may reduce anxiety by modulating the inflammatory response, regulating the HPA axis and improving neurotransmitter metabolism. These approaches may, in the future, complement conventional pharmacological and psychological therapies in the treatment of anxiety. [44, 45]

Link of gut microbiota to neurodevelopmental disorders such as autism

Research on the gut microbiota indicates that it has a significant impact on the development and function of the nervous system, which is of particular importance in the context of neurodevelopmental disorders such as autism spectrum disorders (ASD). Individuals with ASD often exhibit significant changes in the composition of the gut microbiota, referred to as dysbiosis, which can contribute to behavioral and somatic symptoms. Reduced microbiota diversity and an excess of pro-inflammatory bacteria, such as *Clostridium*, can lead to increased inflammation that affects the gut-brain axis.

Mechanisms underlying this relationship primarily involve the action of microbiota metabolites such as short-chain fatty acids (SCFAs). Butyrate, known for its antiinflammatory effects and support of blood-brain barrier function, is often reduced in individuals with ASD. Excess propionate, on the other hand, can negatively affect metabolic pathways in the brain, potentially leading to symptoms typical of autism, such as sensory hypersensitivity, communication difficulties and repetitive behavior. [45]

The microbiota also influences the development of the immune system and the functioning of microglia, which play a key role in the formation of neuronal structures. Microglia dysfunction, resulting from chronic inflammation induced by dysbiosis, can disrupt the processes of synaptogenesis and myelination, which is important in the pathophysiology of ASD.

Moreover, the microbiota affects levels of neurotransmitters such as GABA, dopamine and serotonin, which are critical in regulating mood, behavior and cognitive function. People with ASD often have abnormalities in these neurotransmitter pathways, which may be linked to the microbiota.

Interventions targeting the microbiota, such as the use of probiotics, prebiotics and dietary changes, are promising therapeutic strategies in the context of ASD. Preliminary research indicates that they can improve both gastrointestinal symptoms and some aspects of behavior, such as social interactions and anxiety levels. However, more research is needed to better understand the role of the microbiota in the pathogenesis of neurodevelopmental disorders and to develop effective therapies. [46]

Effects of diet and probiotics on myrobiotics and mental health

Diet is one of the most important factors shaping the composition and function of the gut microbiota, which indirectly affects mental health through the gut-brain axis. Eating a diet rich in fiber, vegetables, fruits, and fermented dairy products promotes the growth of beneficial bacteria such as *Lactobacillus* and *Bifidobacterium*, which support the production of short-chain fatty acids (SCFAs) and neurotransmitters such as serotonin and GABA. These metabolites and compounds modulate inflammation, intestinal barrier permeability and neuroimmune function, which have direct implications for the risk of depression, anxiety or neurodevelopmental disorders. Probiotics - live microorganisms with beneficial health effects - can be used as supplements to help treat mental disorders. Studies have shown that probiotics containing strains of *Lactobacillus rhamnosus* or *Bifidobacterium longum* can lower cortisol levels, regulate stress response, and improve cognitive function and mood. In addition, a diet that eliminates highly processed foods rich in sugars and trans fats reduces dysbiosis and accompanying chronic inflammation, which is crucial for mental stability.

Myrmecobiotic changes due to diet

Diet has a direct effect on the diversity and proportion of gut bacteria, and these changes can both promote health and contribute to the development of psychiatric disorders. The Western diet, characterized by high saturated fat, simple sugars and low fiber, leads to a reduction in the population of SCFA-producing bacteria, such as Faecalibacterium prausnitzii, and an increase in pro-inflammatory bacteria, such as Escherichia coli. Such changes result in increased permeability of the intestinal barrier, leading to the translocation of lipopolysaccharides (LPS) into the bloodstream, triggering inflammation and neuroinflammation, which are associated with depression and anxiety. In contrast, a diet rich in fiber, polyphenols, probiotics and prebiotics can support beneficial bacteria such as Bifidobacterium and Lactobacillus, promoting gut health and reducing the risk of mental disorders. Research confirms that changing to a Mediterranean diet can improve mood and reduce symptoms of depression within weeks by regulating the microbiota and its metabolites. [47, 48]

Research on probiotics and their use in the treatment of mental disorders

Research on probiotics, also referred to as "psychobiotics," indicates their promising potential in the treatment of psychiatric disorders. It has been shown that probiotics containing strains of *Lactobacillus helveticus* and *Bifidobacterium longum* can effectively reduce symptoms of depression and anxiety by reducing inflammatory markers, regulating the HPA (hypothalamic-pituitary-adrenal) axis, and increasing serotonin and GABA production. Clinical studies indicate that the use of probiotics as an adjunct to pharmacotherapy can improve the effectiveness of antidepressants and reduce the time it takes to achieve remission. The use of probiotics in the treatment of neurodevelopmental disorders, such as ADHD and autism, is also the subject of intense research, with results suggesting that modulating the microbiota can improve social behavior and reduce emotional difficulties in patients. Despite the promising results, there is still a need for more long-term and large-scale studies to determine the optimal composition and dosage of probiotics and to understand their mechanisms of action in the context of psychiatric disorders. [49,50]

Research summary and outlook

Modern research on the gut microbiota and its relationship to central nervous system function confirms the important role of the gut microbiota in regulating mental health. Key mechanisms of action include effects on the production of neurotransmitters such as serotonin, GABA and dopamine, modulation of the inflammatory response and regulation of the hypothalamic-pituitary-adrenal (HPA) pathway. Disorders of the gut microbiota, known as dysbiosis, have been linked to a number of psychiatric disorders, including depression, anxiety and neurodevelopmental disorders. Findings from studies to date point to the need to further explore the role of specific bacterial strains and their metabolites in the gut-brain axis, which may contribute to the development of more targeted therapeutic strategies.

Conclusions on the relationship between microbiota and psyche

Accumulating scientific evidence indicates that the gut microbiota plays a fundamental role in the functioning of the gut-brain axis, which is a complex communication system between the gastrointestinal tract and the brain. Dysbiosis of the microbiota leads to an increase in the permeability of the intestinal barrier, which enables the translocation of pro-inflammatory factors, such as lipopolysaccharides, into the systemic circulation. This results in the activation of neuroinflammatory processes that disrupt the balance of neurotransmitters, such as serotonin and dopamine, key to mood and cognitive regulation. These observations support the hypothesis that modulation of the microbiota, such as through a diet rich in fiber, prebiotics or probiotics, may be an effective way to support mental health and treat neuropsychiatric disorders.

Future research directions and clinical application

Perspectives on microbiota research in the context of mental health focus on understanding individual differences in microbiota composition and their impact on the pathogenesis of mental disorders. A key area of interest is the identification of microbial strains and their metabolites with potential therapeutic effects, referred to as psychobiotics. Research into their efficacy and safety in the treatment of depression, anxiety disorders or autism is a promising direction for the development of personalized medicine.

In addition, the implementation of microbiota biomarkers into psychiatric diagnostics may enable early detection of disorders and monitoring of treatment effects. The development of such strategies could transform approaches to treating psychiatric disorders by integrating microbiota modulation with conventional therapeutic approaches.

Disclosure

Author's contribution

Conceptualization: Zofia Martyna Wójcik and Paulina Pietrukaniec; Methodology: Katarzyna Kamińska – Omasta; Software: Olga Krupa; Check: Daria Rybak, Kinga Furtak and Kuba Borys Romańczuk; Formal analysis: Magdalena Agata Czerska; Investigation: Paulina Pietrukaniec; Resources: Katarzyna Kamińska-Omasta; Data curation: Bartosz Omasta; Writing -through preparation: Szymon Przemysław Stolarczyk; Writing -review and editing: Zofia Martyna Wójcik; Visualization: Szymon Przemysław Stolarczyk; Supervision: Paulina Dorota Pietrukaniec; Project administration: Daria Rybak; Receiving funding - no specific funding.

All authors have read and agreed with the published version of the manuscript.

Financing statement This research received no external funding.

Institutional Review Board Statement Not applicable.

Informed Consent Statement Not applicable.

Data Availability Statement Not applicable. Conflict of interest The authors deny any conflict of interest.

Bibliography:

- 1.Sun, Yonggan, et al. "Gut Firmicutes: Relationship with Dietary Fiber and Role in Host Homeostasis." *Critical Reviews in Food Science and Nutrition*, vol. 63, no. 33, Nov. 2023, pp. 12073–88, https://doi.org/10.1080/10408398.2022.2098249.
- 2.Heczko, Piotr Bogumił, et al., editors. Medical Microbiology. PZWL Medical Publishing, 2014.
- Alwali, Amir Y., and Elizabeth I. Parkinson. "Small Molecule Inducers of Actinobacteria Natural Product Biosynthesis." *Journal of Industrial Microbiology and Biotechnology*, vol. 50, no. 1, Feb. 2023, p. kuad019, https://doi.org/10.1093/jimb/kuad019.

- 4.Sun, Desen, et al. "Angiogenin Maintains Gut Microbe Homeostasis by Balancing α-Proteobacteria and Lachnospiraceae." *Gut*, vol. 70, no. 4, Apr. 2021, pp. 666–76, https://doi.org/10.1136/gutjnl-2019-320135.
- 5.Góralczyk-Bińkowska, Aleksandra, et al. "The Microbiota–Gut–Brain Axis in Psychiatric Disorders." *International Journal of Molecular Sciences*, vol. 23, no. 19, Sept. 2022, p. 11245, https://doi.org/10.3390/ijms231911245.
- 6.Breit, Sigrid, et al. "Vagus Nerve as Modulator of the Brain–Gut Axis in Psychiatric and Inflammatory Disorders." *Frontiers in Psychiatry*, vol. 9, Mar. 2018, p. 44, https://doi.org/10.3389/fpsyt.2018.00044.
- 7.Pardo, Ingrid D., et al. "Atlas of Normal Microanatomy, Procedural and Processing Artifacts, Common Background Findings, and Neurotoxic Lesions in the Peripheral Nervous System of Laboratory Animals." *Toxicologic Pathology*, vol. 48, no. 1, Jan. 2020, pp. 105–31, https://doi.org/10.1177/0192623319867322.
- 8.Jewett, Benjamin E., and Bicky Thapa. "Physiology, NMDA Receptor." *StatPearls*, StatPearls Publishing, 2025, http://www.ncbi.nlm.nih.gov/books/NBK519495/.
- 9. Ortega, Miguel A., et al. "Gut Microbiota Metabolites in Major Depressive Disorder-Deep Insights into Their Pathophysiological Role and Potential Translational Applications." *Metabolites*, vol. 12, no. 1, Jan. 2022, p. 50, https://doi.org/10.3390/metabo12010050.
- Donoso, Francisco, et al. "Inflammation, Lifestyle Factors, and the Microbiome-Gut-Brain Axis: Relevance to Depression and Antidepressant Action." *Clinical Pharmacology and Therapeutics*, vol. 113, no. 2, Feb. 2023, pp. 246–59, https://doi.org/10.1002/cpt.2581.
- 11. Terry, Natalie, and Kara Gross Margolis. "Serotonergic Mechanisms Regulating the GI Tract: Experimental Evidence and Therapeutic Relevance." *Handbook of Experimental Pharmacology*, vol. 239, 2017, pp. 319–42, https://doi.org/10.1007/164_2016_103.
- 12. Redondo-Useros, Noemí, et al. "Microbiota and Lifestyle: A Special Focus on Diet." *Nutrients*, vol. 12, no. 6, June 2020, p. 1776, https://doi.org/10.3390/nu12061776.
- 13. Moles, Laura, and David Otaegui. "The Impact of Diet on Microbiota Evolution and Human Health. Is Diet an Adequate Tool for Microbiota Modulation?" Nutrients, vol. 12, no. 6, June 2020, p. 1654, https://doi.org/10.3390/nu12061654.
- 14. Bonaz, Bruno, et al. "The Vagus Nerve at the Interface of the Microbiota-Gut-Brain Axis." Frontiers in Neuroscience, vol. 12, 2018, p. 49, https://doi.org/10.3389/fnins.2018.00049.
- 15. Bravo, Javier A., et al. "Ingestion of Lactobacillus Strain Regulates Emotional Behavior and Central GABA Receptor Expression in a Mouse via the Vagus Nerve." Proceedings of the National Academy of Sciences of the United States of America, vol. 108, no. 38, Sept. 2011, pp. 16050–55, https://doi.org/10.1073/pnas.1102999108.
- 16. Subramanian, Saravanan, et al. "Cell Death of Intestinal Epithelial Cells in Intestinal Diseases." Sheng Li Xue Bao: [Acta Physiologica Sinica], vol. 72, no. 3, June 2020, pp. 308–24.
- 17. Potten, Christopher S. "Radiation, the Ideal Cytotoxic Agent for Studying the Cell Biology of Tissues Such as the Small Intestine1." Radiation Research, vol. 161, no. 2, 2004, pp. 123–36, https://doi.org/10.1667/RR3104.
- 18.Sasso, Janet M., et al. "Gut Microbiome-Brain Alliance: A Landscape View into Mental and Gastrointestinal Health and Disorders." ACS Chemical Neuroscience, vol. 14, no. 10, May 2023, pp. 1717–63, https://doi.org/10.1021/acschemneuro.3c00127.
- 19. Roper, S. D. "Signaling in the Chemosensory Systems: Cell Communication in Taste Buds." Cellular and Molecular Life Sciences, vol. 63, no. 13, 2006, pp. 1494–500, https://doi.org/10.1007/s00018-006-6112-9.

- 20. David, D. J., and A. M. Gardier. "Les bases de pharmacologie fondamentale du système sérotoninergique : application à la réponse antidépressive." L'Encéphale, vol. 42, no. 3, 2016, pp. 255–63, https://doi.org/10.1016/j.encep.2016.03.012.
- Baganz, Nicole L., and Randy D. Blakely. "A Dialogue between the Immune System and Brain, Spoken in the Language of Serotonin." ACS Chemical Neuroscience, vol. 4, no. 1, Jan. 2013, pp. 48–63, https://doi.org/10.1021/cn300186b.
- 22. Bonnin, Alexandre, et al. "A Transient Placental Source of Serotonin for the Fetal Forebrain." Nature, vol. 472, no. 7343, Apr. 2011, pp. 347–50, https://doi.org/10.1038/nature09972.
- 23. Alsegiani, Amsha S., and Zahoor A. Shah. "The Influence of Gut Microbiota Alteration on Age-Related Neuroinflammation and Cognitive Decline." Neural Regeneration Research, vol. 17, no. 11, Nov. 2022, pp. 2407–12, https://doi.org/10.4103/1673-5374.335837.
- 24. Bak, Lasse K., et al. "The Glutamate/GABA-Glutamine Cycle: Aspects of Transport, Neurotransmitter Homeostasis and Ammonia Transfer." Journal of Neurochemistry, vol. 98, no. 3, Aug. 2006, pp. 641–53, https://doi.org/10.1111/j.1471-4159.2006.03913.x.
- 25. Petroff, Ognen A. C. "GABA and Glutamate in the Human Brain." The Neuroscientist: A Review Journal Bringing Neurobiology, Neurology and Psychiatry, vol. 8, no. 6, Dec. 2002, pp. 562–73, https://doi.org/10.1177/1073858402238515.
- 26. Milon, Ripon Baroi, et al. "Recent Advances in the Biosynthesis and Industrial Biotechnology of Gamma-Amino Butyric Acid." Bioresources and Bioprocessing, vol. 11, no. 1, Mar. 2024, p. 32, https://doi.org/10.1186/s40643-024-00747-7.
- 27. Yu, Leilei, et al. "Beneficial Effect of GABA-Rich Fermented Milk on Insomnia Involving Regulation of Gut Microbiota." Microbiological Research, vol. 233, 2020, p. 126409, https://doi.org/10.1016/j.micres.2020.126409.
- 28. Alvariño, Rebeca, et al. "Evaluation of the Protective Effects of Sarains on H2O2-Induced Mitochondrial Dysfunction and Oxidative Stress in SH-SY5Y Neuroblastoma Cells." Neurotoxicity Research, vol. 32, no. 3, 2017, pp. 368–80, https://doi.org/10.1007/s12640-017-9748-3.
- 29. Beaulieu, Jean-Martin, et al. "An Akt/β-Arrestin 2/PP2A Signaling Complex Mediates Dopaminergic Neurotransmission and Behavior." Cell, vol. 122, no. 2, 2005, pp. 261–73, https://doi.org/10.1016/j.cell.2005.05.012.
- 30. Pozzi, Marco, et al. "Emerging Drugs for the Treatment of Attention-Deficit Hyperactivity Disorder (ADHD)." Expert Opinion on Emerging Drugs, vol. 25, no. 4, Oct. 2020, pp. 395–407, https://doi.org/10.1080/14728214.2020.1820481.
- 31. Cui, Changhai, et al. "Neuroimmune Mechanisms of Alcohol and Drug Addiction." International Review of Neurobiology, vol. 118, 2014, pp. 1–12, https://doi.org/10.1016/B978-0-12-801284-0.00001-4.
- 32. Schatzberg, Alan F., et al. "A Corticosteroid/Dopamine Hypothesis for Psychotic Depression and Related States." Journal of Psychiatric Research, vol. 19, no. 1, 1985, pp. 57–64, https://doi.org/10.1016/0022-3956(85)90068-8.
- 33. Mizrahi, Romina, et al. "Increased Stress-Induced Dopamine Release in Psychosis." Biological Psychiatry, vol. 71, no. 6, 2012, pp. 561–67, https://doi.org/10.1016/j.biopsych.2011.10.009.
- 34. Konaka, S., et al. "The Apperance of noradrenaline and adrenaline and the developmental changes in their concentrations in the gut of the chick." British Journal of Pharmacology, vol. 65, no. 2, 1979, pp. 257–60, https://doi.org/10.1111/j.1476-5381.1979.tb07826.x.

- 35. Stjärne, Lennart. "Presynaptic A-receptors Do Not Depress the Secretion of H-noradrenaline Induced by Veratridine." Acta Physiologica Scandinavica, vol. 106, no. 3, 1979, pp. 379–80, https://doi.org/10.1111/j.1748-1716.1979.tb06415.x.
- 36. Westfall, T. C. "Local Regulation of Adrenergic Neurotransmission." Physiological Reviews, vol. 57, no. 4, Oct. 1977, pp. 659–728, https://doi.org/10.1152/physrev.1977.57.4.659.
- 37. Bhatia, Nirav Yogesh, et al. "Gut-Brain Axis and Neurological Disorders-How Microbiomes Affect Our Mental Health." CNS & Neurological Disorders Drug Targets, vol. 22, no. 7, 2023, pp. 1008–30, https://doi.org/10.2174/1871527321666220822172039.
- 38. Asher, Gary N., et al. "Complementary Therapies for Mental Health Disorders." Medical Clinics of North America, vol. 101, no. 5, 2017, pp. 847–64, https://doi.org/10.1016/j.mcna.2017.04.004.
- 39. Zheng, Peng, et al. "The Gut Microbiome from Patients with Schizophrenia Modulates the Glutamate-Glutamine-GABA Cycle and Schizophrenia-Relevant Behaviors in Mice." Science Advances, vol. 5, no. 2, 2019, p. eaau8317, https://doi.org/10.1126/sciadv.aau8317.
- 40. Park, Miey, et al. "Flavonoid-Rich Orange Juice Intake and Altered Gut Microbiome in Young Adults with Depressive Symptom: A Randomized Controlled Study." Nutrients, vol. 12, no. 6, June 2020, p. 1815, https://doi.org/10.3390/nu12061815.
- 41. Parente, Joao, et al. "Neural, Anti-Inflammatory, and Clinical Effects of Transauricular Vagus Nerve Stimulation in Major Depressive Disorder: A Systematic Review." International Journal of Neuropsychopharmacology, vol. 27, no. 3, Mar. 2024, p. pyad058, https://doi.org/10.1093/ijnp/pyad058.
- 42. Foster, Jane A., and Karen-Anne McVey Neufeld. "Gut-Brain Axis: How the Microbiome Influences Anxiety and Depression." Trends in Neurosciences, vol. 36, no. 5, May 2013, pp. 305–12, https://doi.org/10.1016/j.tins.2013.01.005.
- 43. Wang, Hong-Xing, and Yu-Ping Wang. "Gut Microbiota-Brain Axis." Chinese Medical Journal, vol. 129, no. 19, Oct. 2016, pp. 2373–80, https://doi.org/10.4103/0366-6999.190667.
- 44. Cryan, John F., and Timothy G. Dinan. "Mind-Altering Microorganisms: The Impact of the Gut Microbiota on Brain and Behaviour." Nature Reviews. Neuroscience, vol. 13, no. 10, Oct. 2012, pp. 701–12, https://doi.org/10.1038/nrn3346.
- 45. Sorboni, S. G., Moghaddam, H. S., Jafarzadeh-Esfehani, R., & Soleimanpour, S. (2021). A comprehensive review on the role of the gut microbiome in human neurological disorders. Frontiers in Neurology, 10, 838260. https://doi.org/10.3389/fneur.2021.838260
- 46. Fattorusso, Antonella, et al. "Autism Spectrum Disorders and the Gut Microbiota." Nutrients, vol. 11, no. 3, Feb. 2019, p. 521, https://doi.org/10.3390/nu11030521.
- 47. Bibbò, S., Ianiro, G., Giorgio, V., Scaldaferri, F., Masucci, L., Gasbarrini, A., & Cammarota, G. (2016). The role of diet on gut microbiota composition. Nature Reviews Gastroenterology & Hepatology, 13(8), 525–535. https://doi.org/10.1038/nrgastro.2016.98
- 48. Schoeler, M., & Caesar, R. (2019). Dietary lipids, gut microbiota and lipid metabolism. Cell Metabolism, 30(4), 713-723. https://doi.org/10.1016/j.cmet.2019.08.010
- 49. Madabushi, J. S., Khurana, P., Gupta, N., & Gupta, M. (2023). Gut biome and mental health: Do probiotics work? Frontiers in Psychology, 14, 1113475. https://doi.org/10.3389/fpsyg.2023.1113475
- 50. Järbrink-Sehgal, E., & Andreasson, A. (2020). The gut microbiota and mental health in adults. European Neuropsychopharmacology, 30(6), 906-917. https://doi.org/10.1016/j.euroneuro.2020.04.003