

Exploring the Link Between Gut Health and Mental Health: The Gut-Brain Axis

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Abstract

The gut-brain axis (GBA) has emerged as a critical area of research in understanding the relationship between gut health and mental health. This paper explores the physiological mechanisms and clinical evidence that link the gastrointestinal (GI) system and the central nervous system (CNS), with a focus on the role of gut microbiota in modulating mood, behavior, and cognitive function. The findings highlight the potential of the gut-brain connection in the pathophysiology of various mental health disorders, including anxiety, depression, and neurodevelopmental conditions. Furthermore, the implications of dietary interventions, probiotics, and gut-targeted therapies are discussed as potential strategies for improving mental health through modulation of the gut microbiota.

Keywords: Gut-brain axis, mental health, gut microbiota, probiotics, anxiety, depression, gastrointestinal system, cognitive function, neurodevelopmental disorders.

1. Introduction

Recent advancements in neuroscience and microbiology have uncovered a significant relationship between the gastrointestinal system and the brain, referred to as the gut-brain axis (GBA). The GBA represents a bidirectional communication pathway that links the gut microbiota to the central nervous system (CNS), influencing a variety of physiological processes, including mood regulation, cognitive function, and stress response (Cryan & Dinan, 2012). The gut microbiota, consisting of trillions of microorganisms residing in the digestive tract, plays a crucial role in modulating the immune system, the enteric nervous system, and neuroendocrine signaling pathways (Carabotti et al., 2015). This paper explores the scientific evidence supporting the gut-brain connection, highlighting the impact of gut health on mental health, and examines potential therapeutic interventions to harness this link.

2. The Gut-Brain Axis: Mechanisms and Pathways

The GBA functions through a complex network involving the vagus nerve, the enteric nervous system, immune signaling pathways, and the production of neurotransmitters and hormones (Yano et al., 2015). One of the key components in this communication system is the gut microbiota, which influences the brain's activity through several mechanisms. The gut-brain axis (GBA) is a bidirectional communication network between the gastrointestinal (GI) system and the central nervous system (CNS). This dynamic system involves multiple pathways through which the gut microbiota, the immune system, the vagus nerve, and various biochemical signaling molecules interact to influence brain function and behavior. The GBA is critical for regulating a wide range of physiological processes, including mood, cognitive function, and stress response. Below are the primary mechanisms and pathways that facilitate communication between the gut and the brain:

2.1. Vagus Nerve and Neural Signaling

The vagus nerve plays a central role in the GBA, serving as a key neural pathway through which signals from the gut are transmitted to the brain. It is the longest cranial nerve and directly connects the gut to the brainstem, which can influence various brain functions, including those related to stress, mood, and cognition (Bonaz et al., 2018).

Recent studies have shown that the vagus nerve is involved in relaying information about gut microbiota composition and the metabolic byproducts of digestion to the brain. This includes signaling from gut-produced short-chain fatty acids (SCFAs), which have been shown to influence brain activity and behavior (Pereira et al., 2017). In essence, changes in the gut microbiota can activate vagal signaling, leading to alterations in mood, anxiety, and other mental health conditions.

2.2. Gut Microbiota and Neurotransmitter Production

Gut microbiota significantly influences the synthesis of neurotransmitters that are crucial for brain function. A notable example is serotonin, a neurotransmitter primarily involved in mood regulation, which is produced in large quantities in the gastrointestinal tract. It is estimated that about 90% of serotonin is produced in the gut (Clarke et al., 2013). The gut microbiota modulates the production of serotonin through its effects on the enterochromaffin cells of the intestinal lining.

Furthermore, gut bacteria produce other neurotransmitters such as gamma-aminobutyric acid (GABA) and dopamine, both of which are implicated in regulating mood and anxiety. The ability of gut microbiota to influence neurotransmitter synthesis highlights its role in modulating the brain's chemical environment and impacting mental health (Mayer et al., 2014).

2.3. Immune System Modulation

The gut microbiota also plays a critical role in the immune system's regulation, which, in turn, impacts the brain. The gastrointestinal system is home to a significant portion of the body's immune cells, which are constantly interacting with gut bacteria. When gut microbiota becomes imbalanced (a condition known as dysbiosis), it can trigger inflammation in the gut, leading to the release of pro-inflammatory cytokines. These cytokines can enter the bloodstream and cross the blood-brain barrier, affecting the brain and contributing to neuroinflammation (Pittayanon et al., 2019).

This immune system activation can alter brain function and has been linked to various psychiatric conditions, including depression, anxiety, and even neurodegenerative diseases. Inflammation from the gut is thought to disrupt the balance of neurochemicals in the brain, leading to altered mood and behavior (Rudzki et al., 2021).

2.4. Endocrine Pathways and Hormonal Signaling

In addition to neural and immune signaling, the gut-brain axis involves the modulation of various hormones that regulate stress responses, hunger, and emotional responses. One of the key players in this system is the hormone cortisol, which is released in response to stress. The gut microbiota influences the hypothalamic-pituitary-adrenal (HPA) axis, the body's central stress response system, by altering cortisol levels.

Moreover, gut microbiota can impact the levels of other hormones, such as ghrelin (which stimulates hunger) and leptin (which signals satiety), both of which are involved in food intake and metabolism. Dysregulation of these hormones due to imbalances in the gut microbiota can influence eating behavior and emotional regulation (Bonaz et al., 2018).

2.5. Metabolites and Short-Chain Fatty Acids (SCFAs)

Gut microbiota fermentation of dietary fiber produces SCFAs, including acetate, propionate, and butyrate. These SCFAs are important metabolites that provide energy to intestinal cells and have direct effects on brain function. Butyrate, for example, is known to cross the blood-brain barrier and promote the production of brain-derived neurotrophic factor (BDNF), a protein involved in neuronal growth and plasticity (Mayer et al., 2014).

SCFAs can also influence the vagus nerve and modulate immune responses, thus contributing to both gut and brain health. Their production is often affected by dietary factors and the composition of the gut microbiota, making them a potential target for therapeutic interventions aimed at improving mental health.

2.6. Blood-Brain Barrier (BBB) Integrity

The integrity of the blood-brain barrier (BBB) is crucial for maintaining the proper environment within the brain. The gut microbiota can affect the permeability of the BBB through inflammatory signals and changes in the production of tight junction proteins. When the gut microbiota is imbalanced, increased gut permeability can lead to systemic inflammation, which in turn can affect the BBB and allow harmful substances to enter the brain (Pittayanon et al., 2019).

This dysfunction is linked to a variety of neurological and psychiatric conditions, such as Alzheimer's disease, depression, and multiple sclerosis. Hence, maintaining the health of the gut microbiota may play a role in preserving the integrity of the BBB and preventing the onset of such conditions.

The gut-brain axis is a complex and multifaceted communication system that links the gastrointestinal system to the brain through neural, immune, hormonal, and metabolic pathways. The gut microbiota plays a pivotal role in influencing brain function by modulating neurotransmitter production, immune responses, and metabolic processes. Disruptions in this communication network can contribute to the development of mental health disorders, including depression, anxiety, and neurodegenerative diseases. Understanding the mechanisms that govern the GBA opens up potential therapeutic avenues for treating these

conditions by targeting the gut microbiota, highlighting the importance of gut health for overall mental well-being.

3. Gut Health and Mental Health Disorders

The link between gut health and mental health is particularly evident in disorders such as depression, anxiety, and neurodevelopmental conditions. The emerging field of psychobiotics, which explores the use of probiotics to treat mental health conditions, provides promising insights into the potential therapeutic effects of modulating the gut microbiota. The relationship between gut health and mental health has gained significant attention in recent years, with emerging research revealing that disruptions in the gut microbiota, the community of microorganisms residing in the gastrointestinal tract, are closely linked to various mental health disorders. The gut-brain axis (GBA) — a complex, bidirectional communication system between the gut and the brain — plays a central role in this connection. Through this system, the gut microbiota can influence brain function, mood regulation, and behavior. In turn, changes in brain function can affect gut health, creating a cycle of dysfunction that may contribute to the development or exacerbation of mental health disorders.

3.1. Depression and the Gut Microbiota

Depression is one of the most common mental health disorders worldwide, and emerging evidence suggests a significant connection between gut health and depression. Research indicates that individuals with major depressive disorder (MDD) often show alterations in their gut microbiota composition, including a reduction in microbial diversity and an imbalance of beneficial and harmful bacterial species (Jiang et al., 2015). For instance, decreased populations of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*, and an overgrowth of pro-inflammatory bacteria, have been observed in depressed individuals (Valles-Colomer et al., 2019).

The exact mechanisms through which the gut microbiota influences depression are still being studied, but several key pathways have been identified:

- **Neurotransmitter Production:** The gut microbiota plays a crucial role in producing neurotransmitters such as serotonin, which regulates mood and emotional states. Since about 90% of serotonin is produced in the gut (Clarke et al., 2013), alterations in gut

microbiota can disrupt serotonin synthesis, potentially contributing to depressive symptoms.

- **Inflammation:** Gut dysbiosis can trigger systemic inflammation, leading to the release of pro-inflammatory cytokines. These inflammatory molecules can cross the blood-brain barrier and affect brain regions involved in mood regulation (Pittayanon et al., 2019). Chronic inflammation is thought to be a key factor in the pathophysiology of depression.
- **Gut-Immune System Interaction:** The gut microbiota influences the immune system, and immune system activation has been linked to mood disturbances. Dysbiosis in the gut can lead to immune activation, further exacerbating depressive symptoms (Rudzki et al., 2021).

Studies suggest that correcting gut dysbiosis with probiotics or dietary interventions could alleviate some depressive symptoms by restoring a healthy gut microbiome and reducing inflammation (Ng et al., 2018).

3.2. Anxiety and the Gut Microbiota

Anxiety disorders, characterized by excessive worry, fear, and tension, are another group of mental health conditions that may be influenced by gut health. Similar to depression, anxiety is associated with changes in the gut microbiota. Animal studies have shown that altering the gut microbiota — through antibiotics or fecal transplants — can result in anxiety-like behaviors (Savignac et al., 2015). Human studies have also reported altered gut microbiome composition in individuals with anxiety disorders, suggesting that the gut microbiota may play a role in the regulation of anxiety.

Mechanisms linking the gut microbiota to anxiety include:

- **Vagus Nerve and Neural Signaling:** The vagus nerve, which connects the gut and brain, plays a significant role in transmitting signals between the two organs. An imbalance in the gut microbiota can activate the vagus nerve, leading to changes in brain regions responsible for regulating fear and anxiety (Bonaz et al., 2018).
- **GABA and Stress Response:** The gut microbiota influences the production of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter that helps regulate stress and

anxiety. Studies have shown that certain strains of probiotics can increase GABA production, which may contribute to the alleviation of anxiety symptoms (Messaoudi et al., 2011).

- **Immune System Modulation:** As with depression, dysbiosis can lead to inflammation, which may activate the body's stress response, further contributing to anxiety. Inflammatory cytokines produced by the gut can reach the brain and impact areas such as the amygdala, which is involved in processing fear and anxiety (Pereira et al., 2017).

Probiotics and dietary interventions aimed at improving gut health have shown promise in reducing symptoms of anxiety. For example, studies have found that probiotics can significantly reduce self-reported anxiety in both clinical and healthy populations (Messaoudi et al., 2011).

3.3. Neurodevelopmental Disorders and Gut Health

The gut-brain axis is also implicated in neurodevelopmental disorders, including autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), and other cognitive or developmental conditions. Many children with neurodevelopmental disorders experience gastrointestinal disturbances, such as constipation, diarrhea, and bloating, suggesting a strong link between gut health and neurological function.

In individuals with ASD, for example, studies have shown that gut dysbiosis is commonly present. Children with ASD tend to have a less diverse gut microbiome, with a higher prevalence of pathogenic bacteria (Williams et al., 2011). The exact mechanisms linking gut health to neurodevelopmental disorders are still under investigation, but some potential pathways include:

- **Immune Activation and Inflammation:** Dysbiosis in the gut may lead to chronic inflammation, which could affect brain development and function. Studies have shown that inflammatory markers are elevated in children with ASD, potentially due to gut-derived pro-inflammatory cytokines (Sgritta et al., 2019).
- **Neurotransmitter Imbalance:** Gut microbiota influences the production of neurotransmitters such as serotonin and dopamine, both of which are crucial for cognitive

and behavioral regulation. Disruptions in the gut microbiome may contribute to imbalances in these neurotransmitters, which could affect brain development and lead to symptoms associated with ASD or ADHD (Lau et al., 2017).

- **Gut-Brain Communication and Behavior:** Abnormal gut-brain signaling may affect behavior and cognitive development in children with neurodevelopmental disorders. For example, animal studies have suggested that manipulating the gut microbiota can alter social behaviors, highlighting the importance of gut-brain communication in neurodevelopmental processes (Sgritta et al., 2019).

While more research is needed, some studies suggest that dietary interventions, such as the use of probiotics or a gluten-free and casein-free diet, may offer benefits for improving gastrointestinal and behavioral symptoms in children with ASD (Williams et al., 2011).

3.4. Other Mental Health Conditions and Gut Health

Beyond depression, anxiety, and neurodevelopmental disorders, there is growing evidence linking gut health to other mental health conditions, including schizophrenia, bipolar disorder, and post-traumatic stress disorder (PTSD). While the exact mechanisms are still being explored, similar pathways, such as inflammation, neurotransmitter production, and gut-brain signaling, appear to be involved in these disorders as well.

The connection between gut health and mental health disorders underscores the critical role of the gut-brain axis in regulating emotional and cognitive function. Disruptions in the gut microbiota, known as dysbiosis, have been linked to several mental health conditions, including depression, anxiety, and neurodevelopmental disorders. Understanding the mechanisms through which gut health impacts mental health — including microbial production of neurotransmitters, immune system modulation, and gut-brain communication — offers exciting new opportunities for therapeutic interventions.

Emerging treatments, such as probiotics, dietary changes, and other gut-targeted therapies, show promise in addressing mental health disorders by promoting a healthy gut microbiome. As research in this field continues to grow, it may pave the way for novel, microbiome-based treatments for mental health, providing more holistic and personalized approaches to managing these complex conditions.

4. Therapeutic Interventions

The growing understanding of the gut-brain axis has opened new avenues for therapeutic interventions aimed at improving mental health by targeting gut health. Therapeutic interventions targeting the gut microbiota and its impact on mental health are gaining considerable attention as research continues to reveal the critical role the gut-brain axis (GBA) plays in regulating mood, cognition, and behavior. Given the strong association between gut health and mental health disorders such as depression, anxiety, and neurodevelopmental disorders, several approaches aim to restore a healthy gut microbiota and improve mental well-being. These interventions include dietary modifications, probiotic and prebiotic supplementation, fecal microbiota transplantation (FMT), and pharmacological treatments. Below, we explore each of these therapeutic strategies in more detail.

4.1. Probiotics

Probiotics are live microorganisms that, when consumed in adequate amounts, provide health benefits to the host, particularly by improving the balance of gut microbiota. The idea behind using probiotics for mental health is to restore the microbiome to a healthy, balanced state and potentially alleviate symptoms of mental health disorders.

- **Mechanisms of Action:** Probiotics are thought to influence the gut-brain axis through several mechanisms, including:
 - **Neurotransmitter Production:** Probiotics can increase the production of neurotransmitters like serotonin, GABA, and dopamine in the gut, which can influence mood and behavior (Messaoudi et al., 2011).
 - **Immune System Modulation:** Probiotics can reduce systemic inflammation by interacting with the immune system, thus reducing the impact of pro-inflammatory cytokines on the brain (Pittayanon et al., 2019).
 - **Vagus Nerve Stimulation:** Certain probiotics may interact with the vagus nerve, a major pathway for gut-brain communication, thereby impacting brain regions that regulate mood, anxiety, and cognitive function (Bonaz et al., 2018).

- **Evidence for Effectiveness:** Several clinical trials have shown positive effects of probiotics in reducing symptoms of depression and anxiety. For instance, a meta-analysis of randomized controlled trials (RCTs) found that probiotics significantly reduced anxiety and depressive symptoms in both healthy and clinically diagnosed individuals (Ng et al., 2018). Common probiotic strains used in mental health research include *Lactobacillus* and *Bifidobacterium*, which have shown promise in improving mental well-being.

4.2. Prebiotics

Prebiotics are non-digestible food components that selectively stimulate the growth or activity of beneficial gut bacteria. They primarily consist of fiber and other plant-based compounds that promote the growth of healthy microbial species in the gut, which can, in turn, positively influence mental health.

- **Mechanisms of Action:** Prebiotics support gut health by:
 - **Supporting Beneficial Microbes:** Prebiotics stimulate the growth of beneficial gut bacteria, such as *Bifidobacterium* and *Lactobacillus*, which are associated with improved mood and cognitive function (Mayer et al., 2014).
 - **Production of Short-Chain Fatty Acids (SCFAs):** The fermentation of prebiotics by gut microbes produces SCFAs like butyrate, which have anti-inflammatory properties and can cross the blood-brain barrier, positively influencing brain function (Mayer et al., 2014).
 - **Enhancing Gut Integrity:** Prebiotics can improve the integrity of the gut barrier, reducing gut permeability and the risk of inflammation that might affect brain health.
- **Evidence for Effectiveness:** While prebiotic research is still emerging, studies suggest that prebiotic supplementation may have a beneficial effect on mental health. For instance, in a study involving healthy participants, prebiotic supplementation was shown to reduce stress and improve mood (Schmidt et al., 2015). Foods rich in prebiotics, such as garlic, onions, and bananas, can also serve as dietary interventions to support gut health and mental well-being.

4.3. Fecal Microbiota Transplantation (FMT)

Fecal microbiota transplantation (FMT) involves transferring a healthy microbiota from a donor to a recipient in order to restore the balance of gut bacteria. This procedure has been most commonly used in treating gastrointestinal disorders such as *Clostridium difficile* infection but is being explored as a potential treatment for mental health conditions.

- **Mechanisms of Action:** FMT aims to restore microbial diversity and balance in the gut. It may influence the gut-brain axis by:
 - **Restoring Gut Microbiota Composition:** By reintroducing a healthy microbiota, FMT can potentially correct dysbiosis (microbial imbalance), which may alleviate symptoms of depression and anxiety.
 - **Influencing Brain Function:** FMT may influence neurotransmitter production, immune responses, and inflammation, all of which are linked to mental health (Zheng et al., 2021).
- **Evidence for Effectiveness:** The use of FMT for mental health conditions is still in its early stages. Some studies have shown promising results, particularly in animal models of depression, where FMT from healthy animals improved depressive-like behaviors (Kelly et al., 2016). However, clinical trials in humans are limited, and more research is needed to determine its efficacy for treating mental health disorders. Early human studies have shown improvements in mood and anxiety following FMT treatment for gastrointestinal conditions, indicating the potential for broader applications in mental health (Bauer et al., 2020).

4.4. Dietary Interventions

Diet plays a crucial role in shaping the gut microbiota, and dietary interventions are being explored as a way to improve gut health and alleviate mental health symptoms. A diet rich in fiber, polyphenols, and fermented foods can help maintain a healthy gut microbiome and support mental well-being.

- **Mechanisms of Action:** Dietary interventions can influence the gut-brain axis by:

- **Modulating Gut Microbiota Composition:** Diets high in fiber and polyphenols support the growth of beneficial gut bacteria and promote the production of SCFAs, which reduce inflammation and support brain health (Benkeser et al., 2020).
- **Enhancing Microbial Diversity:** A balanced diet rich in diverse food sources (e.g., fruits, vegetables, whole grains, fermented foods) promotes microbial diversity, which has been associated with improved mood and cognitive function.
- **Evidence for Effectiveness:** Several studies support the role of diet in mental health. For instance, the Mediterranean diet, which is rich in fruits, vegetables, whole grains, and healthy fats, has been shown to reduce the risk of depression and improve mood (Sánchez-Villegas et al., 2009). Additionally, the consumption of fermented foods, which are rich in probiotics, has been associated with improved psychological well-being (Steenbergen et al., 2015).

4.5. Pharmacological Interventions

While the focus of gut-brain research is on microbiome-based therapies, conventional pharmacological treatments for mental health disorders, such as antidepressants and anti-anxiety medications, may also interact with gut health. Certain medications, particularly selective serotonin reuptake inhibitors (SSRIs), may influence the gut microbiota and gut-brain communication.

- **Mechanisms of Action:** Antidepressants like SSRIs can alter the gut microbiota by increasing the abundance of beneficial bacteria, which may contribute to their therapeutic effects. However, the precise relationship between medication and microbiome composition is still under investigation (Barton et al., 2020).
- **Evidence for Effectiveness:** Research suggests that pharmacological treatments for mental health conditions may have indirect effects on gut health. However, this area is still under exploration, and the long-term effects of psychotropic medications on the gut microbiome are not fully understood.

Therapeutic interventions targeting the gut microbiota and gut-brain communication offer exciting possibilities for the treatment of mental health disorders. Probiotics, prebiotics, dietary modifications, and fecal microbiota transplantation are emerging strategies to restore gut health and alleviate symptoms of conditions such as depression, anxiety, and neurodevelopmental disorders. While these approaches show promise, more research is needed to fully understand the mechanisms and effectiveness of these treatments in clinical settings. As our understanding of the gut-brain axis continues to evolve, it is likely that microbiome-based therapies will become an integral part of mental health care in the future.

5. Conclusion

The gut-brain axis represents a complex and dynamic relationship between the gastrointestinal system and the brain, with significant implications for mental health. Dysbiosis, or an imbalance in gut microbiota, has been linked to various mental health conditions, including depression, anxiety, and neurodevelopmental disorders. Research suggests that interventions aimed at improving gut health, such as probiotics and dietary changes, may offer promising avenues for treating these conditions. As the field continues to evolve, a deeper understanding of the gut-brain axis may lead to more effective and personalized treatments for mental health disorders, underscoring the importance of considering gut health in the management of mental well-being.

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