The Impact of Microbiome on Mental Disorders

Shakila Hamdy[1,*] - Shahrzad Nasiri Semnani[2]
[1] Islamic Azad University of Zanjan
[2] Islamic Azad University of Zanjan

ABSTRACT

The gut microbiome in particular has important roles in both physical and mental health. The microbiome can influence mental disorders like depression and anxiety, recent research suggests. This paper focuses on the relationship between the microbiome and mental health, how it affects the mechanisms, and how it should be managed.A gut-brain axis is neural, hormonal and immune communication between the gut and the brain, indicating that gut health can have an enormous impact on mood and behavior. There has been a link of increasing symptoms of depression and anxiety to changes in microbiome composition. Furthermore, some bacteria may promote the production of mood regulating neurotransmitters such as serotonin.How the microbiome influences its effects includes production of neurotransmitters, modulation of the immune system, and modulation of stress hormone levels. Maintaining microbiome health and improving mental well being also depends on nutrition. Proper nutrition and probiotics may help manage the microbiome and in turn alleviate symptoms of mental disorders.

***Keywords*: Microbiome, Mental health, Gut-brain axis, Immune, Neurotransmitters, Probiotics.**

1. *INTRODUCTION*

A microbial ecosystem within the human body, especially the gut, the microbiome is important to physical and mental health. New research has found that the microbiome can affect mental disorders like depression, anxiety and mood disorders. In this article, we explore how the microbiome impacts mental disorders, how it works and what could be done to improve mental health with microbiome management.

1.1 Gut-Brain Axis

Gut brain axis is a network of neural, hormonal, and immune connections between the gut and the brain. The vagus nerve, and neurotransmitters and hormones, are also connected. One of the prime communication channel linking the gut and the brain is known as the vagus nerve, which can transmit information about the gut's status to the brain[1]. What this means is that mental conditions can influence gut function and vice versa, that the status of the gut can affect mood and behaviour.
Transmitters and gut microbiome: the gut microbiome can make neurotransmitters like serotonine, dopamine and GABA that have an impact human mood and behavior[2]. For example, the gut makes about 90% of the body's serotonine. This highlights the big role of the microbiome in mood and behavior regulation. In addition, changes in the microbiome composition may result in changes of these neurotransmitters and, consequently, the mental health.

1.1.1 How Mental Disorders Can be Linked to Microbiome

Depression

The gut microbiome may affect mood and behavior, as it does through the gut brain axis, according to research. There are known relationships between depression and changes in gut microbiota composition, with some bacteria linked to inflammatory responses that could play a role in depressive symptoms[3].

There is evidence that changes in gut microbiome composition are linked to worse symptoms of depression[4]. Lactobacillus and Bifidobacterium certain bacteria may help improve mood. For example, in one study people with depression experienced significant reduction in their symptoms after consuming probiotics.[5]. The results indicate that dietary and probiotic interventions may be used as complementary treatments for depression.

Anxiety

Research shows that the gut microbiome can affect levels of stress and anxiety[6]. High anxiety symptoms may result from changes in the diversity of the microbiome. In a second study, mice with altered microbiome had higher levels of anxiety behaviors[1]. This shows the need to keep the gut healthy for handling anxiety. Altered gut microbiota has been associated with anxiety disorders including generalized anxiety disorder (GAD). Mechanisms of neurotransmitter production and immune modulation may be involved in the influence of some bacteria on anxiety levels[8].

Bipolar Disorder

Dysbiosis (microbial imbalance) in the gut microbiome has been linked to bipolar disorder. A few studies suggest that there is a correlation between a particular microbial profile and mood states in bipolar patients[7]. Microbiome changes could affect disorders like bipolar disorder[4]. Probiotic treatments have been shown to help some patients with their symptoms. Also, dietary changes and the consumption of fiber rich foods may affect microbiome composition.

Social Anxiey

Gut microbiota composition could also influence social anxiety disorder, according to emerging studies, which indicate that gut health can impact social behavior and anxiety levels[9].

Autism Spectrum Disorder (ASD)

We are starting to see that people with autism may have different gut microbiomes than the neurotypical. These differences may contribute to the gastrointestinal symptoms often seen in ASD, and could also affect behavior, some studies indicate[10].

Attention Deficit Hyperactivity Disorder (ADHD)

The evidence suggests that gut microbiota might be involved in ADHD symptoms, and some studies have found that children with ADHD have different microbial diversity from their normally developing peers[11].

Schizophrenia

Evidence is emerging that the pathophysiology of schizophrenia may involve alterations in the gut microbiome that can influence immune responses and neuroinflammation[12].

Generalized Anxiety Disorder (GAD)

Like other anxiety disorders, GAD is known to be linked to changes in the gut microbiome, which may impact neurotransmitter levels and stress response[13].

IV. Mechanisms of Action

Some bacteria can make neurotransmitters that affect mood[2]. For instance, Lactobacillus reuteri can increase GABA levels and help mitigate anxiety. Bacteria and neurotransmitters are connected, which makes the microbiome important for mental health.

Neurotransmitter Production

Bacteria can produce neurotransmitters that affect mood[2]. For instance, Lactobacillus reuteri can raise GABA levels to reduce anxiety. Bacteria and neurotransmitters: This is where the microbiome matters to mental health.

Immune System Regulation

The microbiome can modulate immune response which can influence inflammation associated with mental disorders[4]. A major cause of mental disorders is chronic inflammation. Therefore, the microbiome might be managed to reduce inflammation and improve mental health.

Impact on Hormones

Some of the changes in the microbiome can influence stress hormone levels like cortisol[6]. High levels of cortisol are linked to more symptoms of anxiety and depression. Therefore, the ability to control the microbiome status might be able to reduce cortisol levels and therefore reduce anxiety symptoms.

V. Role of Nutrition in Microbiome Health

Mediterranean Diet

Rich in fiber, healthy fats, and plant based proteins, the Mediterranean diet is a positive factor for maintaining microbiome health[4]. By following this diet, you can increase microbiome diversity, and also decrease the symptoms of depression and anxiety.

Probiotics and Prebiotics

In addition, probiotics (live microorganisms) and prebiotics (foods that promote the growth of beneficial bacteria) also are important to supporting microbiome health[5]. Regular intake of these substances can assist in improving mood and reducing anxiety symptoms.

VI. Microbiome-Based Therapies

Probiotics

As complementary treatments for mental disorders[5], probiotics have been investigated. Probiotics have been shown to help decrease symptoms of depression and anxiety.

Dietary Changes

Dietary changes, including increasing the fiber intake and reducing the refined sugars, can also have a positive effect on microbiome composition[1].

Future Research and Challenges

While there is existing evidence demonstrating the microbiome is associated with mental disorders, more research is needed to fully understand that relationship. Furthermore, further studies on the effect of various types of probiotics and prebiotics on mental health are also required[2].

VII. The Influence of the Microbiome on Immunity and Metabolism:

The human body is affected by the microbiome in profound ways, affecting both the immune system and metabolic processes. These are important effects that are needed for maintaining health and preventing different diseases.

Impact on Immunity

The immune system depends on the microbiome. Before birth, exposure to microbes is critical to teach the immune system what harmless and what harmful organisms are. So, for example, commensal bacteria — like those in the gut — interact with immune cells and affect how they respond and help to create immune tolerance[21]. For example, the microbiome controls the production of immune cells, T-regulatory cells, which are crucial for maintaining immune homeostasis and preventing autoimmune responses[22].

Furthermore, the microbiome provides colonization resistance against pathogens, filling niches and producing antimicrobial substances that inhibit pathogenic microorganisms[23]. This exclusion is competitive and prevents harmful pathogens from establishing themselves and decreasing the risk of infections.

Impact on Metabolism

Aiding in the digestion of complex carbohydrates and synthesis of essential vitamins and amino acids, the microbiome makes a large contribution to host metabolism[24]. Short chain fatty acids (SCFAs) produced by gut bacteria from dietary fibers are used as energy sources for colon cells and have systemic metabolic effects. In addition, these SCFAs are anti-inflammatory and involved in glucose and lipid metabolism[25]. Dysbiosis (i.e. imbalance in the microbial community) has been associated with metabolic disorders, such as obesity and type 2 diabetes[26]. Microbiome influences overall energy balance and metabolic health by influencing energy harvest from food and fat storage.

VII. *Impact of SCFAs on the Brain*

Short chain fatty acids (SCFAs) are produced by gut microbiota fermentation of dietary fibers and have been reported to exert different effects on brain.

Neuroinflammation Reduction
SCFAs, and butyrate in particular, have anti-inflammatory properties, capable of reducing neuroinflammation. This is important because chronic brain inflammation is linked to a number of neurodegenerative diseases and psychiatric disorders[14].

Blood-Brain Barrier Integrity
SCFAs can strengthen the blood-brain barrier (BBB). The BBB is important for protecting the brain from harmful substances and maintaining homeostasis, and a healthy BBB is essential[15].

Neurotransmitter Production
SCFAs can influence the production of neurotransmitters, such as serotonin and gamma-aminobutyric acid (GABA). Butyrate, for instance, has been found to increase serotonin levels in the brain, and increasing serotonin in the brain might be a good way to regulate mood[16].

Cognitive Function

SCFAs may be involved in cognitive functions such as learning and memory, according to evidence. In fact, butyrate, in particular, has been shown to improve cognitive performance in animal models[17].

.**Mood Regulation**

SCFAs may also play a role in the development of mood disorders, such as anxiety and depression. The gut brain axis implicates that gut microbiota changes

VIII. *The Connection Between the Microbiome and Mental Health*

As an emerging area of research, the relationship between gut microbiome and mental health has received a lot of attention in recent years. In this connection the gut brain axis, a bidirectional communication system between the central nervous system and the gastrointestinal tract, is important[1]. Many of the functions of the brain can be affected by the gut microbiome through neurotransmitter production, immune modulation, and the production of short-chain fatty acids that affect brain physiology[19]. Dysbiosis, or an imbalance of the gut microbiota, has been linked to psychiatric disorders including depression, anxiety and autism spectrum disorders[20]. If we understand how the gut microbiome contributes to mental health, then it could mean innovative treatments like microbiome targeted therapies that try to rebalance the microbial balance, which could help produce better psychiatric outcomes.

IX. The Prevalence and Impact of Mental Health Disorders on Individual and Social Life

Mental health disorders are a major public health problem of global magnitude (WHO, 2011). Depression, anxiety, bipolar disorder, and schizophrenia are the most common disorders and have all far reaching implications for individual and society.

Mental Health Disorders prevalence

World Health Organization (WHO) estimates that depression is the leading cause of disability in the world, with more than 264 million people affected[27]. There are also 284 million people worldwide who suffer from anxiety disorders[28]. Often these disorders co-occur and make diagnosis and treatment more difficult. Mental disorders are more prevalent in certain regions and in particular demographic groups, with these differences influenced by socioeconomic status, environmental stressors, and genetic predispositions[29].

Impact on Individual Life

Mental health disorders seriously affect an individual's quality of life. Acute episodes can disrupt daily functioning, academic and occupational performance and interpersonal relationships[30]. For example, depression can be very severe emotionally, cause people to be unmotivated, tired, and unable to work or go to school[31]. Persistent worry and panic attacks that interfere with social interactions and destroy self confidence[32]are an example of anxiety disorders.

Impact on Social Life

Mental health disorders have as much of an impact on society. They cause substantial economic costs through lost productivity, healthcare costs and social welfare programs[33]. Stigmatization and discrimination of people with mental health problems can result in social isolation and reduced social cohesion[34]. This is a huge burden on healthcare systems requiring comprehensive public health strategies for prevention, early intervention and effective treatment[35].

X. FMT

Fecal Microbiota Transplantation (FMT) is a medical procedure where feces (fecal matter) from a healthy donor is transferred into the gastrointestinal tract of a recipient. The first objective is to restore gut microbiota balance that can be compromised by certain conditions, such as antibiotic use, infection, or inflammatory bowel disease (IBD), or Clostridium difficile infection (CDI).

Key Aspects of FMT

Mechanism of Action

The basic idea behind FMT is to reintroduce a diverse array of beneficial bacteria into the recipient's gut. It can facilitate microbial diversity restoration, enhance gut barrier function and alter immune response. A healthy microbiota can restore the digestion, promote immune function, and may even reduce gastrointestinal and systemic symptoms[36].

Indications:

FMT is used most commonly for recurrent Clostridium difficile infections that fail to respond to standard antibiotic treatment. It has also been explored for other conditions, including[37]:

- *Inflammatory bowel diseases (including ulcerative colitis and Crohn's disease)*

- *Irritable bowel syndrome (IBS)*

- *Metabolic disorders (e.g. obesity and type 2 diabetes)*

- *Some neurological conditions (autism spectrum disorders, for ex)*

Procedure

The FMT procedure can be performed via several routes, including:

Colonoscopy

Enema

Nasogastric tube

Oral capsules

Safety and Efficacy

The success rates with FMT in treating recurrent CDI are often greater than 80%. Generally considered safe, FMT comes with some risks: infections can be transmitted, and you can have an adverse reaction. These risks can be minimized by rigorous screening of donors and proper processing of fecal material[38].

Future Directions

FMT research is ongoing to understand the mechanisms that drive the outcome of FMT, determine which donor characteristics are optimal, and to explore the potential use of FMT in other diseases. Furthermore, studies are underway to determine if specific microbial consortia or isolated bacterial strains can be used instead of whole fecal transplant[39].

Conclusion

The complexity and multifaceted nature of the interplay between mental health disorders and the microbiome suggests therapeutic interventions that can be achieved through dietary and probiotic strategies, as a means of restoring a healthy microbiome. Through a variety of mechanisms, SCFAs are important for brain health, including decreasing neuroinflammation, improving blood brain barrier integrity, modulating neurotransmitter production and possibly mood and cognitive function. FMT is being developed as a potential therapeutic for restoring the balance of the gut microbiota and treating recurrent CDI. More research will be done to see if its applications will expand to a wider range of health conditions.

REFERENCES

[1] *Foster, J.A., & McVey Neufeld, K.A. (2013). Gut-brain axis: how the microbiome influences anxiety and depression. Trends in Neurosciences, 36(5), 287-296.*

[2] *Cryan, J.F., & Dinan, T.G. (2012). Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. Nature Reviews Neuroscience, 13(10), 701-712.*

[3] *Jiang, H., et al. (2015). "Altered gut microbiota profile in patients with major depressive disorder." *Brain, Behavior, and Immunity*, 48, 186-194. doi:10.1016/j.bbi.2015.03.016.*

[4] *Mörkl, S., et al. (2018). The role of the gut microbiome in the pathophysiology of depression: a review of the literature and future directions for research. Psychiatry Research, 269, 122-133.*

[5] *O'Mahony, S.M., et al. (2015). The role of the gut microbiota in the development of anxiety and depression: a review of the literature and future directions for research. Neuroscience & Biobehavioral Reviews, 58, 115-126.*

[6] *Sudo, N., et al. (2004). Postnatal microbial colonization programs the hypothalamic-pituitary-adrenal system for stress response in mice. Journal of Physiology, 558(1), 263-275.*

[7] *O'Mahony, S. M., et al. (2015). "The role of the microbiome in bipolar disorder." *Psychiatry Research*, 229(1-2), 70-75. doi:10.1016/j.psychres.2015.06.010.*

[8] *Kelly, J. R., et al. (2016). "Transferring the blues: depression-associated gut microbiota induces neurobehavioural changes in the rat." *Journal of Psychiatric Research*, 82, 109-118. doi:10.1016/j.jpsychires.2016.07.008.*

[9] *Aizawa, E., et al. (2019). "Gut microbiota and social anxiety: A review." *Frontiers in Microbiology*, 10, 903. doi:10.3389/fmicb.2019.00903.*

[10] *Kang, D.-W., et al. (2017). "Dysbiosis of the gut microbiota in disease." *Microbial Ecology in Health and Disease*, 28(1), 1344890. doi:10.1080/16512235.2017.1344890.*

[11] *Aarts, E. O., et al. (2021). "The gut microbiome in children with attention-deficit/hyperactivity disorder: A systematic review." *European Child Adolescent Psychiatry*, 30(8), 1123-1132. doi:10.1007/s00787-020-01734-4.*

[12] *Zhang, X., et al. (2020). "The role of gut microbiota in schizophrenia." *Frontiers in Psychiatry*, 11, 606. doi:10.3389/fpsyt.2020.00606.*

[13] Sudo, N., et al. (2004). "Postnatal microbial colonization programs the hypothalamic-pituitary-adrenal system for stress response in mice." *Journal of Physiology*, 558(1), 263-275. doi:10.1113/jphysiol.2004.063388.

[14] Zhang, C., et al. (2020). "Short-chain fatty acids: A novel therapeutic target for neuroinflammation." *Frontiers in Immunology*, 11, 2043. doi:10.3389/fimmu.2020.02043.

[15] Harris, P. J., et al. (2018). "Butyrate protects against blood-brain barrier dysfunction in a mouse model of multiple sclerosis." *Frontiers in Neuroscience*, 12, 751. doi:10.3389/fnins.2018.00751.

[16] Yano, J. M., et al. (2015). "Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis." *Cell*, 161(2), 264-276. doi:10.1016/j.cell.2015.03.018.

[17] Gao, K., et al. (2018). "Short-chain fatty acids facilitate the production of neurotrophic factors in the rat brain." *Journal of Nutritional Biochemistry*, 57, 183-190. doi:10.1016/j.jnutbio.2018.02.002.

[18] Miller, A. H., et al. (2018). "Inflammation and its discontents: The role of cytokines in depression." *Biological Psychiatry*, 83(1), 73-82. doi:10.1016/j.biopsych.2017.09.006.

[19] Sampson, T. R., & Mazmanian, S. K. (2015). Control of brain development, function, and behavior by the microbiome. Cell Host & Microbe, 17(5), 565-576.

[20] Foster, J. A., & McVey Neufeld, K.-A. (2013). Gut-brain axis: how the microbiome influences anxiety and depression. Trends in Neurosciences, 36(5), 305-312.

[21] Belkaid, Y., & Hand, T. W. (2014). Role of the microbiota in immunity and inflammation. Cell, 157(1), 121-141.

[22] Round, J. L., & Mazmanian, S. K. (2009). The gut microbiota shapes intestinal immune responses during health and disease. Nature Reviews Immunology, 9(5), 313-323.

[23] Buffie, C. G., & Pamer, E. G. (2013). Microbiota-mediated colonization resistance against intestinal pathogens. Nature Reviews Immunology, 13(12), 790-801.

[24] H. J., Scott, K. P., Louis, P., & Duncan, S. H. (2012). The role of the gut microbiota in nutrition and health. Nature Reviews Gastroenterology & Hepatology, 9(10), 577-589.

[25] Koh, A., De Vadder, F., Kovatcheva-Datchary, P., & Bäckhed, F. (2016). From dietary fiber to host physiology: Short-chain fatty acids as key bacterial metabolites. Cell, 165(6), 1332-1345.

[26] Turnbaugh, P. J., Ley, R. E., Mahowald, M. A., Magrini, V., Mardis, E. R., & Gordon, J. I. (2006). An obesity-associated gut microbiome with increased capacity for energy harvest. Nature, 444(7122), 1027-1031.

[27] World Health Organization. (2020). Depression and Other Common Mental Disorders: Global Health Estimates. Retrieved from WHO

[28] World Health Organization. (2020). Global Health Estimates 2019. Retrieved from WHO

[29] Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry, 62(6), 593-602.

[30] Murray, C. J., & Lopez, A. D. (1996). The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Harvard School of Public Health.

[31] *Layard, R. (2005). Mental health: Britain's biggest social problem? Centre for Economic Performance, London School of Economics.*

[32] *Kessler, R. C., Chiu, W. T., Demler, O., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry, 62(6), 617-627.*

[33] *Trautmann, S., Rehm, J., & Wittchen, H.-U. (2016). The economic costs of mental disorders: Do our societies react appropriately to the burden of mental disorders? EMBO Reports, 17(9), 1245-1249.*

[34] *Corrigan, P. W., & Watson, A. C. (2002). Understanding the impact of stigma on people with mental illness. World Psychiatry, 1(1), 16-20.*

[35] *Patel, V., Saxena, S., Lund, C., Thornicroft, G., Baingana, F., Bolton, P., ... & UnÜtzer, J. (2018). The Lancet Commission on global mental health and sustainable development. The Lancet,392(10157), 1553-1598.*

[36] *Cammarota, G., et al. (2017). "Fecal microbiota transplantation for treating Clostridium difficile infection: A systematic review and meta-analysis." *Therapeutic Advances in Gastroenterology*, 10(3), 191-210. doi:10.1177/1756283X16683460.*

[37] *Kassam, Z., et al. (2013). "Fecal microbiota transplantation for the treatment of Clostridium difficile infection: A systematic review." *Annals of Internal Medicine*, 159(2), 130-137. doi:10.7326/0003-4819-159-2-201307160-00008.*

[38] *Bafeta, A., et al. (2018). "Fecal microbiota transplantation for the treatment of Clostridium difficile infection: A systematic review and meta-analysis." *BMC Gastroenterology*, 18(1), 1-11. doi:10.1186/s12876-018-0905-6.*

[39] *Zhou, L., et al. (2020). "Fecal microbiota transplantation: A novel approach to treat diseases." *Frontiers in Microbiology*, 11, 574287. doi:10.3389/fmicb.2020.574287.*