International Journal of Medical, Pharmacy and Drug Research (IJMPD)
[Vol-5, Issue-4, Jul-Aug, 2021]
ISSN: 2456-8015
https://dx.doi.org/10.22161/ijmpd.5.4.4
Peer-Reviewed Journal

The Microbiome's Impact on Human Health: Unraveling the Gut-Brain Connection

Dr. Jalla Ram

Lecturer, Anar Devi Govt. Senior Secondary School Nagar, Bharatpur, Rajasthan, India

Received: 11 Jul 2021; Received in revised form: 05 Aug 2021; Accepted: 14 Aug 2021; Available online: 24 Aug 2021

Abstract

The human body hosts a diverse community of microorganisms known as the microbiome, with a significant population residing in the gut. Recent scientific discoveries have illuminated a fascinating interplay between the gut microbiome and the brain, giving rise to the concept of the gut-brain connection. This abstract encapsulates a comprehensive study exploring the intricate impact of the microbiome on human health, specifically focusing on the emerging understanding of the gut-brain axis. The human microbiome, a complex ecosystem of microorganisms inhabiting various body sites, has garnered increasing attention for its pivotal role in health and disease. Within this vibrant microbiome, the gut stands out as a major hub, hosting a myriad of microorganisms that contribute to digestion, immune function, and overall well-being. This study delves into the profound impact of the gut microbiome on human health, unraveling the intricate web of the gut-brain connection. A multidisciplinary approach will be adopted, involving literature reviews, molecular studies, and clinical investigations. Microbiome sequencing techniques will be used to analyze gut microbiome composition in relation to mental health outcomes. Neuroscientific methodologies will be employed to elucidate the neural pathways and biochemical signaling underlying the gut-brain communication.

***Keywords*— Human, Health, Biochemical, microorganisms, Molecular, microbiome**

I. INTRODUCTION

The intricate web of life within the human body extends far beyond what meets the eye. Within our digestive tracts resides a bustling ecosystem of microorganisms known as the gut microbiome, which is increasingly recognized as a pivotal player in shaping human health and well-being. Emerging research has unveiled an unexpected dimension of this complex symbiosis - the profound influence of the gut microbiome on the intricate network of our brain, setting the stage for a captivating exploration of the gut-brain connection. The human gut is home to trillions of microorganisms, including bacteria, viruses, fungi, and other microorganisms. This collective microbial community, the gut microbiome, is a dynamic and diverse ecosystem that influences various aspects of our health, from digestion and nutrient absorption to immune function and metabolism.

Recent scientific inquiries have revealed that the gut-brain connection extends beyond the confines of their respective anatomical locations. The "mind-gut axis" is an intricate communication network that links the gut microbiome to the central nervous system, paving the way for bi-directional signaling between the gut and the brain. Through a complex interplay of biochemical messengers, neural pathways, and immune responses, the gut microbiome communicates with the brain, impacting mood, emotions, cognition, and behavior. This communication occurs through various mechanisms, including the release of neurotransmitters, hormones, and metabolites.

The implications of the gut-brain connection extend far beyond digestion. Research suggests that alterations in the gut microbiome composition, known as dysbiosis, are associated with a range of conditions including anxiety, depression, neurodegenerative diseases, and even autism spectrum disorders. The microbiome's influence on immune responses and inflammation further underscores its significance in maintaining systemic health. The revelation of the gut-brain connection opens doors to innovative approaches for addressing mental health and neurological disorders. Probiotics, prebiotics, dietary interventions, and even fecal microbiota transplantation are emerging as potential therapeutic strategies to modulate the gut microbiome and alleviate symptoms of brain-related conditions. While the understanding of the gut-brain connection is rapidly expanding, many questions remain unanswered. The exact mechanisms of communication, the role of specific microbial species, and the long-term implications of microbiome modulation on mental health are areas of ongoing research. The revelation of the gut-brain connection serves as a reminder of the intricacies of the human body and its symbiotic relationship with the microbial world. As research continues to unveil the myriad ways in which the gut microbiome impacts human health, it offers a promising avenue for innovative therapeutic interventions and a deeper understanding of the profound interplay between our gut and our brain. This exploration of the gut-brain connection beckons us to reimagine the boundaries of human health and to appreciate the complex harmony that exists within us.

II. LITERATURE REVIEW

Longsha Liu, (2022) Following the recent discovery that the gut microbiome, which contains an estimated 100 trillion bacteria, plays a role in the emergence of both health and illness, multidisciplinary research into gut microbiology has exploded. The increasing evidence concerning the function of the gut microbiota in neurodegenerative and neurodevelopmental illnesses, such as central nervous system (CNS) cancers, has to be properly understood and placed in perspective among all this hoopla. To better understand microbiota-mediated pathogenesis, potential noninvasive prognostic tools, and treatment strategies based on microbiota-gut-brain-axis modulations, the purpose of this review is to disentangle the intricate connections between the microbiota, the gut, and the brain. We also explore the limits of existing techniques and give insights into the continuing translation from the laboratory to the clinic. We conclude by advocating for the continuous development of synergistic therapeutic models that take into account the wide variety of gut-resident bacteria that hold the promise of making major advances in the treatment of numerous neurological illnesses.

Shivani Ghaisas (2017) The microbiome in our gastrointestinal tract is made up of the genomes of the billions of bacteria that live there. Irritable bowel syndrome (IBS), ulcerative colitis (UC), and other gastrointestinal (GI) disorders, as well as neurological (CNS) diseases like Alzheimer's and Parkinson's, may all be prevented or treated in part by manipulating the complex relationship between the host and its gut microbiome. This review aims to synthesize current understanding of the gut microbiome, its role in disease progression, and the bacterial and biochemical targets that should be the focus of future studies. Insights gained from studying the gut microbiome's activities and proliferation processes may lead to the development of new treatment approaches.

Helianthous Verma (2020) Human health relies heavily on the microorganisms living in the digestive tract, which have been found to affect a wide range of physiological reactions, including neurological ones. Evidence for the importance of the gut microbiome to mental health has been increasing in recent years. Microbes influence the brain-gut relationship via neurotransmitters, neurotransmitter precursors, hormones, cytokines, and bioactive metabolites, all of which travel through neuronal, neuroendocrine, and metabolic pathways. When this link isn't working properly, mental illness may show up in people's lives. It's estimated that almost a billion people worldwide struggle with conditions such as mental illness, addiction, or a lack of intellectual capacity. Knowing how gut bacteria contribute to mental illnesses is thus crucial. It is crucial to have a comprehensive knowledge of gut dysbiosis in mental illnesses due to the fact that the diseases linked with these disorders vary and some share symptoms. In this article, we provide the most up-to-date information on the link between changes in gut microorganisms and a wide range of neurological, psychiatric, and neurodegenerative illnesses. In light of these findings, a number of research have been conducted on the effects of therapeutic treatments, such as the introduction of live microorganisms (psychobiotics), on the gut microbiota in attempt to treat mental health illnesses and/or associated symptoms. We discuss these studies and propose a personalized and integrative approach to the treatment of mental disorders, wherein combinations of microbe-based therapeutic interventions to modulate gut microbes and in-use psychological treatment practices can be integrated and based on the patient's gut microbiome.

Willem M de Vos (2022) It is now well accepted that the gut microbiota plays a critical role in the control of host health. Microbes colonize almost every surface of our bodies, indicating that they engage in a wide variety of crosstalk with our internal organs. The evolution of molecular methods and technologies has allowed scientists to better understand the intricate relationships between the host and many bacteria. Obesity, type 2 diabetes, hepatic steatosis, inflammatory bowel disease (IBD), and numerous forms of cancer have all been related to changes in the gut microbiota in recent years. Immune function, energy production, cholesterol and glucose metabolism, and maybe other processes are impacted. A critical assessment of the state of knowledge in this area is a primary focus of this study. Several potential biological processes connecting gut bacteria to either illness prevention or development are presented. Some of the metabolites we look at include short-chain fatty acids, bile acids, and trimethylamine N-oxide, but we also include more recently discovered metabolites and their receptors, such as the peroxisome proliferator-activated receptor alpha and gamma, the aryl hydrocarbon receptor, and the G protein-coupled receptors GPR41, GPR43, GPR119, and Takeda G protein-coupled receptor 5. New medicines are being developed, and knowing the intricacy and molecular components relating gut microorganisms to health is essential

Qianquan Ma (2019) Both intrinsic and peripheral signals control central nervous system (CNS) development. In both normal and pathological states, the brain's neural functions have been shown to be influenced by their external context. Emerging data has shown a two-way connection between the gut microbiota and the brain, despite the physical barriers that separate them. Basic neurogenerative processes, neurodegenerative illnesses, and CNS malignancies may all be affected by the communication between the gut microbiota and the brain. Here, we take a look at the gut-brain axis, or the biological connection between the two, and how that connection may become imbalanced in neurological disorders. We also emphasize recent advances in our understanding of how altering the makeup of one's gut microbiota might be a useful treatment strategy for dealing with neurological conditions.

III. RESEARCH METHODOLOGY

Microbiome Sampling and Analysis: Gut microbiome samples will be collected from a diverse range of participants, including individuals with varying mental health statuses. State-of-the-art DNA sequencing techniques will be used to analyze microbial composition, diversity, and abundance. Bioinformatics tools will aid in identifying specific microbial taxa associated with mental health outcomes.

Neuroscientific Investigations: Neuroscientific methods, such as functional magnetic resonance imaging (fMRI) and electroencephalography (EEG), will be employed to study the neural mechanisms underlying the gut-brain connection. These techniques will help map brain regions activated by gut signals and investigate how neurotransmitters and hormones mediate communication between the two systems.

Clinical Assessments: Psychometric assessments will be conducted to evaluate participants' mental health, mood, cognition, and behavioral patterns. Questionnaires and standardized scales will provide quantitative data to correlate microbial composition with mental health variables.

Molecular Analysis of Signaling Molecules: Blood and fecal samples will be analyzed to measure concentrations of neurotransmitters, cytokines, and other signaling molecules that are involved in the gut-brain communication. This analysis will provide insights into the biochemical pathways through which the microbiome influences the brain.

Correlation and Statistical Analysis: Statistical analyses, including correlation and regression analyses, will be performed to identify associations between specific microbial taxa, signaling molecules, neural activation patterns, and mental health outcomes. These analyses will provide insights into potential causal relationships and predictive models.

Integrative Data Analysis: By integrating microbiome data, neuroscientific findings, and clinical assessments, a comprehensive picture of the gut-brain connection's impact on human health will be constructed. This integration will allow for a deeper understanding of the mechanisms underlying this relationship.

Ethical Considerations: Ethical guidelines will be followed throughout the study, ensuring the well-being and privacy of participants. Informed consent will be obtained, and ethical approval will be sought from relevant research ethics committees.

IV. DATA ANALYSIS

The central nervous system (CNS) and the enteric nervous system (ENS) are linked in a bidirectional pathway known as the gut-brain axis (GBA). The brain's centers for emotion, memory, and cognition are directly and indirectly linked to the intestine's peripheral activities. The interplay between the endocrine system, the immunological system, and the ANS is particularly intricate. The permeability of the GI tract, hormone secretion, bile salt and mucus synthesis, and the creation of mucus are all typical physiological activities that require these signaling stations. The equilibrium of the gastrointestinal tract is disrupted by dysregulation anywhere in the network. Through the GBA's neurological and hormonal linkages, the brain may control the actions of the intestine's functional effector cells such immune cells, enteric neurons, muscle cells, epithelial cells, and so on. The gut microbiota influences these cells and, by extension, the GBA. The role of gut microbiota in controlling the transmission of information between the digestive tract and the brain has expanded the original notion of GBA into what is now known as the Microbiota-Gut-Brain axis. The Microbiota-Gut-Brain axis is shown in Figure 1 from a structural and functional perspective. There are three primary channels via which the gut microbiota may interact with the brain, as shown in the image above: the nervous system, the immunological system (cytokines), and the endocrine system. (Fig. 1). To control intestinal motility, permeability, hormone production, and defecation, the vagus nerve uses efferent fibers to activate several gut targets. Afferent vagus nerve fibers provide signals to the brain about appetite, fullness, inflammation, and metabolism. Gut neuropod cells and vagal neurons create synapses via their interactions. Numerous metabolites produced by gut microbiota, such as neurotransmitters (such as serotonin and gamma-aminobutyric acid; GABA); short chain fatty acids (SCFAs) (such as butyric acid and propionic acid); catecholamines (such as dopamine and norepinephrine); amino acids (such as tryptophan); and serotonin and glycine) (Fig. 1, 1–6) Metabolites produced by microbes may either act locally on the enteric nervous system (ENS) and vagus nerve (3) or penetrate the bloodstream and reach the brain (4). Also, gut microbiota induce the release of cytokines (5) and hormones (6) by acting locally on gut immune cells.

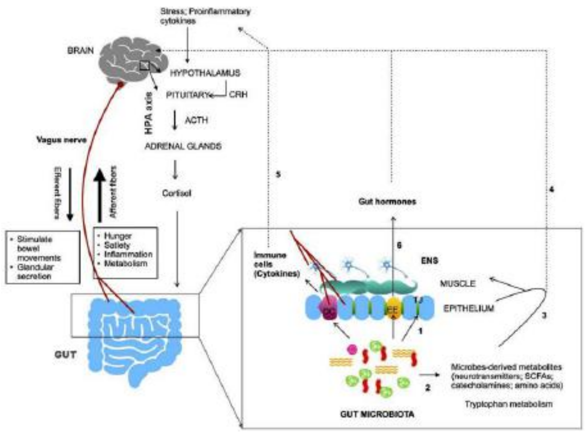

Fig. 1 Microbiota and the gut-brain axis.

Approximately 1 in 7 Indians, or about 197 million individuals, had a moderate to severe mental condition in 2017, almost doubling the prevalence of mental health issues since 1990. The relative prevalence of many types of mental illness in India is shown in Figure 2.

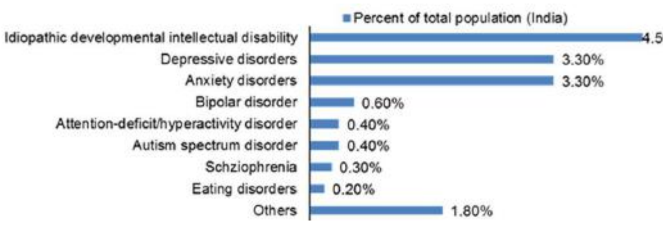

Fig. 2 Burden share of various mental disorders in India

Having a thorough knowledge of the function of the gut microbiota in diverse mental diseases is crucial in light of the worrisome rise in the burden of mental disorders and the evidences of link that exist between the gut microbiota and mental health. Here, we compile the research (Table 1) that may help us figure out how to reduce the distressing effects of different mental diseases via effective treatment methods. Table 1 includes some of the therapy methods that were used and the results of those methods.

Mental health disorder	Change in gut microbiota	Consequences of microbial dysbiosis	Therapeutic interventions	Observations after treatment/ therapy
Autism spectrum disorder (ASD)	Alterations in Bacteroidetes/firmicutes ratio Increase abundance of *Bacteroides, Barnesiella, Clostridium* and *Roseburia* Decreased abundance of *Bifidobacterium, Coprococcus, Dialister, Faecalibacterium, Prevotella*, and *Streptococcus*	Less production of butyrate and lactate; mucin degradation	FMT Changes in diet Antibiotics	Increased abundance of *Bifidobacterium, Prevotella*, and *Desulfovibrio* FMT associated changes in GI and ASD symptoms
Attention-deficit/ hyperactivity disorder (ADHD)	Increase abundance of *Bifdobacterium* *Neisseria*	Predicted enhanced biosynthesis of cyclohexadienyl dehydratase—enzyme required for dopamine synthesis	Micronutrient supplementation	Decline in abundance of *Bifdobacterium*
General anxiety disorder (GAD)	Increase abundance of *Fusobacterium, Ruminococcus* and *Escherichia- Shigella* Decrease in SCFAs-producing genera—*Faecalibacterium, Eubacterium and Suttereella*	Immune activation Degradation of mucin	Non-probiotic (supplementary of the resistant dextrin)	Improvement in anxiety symptoms
Depression	Abundance of *Prevotella, Klebsiella, Enterobacteriaceae* and *Alistipes* Decrease in *Faecalibacterium, Coprococcus, Dialister, Ruminococcus* species *Lachnospiraceae* family *Lactobacillus* and *Bifidobacterium*	Butyrate production decline Increased intestinal inflammation	FMT—capsule administration	Reduction in the psychological distress

V. CHALLENGES AND FUTURE DIRECTIONS

Although the role of the gut microbiome in a number of mental health disorders has become increasingly clear over the past two decades, more definitive data and clinical studies are needed to establish the direct role of gut microbiota in restoring mental health balance before we can rely on microbe-based therapeutic interventions. To better understand the causative or effector relationship between gut microbiota and a broad spectrum of mental health diseases, several obstacles must be overcome. First, most clinical research are cross-sectional; for a more complete picture of the role of gut microbiota in mental health problems or the efficacy of therapeutic interventions aimed at altering gut microbiota, longitudinal studies are required [69]. Second, the consistency and repeatability of the findings are hampered by factors such as the small sample size, the absence of robust and consistent sampling technique, and the lack of bioinformatics tools. Incomplete symptom assessments, biases based on gender, and the fact that symptoms are often reported by the patient themselves (as is the case with gastrointestinal symptom questionnaires) may all contribute to incorrect conclusions. Despite this, researchers have acknowledged the problems and are now better planning and conducting their investigations. Thirdly, it's been well acknowledged that one's food plays a complex function in determining the make-up of his or her gut microbiota, and that even temporary dietary modifications may have a noticeable impact on the variety and richness of gut microbiota [70]. It's further complicated since most forms of mental illness are known to have an effect on patients' appetite and metabolism. Therefore, it may provide us with better knowledge for devising the treatment programs if we track the nutrition and lifestyle of both patients and healthy people under investigation. In addition, several clinical trials have omitted crucial information on other treatments, such as drugs and co-morbidities. One last obstacle is that people may respond differently to treatments like FMT, nutrition therapy, psychobiotics, etc. due to their individualized gut microbiota, which is influenced by their food, genetics, and lifestyle. Since the'microbiota-gutbrain' connection is a complex system that includes many ways to modulate the gut microbiota and many mechanisms to affect the brain's functioning, an integrative approach can be taken in which different therapeutic interventions are used in tandem to treat or alleviate the disorder or its symptoms. Due to individual differences in microbiota and environmental influences, tailored microbial-based therapies should be explored.

VI. CONCLUSION

Due to the differences between people and rodents, further clinical investigations are needed to better understand the role of the gut microbiota in mental health problems. Future technological advances and the resolution of the issues raised here will pave the way for a more complete comprehension of the role gut microbiota plays in determining the prevalence of mental health problems and how this knowledge may be leveraged in the development of successful treatment interventions. Together, psychiatrists and microbiologists have been presented with a crucial new viewpoint on the manifestation of mental health issues, and they may work toward reaching or restoring the natural balance of mental health in the human population. There has been a lot of advancement in the previous twenty years. The study of the relationship between the gut microbiota and health has progressed from early clinical findings to more mechanistic techniques, and now to indisputable causal correlations. However, there are still a great deal of research that attribute causation when none exists. As promising as it is to think about designing therapies based on the modification of the gut microbiota or by utilizing particular active chemicals, it is still necessary to get from correlation to causation. As a result of many people's hard work and the development of omics analysis, the scientific community is making slow but steady progress toward personalized medicine, and the microbiome era is obviously a key component of this paradigm shift.

REFERENCES

[1] Korpela K, de Vos WM. Early life colonization of the human gut: microbes matter everywhere. Curr Opin Microbiol 2018;44:70–8.

[2] Korpela K, Helve O, Kolho K-L, et al. Maternal fecal microbiota transplantation in Cesarean-Born infants rapidly restores normal gut microbial development: a proof-of-concept study. Cell 2020; 183:324–34.

[3] Lloyd-Price J, Mahurkar A, Rahnavard G, et al. Strains, functions and dynamics in the expanded human microbiome project. Nature 2017; 550:61–6.

[4] Barlow JT, Leite G, Romano AE, et al. Quantitative sequencing clarifies the role of disruptor taxa, oral microbiota, and strict anaerobes in the human small-intestine microbiome. Microbiome 2021; 9:214.

[5] Seekatz AM, Schnizlein MK, Koenigsknecht MJ, et al. Spatial and temporal analysis of the stomach and small-intestinal microbiota in fasted healthy humans. mSphere 2019;4:e00126–19.

[6] Leite GGS, Weitsman S, Parodi G, et al. Mapping the segmental Microbiomes in the human small bowel in comparison with stool: a REIMAGINE study. Dig Dis Sci 2020; 65:2595–604.

[7] Zoetendal EG, Rajilic-Stojanovic M, de Vos WM. High-Throughput diversity and functionality analysis of the gastrointestinal tract microbiota. Gut 2008; 57:1605–15.

[8] Qin J, Li R, Raes J, et al. A human gut microbial gene Catalogue established by metagenomic sequencing. Nature 2010; 464:59–65.

[9] Rajilić-Stojanović M, de Vos WM. The first 1000 cultured species of the human gastrointestinal microbiota. FEMS Microbiol Rev 2014; 38:996–1047.

[10] Li J, Jia H, Cai X, et al. An integrated catalog of reference genes in the human gut microbiome. Nat Biotechnol 2014; 32:834–41.

[11] van Nood E, Vrieze A, Nieuwdorp M, et al. Duodenal infusion of donor feces for recurrent Clostridium difficile. N Engl J Med 2013; 368:407–15.

[12] Lynch SV, Pedersen O. The human intestinal microbiome in health and disease. N Engl J Med 2016; 375:2369–79.

[13] Fan Y, Pedersen O. Gut microbiota in human metabolic health and disease. Nat Rev Microbiol 2021; 19:55–71.

[14] Hanssen NMJ, de Vos WM, Nieuwdorp M. Fecal microbiota transplantation in human metabolic diseases: from a murky past to a bright future? Cell Metab 2021; 33:1098–110.

[15] Wang R, Tang R, Li B, et al. Gut microbiome, liver immunology, and liver diseases. Cell Mol Immunol 2021; 18:4–17. 16 O'Grady J, Murphy CL, Barry L, et al