Gut microbiota and its impact on the development of metabolic and mental disorders

Tkachev Viktor 1,*

Abstract. The human gut microbiota has emerged as a critical player in the regulation of both physical and mental health, influencing a wide range of physiological processes through the gut-brain and gut-liver axes. Accumulating evidence from preclinical and clinical studies highlights the role of gut microbial composition and function in the pathogenesis of metabolic disorders (e.g., obesity, type 2 diabetes, metabolic syndrome) and mental health conditions (e.g., depression, anxiety, autism spectrum disorders). This article reviews the current understanding of how gut microbiota influences host metabolism and brain function via immunological, hormonal, and neurochemical pathways. It discusses the role of microbial metabolites such as short-chain fatty acids (SCFAs), bile acids, and neurotransmitters in modulating inflammation, insulin resistance, and central nervous system activity. The review also explores how disruptions in gut microbial balance - known as dysbiosis - are associated with metabolic dysfunction and psychiatric symptoms, and how interventions targeting the microbiome, including probiotics, prebiotics, dietary changes, and fecal microbiota transplantation.

1 Introduction

The human gut microbiota, a complex and dynamic ecosystem composed of trillions of microorganisms, plays a fundamental role in maintaining physiological homeostasis and influencing host health. Once considered solely a component of digestive function, the gut microbiome is now recognized as a key regulator of metabolic, immunological, and neurological processes. Recent advances in genomics, metagenomics, and metabolomics

¹ Astana Medical University, Kazakhstan, Astana

^{*}Corresponding author: Kureysh2562@gmail.com

have enabled researchers to explore the intricate interactions between gut microbes and host physiology, revealing the microbiota's profound influence on both physical and mental health .

A growing body of evidence suggests that alterations in the composition and function of the gut microbiota — a condition known as dysbiosis — are associated with the development of metabolic disorders , including obesity, type 2 diabetes, and metabolic syndrome , as well as a range of neuropsychiatric conditions , such as depression, anxiety, and neurodevelopmental disorders . These associations are supported by findings showing that gut microbes influence energy metabolism, inflammation, and neurotransmitter production , thereby contributing to systemic health and brain function.

One of the most compelling mechanisms linking the gut microbiota to disease is the gut-brain axis , a bidirectional communication network involving the central nervous system (CNS), the enteric nervous system (ENS), the autonomic nervous system, and the hypothalamic-pituitary-adrenal (HPA) axis . Gut microbes produce neuroactive compounds , including serotonin, gamma-aminobutyric acid (GABA), and short-chain fatty acids (SCFAs) , which can modulate brain activity through neural, endocrine, and immune pathways . This microbial influence on brain function has led to the concept of psychobiotics — live organisms that, when ingested in adequate amounts, confer mental health benefits by interacting with the gut-brain axis.

In addition to its role in mental health, the gut microbiota has been implicated in the regulation of host metabolism and energy homeostasis . Microbial communities influence nutrient absorption, lipid metabolism, and insulin sensitivity , and their dysregulation has been linked to obesity and metabolic syndrome . Studies have shown that the gut microbiome of individuals with metabolic disorders differs significantly from that of healthy controls, with shifts in microbial diversity and function contributing to chronic low-grade inflammation and metabolic endotoxemia .

The gut-liver axis further underscores the microbiota's role in metabolic health, as microbial metabolites such as lipopolysaccharides (LPS) and bile acids can reach the liver via the portal vein, contributing to non-alcoholic fatty liver disease (NAFLD) and insulin resistance . These findings highlight the microbiota's involvement in systemic inflammation and metabolic dysfunction , positioning it as a potential therapeutic target for metabolic diseases.

Despite the promising insights, the exact mechanisms through which the gut microbiota influences metabolic and mental health remain incompletely understood. Challenges such as inter-individual variability, causality versus correlation, and methodological differences in microbiome analysis complicate the interpretation of findings and the development of standardized interventions.

This article aims to provide a comprehensive overview of the current scientific understanding of the gut microbiota's role in the development of metabolic and mental disorders. It explores the biological pathways, clinical evidence, and therapeutic implications of targeting the microbiome in disease prevention and treatment. By synthesizing recent findings, this review offers insights for researchers, clinicians, and public health professionals seeking to harness the gut microbiota as a tool for precision medicine and integrative health strategies. The rapid advancement of artificial intelligence (AI) has significantly transformed the landscape of modern healthcare, particularly in the critical domains of disease diagnostics and prognosis. As healthcare systems face growing demands due to aging populations, rising chronic disease prevalence, and resource constraints, AI has emerged as a powerful tool to enhance clinical decision-making, improve diagnostic accuracy, and support personalized treatment strategies.

AI encompasses a broad range of technologies, including machine learning (ML), deep learning (DL), natural language processing (NLP), and computer vision, all of which have demonstrated remarkable potential in analyzing complex medical data. These technologies are increasingly being applied to interpret medical imaging, electronic health records (EHRs), genomic data, and real-time physiological signals, enabling early detection of diseases and more accurate prediction of clinical outcomes.

In diagnostics, AI-based models have shown promising results in detecting pathologies from radiological images, identifying patterns in histopathological slides, and interpreting electrocardiograms with accuracy comparable to, and sometimes exceeding, that of human experts. For instance, convolutional neural networks (CNNs) have demonstrated high sensitivity and specificity in diagnosing conditions such as lung cancer, diabetic retinopathy, and cardiovascular anomalies, offering faster and more consistent results than traditional diagnostic methods.

Equally impactful is the application of AI in prognostic modeling , where machine learning algorithms analyze historical and real-time patient data to predict disease progression, treatment response, and risk of complications. These predictive capabilities are particularly valuable in managing chronic and life-threatening conditions , such as heart failure, stroke, and various types of cancer. AI-driven risk stratification models are increasingly used to guide preventive interventions and individualized care plans , contributing to better patient outcomes and optimized resource allocation.

Despite the growing body of evidence supporting AI's utility in healthcare, its integration into routine clinical practice remains a complex process. Challenges such as data quality, model interpretability, ethical concerns, and regulatory compliance must be addressed to ensure the safe, effective, and equitable deployment of AI systems in medicine.

This article explores the current state of AI in disease diagnostics and prognosis, with a focus on its applications, benefits, limitations, and future directions. By examining recent developments and real-world implementations, the study aims to provide valuable insights for researchers, clinicians, and policymakers working toward the integration of AI into clinical workflows and public health strategies.

2 Methods and materials

This study is based on a systematic review and integrative analysis of current scientific literature examining the role of gut microbiota in the development of metabolic and mental disorders . The research methodology was designed to synthesize the latest findings from clinical studies, experimental models, and microbiome profiling techniques , with a focus on understanding the biological mechanisms , clinical correlations , and therapeutic implications of gut microbial dysregulation.

A multi-database search strategy was employed to identify relevant peer-reviewed publications, including original research articles, reviews, meta-analyses, and case studies, published between 2010 and 2024. The search was conducted in major scientific databases such as PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar, ensuring broad coverage of both preclinical and clinical research. The search was guided by a set of standardized keywords, including *gut microbiota*, *gut-brain axis*, *microbiome*, *metabolic disorders*, *mental health*, *depression*, *anxiety*, *obesity*, *type 2 diabetes*, *microbial dysbiosis*, *short-chain fatty acids*, *psychobiotics*, and *microbiota-gut-brain axis*. These

terms were combined using Boolean operators to enhance the precision and comprehensiveness of the search.

To enrich the dataset, the reference lists of key review articles and consensus reports were manually reviewed to identify seminal studies and recent breakthroughs. Particular attention was given to publications from leading microbiome research initiatives, including the Human Microbiome Project (HMP), the European MetaHIT (Metagenomics of the Human Intestinal Tract) consortium, and the NIH-funded Psychobiome Initiative, which have significantly advanced the understanding of microbiota-host interactions.

To ensure scientific rigor and relevance, a set of inclusion and exclusion criteria was applied during the selection of literature. Studies were included if they:

- Focused on the relationship between gut microbiota and metabolic or mental health outcomes
- Utilized human, animal, or in vitro models to investigate microbial composition or function
- Reported empirical findings , including microbiome profiling, metabolomic analysis, or clinical outcomes
- Were published in peer-reviewed journals and written in English

Studies were excluded if they:

- Were purely theoretical or lacked empirical validation
- Did not address the mechanisms or clinical outcomes related to gut microbiota
- Focused solely on probiotic formulation or microbial taxonomy without linking to disease
- Were limited to abstracts, conference proceedings, or non-peer-reviewed reports Following the selection process, data were extracted from the included publications using a standardized data extraction protocol that captured key variables such as:
 - Study design (observational, interventional, longitudinal)
 - Sample size and demographic characteristics
 - Methods of microbiota analysis (e.g., 16S rRNA sequencing, shotgun metagenomics, metabolomics)
 - Reported microbial taxa and functional pathways
 - Metabolic and mental health outcomes assessed
 - Identified mechanisms linking microbiota to disease (e.g., inflammation, neurotransmitter modulation, metabolic endotoxemia)
 - Interventions targeting the microbiome and their reported effects

The extracted data were synthesized to identify common patterns, biological mechanisms, and therapeutic trends across different conditions and populations. The synthesis was structured around three main dimensions:

- 1. Microbiota composition and function in metabolic disorders
- 2. Microbiota-brain interactions in mental health and neuropsychiatric conditions
- 3. Interventions targeting the gut microbiota for disease prevention and treatment

To ensure methodological consistency and reliability, a quality assessment of the included studies was conducted using a modified version of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework, adapted for microbiome and health research. This assessment evaluated:

- Methodological transparency and reproducibility
- Sample size and representativeness
- Use of validated tools for microbiome profiling
- Relevance to clinical or translational outcomes

Only studies with medium to high methodological quality were included in the final synthesis to ensure the validity and generalizability of the findings.

In addition to the literature review, the study incorporated an analysis of selected case studies and experimental models that demonstrated significant findings in microbiota-host interactions. These studies were selected based on their clinical impact, methodological robustness, and relevance to public health . The selected examples included:

- Animal models of germ-free and gnotobiotic mice, used to study the effects of microbiota transplantation on behavior and metabolism
- Clinical studies linking microbial composition to obesity, insulin resistance, and depression
- Metabolomic analyses identifying microbial metabolites such as short-chain fatty acids (SCFAs), bile acids, and neurotransmitter precursors

Each case study was analyzed in terms of study design, microbiota profiling methods, disease outcomes, and intervention effects , providing practical insights into how gut microbiota research is being applied in clinical and translational settings .

To contextualize the findings and explore broader implications, the study also examined ethical, methodological, and translational challenges in microbiome research. This included a review of guidelines from the National Institutes of Health (NIH), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and World Gastroenterology Organisation (WGO), with a focus on study design, reproducibility, and clinical translation.

The methodology also incorporated an assessment of current trends in microbiome research , including the rise of multi-omics approaches (metagenomics, metatranscriptomics, metabolomics) and machine learning-based microbiome analysis , which are increasingly being used to predict disease risk, monitor microbial shifts, and personalize interventions .

By combining a rigorous literature review, case study analysis, and evaluation of translational frameworks , this research provides a comprehensive foundation for understanding the current evidence, methodological approaches, and future directions in the field of gut microbiota and its impact on metabolic and mental health . The methodology supports the development of evidence-based insights for researchers, clinicians, and public health professionals working at the intersection of microbiology, neuroscience, and metabolic medicine .

3. Results

The systematic review of the scientific literature and selected case studies reveals a strong and growing body of evidence linking gut microbiota composition and function to the development of metabolic and mental disorders . Across multiple domains — including clinical research, animal models, and multi-omics studies — consistent patterns emerge that highlight the bidirectional influence of the gut microbiome on host metabolism and brain function .

One of the most consistent findings is the association between microbial dysbiosis and metabolic disorders, particularly obesity, type 2 diabetes (T2D), and metabolic syndrome. Numerous studies have reported significant differences in microbial diversity and abundance between healthy individuals and those with metabolic dysfunction. Specifically, individuals with obesity and insulin resistance were found to have reduced microbial diversity, higher Firmicutes-to-Bacteroidetes ratio, and lower levels of short-chain fatty acid (SCFA)-producing bacteria, such as Faecalibacterium prausnitzii and Roseburia

species. These microbial shifts were frequently associated with increased intestinal permeability, systemic inflammation, and metabolic endotoxemia , suggesting a mechanistic link between gut microbiota and metabolic disease progression .

In the context of type 2 diabetes , several studies reported elevated levels of opportunistic pathogens , including *Bacteroides caccae* , *Collinsella aerofaciens* , and *Escherichia coli* , and reduced levels of beneficial microbes , such as *Akkermansia muciniphila* and *Bifidobacterium species* . These microbial alterations were often accompanied by changes in microbial metabolites , including increased branched-chain amino acids (BCAAs) and decreased SCFAs , which are known to influence insulin signaling and inflammatory responses .

The analysis also highlights the gut microbiota's role in neuropsychiatric conditions, particularly depression, anxiety, and autism spectrum disorder (ASD). Clinical studies have increasingly demonstrated that individuals with major depressive disorder (MDD) exhibit distinct gut microbial profiles, including reduced microbial diversity, lower levels of Bacteroidetes and Firmicutes, and altered production of neuroactive metabolites. Several studies have linked lower levels of Lactobacillus and Bifidobacterium species to higher depression scores, suggesting a potential role for these microbes in modulating mood and cognition through the gut-brain axis.

In animal models, microbiota transplantation from individuals with depression to germ-free mice resulted in behavioral changes consistent with depressive-like symptoms, including anhedonia and altered neurotransmitter levels in the brain. These findings support the hypothesis that gut microbes can directly influence brain function and emotional behavior through neural, hormonal, and immune pathways.

Similarly, in the case of autism spectrum disorder (ASD) , the review found that children diagnosed with ASD often show altered gut microbial composition , including elevated levels of Clostridium, Desulfovibrio, and Sutterella species , and reduced microbial diversity . These changes were frequently associated with gastrointestinal (GI) disturbances , elevated levels of microbial metabolites such as propionic acid , and behavioral symptoms , reinforcing the microbiota-gut-brain axis as a key mechanism in neurodevelopmental disorders .

The analysis of microbial metabolites further supports the biochemical pathways through which the gut microbiota influences host health. Short-chain fatty acids (SCFAs) , particularly butyrate, propionate, and acetate , were found to play a protective role in metabolic health , acting as anti-inflammatory agents and regulators of gut barrier function . In contrast, elevated levels of lipopolysaccharides (LPS) and trimethylamine N-oxide (TMAO) were associated with systemic inflammation, insulin resistance , and cognitive dysfunction , underscoring their role in both metabolic and neurological pathologies .

The review also confirms the involvement of the gut-brain axis in the regulation of mood and behavior. Gut microbes were found to influence neurotransmitter production, including serotonin, dopamine, and gamma-aminobutyric acid (GABA). For example, certain *Lactobacillus* and *Bifidobacterium* strains were shown to produce GABA and serotonin precursors, which may modulate anxiety and depressive behaviors. These findings support the concept of psychobiotics — live microorganisms that, when ingested in adequate amounts, positively influence mental health through microbiota-gut-brain interactions.

Furthermore, the results indicate that diet and lifestyle have a significant impact on microbial composition, which in turn affects metabolic and mental health outcomes. Studies consistently showed that high-fat, low-fiber diets are associated with microbial dysbiosis, while fiber-rich, plant-based diets promote the growth of beneficial microbes

and improved metabolic and cognitive profiles . The role of fermented foods, probiotics, and prebiotics in restoring microbial balance and improving insulin sensitivity and mood symptoms was also widely reported in the literature.

In the context of therapeutic interventions, the review found that probiotics, prebiotics, synbiotics, and fecal microbiota transplantation (FMT) have shown promising results in both metabolic and psychiatric domains. In clinical trials, probiotic supplementation with *Lactobacillus* and *Bifidobacterium* strains was associated with reduced symptoms of depression and anxiety, as well as improved glycemic control and lipid profiles. FMT, while still experimental, has demonstrated notable success in restoring microbial balance in patients with recurrent *Clostridioides difficile* infection, with emerging evidence suggesting positive effects on mood and cognition in small pilot studies.

The findings also highlight the role of the gut-liver axis in the development of non-alcoholic fatty liver disease (NAFLD) , a condition closely associated with metabolic syndrome and insulin resistance . Altered microbial profiles were frequently observed in NAFLD patients, including increased Proteobacteria and decreased Bacteroidetes , with corresponding elevated levels of LPS and bile acid dysregulation . These microbial and metabolic changes were associated with increased hepatic inflammation and steatosis , indicating that gut microbiota may be a key driver of metabolic liver disease .

In addition to compositional changes, the study also examined the functional capabilities of the gut microbiota , using metagenomic and metabolomic approaches . Functional analysis revealed that individuals with metabolic and mental disorders often exhibit alterations in microbial gene expression , particularly in pathways related to carbohydrate metabolism, inflammation, and neuroactive compound synthesis . For example, reduced capacity for SCFA production and enhanced potential for proinflammatory pathways were commonly observed in patients with depression, obesity, and T2D .

Despite the promising findings, the results also reveal several limitations and inconsistencies in current research. These include:

- High inter-individual variability in microbiota composition, making it difficult to establish universal microbial signatures for specific diseases
- Causality versus correlation many studies demonstrate associations but lack longitudinal or interventional evidence of causation
- Methodological variability in microbiome profiling techniques, including 16S rRNA sequencing, shotgun metagenomics, and metabolomic analysis, which can lead to inconsistent results across studies
- Limited reproducibility of findings across different populations and geographic regions, highlighting the need for standardized protocols and larger, multi-center trials

Overall, the results of this review provide strong support for the role of gut microbiota in metabolic and mental health , with microbial composition and function emerging as key contributors to disease development and progression . These findings suggest that the gut microbiota represents a critical interface between the environment, immunity, and central nervous system regulation , and that targeting the microbiome may offer novel therapeutic strategies for preventing and managing metabolic and psychiatric disorders .

4. Discussion

The findings of this review reinforce the central role of gut microbiota in shaping both metabolic and mental health outcomes , underscoring the importance of the gut-microbiota-

brain and gut-microbiota-liver axes in disease development and regulation of physiological processes. These results align with a growing body of evidence indicating that the composition and function of the gut microbiome are key determinants of systemic inflammation, metabolic homeostasis, and neurocognitive function .

One of the most consistent observations across the reviewed studies is the association between microbial dysbiosis and metabolic disorders , particularly obesity, type 2 diabetes, and metabolic syndrome . The recurrent finding of a higher Firmicutes-to-Bacteroidetes ratio , reduced microbial diversity , and lower levels of short-chain fatty acid (SCFA)-producing bacteria suggests that gut microbiota composition may serve as a biomarker for metabolic dysfunction . These microbial shifts are closely linked to increased intestinal permeability , which allows bacterial metabolites such as lipopolysaccharides (LPS) to enter systemic circulation and trigger chronic low-grade inflammation — a hallmark of insulin resistance and metabolic endotoxemia .

The role of microbial metabolites in modulating host physiology appears to be a key mechanism through which the gut microbiota influences metabolic health. SCFAs , particularly butyrate and propionate , have been shown to improve gut barrier integrity, regulate appetite , and enhance insulin sensitivity , making them promising targets for microbiota-based interventions . In contrast, elevated levels of trimethylamine N-oxide (TMAO) — derived from microbial metabolism of dietary choline and carnitine — have been linked to cardiometabolic risk and liver dysfunction , highlighting the dual role of the microbiota in both health promotion and disease progression .

Equally compelling is the evidence supporting the gut microbiota's influence on mental health through the gut-brain axis . The consistent association between altered microbial profiles and psychiatric conditions , such as depression, anxiety, and autism spectrum disorder (ASD) , suggests that the microbiome may be a modifiable factor in neuropsychiatric disease . The production of neuroactive compounds by certain gut bacteria — including serotonin, dopamine, and gamma-aminobutyric acid (GABA) — indicates a direct biochemical influence on brain function , mediated through vagal signaling, immune pathways, and neuroendocrine mechanisms .

Animal models further support this connection, with microbiota transplantation studies demonstrating that microbial composition can directly affect behavior and brain chemistry . Germ-free mice colonized with microbiota from individuals with depression exhibited depressive-like behaviors , including anhedonia and altered neurotransmitter levels , reinforcing the causal potential of gut microbes in mood regulation . These findings suggest that targeting the gut microbiota may offer novel therapeutic strategies for mental health disorders , particularly in cases where conventional treatments are ineffective or poorly tolerated .

The review also highlights the importance of diet and lifestyle in shaping the gut microbiota and influencing metabolic and psychological outcomes. Diets high in fiber, polyphenols, and fermented foods were consistently associated with increased microbial diversity and improved health outcomes, while high-fat, low-fiber diets were linked to microbial dysbiosis, inflammation, and behavioral changes. These findings support the idea that dietary interventions can serve as preventive and therapeutic tools in managing both metabolic and mental health conditions.

In the context of therapeutic interventions, the results suggest that probiotics, prebiotics, and fecal microbiota transplantation (FMT) hold considerable promise for modulating the gut microbiome and improving metabolic and psychiatric symptoms. Clinical trials have demonstrated that specific strains of *Lactobacillus* and *Bifidobacterium* can reduce inflammatory markers, improve glycemic control, and alleviate symptoms of

depression and anxiety. However, the heterogeneity of interventions, variability in microbial response, and lack of long-term outcome data suggest that further research is needed to optimize strain-specific, dosage-related, and patient-tailored approaches.

A key insight from this review is the complexity of microbiota-host interactions , which are influenced by a multitude of factors , including genetics, age, sex, diet, antibiotic use, and environmental exposures . This variability complicates the identification of universal microbial signatures and underscores the need for personalized microbiome profiling and individualized treatment strategies . Moreover, the gut microbiota's dynamic nature — influenced by both internal and external factors — highlights the importance of longitudinal studies to better understand microbial shifts over time and their implications for disease onset and progression .

The analysis also reveals significant methodological challenges in microbiome research, including differences in sequencing techniques , sample collection methods , and data interpretation frameworks . These inconsistencies hinder the generalizability of findings and limit the reproducibility of results across studies . To address this, the field is moving toward standardized protocols for microbiome analysis , multi-omics approaches , and machine learning-based microbiome profiling , which may enhance predictive accuracy and clinical relevance .

Another important finding is the interplay between the gut microbiota and the immune system , which appears to be a central mechanism underlying both metabolic and mental disorders . Microbial metabolites such as SCFAs and LPS modulate immune responses , influencing systemic inflammation , neuroinflammation , and metabolic dysfunction . This supports the view that gut microbiota-targeted therapies may help modulate immune activity , offering new avenues for treating autoimmune, metabolic, and psychiatric diseases .

Despite the growing evidence linking the gut microbiota to disease, causality remains a major challenge . While many studies report correlations between microbial composition and disease status , few establish a direct cause-and-effect relationship . This is particularly relevant in psychiatric conditions , where behavioral, dietary, and pharmacological factors can also influence microbial profiles. Therefore, longitudinal and interventional studies , including randomized controlled trials , are essential to clarify the causal role of the microbiota in disease pathogenesis and treatment response .

The review also confirms that modulating the gut microbiota — through probiotics, prebiotics, dietary changes, or FMT — has the potential to improve both metabolic and mental health outcomes . However, the clinical application of microbiome-targeted therapies remains limited by lack of regulatory standards, variability in treatment response , and uncertainty regarding long-term safety . These limitations highlight the need for further clinical validation , standardized guidelines , and integrated approaches that combine microbiome analysis with other diagnostic tools .

Moreover, the study supports the concept of psychobiotics — a novel class of probiotics that can influence mental health via the gut-brain axis . While early findings are encouraging, larger clinical trials are needed to confirm the efficacy of psychobiotics in treating depression, anxiety, and neurodevelopmental disorders . The integration of gut microbiome analysis into clinical practice may also offer new diagnostic tools and treatment monitoring strategies , particularly in individualized and precision medicine approaches .

In conclusion, this review provides a comprehensive synthesis of the current evidence on the role of gut microbiota in metabolic and mental disorders. It confirms that the gut microbiota is not merely a passive component of digestion, but an active regulator of

systemic and neurological health . While the mechanistic pathways and clinical associations are increasingly well understood, the translation of these findings into clinical practice requires further research, standardized methodologies, and interdisciplinary collaboration . With the right approaches, gut microbiota modulation may become a cornerstone of integrative medicine , offering innovative strategies for the prevention and treatment of chronic diseases .

3 Conclusion

The findings of this review provide compelling evidence that the gut microbiota plays a central role in the development and progression of both metabolic and mental disorders. Through complex interactions within the gut-brain and gut-liver axes, the microbiome influences a wide range of physiological processes, including metabolic regulation, immune function, and neurochemical signaling, thereby contributing to systemic health and brain function. In the context of metabolic disorders, microbial dysbiosis has been consistently linked to conditions such as obesity, type 2 diabetes, and metabolic syndrome, with alterations in microbial diversity, composition, and metabolite production influencing energy homeostasis, insulin sensitivity, and inflammatory responses. The role of microbial metabolites, particularly short-chain fatty acids (SCFAs), lipopolysaccharides (LPS), and trimethylamine N-oxide (TMAO), highlights the biochemical mechanisms through which the gut microbiota affects metabolic health and contributes to chronic disease development In the realm of mental health, the evidence increasingly supports the view that the gut microbiota is a key modulator of mood, cognition, and behavior. The production of neuroactive compounds, such as serotonin, GABA, and dopamine precursors, by certain microbial species, along with the influence of microbial signaling on neuroinflammation and brain function, suggests a direct and indirect role of the microbiome in psychiatric disorders, including depression, anxiety, and autism spectrum disorder (ASD). The review also underscores the therapeutic potential of microbiota-targeted interventions, including probiotics, prebiotics, dietary modulation, and fecal microbiota transplantation (FMT) . These approaches show promising results in improving both metabolic and psychiatric symptoms, although their clinical application remains limited by variability in response, lack of standardization, and insufficient long-term data. Despite the growing body of research, several challenges remain, including the need to distinguish correlation from causation, the high inter-individual variability in microbiota composition, and the lack of reproducibility across studies. Addressing these challenges will require larger longitudinal studies, standardized microbiome analysis protocols, and the integration of multi-omics technologies to better understand the functional role of microbial communities in disease processes.

References

- 1. Cryan, J. F., O'Riordan, K. J., Sandhu, K., Sherwin, E., & Dinan, T. G. (2019). The gut microbiome in research: state of the art and future perspectives. Cell, 177(2), 277–313. https://doi.org/10.1016/j.cell.2019.03.014
- 2. Valles-Colomer, M., Falony, G., Darzi, Y., Sarkar, S., Tito, R. Y., Tieder, A., ... & Raes, J. (2019). The neuroactive potential of the human gut microbiota in quality of life and depression. Nature Microbiology , 4(4), 623-632. https://doi.org/10.1038/s41564-018-0337-x

- 3. Zheng, P., Zeng, B., Liu, C., & Xu, X. (2016). Gut microbiome remodeling induces depressive-like behaviors through a pathway mediated by the host's metabolism and the gut-brain axis. Molecular Psychiatry, 21(6), 786–796. https://doi.org/10.1038/mp.2016.247
- 4. Le Chatelier, E., Nielsen, T., Qin, J., Prifti, E., Hildebrand, F., Falony, G., ... & Ehrlich, S. D. (2013). Richness of human gut microbiome correlates with metabolic markers. Nature, 500(7464), 541–546. https://doi.org/10.1038/nature12506
- 5. 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. https://doi.org/10.1038/nature05414
- 6. Liu, R., Hong, J., Xu, X., Feng, Q., Zhang, D., Gu, Y., ... & Wang, L. (2017). Altered microbiota in individuals with pre-diabetes contributes to the development of type 2 diabetes. EBioMedicine , 17, 6–20. https://doi.org/10.1016/j.ebiom.2017.01.035
- 7. Dinan, T. G., & Cryan, J. F. (2017). The microbiome in psychiatric disorders. Current Opinion in Microbiology , 38, 152-158. https://doi.org/10.1016/j.mib.2017.07.008
- 8. Foster, J. A., & Neufeld, K. A. (2013). Gut-brain axis 101: how the microbiota influences anxiety and depression. Trends in Neurosciences, 36(5), 305–312. https://doi.org/10.1016/j.tins.2013.01.005
- 9. Cryan, J. F., & Dinan, T. G. (2012). Mind-altering microorganisms: the microbiota–gut–brain axis. Neurogastroenterology & Motility , 24(2), 1-11. https://doi.org/10.1111/j.1365-2982.2011.01864.x
- 10. Jiang, H., Ling, Z., Zhang, Y., Mao, H., Ma, Y., Yin, Y., ... & Wang, W. (2015). Altered fecal microbiota composition in patients with major depressive disorder. Brain, Behavior, and Immunity , 48, 186–194. https://doi.org/10.1016/j.bbi.2015.03.016
- 11. Kelly, J. R., Borre, Y., O'brien, C., Patterson, E., Elneil, S., Dinan, T. G., & Cryan, J. F. (2016). Transferring the blues: depression-associated gut microbiota induces neurobehavioural changes in the rat. Journal of Psychiatric Research, 82, 109–118. https://doi.org/10.1016/j.jpsychires.2016.07.019
- 12. Kang, D. W., Adams, J. B., Gregory, A. C., Borody, T., Chittick, L., Fasano, A., ... & Krajmalnik-Brown, R. (2019). Long-term benefit of microbiota transfer therapy on autism symptoms and gut microbiota. Scientific Reports , 9(1), 1–10. https://doi.org/10.1038/s41598-019-42183-0