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The Gut-Brain Axis: A Physiological Review

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Abstract

The Greek physician Hippocrates held the view that the digestive tract is the origin of all illness. We now know that important physiological and homeostatic processes are regulated by bidirectional gut-brain (GB) interactions, thanks to modern research into gut-brain interactions. There is evidence that gastrointestinal dysfunction and persistent stomach pain may be caused by changes in GB interactions. As research into the microbiome has progressed rapidly, the conventional wisdom about the gut-brain-microbiome (GBM) axis has given way to a more systems-based perspective. Psychiatric and neurological diseases, chronic pain, and brain-gut issues are all linked to shifts in these connections, according to research. Although there is limited evidence linking the BGM axis to specific health outcomes, it is an exciting new therapeutic target due to its involvement in both basic and disease-prone processes. The gut is home to the vast majority of the trillions of microorganisms that make up the human microbiota, which plays a pivotal role in determining human well-being. Yeasts, archaea, parasites, viruses, and protozoa are just a few of the many microbes that call the digestive tract home. Metabolic equilibrium relies on the gut-brain axis, a two-way signaling mechanism for hormones and neurons. A person's caloric intake, metabolic rate, and blood sugar levels are all controlled by the gut-brain axis. This negative feedback is complex on a physiological and neurological level, and new studies have cast doubt on vagal signaling mediated by gastrointestinal peptides. In addition to being an important regulator of host physiology, the gut microbiome is crucial in regulating brain function and metabolic balance. The neuro-immunoendocrine system is thought to rely heavily on short-chain fatty acids (SCFAs). Mood, cognition, and mental health are all affected by the gut-brain axis. Functional gastrointestinal disturbances and alterations to the gut flora are associated with psychiatric illnesses. Psychiatric symptoms and bacterial infections can be helped by taking probiotic and prebiotic supplements. Microbiome-based medicines, like probiotics and prebiotics, can be used to treat neurodegenerative illnesses. Prebiotics encourage the development of good bacteria, whereas probiotics boost the creation of health-promoting compounds and microbiome pathways. One approach to modulating the gut microbiota is fecal microbiota transplantation (FMT), which is both extensive and mostly untargeted. Intestinal pH, inflammation, and harmful bacteria can all be diminished with the use of probiotics, which can also restore a healthy microbiota.

Keywords: Gut-brain Axis, Diet interactions, Microbiome, CNS.

Introduction

All disease begins in the gut"-Hippocrates of Kos, sometimes known as Hippocrates of the Kos: date. (around 460–370 BCE). The Greek physician Hippocrates, often regarded as the founder of modern medicine, supposedly made this declaration more than two millennia ago. Regardless of the veracity of its attribution to Hippocrates, the wisdom contained within it has and will continue to have an impact on medical scholars and practitioners. The connections between rural Michigan and classical Greece may not be immediately apparent, yet it was in the 1800s that an Inspired by the teachings of Hippocrates and the other great Greek physician-philosopher, Galen of Pergamon (1001) [1], the tragic accident suffered by Canadian fur-trader Alexis St. Martin provided a favorable chance to further research into the digestive system and the intestines.

"What are gut-brain interactions?" is the new question that has emerged.

The management of the immune system, the regulation of food intake, and sleep are all important homeostatic processes that are influenced by the bidirectional gut-brain (GB)

interactions. A shift in terminology from functional gastrointestinal disorders to disorders of altered GB interactions has only just been acknowledged by major professional societies, despite the long-standing hypothesis that alterations of GB interactions are central to chronic abdominal pain symptoms and gastrointestinal (GI) dysfunction. There has been a lot of progress in understanding the pathophysiology of GB disorders like functional dyspepsia and irritable bowel syndrome (IBS) over the past decade. However, there is still disagreement about which mechanisms—the brain or the gut—are more responsible for symptom generation in these diseases and other, often comorbid syndromes like functional chest pain and functional abdominal pain. On the other hand, there is a growing consensus that chronic abdominal pain is caused by a dysregulation of the interaction among signaling events in the gut, enteric microbiota, enteric nervous system (ENS), and central nervous system (CNS).

Mood, immunological function, visceral sensitivity, and alterations in gut motility and regional transit are all linked to this imbalance.

In the past fifteen years, research on the microbiome has progressed at a rapid pace, and with it, our understanding of the traditional gut-brain-microbiome (GBM) axis. This new perspective emphasizes the bidirectional interplay between the brain and the gut, including the gut-associated immune system, the enteric neuroendocrine system, the ENS, and the gut microbiome. [2]

A number of recent preclinical investigations have provided significant evidence in favor of the idea of BGM interactions, which stand for brain-gut-microbiome interactions that go both ways. A wide variety of mental and neurological diseases, such as irritable bowel syndrome (IBS), multiple sclerosis, affective disorders, autism spectrum disorders (ASD), Parkinson's disease, and a host of functional gastrointestinal disorders, have been linked to changes in these interactionspersistent discomfort. Evidence for a causal relationship is lacking, despite the fact that the majority of the literature links the makeup of the gut microbiota to human health, development, and illness. The interaction between the BGM axis and basic and disease-prone functions, making it an innovative therapeutic target, however, there is still a lack of understanding about this network that prevents intervention. Here we discuss the most recent findings that point to both bottom-up and top-down signaling along the BGM axis. and the growing body of data linking it to illnesses in humans [3].

Background

A Historical Perspective on the Digestive-Brain Axis during 19th century

When it came to patient care in the nineteenth century, doctors started looking at the patient as a whole, not just their organs. The gastrointestinal system, though, was their primary focus. Evoking happy feelings, they hypothesized, was the job of nerve endings. Conversely, they may experience bad emotions as a result of dietary blunders, such as consuming alcohol or unhealthy food. According to Royal physician James Johnson's 1827 writing, "strange antipathies, disgusts, caprices of temper, and eccentricities, which are considered solely as obliquities of the intellect, have their source in corporeal disorder." This is why they believed this.

Two Centuries: 1950s and 2000s

At the turn of the twentieth century, researchers began to focus more on the stomach from an anatomical or surgical perspective, in contrast to the 19th century's holistic approach to gastrointestinal study. British doctor Peter Down proposed a mental disorder diagnosis for anyone with gastrointestinal problems that could not be explained by any physical reason. All functional impairments would thereafter be categorized as primarily caused by psychological discomfort. The widespread availability of enemas and herbal cures for constipation, as well as the widespread belief in diet gurus like John Harvey Kellogg, helped to debunk the autointoxication theory in the twentieth century. [4]

Diversity of Microbes: Friends with Benefits

Our environment is filled with microbes. In contrast to humans, bacteria have been around for a lot longer—hundreds of millions of years—and our bodies have always been susceptible to signals transmitted by germs. All the trillions of microbes that inhabit our bodies are collectively known as the human microbiota (1532). Rapid advancements in understanding the microbiome over the last two decades have shed light on the many ways in which these tiny organisms influence our everyday lives. It has recently become clear that the microbiota plays a pivotal role in regulating host physiology and in determining human health and illness. The sheer magnitude of the microbiota is staggering when expressed in numerical terms.[1]
An individual's microbiome is unique to their specific bodily niche. To be sure, microbes mostly colonise humans' skin, airways, urogenital tract, eyes, and gastrointestinal tract. The majority of our microbes live in our gut, however other locations like the oral (795) and pulmonary (939) microbiota are also essential. Although the bacterial population is now the most thoroughly studied, the gut is home to a wide variety of microbes, including yeasts, archaea, parasites (including helminths), viruses, and protozoa.

At least 2,776 different types of prokaryotic organisms have been found in human faces, according to recent data from the Human Microbiome Project and MetaHIT. The microbiome is composed of eleven distinct phyla; the majority, 90%, is made up of Proteobacteria, Firmicutes, Actinobacteria, and Bacteroidetes, with only a small percentage coming from Fusobacteria and Verrucomicrobia. Although this technique of categorization is three separate enterotypes have been postulated, each defined by relatively high amounts of one microbial genus: Bactericides, Prevotella, or Ruminococcus. This classification is both oversimplified and contentious. With the Bacteroides enterotype linked to high-fat or high-protein diets and the Prevotella enterotype being related with low-fat or low-protein diets, it appears that these enterotypes do have some functional significance,high-carbohydrate diets and enterotypes.[1]

Review

The GUT-BRAIN-AXIS's metabolic role in the metabolism of glucose and energy

Obesity and type 2 diabetes (T2D) are on the rise globally because people are leading more sedentary lives and eating more sugary and fatty food. This is mostly caused by the Western way of life. Nearly 75% of American individuals are categorized as
43% of the population is overweight, and that number has virtually tripled in the last 40 years. Similarly, diabetes has more than quadrupled in the previous 40 years, with a global prevalence of 9.3% in 2019. Diabetes has the same death rate, comorbidity rates, and health care costs as obesity.

There are few effective treatment options for metabolic illnesses, despite the critical need for their prevention and amelioration. To that end, the gastrointestinal tract (GI) is also the target of some of the most exciting pharmaceutical treatments. For instance, the signaling systems originating in the gut are the source of the glucagon-like peptide-1 (GLP-1) agonists and di peptidyl peptidase-4 inhibitors utilized to treat type 2 diabetes. Research has shown that metabolic illness therapy that focusses on the gastrointestinal system (GI tract) can have an effect on metabolic homeostasis and the efficacy of other treatments, including gastric bypass surgery and metformin.

In their entirety, these findings shed information on the GI tract's role as a therapeutic target and its function in the maintenance of metabolic disorders.An intricate network of neuronal and hormonal signals that extends from the digestive tract to the central nervous system is known as the gut-brain axis. The control of metabolic homeostasis is a brain-gut process that is mediated by several pathways. Traditionally, when nutrients enter the digestive tract during a meal, signals are transmitted to the brain via the gut, which inform the central nervous system (CNS) about the amount and type of food consumed. In order to regulate food intake, the brain, namely the hypothalamus, takes in signals from the gut and other sourcesspending energy and maintaining a steady blood sugar level. Postprandial gut feedback is mediated by enteroendocrine cells (EECs), which are specialized neuroendocrine cells of the intestinal epithelium. EECs perceive the luminal environment and secrete gut peptides including cholecystokinin and GLP-1, which impact metabolic homeostasis.

Both paracrine and endocrine effects of nutrient-induced gut peptides on the brain and other peripheral organs involved in metabolic homeostasis have been described. Paracrine effects entail the activation of vagal neurons, which innervate tissue close to the intestinal epithelium and transmit signals to the brain. New research challenges the gut peptide-mediated vagal signaling and emphasizes the physiological and neurological complexity of the postprandial gut-brain signaling in energy and glucose homeostasis, despite the well-established importance of this signaling in these processes.

An outline of what is now known about how sensory information from the gastrointestinal tract is processed was asserted by **Richards P et al. in 2021.** system is transmitted to the brain via the central nervous system, particularly to the circuits that control metabolism and nutrition. They go into detail on how new tech is helping us comprehend this system at the molecular level, which is shedding light on gut-brain communication in ways we never imagined. We also go over some of the existing treatments for diabetes, obesity, and associated conditions that take use of the gut-brain axis, and we detail some of the new possibilities made possible by recent research.

Important findings: the gut-brain axis is critical for appetite regulation and glucose homeostasis, and this system is essential for mediating the effectiveness of treatments that have significantly improved the treatment of type 2 diabetes and obesity. New technologies are allowing a greater understanding of how signals from these components are organized to govern metabolism, which is a departure from the traditional focus on investigating individual components in gut-brain axis research. New insights are already being used to explore fundamentally new approaches to treating metabolic diseases[6], even if this work exposes an even greater complexity of signaling than previously realized.

Immune systems for communication between gut microbiota and the brain

Gut homeostasis—the delicate balancing act between commensal microbes' homeostatic tolerance and the simultaneous safeguarding the body against harmful microbial infiltration. Furthermore, immunity is also essential for relaying messages from the ENS to the brain, the gut microbiota, and the gut. peptidoglycans and toll-like receptors (TLRs) (PGNs) play a key role in the immune response to microorganisms by sensing certain components of bacteria. The development of systemic immune activation and the improper activation of immune cells are both prevented by an intact intestinal barrier.

Bacteria can enter the brain through the blood when they emit immune agonists such lipopolysaccharide and PGN. TLRs have been discovered in the microglia of disease-model mice brains; their role in the onset of Alzheimer's disease, Parkinson's disease, visceral pain, and depression has been investigated. It appears that gene expression in the brain is susceptible to alteration of the microbiota, since both GF and antibiotic-treated animals show a decrease in the expression of many PGN receptors in the striatum. Loss of peptidoglycan sensing ability leads to host behavioral changes, as demonstrated by an increase in sociability in mice following suppression of a PGN-sensing receptor, PGN-recognition protein 2. However, further investigation is required to understand the long-term effects of immunological signaling in both health and illness.

When the mucus layer in the gut becomes damaged due to dietary changes, luminal microorganisms are able to access the extensions of dendritic cells. This opens the door for both commensals and pathogens to activate these cells. As a result of local immunological activation, the intestinal barrier can be further compromised due to increased permeability of the epithelial tight junctions. Some types of depression and neurodegenerative diseases may have their roots in metabolic endotoxemia, a condition in which immune mediators released into the systemic circulation as a result of dietary changes activate the immune system in various organs, including the brain.diseases, including dementias and PD. [7]

Some issues might arise from an imbalance, often known as dysbiosis.

According to a 2016 analysis by Rogers GB et al., the human body is home to a vast variety of microorganisms that carry out many important and helpful jobs. In recent years, our understanding of how these microbial communities impact various parts of human physiology has significantly expanded. An increasing number of diseases are linked to disruptions in the commensal microbiota in humans, and we know that animals raised in germ-free environments show significantly different immunological and metabolic functions. Recent evidence suggests that changes in behavior can alter the composition of gut microbiota, and that modifications to the microbiome can induce depressive-like behaviors. This suggests that the gut microbiome can influence neural development, cognition, and behavior through interactions with the gut-brain axis, a bidirectional communication system between the central nervous system and the gastrointestinal tract. Although there has long been acknowledgement of a link between enteropathy and specific mental disorders, it now seems that microorganisms in the gut affect psychopathology directly. In this article, we take a look at the gut microbiome and how it affects neurological function, brain development, and mental illness. We go on to talk about how this intriguing new area of study can teach us about the microbiota and how that knowledge can guide the development of new treatments.

According to Kandpal M et al. (2022), the gut-brain axis is a network that allows for two-way communication between the central nervous system and the gastrointestinal tract. The axis links the well-being of the digestive tract to the higher brain regions responsible for cognition by monitoring and integrating gastrointestinal activity. Alterations to the gastrointestinal system and neurological issues may result from a breakdown of this link. The deterioration of particular populations of neurons is the hallmark of neurodegenerative illnesses and the determinant of their clinical manifestations. Characteristic of neurodegenerative retinopathies are cellular toxicity and the collapse of cellular proteostasis due to misfolded protein aggregates. Alterations in the neural compartment are just one of several non-neural variables that might lead to these illnesses. It is becoming increasingly clear that the central nervous system (CNS) regulates most GI physiologies and mechanics. Although the exact mechanism at work is still a mystery, the gut microbiota is known to have an important role in brain regulation and physiological function. Emerging evidence suggests that dysbiosis of the gut microbial composition may have a role in the onset and development of numerous neurodegenerative diseases. This study primarily aims to provide a current understanding of the research concerning the association between intestinal dysbiosis and the development of specific neurological disorders. These diseases include Alzheimer's disease, Parkinson's disease, Huntington's disease, and multiple sclerosis. At the beginning of neuropathology, this paper explored the potential entrance mechanism of secretions and poisons associated with pathogens into the central nervous system compartment. Also mentioned is a potential mechanism that, according to our current knowledge, could prevent infections, their metabolites, and other interactions from having a synergistic effect.[9]

Function of Fatty Acids with Short Chains

Amazing new research in the last several years has increased our understanding of how bacteria and hosts communicate, but the foundations of microbiota-gut-brain interaction are still up in the air. The primary byproducts of bacterial fermentation of resistant starch and dietary fibers in the colon, short-chain fatty acids (SCFAs), are believed to have important functions in the control of neuro-immunoendocrine systems. Unfortunately, the exact ways in which SCFAs may affect brain physiology and behavior remain unclear. Scope of SCFA involvement in microbiota-gut-brain interactions is summarized in this article. By delving into the function of SCFAs in overseeing the control of systemic neuro-immunoendocrine regulation.[10]

A synopsis of the gut-brain axis's role in mood disorders and others

A network of connections between the enteric and central nervous systems, the gut-brain axis allows for two-way communication. In addition to being anatomical, this network extends to incorporate not just metabolic but also endocrine, humoral, and immunological pathways of communication. Brain signals can affect intestinal processes, such as the activity of functional immune effector cells, and gut signals can impact mood, cognition, and mental health via the autonomic nervous system, the hypothalamic-pituitary-adrenal (HPA) axis, and nerves within the gastrointestinal (GI) tract. The gut-brain connection (i.e., the control of emotions, neuromuscular function, and the HPA) is heavily and deeply impacted by the enteric microbiota, according to clinical, epidemiological, and immunological findings. The direct and indirect effects of microbiota on the brain's emotional and cognitive centers are still a mystery, but recent studies have shown that changes in these communication systems are associated with fluctuations in the microbiota.

For instance, a number of mood disorders, including anxiety, depression, and autism spectrum disorders now have well-established connections to functional gastrointestinal disturbances, while gastrointestinal disorders (such as irritable bowel syndrome or irritable bowel disease) frequently incorporate psychological co-morbidities linked to changes in the gut microbiome. Not surprisingly, studies have shown that the make-up of the gut flora has an effect on the development of the nervous system in fetuses and newborns. The effects of the gut microbiota on cognitive function can be modulated by dietary changes. Disturbances in people's cognitive processes, emotional regulation, and behavioral patterns are symptoms of psychiatric diseases, which are a leading cause of disability globally. Research in the field of neuropharmacology has focused on the gut microbiota and its function in modifying various illnesses in an effort to find new treatments and push the profession's frontiers. The brain-gut axis is a complex bidirectional system that links the enteric and central nervous systems; these changes may impact brain functions through it. Therefore, dietary supplements that aim to improve gut health, such as probiotics and prebiotics, may have a significant impact on the reduction of mental health symptoms, including the cognitive hallmarks of schizophrenia, major depressive disorder, anxiety, and other similar disorders. Psychotropic medication use has also been shown to alter microbiome diversity in predictable ways, which may have applications in the fight against bacterial diseases [11,12,13].

The relationship between the enteric nervous system and the bacteria in the digestive tract

A network of connections between the brain's emotional and cognitive centers and the gut's peripheral functions, the gut-brain axis (GBA) allows for two-way communication between the brain and the enteric nerve system. New findings highlight the role of gut microbes in shaping these relationships. It seems that the relationship between microbiota and GBA is two-way, working via neurological, endocrine, immunological, and humoral pathways from the gut microbiota to the brain and vice versa. We summarize the existing evidence for these connections and the potential pathophysiological mechanisms at work in this review. Studies on infections, probiotics, antibiotics, and germ-free animal models have provided the bulk of the data. Evidence of microbiota-GBA interactions in clinical practice derives from the correlation of dysbiosis with CNS diseases (such as autism and anxiety-depressive behaviors) and FGIDs. Irritable bowel syndrome is one condition that results from disruption of these interconnected processes; further research into these changes may lead to the development of more precise treatments for this condition.[14]

Influence of the microbiota on the diet

Several chronic diseases, such as inflammatory bowel disease, obesity, type 2 diabetes, cardiovascular disease, and cancer, may be influenced by the intestinal microbiome, according to recent studies. Simultaneously, it is now known that diet significantly influences the microbiome, with studies demonstrating that changes in diet can cause temporary shifts in microbes within 24 hours. Considering this correlation, dietary changes that affect microbiome composition may have substantial therapeutic value. The effects of many common food components on intestinal microbiota are comprehensively evaluated in this review of current research. We demonstrate that existing host bacterial genera undergo predictable changes in response to specific dietary factors. Moreover, these bacteria' identities impact host immunological and metabolic factors, which in turn impacts human health in a broad way. Both the practitioner and the patient will benefit greatly

from being familiar with these associations.[15]

Hopeful endpoint for novel treatments involving microbiota and the gut-brain axis

A number of chronic disorders, including as cancer, inflammatory bowel disease, obesity, type 2 diabetes, cardiovascular disease, and type 2 diabetes, may be influenced by the intestinal microbiome, according to recent research. Simultaneously, it is now known that food plays a major influence in moulding the microbiome; studies have shown that changes in food can cause big, transient changes in microbes within a day. Considering this correlation, dietary changes that affect microbiome composition may have substantial therapeutic value. The effects of many common food components on intestinal microbiota are comprehensively evaluated in this review of current research. We demonstrate that existing host bacterial genera undergo predictable changes in response to specific dietary factors. Moreover, these bacteria' identities impact host immunological and metabolic factors, which in turn impacts human health in a broad way. The practitioner and patient will both benefit greatly from being familiar with these relationships.

For autistic youngsters, a comparable situation could play out.In addition to calming anxiety and hyperactivity, what if dietary influences on the gut flora may alleviate GI irritation? And what if specific foods, like probiotics, might supplement pharmacological and psychological treatment for schizophrenia? Possibly, these aspirations are within reach. In response to their work, an increasing number of researchers have launched new businesses focused on studying the potential of small molecule medicines to modulate the microbiome in the treatment of neurological and other diseases. Much of the funding for their clinical research comes from private investors.[16,17]

Potential microbiome-based treatments for neurodegenerative illnesses

Probiotics are defined as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" by the International Scientific Association for Probiotics and Prebiotics (ISAPP).

The goal of administering probiotics is typically to introduce specific microbial strains to promote the microbiome's health-promoting pathways and enhance metabolite production. Probiotics have expanded their role in the human gut microbiome thanks to advances in cultivation and sequencing technologies and our growing understanding of this ecosystem. Probiotics of the next generation, include Lactobacillus and Bifidobacterium. Among the NGPs, we find A. these bacteria: Muciniphila, Faecalibacteriumprausnitzii, Roseburia intestinalis, and Bacteroides fragilis.

Conversely, according to ISAPP, a prebiotic is "a substrate that is selectively utilised by host microorganisms conferring a health benefit.". A prebiotic is a non-digestible material that promotes the growth of good bacteria and their related metabolites. Among the several prebiotics, inulin, FOS, and GOS have the best track records for encouraging the development of beneficial bacteria like Lactobacillus and Bifidobacterium. However, thanks to scientific and technical advancements, prebiotics are now targeted at a wider variety of gut microorganisms that promote health, not only Lactobacillus and Bifidobacterium.

Transplantation of fecal microbiota (FMT)

Functional microbiome transplantation (FMT) is the process of introducing the microbiome of a healthy donor into the digestive system of a sick person in order to improve the latter's microbiome and treat disorders linked to dysbiosis in the gut. Considered a general and mostly unfocused approach to modulating the gut microbiota, it pits the recipient's microbial environment against the donor's. From its humble beginnings as a method of transporting fresh donor stool to its current status as a standard treatment option, FMT has come a long way.[18] **In 2024, Kumar A et al**. asserted that the human gastrointestinal tract is home to diverse microbial populations that are vital for defense against infections, digestion, drug metabolism, intestinal integrity, and immunology. New research has shown that the gut microbiota (GM) communicates with the brain via a two-way communication pathway called the gut-brain axis. Brain, endocrine, humoral, and immunological pathways are all involved in this communication. Gut dysbiosis disrupts these routes of communication in a bad wayresults in brain damage and cognitive impairments. A number of benefits of probiotics have been shown in both animal and human trials, including the restoration of healthy GM, the reduction of intestinal pH, inflammation, and harmful microorganisms. Probiotics also boost BBB-derived neurotrophic factors and enhance cell-to-cell signaling. Despite these encouraging results, there are still safety concerns and hazards associated with probiotics that make them an unproven strategy for treating neurological problems and cognitive impairments. The use of probiotics needs to be carefully observed and handled. A concise synopsis of probiotics' function and relevance to mental wellness is presented in this review article. [19]

Conclusion

Alterations to the bidirectional gut-brain axis have been associated to gastrointestinal dysfunction and chronic pain. This axis affects homeostatic and physiological activities. Studies have linked alterations in these interactions to brain-gut problems, mental, neurologic illnesses, chronic pain, and the gut microbiome making it a critical predictor of human health and disease.

References

1 Craig , J. f, O ’ riordan, K. j, & Cowan , C. s m. (2019). The microbiota-gut-brain axis. *American Physiological Society* , 99(10), 1877-2013.

2 Mayer, E. A., Nance, K., & Chen, S. (2022). The Gut–Brain Axis. *Annual Review of Medicine*, 73(1), 439-453. https://doi.org/10.1146/annurev-med-042320-014032.

3 Martin, C. R., Osadchiy, V., Kalani, A., & Mayer, E. A. (2018). The Brain-Gut-Microbiome Axis. *Cellular and Molecular Gastroenterology and Hepatology*, 6(2), 133-148. https://doi.org/10.1016/j.jcmgh.2018.04.003

4 Lewandowska-Pietruszka, Z., Figlerowicz, M., & Mazur-Melewska, K. (2022). The History of the Intestinal Microbiota and the Gut-Brain Axis. *Pathogens*, 11(12), 1540. https://doi.org/10.3390/pathogens11121540

5 Wachsmuth, H. R., Weninger, S. N., & Duca, F. A. (2022). Role of the gut–brain axis in energy and glucose metabolism. *Experimental & Molecular Medicine*, 54(4), 377-392. https://doi.org/10.1038/s12276-021-00677-w

6 Richards, P., Thornberry, N. A., & Pinto, S. (2021). The gut–brain axis: Identifying new therapeutic approaches for type 2 diabetes, obesity, and related disorders. *Molecular Metabolism*, 46, 101175. https://doi.org/10.1016/j.molmet.2021.101175

7 Margolis, K. G., Cryan, J. F., & Mayer, E. A. (2021). The Microbiota-Gut-Brain Axis: From Motility to Mood. *Gastroenterology*, 160(5), 1486-1501. https://doi.org/10.1053/j.gastro.2020.10.066

8 Rogers, G. B., Keating, D. J., Young, R. L., Wong, M.-L., Licinio, J., &Wesselingh, S. (2016). From gut dysbiosis to altered brain function and mental illness: Mechanisms and pathways. *Molecular Psychiatry*, 21(6), 738-748. https://doi.org/10.1038/mp.2016.50

9 Kandpal, M., Indari, O., Baral, B., Jakhmola, S., Tiwari, D., Bhandari, V., Pandey, R. K., Bala, K., Sonawane, A., & Jha, H. C. (2022). Dysbiosis of Gut Microbiota from the Perspective of the Gut–Brain Axis: Role in the Provocation of Neurological Disorders. *Metabolites*, 12(11), 1064. https://doi.org/10.3390/metabo12111064

10 Silva, Y. P., Bernardi, A., &Frozza, R. L. (2020). The Role of Short-Chain Fatty Acids From Gut Microbiota in Gut-Brain Communication. *Frontiers in Endocrinology*, 11. https://doi.org/10.3389/fendo.2020.00025

11 Appleton , J. (2018). The Gut Brain Axis . Influence of microbiota on mood and mental health . *Integrative Medicine* , 17(4), 28-32.

12 Toader, C., Dobrin, N., Costea, D., Glavan, L.-A., Covache-Busuioc, R.-A., Dumitrascu, D.-I., Bratu, B.-G., Costin, H.-P., & Ciurea, A. V. (2024). Mind, Mood and Microbiota—Gut–Brain Axis in Psychiatric Disorders. *International Journal of Molecular Sciences*, 25(6), 3340. https://doi.org/10.3390/ijms25063340

13 Toader, C., Dobrin, N., Costea, D., Glavan, L.-A., Covache-Busuioc, R.-A., Dumitrascu, D.-I., Bratu, B.-G., Costin, H.-P., & Ciurea, A. V. (2024). Mind, Mood and Microbiota—Gut–Brain Axis in Psychiatric Disorders. *International Journal of Molecular Sciences*, 25(6), 3340. https://doi.org/10.3390/ijms25063340

14 Carbotti, M., Scirocco, A., Maselli, M. A., &Severi , C. (2015). The gut-brain axis: Interactions between enteric microbiota, central and enteric nervous systems. *Annals of Gasteroenterology* , 28(2), 203-209.

15 Singh, R. K., Chang, H.-W., Yan, D., Lee, K. M., Ucmak, D., Wong, K., Abrouk, M., Farahnik, B., Nakamura, M., Zhu, T. H., Bhutani, T., & Liao, W. (2017). Influence of diet on the gut

microbiome and implications for human health. *Journal of Translational Medicine*, 15(1). https://doi.org/10.1186/s12967-017-1175-y

16 Chakrabarti, A., Geurts, L., Hoyles, L., Iozzo, P., Kraneveld, A. D., La Fata, G., Miani, M., Patterson, E., Pot, B., Shortt, C., &Vauzour, D. (2022). The microbiota–gut–brain axis: Pathways to better brain health. Perspectives on what we know, what we need to investigate and how to put knowledge into practice. *Cellular and Molecular Life Sciences*, 79(2). https://doi.org/10.1007/s00018-021-04060-w

17 Liu, L., Huh, J. R., & Shah, K. (2022). Microbiota and the gut-brain-axis: Implications for new therapeutic design in the CNS. *EBioMedicine*, 77, 103908. https://doi.org/10.1016/j.ebiom.2022.103908

18 Loh, J. S., Mak, W. Q., Tan, L. K. S., Ng, C. X., Chan, H. H., Yeow, S. H., Foo, J. B., Ong, Y. S., How, C. W., & Khaw, K. Y. (2024). Microbiota–gut–brain axis and its therapeutic applications in neurodegenerative diseases. *Signal Transduction and Targeted Therapy*, 9(1). https://doi.org/10.1038/s41392-024-01743-1

19 Kumar, A., Sivamaruthi, B. S., Dey, S., Kumar, Y., Malviya, R., Prajapati, B. G., &Chaiyasut, C. (2024). Probiotics as modulators of gut-brain axis for cognitive development. *Frontiers in Pharmacology*, 15. https://doi.org/10.3389/fphar.2024.1348297