



GUT MICROBIOME AND HUMAN HEALTH: A REVIEW

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Article History Received: 28 September 2023 Revised: 21 October 2023 Accepted: 02 November 2023	Abstract Our body is comprised of trillions of bacteria, virus, fungi etc. The "microbiome" refers to them all together. In contrast to human health, some of the bacteria are linked to illnesses that are critical to the immune system, and weight. In fact, most of the microbes in our intestines are found in a part of our large intestine called the caecum. They are referred to as a gut microbiome. In fact, there are more bacterial cells in our body than human cells. There are roughly 40 trillion of bacterial cells in our body while the number of human cells are nearly 30 trillion. The gut microbiome refers to all of the microbes present in our intestine, which acts as another organ to live with microbes with millions of years. In the present review the composition of the gut microbiome and their function towards human health is discussed. Microbes have played a very important role in human body. From birth and throughout life, the gut microbiota influences the body by regulating the immune system, central nervous system, and other physiological processes as well as digestion. The gut microbiota and its benefits for human health are the topics of this review. Key Words: Microbiota, Alzheimer disease, Neurodegenerative disease, gut-brain axis, probiotics.
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Introduction:

Considering its significant impact on human health and disease, the microbiota has even been dubbed our "forgotten organ" (Ogunrinola et al. 2020). Among the many metabolic functions carried out by the microbiota is the digestion and absorption of undigested carbohydrates (Fan et al., 2020). This process has probably served as a strong evolutionary push for the evolution of bacteria into human symbionts. Perhaps even more important is the relationship between the immune system and the gut microbiota, which communicates to promote immune cell maturation and the appropriate development of immunological activities (Ogunrinola et al. 2020).

In this study, we give a summary of the current understanding of the gut microbiota and its impact on health. We also present interactions between viruses, eukaryotes, bacteria, and the host immune system

that commonly occur in the human stomach in order to further characterise this healthy microbiome. Next, we explore the connection between disorders like obesity and Crohn's disease and abnormalities in the microbiota's composition and the resulting modifications in the host's relationships (Hou et al., 2022). We argue that taking an integrated approach will promote a deeper understanding of the numerous diseases linked to disruption of the microbiota and result in microbiota-based therapeutic options for treating these diseases. In each section, we highlight lessons learned about various interacting components of the microbiota. We then discuss the relationship between imbalances in the composition of the microbiota and changes in the way it interacts with the host, as seen in the cases of obesity and Crohn's disease (Robertson et al., 2023).

Gut microbiome

The gut microbiota is a diverse community of microorganisms that live throughout the length and width of the mammalian gastrointestinal tract. It is host specific, changes over the course of an individual's lifetime, and can be affected by both endogenous and exogenous modifications [Robertson et al., 2023]. The microbiota is closely related to many aspects of normal host physiology, including behaviour, stress response, and nutritional status. It can be both aerobically and anaerobically, and can multiply the aerobes by up to 100 times (Ogunrinola et al., 2020). Nonetheless, to date, the human gut has been found to contain more than 50 different bacterial phyla (Fan et al. 2020). There are just two phyla that dominate the microbiota: Firmicutes and Bacteroidetes. The majority of microbiota estimates are attributed to the Bacteroidetes and Firmicutes, despite the fact that more than 50 bacterial phyla have been found in the human gut to date (Eggersdorfer et al. 2018). Studies have found a wide variety of bacterial species in the human gut, although it is generally accepted that individuals have more than 1000 microbial, species-level phylotypes.

Composition of gut microbiome

The baby's gut microbiota undergoes a number of changes as they go from being breastfed or formula-fed to being weaned and introduced to solid food (Afzaal et al., 2022). The kind of food eaten, feeding habits, and the microbiota in the surrounding environment are examples of extrinsic factors in addition to the mother's microbiome. Temperature and nutrition-related stresses can also have an impact on the succession of microorganisms. The colonisation of human gut microbes begins at birth. The baby's intestines are assumed to be sterile or to have very few microorganisms before birth (AboNahas et al. 2022). The infant interacts with the mother's vaginal microbiota as it passes through the delivery canal. The growth of the baby's gut microbiota is impacted by this contact, which is comparable to the mother's vaginal tract flora (Lagier et al, 2016). Compared to babies born spontaneously, cesarean-born babies had fewer microorganisms in their gastrointestinal tracts at one month, but these changes did not last past that point (Afzaal et al., 2022).

Human gut microbial communities

The gut flora of gastrointestinal tract offers significant advantages to your host. Changes in the populations of microbes can cause immunological dysregulation, which can lead to autoimmune diseases (Wang et al. 2017). The microbiome is critical to the body's defence against infections when it is in a state of equilibrium.

The human gut microbiota affects various aspects of human health, including the pathogen, inflammation caused by interactions with mucosa, vitamin synthesis, energy production, fibre and fatty acid creation, and brain development and appropriate function. Additionally, the formation and operation of the immune system are influenced by the human gut microbiota (Piccioni et al. 2022). The

gut microbiota also plays a role in the integrity of the blood- brain barrier (BBB). Firmicutes are the most abundant bacteria, accounting for 51% of the human gut microbiota, while Bacteroidetes are the second most abundant bacteria (48%). Bacteroidetes also include several bacteria like *Clostridium coccoides* (*Clostridium clostridiumclavulorumclavulorum*), *Clostridium luteum leptum* (*Lactobacillus leptum* (*clostridium fungalumclavulorum*)) (*Lactobacillus lactobacillus luteum*, Lact.

Probiotics

Probiotics are defined as "live microorganisms that provide health benefits to the host when administered in sufficient amounts" by the Food and Agriculture Organisation (FAO) and the World Health Organisation (WHO) (Afzaal et al. 2022). Probiotics were first introduced to the scientific world by Nobel laureate Elia Metchnikov. In his seminal paper, he linked the longevity of the Bulgarian people to their consumption of fermented dairy products containing viable lactobacilli (Piccioni et al. 2022).

The mechanisms of probiosis are as follows:

- Manipulating intestinal microbial communities
- Suppressing pathogens
- Immunomodulating epithelial cells
- Stimulating differentiation and fortifying the intestinal barrier.

Prebiotics

Prebiotics are a vital part of human health (Wang et al. 2017). Asparagus, sugar beetroot, garlic, chicory, onion, Jerusalem artichokes, wheat, honey, banana, barley, tomato, rye, soybean, human and cow's milk, peas and beans are only a few of the foods that naturally contain them. [Figure 1].

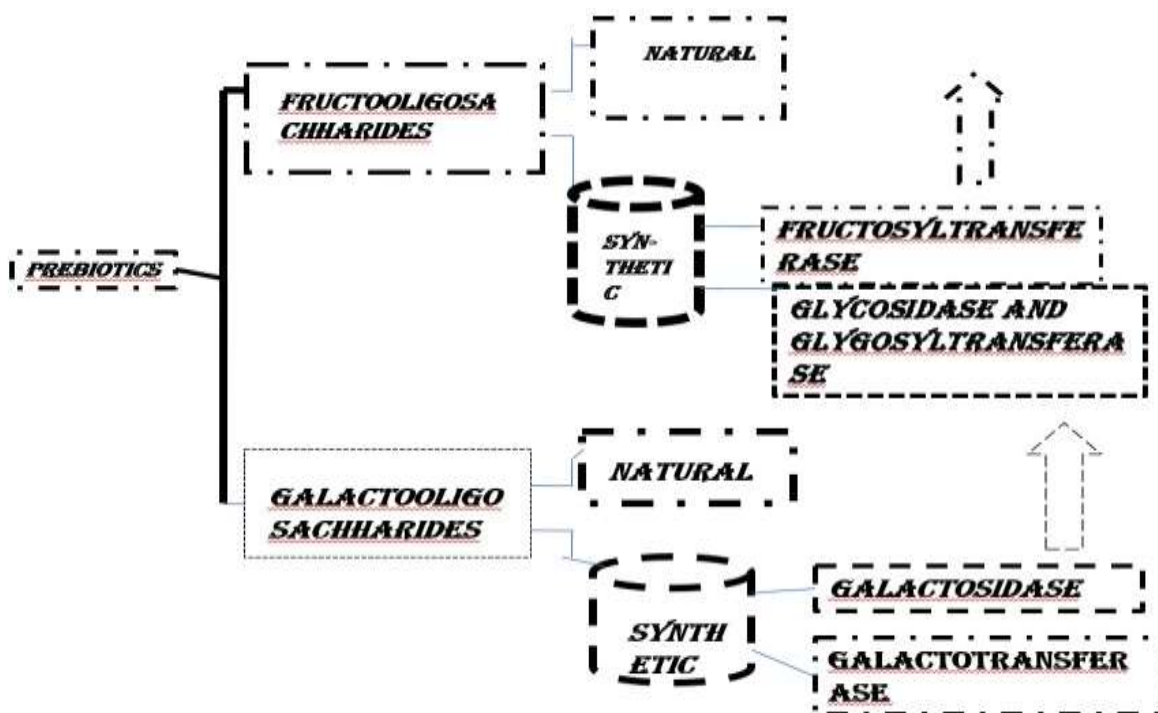


Figure 1: Sources and production of major prebiotics, including fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS).

Function of gut microbiome

The host's gut microbiome has a significant role in their overall health, in both humans and animals. It is essential for metabolism, immune system instruction and regulation, and pathogen defence. The human body would not be able to function without the gut microbiome. Vitamins and amino acids are among the essential nutrients that the gut microbiome provides.

The most prevalent fatty acid in the gut microbiota, short chain fatty acids, are produced by these cells. Although butyrate is a significant source of SCFA, acetate is the main kind of SCFA produced by the gut microbiome (Fava et al., 2019).

Butyrate is involved in several important functions, including the induction of colon cancer cell apoptosis and intestinal gluconeogenesis, which is important for energy regulation and diabetes (Lagier et al. 2015) Propionate regulates hepatic gluconeogenesis and stimulates satiety signalling, which are both related to glucose homeostasis. Acetate is also involved in controlling lipogenesis and cholesterol metabolism in extra-intestinal tissues.

In order to defend the host, the human gut microbiota colonises any niche that becomes available, vying for space with potentially hazardous microbes (Fava et al. 2019). A well-balanced community is essential for keeping pathogens away, which is one of the main reasons fecal transplantation is so effective in treating infections with *C. difficile*.

The microbiome also helps to protect the host by helping to train the immune system. Immune cells in the intestine actively interact with microorganisms to increase immune tolerance (Browne et al,2016). Lack of beneficial bacteria, or dysbiosis, is thought to increase inflammation by forcing changes in the composition of Microbial components enter the body by attacking the intestinal epithelium, leading to a gut leak (Fava et al. 2019). Bacterial components, such as lipoproteins (LPS), can leak out of the intestine. In recent years, it has been found to play a direct role in mental health. Studies have shown that the gut microbiota can influence the normal functioning and development of the brain (Thaiss et al. 2016). A comparison between children with ADHD or autism and those without the condition has revealed that those with the condition have a different gut bacterial composition. Diabetes, autoimmune and inflammatory illnesses, metabolic disorders, and cancer have all been related to the gut microbiome (Fava et al 2019).

There is also growing interest in understanding how the gut microbiome plays a role in drug metabolism, as it can affect how many active drugs are made available to the host.

Gut brain axis

A gut leak results from an attack on the intestinal epithelium by microbiological components. Lipoproteins (LPS), one type of bacterial component, can seep out of the intestine. Both local and systemic inflammation may result from elevated amounts of lipoproteins or changes in the kinds of lipoproteins the immune system comes into contact with (Thaiss et al. 2016). A comparison between children with ADHD or autism and those without the condition has revealed that those with the condition have a different gut bacterial composition. The gut microbiome has also been linked to cancer, inflammatory and autoimmunity conditions, metabolic diseases, and diabetes (Fava et al. 2019).

The connection between the gut and the brain is a two-way pathway that connects the Endocannabinoid System (ENS) and the Central Nervous System (CNS). Microorganisms in the gastrointestinal tract play a role in the development and functioning of the central nervous system (CNS) and endocannabinoid system (ENS) (Lloyd-price et al. 2016). The CNS is responsible for regulating the gastrointestinal

system through the Endo-Nervous System (ENS), which is connected to the hypothalamic-pituitary-adrenal (HPA) and peripheral nerves. When migrating contractions are reduced, constipation is present, while when migrating contractions are increased, diarrhea-dominant IBS is present. The frequency of food is associated with the migration of gut contractions. The ANS regulates the secretion of mucus, the size, and the quality of the intestinal mucus layer and the intestinal epithelial cells (Fava et al. 2019). The gut epithelial cell controls the gut immune cell and induces an intestinal mucosal response (Sender et al. 2016). Neuroendocrine molecules (Serotonin, Dynorphin, γ -Amino Butyric Acid (GABA) and Cytokines) released into the intestinal lumen (Sender et al. 2016) are modulated in the nervous system by the central nervous system (CNS). Synthetic ceCeA (Norepinephrine) also enhances the pathogenic activity of the enteric strains (Fava et al. 2019) as well as their proliferation (sender et al. 2016).

Diagnosis, management, and treatment of neurological disorders are dependent on the relationship between GM alteration and brain pathology. However, the relationship between when the GM- brain axis is altered, the gut microbiota changes, and the brain functions are affected. The Bacteroides abundance was reduced and the increase abundance of the clostridium bacterium was increased. The other bacterial genera were also significantly altered (Silva et al. 1999).

Involvement of microbiome in neurodegenerative disease

Alzheimer's disease

Dementia or cognitive impairment is the most common degenerative disease in the elderly central nervous system (CNS). A steady deterioration in cognitive function (AD) is its defining feature. According to this research, amyloid protein and associated bacterial buildup may both be involved in cognitive decline (Collins et al. 2014).

AD is caused directly by crossing the blood-brain barrier or intestinal barrier that has been compromised by ageing or illness. Alternatively, it might cause AD indirectly by acting on protective physiological barriers, such as lipoproteins, amyloid-induced cytokines, and tiny pro-inflammatory molecules (Collins et al. 2014). The microbiomes of older persons with AD contain more taxa linked to pro-inflammatory states and a reduced percentage of butyrate-generating bacteria, which help regulate immunity and anti-inflammatory responses (Collins et al. 2014). Modulating intestinal homeostasis (reducing inflammatory, increasing anti-inflammatory microbial metabolism) is a potential therapy for AD. Fecal microbiota transfer therapy has been shown to improve amyloidosis and tau pathology, as well as reactive gliosis and cognitive impairment, in AD mice (Collins et al. 2014)

Parkinson's Disease (PD)

Parkinson's disease (PD) patients are thought to make up 1%–2% of the global population. Non-muscular symptoms are widespread in PD patients, with gastrointestinal dysfunction being the most prevalent complaint. Additionally, gut inflammation might have a role in the pathophysiology of Parkinson's disease. Moreover, intestinal microbiota sequencing demonstrated a relationship between the relative abundance of postural stability and gait difficulty in the faeces of Parkinson's disease patients and controls (Anitha et al. 2012). This in turn may lead to an over-expression of α -syn in the colon, and potentially in the brain. Furthermore, the microbiomes of PD patients are characterized by a decrease in bacteria that produce butyrate and an increase in pro-inflammatory bacteria, which may lead to inflammation-induced misfolding of α -syn (Anitha et al. 2012).

In conclusion, it has been demonstrated that the gut microbiome can play a role in the onset, progression, and alleviation of motor deficits in PD mice, as well as the reduction of dopaminergic neuron loss [Figure 2]

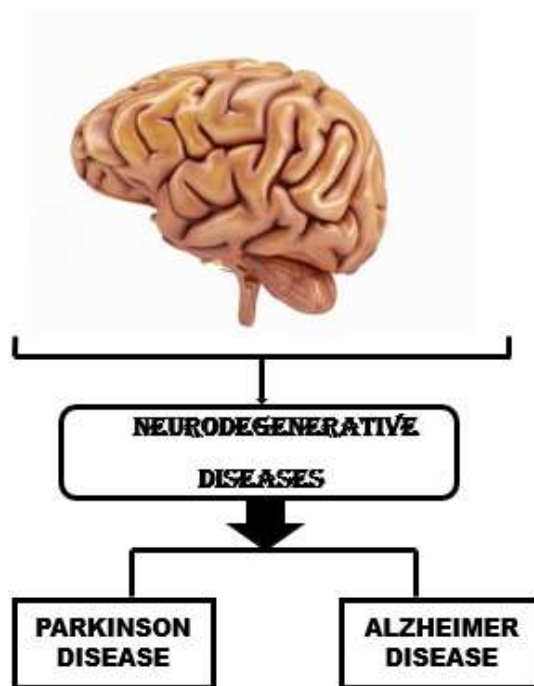


Figure 2: Involvement of microbiome in neurodegenerative disease

Conclusion and Future Perspective

The link between the gut microbiota and the host immune system, as well as its crucial role in immunological dysfunction, are better understood as a result of this work. Additionally, it sheds light on the possible consequences of changing the course of future study to ascertain the course and pathogenicity of human neurodegenerative disease in connection to gut bacteria. To determine whether the pathogenic bacteria are present, bacterial communities from healthy people and disease patients can be compared. We have discussed the function of the gut microbiota and how it affects health in this review. We also go over a number of computational techniques for analysing how the human gut microbiome affects neurodegenerative illnesses. As technology advances, new methods for researching the microbiome are constantly being developed and improved. It is anticipated that other multi-omics techniques will emerge soon. Prices will keep going down, and restrictions will eventually be lifted. This method can investigate the reciprocal relationship between neurodegenerative diseases and the gut microbiota by combining a number of contemporary technologies. Numerous analyses of the gut microbiome show a connection between the brain and gut microbes.

Conflict of Interest

Authors declare no competing interest.

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