DOI: *10.15613/fijrfn/2025/v12i2/50536*
ISSN (Print) : 2349-8897
***FoodSci*: Indian Journal of Research in Food Science and Nutrition,** *Vol 12(2), 62-74, July-December 2025* *ISSN (Online) : 2350-1006*

The Gut Microbiota-Parkinson's Disease Nexus: A Comprehensive Review on Dysbiosis, Nutrition, and Neurodegeneration

S. Abhigna*, V. Aishwarya Patil and S. Bhavana

Department of Food Technology, M. S. Ramaiah University of Applied Sciences, Bengaluru-560054, India; abhigna2002@gmail.com

Abstract

The loss of dopaminergic neurons is the hallmark of Parkinson's Disease (PD), a progressive neurodegenerative illness that mostly impairs motor function. According to new research, the gut-brain axis and gut bacteria are key players in the pathophysiology of Parkinson's disease. An imbalance in the makeup of gut microbes, known as dysbiosis, accelerates the progression of disease by causing neuroinflammation, α-synuclein aggregation, and increased intestinal permeability. Oxidative stress, mitochondrial dysfunction, and immunological dysregulation result from a decrease in bacteria that produce Short-Chain Fatty Acids (SCFAs) and an increase in pro-inflammatory microorganisms. The composition of the gut microbiota is greatly influenced by dietary factors; diets high in fiber encourage the generation of SCFA and have anti-inflammatory properties, whereas diets heavy in fat or processed foods worsen dysbiosis. Prebiotics, probiotics, and foods high in polyphenols are examples of nutritional therapies that may help reestablish microbial equilibrium and lessen the symptoms of Parkinson's disease. Furthermore, diet-based therapy and Fecal Microbiota Transplantation (FMT) are becoming recognized as viable approaches to delay the progression of the disease. A potential biomarker for early Parkinson's disease identification and disease monitoring is gut microbiota profiling. The potential of dietary therapies that target the gut microbiota in the management of Parkinson's disease is highlighted in this review, which examines the relationship between gut microbiota, nutrition, and PD.

Keywords: Fecal Microbiota Transplantation (FMT), Gut-Brain Axis (GBA), Gut Microbiota (GM), Parkinson's Disease (PD), Short-Chain Fatty Acids (SCFAs)

1. Introduction

The primary cause of Parkinson's Disease (PD), a progressive neurodegenerative illness, is the death of dopaminergic neurons in the substantia nigra, which impairs motor function. Affecting about 10 million individuals globally, it is the second most prevalent neurological disease after Alzheimer's disease[1]. A growing body of research indicates that non-motor symptoms, especially Gastrointestinal (GI) problems, are important in the pathophysiology of Parkinson's Disease (PD), despite the fact that the disease is typically defined by motor symptoms such bradykinesia, rigidity, and tremors[2]. Chronic constipation, which might emerge years before motor symptoms do, is one of the first non-motor symptoms of Parkinson's disease. Researchers are now looking into the gut-brain axis, which is a network of communication that runs both ways between the Central Nervous System (CNS), the Enteric Nervous System (ENS), and the gut microbiota[3]. We now know from numerous studies that gut dysbiosis (microbial imbalance) is linked to Parkinson's Disease (PD) and may be a factor in dopaminergic neurodegeneration, α-synuclein aggregation, and neuroinflammation[4].

According to a study that compared the gut microbiota of PD patients and healthy controls, PD patients had higher levels of pro-inflammatory bacteria like *Proteobacteria* and *Enterobacteriaceae* and significantly lower levels of bacteria that produce Short-Chain Fatty Acids (SCFA), such as *Faecalibacterium prausnitzii* and

*Author for correspondence

Roseburia[5]. By increasing intestinal permeability (also known as "leaky gut"), these microbial changes can let bacterial endotoxins—like Lipopolysaccharides, or LPS—enter the bloodstream and cause systemic inflammation, which can then travel through the vagus nerve to the brain[6]. Further supporting the link between gut dysbiosis and PD progression is the observation that transplanting gut microbiota from PD patients into germ-free animals exacerbates motor deficits and α-synuclein aggregation[7].

According to the Braak Hypothesis, some researchers have even suggested that Parkinson's Disease (PD) starts in the gut before moving on to the brain[8]. Probiotics, prebiotics, Fecal Microbiota Transplantation (FMT), and dietary interventions aresome of the new therapy options made possible by an understanding of the gut microbiota's role in Parkinson's Disease (PD) and may help control the course of the illness[9]. This review examines the connection between Parkinson's Disease (PD) and gut microbiota, going over recent research results, potential causes, and newly developed gut-targeted treatments[10].

2. Alterations in Gut Microbiota Composition in Parkinson's Disease

Recent studies have revealed notable variations in the gut microbiota composition between people with Parkinson's Disease (PD) and healthy controls. These changes—often called dysbiosis—may be essential to the etiology and development of Parkinson's disease.

2.1. Decreased Beneficial Bacteria

Beneficial gut bacteria, especially *Prevotellaceae*, which are essential for preserving gut homeostasis and generating Short-Chain Fatty Acids (SCFAs), are significantly reduced in Parkinson's Disease (PD) patients, according to several studies[11]. Butyrate and other SCFAs support the integrity of the gut barrier and have anti-inflammatory properties, which may help prevent neurodegeneration. Increased intestinal permeability, which permits toxic chemicals to enter the bloodstream and cause systemic inflammation, is linked to a decrease in *Prevotellaceae*[12]. Additionally, PD patients have reduced numbers of two bacterial genera that produce SCFA, *Blautia* and *Roseburia*, which further contribute to an inflammatory gut environment[13]. The necessity for microbiome-targeted therapy methods is highlighted by the reduction of beneficial bacteria, which raises the possibility of a gut-brain link in PD pathogenesis[14].

2.2. Increased Pathogenic Bacteria

PD patients had an excess of potentially dangerous bacteria, including *Enterobacteriaceae*, *Proteobacteria*,

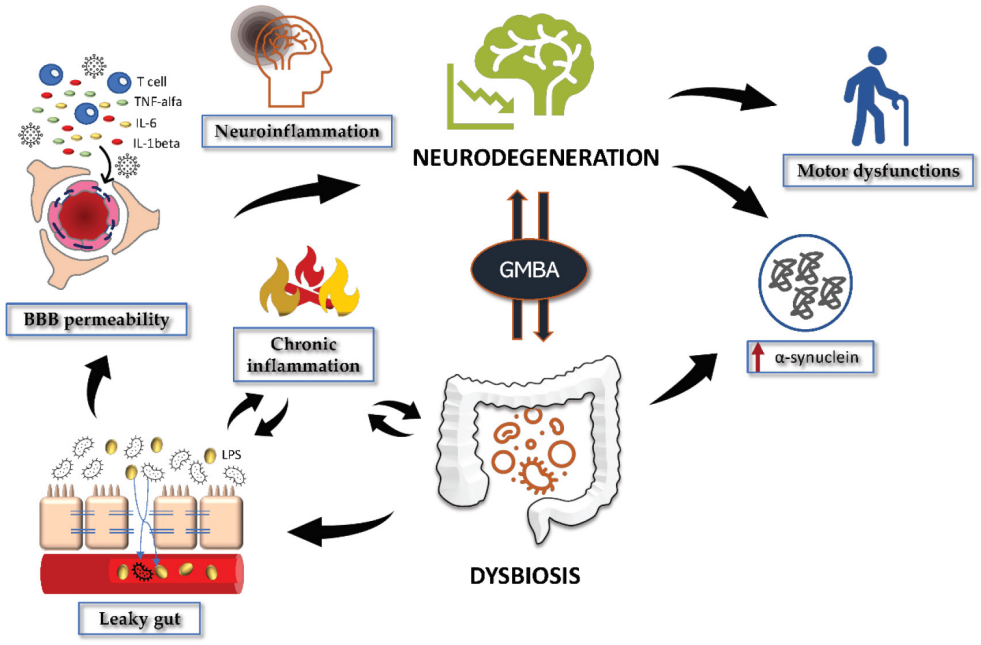


Figure 1. The interplay between gut microbiota and Parkinson's disease. (Source: Varesi, A. *et al.*, (2022).

and *Desulfovibrio*, in contrast to the decrease of helpful microbes[15]. Endotoxins, like Lipopolysaccharides (LPS), are known to be produced by *Enterobacteriaceae* species and have the ability to weaken the gut barrier and cause chronic inflammation[16]. Increased blood levels of LPS have been associated with neuroinflammation and microglial activation, both of which accelerate the course of Parkinson's disease[17]. Hydrogen sulfide, which is also produced by *Desulfovibrio bacteria*, can harm the intestinal lining and interfere with neuronal mitochondrial activity[18]. Further linking gut dysbiosis to the development of PD, these pathogenic bacteria may affect alpha-synuclein aggregation[19].

2.3. Functional Implications of Dysbiosis

In addition to compositional abnormalities, gut dysbiosis in PD patients causes functional changes that impact immunological signalling and neurotransmitter metabolism. Tyrosine and phenylalanine, two dopamine precursors necessary for dopamine synthesis in the brain, are synthesized in large part by the gut microbiota[20]. Additionally, serotonin and Gamma-Aminobutyric Acid (GABA), which control mood and motor function, may be affected by dysbiosis[21]. Furthermore, oxidative stress and inflammation—two important factors in the development of Parkinson's disease—are influenced by certain bacterial metabolites, such as bile acids and SCFAs[22]. Thus, by encouraging neuroinflammation and oxidative damage, an imbalance in microbial metabolism may worsen neurodegeneration[23].

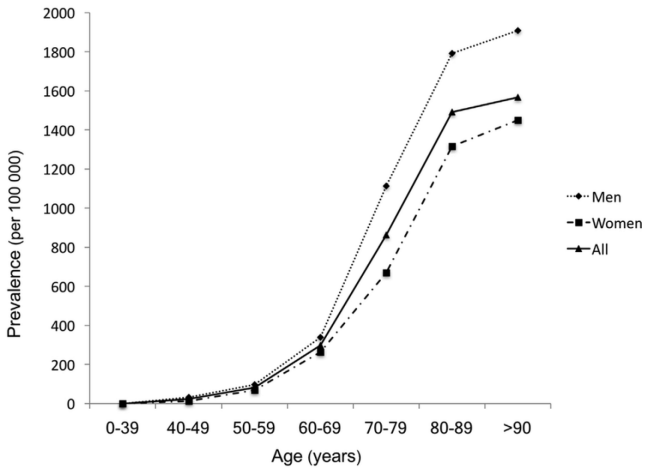


Figure 2. Age-and sex-specific prevalence of Parkinson's disease.(Source: Fleury *et al.*, 2018).

2.4. Variability Across Populations

Although dysbiosis patterns are evident in PD patients, differences in microbial composition across geographic regions and dietary habits highlight the complexity of the gut-brain axis. Studies comparing Western and Asian populations have found variations in microbial taxa associated with PD, possibly due to differences in fiber intake, fermented food consumption, and medication use[24]. Genetic predisposition and environmental exposures, such as pesticide exposure and lifestyle factors, also influence gut microbiota composition in PD patients[25]. These variations underscore the need for standardized microbiome studies that consider demographic and lifestyle factors to identify universally applicable microbial biomarkers for PD diagnosis and treatment[26].

The gut microbiota in PD patients exhibits significant alterations, characterized by a depletion of beneficial bacteria and an enrichment of pathogenic microbes. These changes contribute to neuroinflammation, oxidative stress, and metabolic dysfunctions that exacerbate PD pathology. Understanding these microbial shifts provides potential avenues for microbiome-based therapies, such as probiotics, prebiotics, and fecal microbiota transplantation, which may help restore gut homeostasis and mitigate disease progression[27].

3. Mechanisms Linking Gut Dysbiosis to Parkinson's Disease Pathology

3.1. Increased Intestinal Permeability and Inflammation

Increased intestinal permeability brought on by gut dysbiosis in Parkinson's Disease (PD) is referred to as "leaky gut"[28]. This malfunction speeds up the onset of Parkinson's disease by allowing bacterial endotoxins, like Lipopolysaccharides (LPS), to enter the bloodstream and cause systemic and neuroinflammation[29]. α-synuclein aggregation, a major clinical characteristic of Parkinson's disease, has also been connected to chronic gut inflammation[30]. According to research, gut dysbiosis causes an imbalance between good and bad bacteria, which fuels chronic low-grade inflammation. This inflammation exacerbates neurodegenerative processes by upsetting the gut-brain axis. Even before motor symptoms appear,

increased intestinal permeability has been seen in PD patients, indicating that it may act as an early biomarker[31]. Furthermore, inflammation originating from the stomach is believed to affect microglial activation, which in turn promotes neurotoxicity. Bacterial metabolites in the bloodstream can aggravate brain injury by impairing mitochondrial function. According to some researchers, probiotics and dietary changes that focus on gut health may help reduce the onset of Parkinson's disease. New treatment approaches may result from an understanding of the connection between intestinal permeability and Parkinson's disease[32].

3.2. α-Synuclein Aggregation and Gut-Brain Transmission

Gut dysbiosis has been connected to the buildup and misfolding of α-synuclein, a neuronal protein implicated in Parkinson's disease. According to the Braak hypothesis, α-synuclein disease begins in the Enteric Nervous System (ENS) and then travels through the vagus nerve to the brain. According to research, α-synuclein misfolding can be facilitated by exposure to gut microbial metabolites, such as bacterial amyloids, which can aid in the pathogenic cascade of Parkinson's disease. The gut-brain axis theory is further supported by the finding that vagotomy, or the surgical removal of the vagus nerve, is linked to a lower chance of developing Parkinson's disease. This pathogenic process has been linked to changes in the makeup of the gut microbiota, namely a rise in *Proteobacteria* and a fall in *Firmicutes*[33].

3.3. Microbiota Influence on Dopamine Metabolism

Gut bacteria affect the synthesis of dopamine, a crucial neurotransmitter in Parkinson's disease, from dietary precursors such L-tyrosine and L-DOPA. While some microbial species, such as *Bifidobacterium* and *Lactobacillus*, aid in the digestion of dopamine precursors, an imbalance in the gut microbiota may result in decreased dopamine bioavailability[34]. Furthermore, Levodopa (L-DOPA) medication, the main treatment for Parkinson's Disease (PD), may be less effective due to microbial dysbiosis since some bacteria, such *Enterococcus faecalis*, have been demonstrated to metabolize L-DOPA before it reaches the brain[40]. This implies that PD treatment outcomes could be enhanced by focusing on gut microbes[35].

3.4. Neuroinflammation and Oxidative Stress

Chronic neuroinflammation and oxidative stress are major causes of Parkinson's disease pathology, and gut dysbiosis is a major factor in making these processes worse. Trimethylamine-N-oxide (TMAO), one of the pro-inflammatory compounds produced by dysbiotic microbiota, can cause systemic inflammation and neurodegeneration. Furthermore, lower levels of regulatory T cells (Tregs), which aid in regulating inflammation in the gut and brain, have been connected to decreased levels of SCFAs in PD patients. Dopaminergic neurons in the substantia nigra are lost as a result of oxidative stress, which is exacerbated by gut-derived inflammation and is caused by an excess of Reactive Oxygen Species (ROS) and mitochondrial dysfunction. Therefore, altering gut microbiota may be a useful tactic to lessen oxidative damage and neuroinflammation in Parkinson's disease[36].

4. Gut Microbiota as a Biomarker and Therapeutic Target in Parkinson's Disease

The pathophysiology of Parkinson's Disease (PD) has been increasingly associated with changes in gut microbiota composition, with mounting evidence that it may be a biomarker for early diagnosis. Research shows that PD patients have an imbalance in microbial diversity, specifically an increase in pro-inflammatory bacteria like Enterobacteriaceae and a decrease in beneficial microbes like *Lactobacillus* and *Faecalibacterium*. This dysbiosis may promote intestinal permeability (leaky gut), systemic inflammation, and neuroinflammation through gut-brain axis interactions[37]. Additionally, metabolomic analyses have shown significant decreases in microbial-derived Short-Chain Fatty Acids (SCFAs), such as butyrate, which are crucial for gut health and neuroinflammatory responses.Alpha-synuclein aggregation, a defining feature of Parkinson's disease pathology, has been linked to a decrease in these SCFAs. According to these results, tracking particular bacteria profiles and the byproducts of their metabolism may be a non-invasive diagnostic method and lead to novel approaches for focused gut-based treatment[38].

4.1. Probiotic and Prebiotic Interventions

Prebiotics and probiotics are showing promise as therapeutic approaches to alter gut microbiota in Parkinson's disease. Probiotics, especially *Lactobacillus* and *Bifidobacterium* strains, have been shown to have neuroprotective effects via improving the integrity of the gut barrier, lowering systemic inflammation, and modifying the production of neurotransmitters like serotonin and Gamma-Aminobutyric acid (GABA)[39]. Clinical trials suggest that probiotic supplementation may reduce PD-related gastrointestinal symptoms like as constipation, which is a prevalent non-motor symptom of the condition. Furthermore, by inhibiting pro-inflammatory cytokines and encouraging anti-inflammatory pathways, probiotics might lessen neuroinflammation and possibly halt the progression of disease. Beneficial gut bacteria are fed by prebiotics such Fructooligosaccharides (FOS) and inulin, which promotes their development and activity. These substances promote the synthesis of SCFAs, which support dopamine metabolism, control immunological responses, and fortify the intestinal lining[40]. According to a number of studies, giving PD patients prebiotic supplements can restore the balance of gut microbes, reduce constipation, and possibly even enhance cognitive and motor abilities. Additionally, probiotics and prebiotics combined, known as synbiotics, have demonstrated synergistic effects in reducing inflammation and reestablishing gut microbial diversity. These treatments present a viable, non-invasive approach to treating neurological and gastrointestinal problems in PD patients, but more extensive clinical research is required[41].

4.2. Fecal Microbiota Transplantation (FMT) in PD

Fecal Microbiota Transplantation (FMT) is an emerging therapeutic strategy aimed at restoring gut microbial balance by transferring microbiota from a healthy donor to a recipient[42]. In the context of Parkinson's Disease (PD), FMT has gained interest due to its potential to modulate gut dysbiosis, reduce inflammation, and improve motor and non-motor symptoms. Preclinical studies in PD animal models have shown that FMT can enhance dopamine production, decrease α-synuclein aggregation, and improve gut-brain axis communication. Early clinical trials suggest that PD patients undergoing FMT exhibit improvements in constipation, motor function, and mood disorders, potentially due to increased levels of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*[43].

Despite its promise, FMT remains an experimental approach in PD treatment. The long-term safety, optimal donor selection, and standardized administration protocols require further investigation. Ongoing clinical trials aim to determine the efficacy of FMT in slowing PD progression and improving patient outcomes[44].

5. Future Directions and Challenges in Gut Microbiota Research for Parkinson's Disease

New methods for diagnosing and treating Parkinson's Disease (PD) are being developed as research on the gut-brain axis progresses. Nonetheless, there are still issues with standardizing procedures, comprehending the dynamic character of the microbiome, and converting research results into useful clinical applications. In order to fully utilize the promise of gut microbiota-based therapies in the therapy of Parkinson's disease, this section identifies the crucial areas that need more research[45].

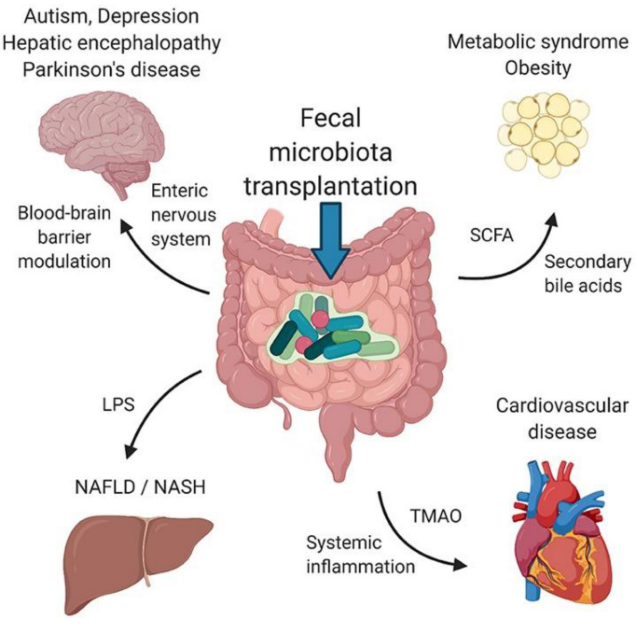


Figure 3. Fecalmicrobiota transplantation as a tool for therapeutic modulation of non-gastrointestinal disorders. (Source :Liptak, R., *et al.,* (2021).

5.1. Advancements in Microbiome Sequencing Technologies

Our knowledge of the composition of the gut microbiota and its connection to Parkinson's Disease (PD) has greatly increased as a result of the quick development of microbiome sequencing technology. Researchers may now identify microbial diversity and detect changes in microbial communities linked to Parkinson's Disease (PD) thanks to Next-Generation Sequencing (NGS) tools like metagenomic analysis and 16S rRNA sequencing. These methods shed more light on the potential roles that dysbiosis may play in neuroinflammation, compromised gut barrier function, and disturbances of the gut-brain axis.Recent developments, such as whole-genome sequencing and shotgun metagenomics, enable a more thorough examination of microbial communities at the strain level, identifying certain bacterial species connected to the pathophysiology of Parkinson's disease[46]. Furthermore, a more accurate understanding of host-microbe interactions is now available because to single-cell sequencing technologies, which enable the investigation of the functional roles of individual microbial cells. By examining metabolites generated by microorganisms, such as Short-Chain Fatty Acids (SCFAs), neurotransmitter precursors, and pro-inflammatory substances that may affect the course of Parkinson's Disease (PD), techniques like metabolomics and meta transcriptomics enhance these sequencing methodologies.There are still issues with standardizing microbiome research in spite of these technical advancements. Inconsistencies between research may result from variations in sample collection, DNA extraction techniques, sequencing processes, and bioinformatics pipelines. The conversion of microbiome sequencing results into clinically meaningful biomarkers and treatment targets for Parkinson's disease will require the establishment of uniform standards for data interpretation and the harmonization of methodology among various research teams. It is anticipated that continued attempts to incorporate multi-omics techniques, such as proteomics and lipidomics, will offer a more comprehensive understanding of changes in the gut microbiota in Parkinson's disease, opening the door for customized microbiome-based therapies[47].

5.2. Personalized Microbiota-Based Therapeutics

The growing evidence of gut dysbiosis in Parkinson's Disease (PD) has led to an increase in interest in tailored microbiota-based treatments. Through the use of carefully chosen donor microbiota that is customized for each patient, Precision Microbiota Transplantation (PMT) seeks to restore microbial balance. Dietary therapies, including ketogenic or fiber-rich diets, alter the composition of the gut microbiota and have an impact on neuroinflammatory pathways. Based on a patient's microbiome profile, customized probiotic formulations can promote gut-brain connection and increase beneficial bacterial populations. The best treatment plans for every patient can be found thanks to developments in Artificial Intelligence (AI) and microbiome analysis. Gut microbial diversity is further increased by prebiotic supplementation, which targets particular microbial shortages[48]. Postbiotics, including microbial-derived metabolites like short-chain fatty acids, offer another promising approach. These techniques may help with both motor and non-motor symptoms when combined with traditional PD therapy. To determine their effectiveness, safety, and long-term impacts, extensive clinical trials are required[49].

5.3. Role of Gut-Brain Axis in Disease Progression

By connecting changes in the gut microbiota to neurodegeneration, the gut-brain axis plays a critical role in the development of Parkinson's Disease (PD). Short-Chain Fatty Acids (SCFAs) and bacterial endotoxins are examples of gut-derived metabolites that affect neuroinflammation and α-synuclein aggregation. Increased intestinal permeability brought on by dysbiosis makes it possible for dangerous bacterial compounds to reach the bloodstream and set off immunological reactions[50]. Decreased SCFA levels damage the integrity of the intestinal barrier and interfere with dopaminergic transmission. Bidirectional communication between the gut and the brain is facilitated by vagus nerve pathways, which contribute to the pathophysiology of Parkinson's disease. Neuronal injury and oxidative stress are made worse by chronic inflammation brought on by gut dysbiosis. Modulating SCFA synthesis by focusing on

the microbiota may have neuroprotective advantages. Restoring microbial equilibrium may be aided by probiotic and nutrition therapies that are tailored to the individual. New treatment approaches could result from a better understanding of gut-brain connections. To validate these pathways and therapeutic modalities, more research is required[51].

5.4. Challenges in Translating Research into Clinical Applications

Despite encouraging results, a number of obstacles prevent gut microbiota research in Parkinson's Disease (PD) from being used clinically. The repeatability of results is impacted by variations in patient populations, sample collection, and study design. Data interpretation and cross-study comparison are made more difficult by the absence of defined procedures for microbiome investigation[52].The broad use of FecalMicrobiota Transplantation (FMT) as a therapeutic alternative is constrained by ethical issues and legal restrictions. There is currently a lack of long-term safety and effectiveness data for therapies based on microbiota. Personalized treatments are complicated by individual variations in microbiome composition. Because the gut microbiota is dynamic, effective therapies necessitate ongoing monitoring. It is still difficult to fully comprehend the causal links between dysbiosis and the development of Parkinson's disease. It takes interdisciplinary cooperation to incorporate microbiota-based therapies into routine PD care. For microbiome-targeted treatments to advance in clinical practice, these challenges must be overcome[53].

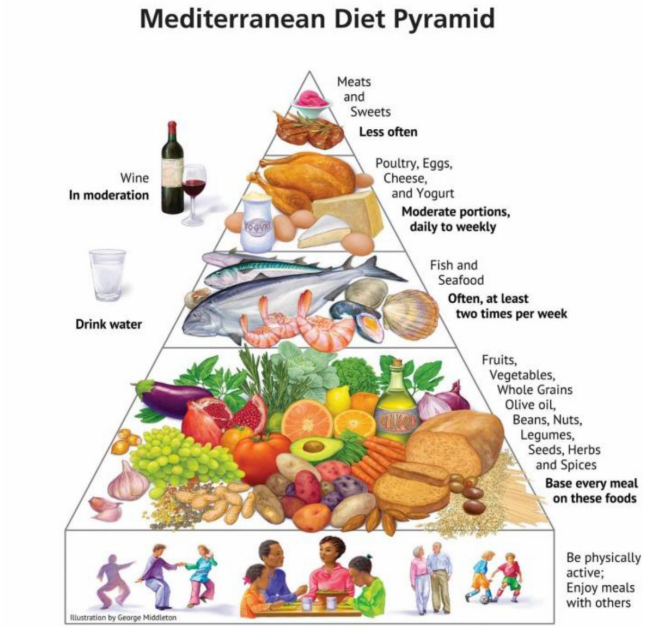


Figure 4. Defining features of the Mediterranean dietary pattern. (Source: Maggi *et al.*, 2023).

6. Nutritional Interventions Targeting Gut Microbiota in Parkinson's Disease

The composition of the gut microbiota is modulated by diet, which also affects inflammation, neuroprotection, and the course of Parkinson's Disease (PD). Numerous dietary strategies have been investigated to improve gut-brain communication, restore microbial balance, and lessen Parkinson's disease symptoms. Important dietary tactics that could control gut dysbiosis and enhance overall illness outcomes are covered in this section[54].

6.1. Mediterranean Diet and its Neuroprotective Effects

The anti-inflammatory and neuroprotective qualities of the Mediterranean Diet (MD) are well known. While limiting processed foods and red meat, it promotes a high intake of fruits, vegetables, whole grains, legumes, nuts, olive oil, and fish. Rich in fiber, omega-3 fatty acids, and antioxidants, MD supports the growth of beneficial bacterial species including *Bifidobacterium* and *Faecalibacterium prausnitzii* and adds to the diversity of the gut microbiota[55]. Short-Chain Fatty Acids (SCFAs), such butyrate, are produced by these bacteria and aid in preserving the integrity of the intestinal barrier and controlling neuroinflammation[49]. Furthermore, MD's polyphenols have been connected to a decrease in oxidative stress, which is a significant cause of Parkinson's disease pathology[56]. According to a recent study, following MD was linked to a decreased risk of Parkinson's Disease (PD), which may indicate that the beneficial effects of MD on gut microbiota have neuroprotective advantages[57].

6.2. Role of Probiotics and Prebiotics

Probiotics are live bacteria that improve gut barrier function, alter immunological responses, and improve the composition of the gut microbiota. Numerous strains, including *Bifidobacterium longum*, *Lactobacillus acidophilus*, and *Lactobacillus rhamnosus*, have

demonstrated promise in lowering inflammation and gastrointestinal disorders in PD patients[58]. Non-digestible fibers called prebiotics, which are present in foods like asparagus, garlic, onions, and bananas, specifically promote the growth of good bacteria, increasing the generation of SCFA and enhancing gut-brain connection[59]. Probiotic use for 12 weeks relieved gastrointestinal symptoms and decreased systemic inflammation markers in PD patients, according to a randomized clinical trial[60]. Additionally, probiotics and prebiotics, or synbiotics, have demonstrated promise in reestablishing the balance of gut microbes, which may help reduce neuroinflammation associated with Parkinson's disease[61].

6.3. Impact of High-Fiber Diets on Gut Microbiota

Because it acts as a substrate for fermentation, which produces SCFA, dietary fiber is essential for the regulation of the gut microbiota. It has been demonstrated that SCFAs, including butyrate, acetate, and propionate, improve gut integrity, lower inflammation, and promote neuroprotection[62]. Research has shown that PD patients frequently consume less dietary fiber, which is linked to an increase in pro-inflammatory species such as *Proteobacteria* and *Enterobacteriaceae* and a decrease in good gut bacteria[63]. It has been demonstrated that high-fiber diets, such as plant-based and whole-food diets, enhance *Akkermansia muciniphila*, a bacteria that supports gut barrier function and lowers intestinal permeability, a major contributing factor to gut dysbiosis associated with Parkinson's disease[64]. The significance of fiber consumption in PD management was highlighted by a study looking at the effects of fiber supplementation in PD patients, which found improvements in constipation, a frequent non-motor symptom of the condition[65].

6.4. Ketogenic Diet and its Potential Benefits

The Ketogenic Diet (KD) is a low-carb, high-fat eating plan that puts the body into a metabolic state called ketosis, when the brain uses ketone bodies as its

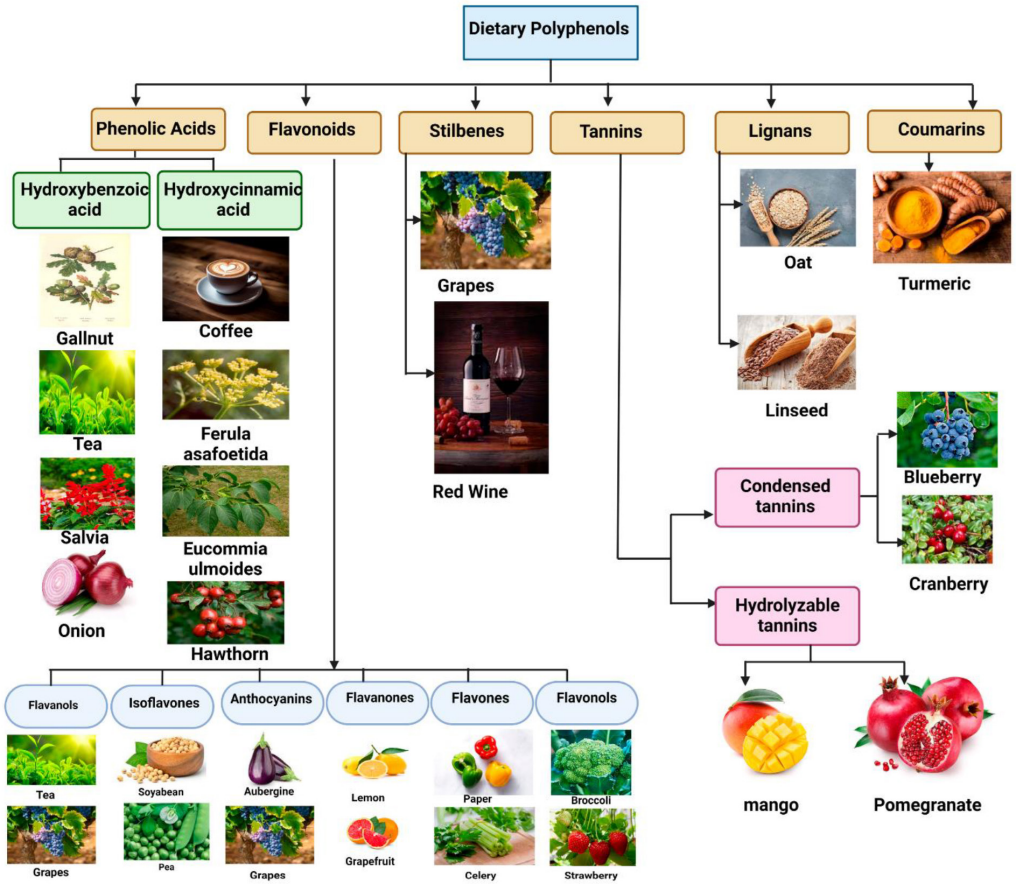


Figure 5. Various sources of dietary polyphenols. (Source: (Rudrapal *et al.*, 2024).

main energy source[66]. The neuroprotective benefits of KD have been thoroughly investigated, especially in relation to neurological conditions like epilepsy and Parkinson's disease. It has been demonstrated to change the composition of the gut microbiota by lowering pro-inflammatory bacteria linked to Parkinson's disease and increasing beneficial bacterial species such as *Akkermansia muciniphila*[67]. Furthermore, ketone bodies like β-hydroxybutyrate have anti-inflammatory and antioxidant qualities that could prevent dopaminergic neurons from degenerating[68]. In a PD mouse model, a preclinical investigation showed that KD decreased neuroinflammation and enhanced motor performance[69]. Long-term adherence to KD is still difficult, though, and more clinical research is required to determine its safety and effectiveness in PD patients[70].

6.5. Dietary Polyphenols and Microbiota Modulation

Plant-based bioactive substances called polyphenols can be found in foods including red wine, green tea, berries, and cocoa. By specifically promoting the growth of advantageous gut bacteria, such *Lactobacillus* and *Bifidobacterium*, while preventing the growth of pathogenic species, they have been demonstrated to exhibit prebiotic-like effects[71]. By modifying inflammatory pathways and lowering oxidative stress, two factors linked to Parkinson's disease pathogenesis, polyphenols also affect gut-brain transmission[72]. In preclinical models, resveratrol, a polyphenol present in grapes, has been shown to enhance mitochondrial activity and decrease α-synuclein aggregation, a defining feature of Parkinson's disease[73]. Furthermore, it has been demonstrated that green tea's main ingredient, Epigallocatechin Gallate (EGCG), enhances neuroprotection by modifying the composition of the gut microbiota and lowering neuroinflammation in PD models[74]. Thus, including foods high in polyphenols in the diet may be a viable dietary approach to controlling Parkinson's disease symptoms and delaying the course of the illness[75].

7. Conclusion

The complex connection between gut microbiota and Parkinson's Disease (PD) has drawn a lot of attention, emphasizing how important it is to the development and course of the illness. A significant communication network is the gut-brain axis, where changes in the composition of the gut microbiota cause chronic inflammation, increased intestinal permeability, and α-synuclein aggregation, all of which contribute to neurodegeneration[11,14,19,25,28]. A decrease in beneficial bacterial species and an increase in pro-inflammatory microorganisms are hallmarks of dysbiosis in Parkinson's Disease (PD) patients, which exacerbates oxidative stress and neuroinflammatory reactions[32,36,39]. In Parkinson's disease pathophysiology, the function of microbial metabolites, such as Lipopolysaccharides (LPS) and Short-Chain Fatty Acids (SCFAs), is especially important. Increased inflammation and compromised gut barrier integrity result from PD's substantial reduction in SCFAs, which have neuroprotective properties[43,45,48,50]. However, LPS causes systemic inflammation, which in turn activates microglial cells and leads to the death of dopaminergic neurons in the substantia nigra[51,53,55]. Promising outcomes have been seen from potential treatment therapies meant to restore gut balance. The potential of probiotics and prebiotics to relieve gastrointestinal symptoms and increase microbial diversity in individuals with Parkinson's disease has been investigated; some trials have shown modest benefits in both motor and non-motor symptoms[57,59,61]. Preliminary research suggests that FecalMicrobiota Transplantation (FMT), a novel strategy for reestablishing gut microbiota balance, may help reduce symptoms associated with Parkinson's disease[62,64,66]. Additionally, nutritional tactics are essential for adjusting the composition of the gut microbiota. Because of its anti-inflammatory and neuroprotective qualities, the mediterranean diet, which is high in fiber, polyphenols, and healthy fats, has been linked to a decreased risk of Parkinson's disease progression[67,68]. Flavonoids and phenolic acids are examples of dietary polyphenols that have positive effects via scavenging free radicals, regulating gut flora, and lowering neuroinflammation[53,55,58,60,64]. One promising approach to managing Parkinson's disease is to target the gut bacteria. Even though there is currently evidence linking gut microbiota to the etiology of Parkinson's disease, more extensive clinical studies are required to develop standardized dietary and microbial-based therapies. Future PD management strategies may become more individualized and successful if gut-targeted medicines are combined with traditional treatments.

8. References

1. Lau D, LML,Breteler, MMB2006. Epidemiology of Parkinson's disease. The Lancet Neurology, 5(6), 525-535. https://doi.org/10.1016/S1474-4422(06)70471-9PMid:16713924
2. PfeifferRF 2016. Non-motor symptoms in Parkinson's disease. Parkinsonism andrelated disorders, 22(Suppl 1), S119-S122. https://doi.org/10.1016/j.parkreldis.2015.09.004PMid:26372623
3. Carabotti M, Scirocco A, Maselli MA, Severi C2015. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. Annals of Gastroenterology, 28(2), 203-209.
4. Sampson TR, Mazmanian SK2015. Control of brain development, function, and behavior by the microbiome. Cell host andmicrobe, 17(5), 565-576. https://doi.org/10.1016/j.chom.2015.04.011PMid:25974299 PMCid:PMC4442490
5. Keshavarzian A, GreenSJ, EngenPA, *et al.*, 2015. Colonic bacterial composition in Parkinson's disease. Movement disorders, 30(10), 1351-1360. https://doi.org/10.1002/mds.26307PMid:26179554
6. Forsyth CB, Shannon KM, KordowerJH,*et al.*, 2011. Increased intestinal permeability correlates with sigmoid mucosa α-synucleinst,aining and endotoxin exposure markers in early Parkinson's disease. PLOS ONE, 6(12), e28032. https://doi.org/10.1371/journal.pone.0028032PMid:22145021 PMCid:PMC3228722
7. SampsonTR, DebeliusJW, ThronT, *et al.*, 2016. Gut microbiota regulate motor deficits and neuroinflammation in a model of Parkinson's disease. Cell, 167(6), 1469-1480.e12. https://doi.org/10.1016/j.cell.2016.11.018PMid:27912057 PMCid:PMC5718049
8. Braak, H., Del Tredici, K., Rüb, U., et al. (2003). Staging of brain pathology related to sporadic Parkinson's disease. Neurobiology of Aging, 24(2), 197-211. https://doi.org/10.1016/S0197-4580(02)00065-9PMid:12498954
9. BoertienJM, Pereira PA, Aho VTE, *et al.*, (2019). Increasing comparability and utility of gut microbiome studies in Parkinson's disease: A systematic review. J Parkinsons Dis. 9(s2), S297-S312. https://doi.org/10.3233/JPD-191751 PMid:32176653 PMCid:PMC8203232
10. Varesi, A., Pierella, E., Romeo, M., et al. (2022). The interplay between gut microbiota and Parkinson's disease: Implications on diagnosis and treatment. International Journal of Molecular Sciences, 23(20), 12289. https://doi.org/10.3390/ijms232012289 https://doi.org/10.3390/ijms232012289PMid:36293176 PMCid:PMC9603886
11. ScheperjansF, Aho V, PereiraPA, KoskinenK, Paulin L, PekkonenE, Auvinen P. 2015. Gut microbiota are related to Parkinson's disease and clinical phenotype. Movement disorders, 30(3), 350-358. https://doi.org/10.1002/mds.26069PMid:25476529
12. NuzumND, Loughman A, Szymlek-GayEA, Hendy A, TeoWP, Macpherson H. (2020). Gut microbiota differences between healthy older adults and individuals with Parkinson's disease: A systematic review. J Parkinsons Dis. 10(3), 893-917. https://doi.org/10.3233/JPD-191800PMid:31868685
13. Hill-Burns EM, DebeliusJW, Morton JT, WissemannWT, Lewis MR, Wallen ZD, Knight R 2017. Parkinson's disease and Parkinson's disease medications have distinct signatures of the gut microbiome. Movement Disorders, 32(5), 739-749. https://doi.org/10.1002/mds.26942PMid:28195358 PMCid:PMC5469442
14. Bedarf JR, Hildebrand F, CoelhoLP, Sunagawa S, Bahram M, Goeser F, Bork P. 2017. Functional implications of microbial and viral gut metagenome changes in early-stage L-DOPA-naïve Parkinson's disease patients. Genome medicine, 9(1), 39. https://doi.org/10.1186/s13073-017-0428-yPMid:28449715 PMCid:PMC5408370
15. Unger MM, Spiegel J, Dillmann KU, Grundmann D, Philippeit H, Bürmann J, Schäfer KH; 2016. Short chain fatty acids and gut microbiota differ between patients with Parkinson's disease and age-matched controls. Parkinsonism andrelated disorders, 32, 66-72.https://doi.org/10.1016/j.parkreldis.2016.08.019PMid:27591074
16. Zhang F, Wang Y, WangX, Zhu X, Zhang Q, Ni.Y; 2020. Gut microbiota dysbiosis in Parkinson's disease: Current and potential impact on pathogenesis. Frontiers in Neurology, 11, 865. https://doi.org/10.3389/fneur.2020.00865PMid:32922359 PMCid:PMC7457056
17. Liu B, Fang F, Pedersen NL, Tillander A, Ludvigsson JF, Ekbom A, SvenningssonP 2017. Vagotomy and Parkinson disease: A Swedish register-based matched-cohort study. Neurology, 88(21),1996-2002.https://doi.org/10.1212/WNL.0000000000003961 PMid:28446653 PMCid:PMC5440238
18. DevosD, Lebouvier T, Lardeux B, Biraud, M, Rouaud T, Pouclet H, Derkinderen P 2013. Colonic inflammation in Parkinson's disease. Neurobiology of disease, 50, 42-48. https://doi.org/10.1016/j.nbd.2012.09.007PMid:23017648
19. ShenT, YueY, He T, Huang C, Qu B, Lv W2021. The association between the gut microbiota and Parkinson's disease, a meta-analysis. Frontiers in aging euroscience, 13, 636545. https://doi.org/10.3389/fnagi.2021.636545PMid:33643026 PMCid:PMC7907649
20. Enright EF,Gahan CGM, Joyce SA, Griffin BT2016. The impact of the gut microbiota on drug metabolism and clinical outcome. Yale J Biol Med, 89(3), 375-382.
21. Fung TC2020. The microbiota-immune axis as a central mediator of gut-brain communication. Neurobiol. Dis., 136, 104714. https://doi.org/10.1016/j.nbd.2019.104714PMid:31846737

22. Dutta SK, Verma S, Jain A2022. Parkinson's disease and the microbiome. J Neurol, 269(6), 2943-2956. https://doi.org/10.1007/s00415-021-10887-3
23. Houser MC, Tansey MG2017. The gut-brain axis: Is intestinal inflammation a silent driver of Parkinson's disease pathogenesis? NPJ Parkinson's Disease, 3, 3. https://doi.org/10.1038/s41531-016-0002-0PMid:28649603 PMCid:PMC5445611
24. Heintz-BuschartmA, Pandey U, Wicke T, *et al*., 2018. The nasal and gut microbiome in Parkinson's disease and idiopathic rapid eye movement sleep behavior disorder. Movement disorders, 33(1), 88-98. https://doi.org/10.1002/mds.27105PMid:28843021 PMCid:PMC5811909
25. Acuña CJ, Elgueta D, Pacheco R 2019. T-cell-driven inflammation as a mediator of the gut-brain axis involved in Parkinson's disease. Frontiers in immunology, 10, 239. https://doi.org/10.3389/fimmu.2019.00239PMid:30828335 PMCid:PMC6384270
26. Fleury V, Funk GC, Lazzeri C, *et al*., 2018. Age- and sex-specific prevalence of Parkinson's disease: A systematic review and meta-analysis. Parkinsonism andrelated disorders, 48, 29-35. https://doi.org/10.1016/j.parkreldis.2017.12.010PMid:29249680 PMCid:PMC5826846
27. Boertien JM, PereiraPA, Aho VTE, *et al*., 2019. Increasing comparability and utility of gut microbiome studies in Parkinson's disease: A systematic review. J Parkinsons Dis. 9(S2), S297-S312. https://doi.org/10.3233/JPD-191721PMid:31498132 PMCid:PMC6839496
28. TamtajiOR, Taghizadeh M, Kakhaki DR, *et al*., 2019. Clinical and metabolic response to probiotic administration in people with Parkinson's disease: A randomized, double-blind, placebo-controlled trial. Clinical nutrition, 38(3), 1031-1035. https://doi.org/10.1016/j.clnu.2018.05.007PMid:31060718
29. Kelly JR, Kennedy PJ, Cryan JF, *et al*., 2015. Breaking down the barriers: The gut microbiome, intestinal permeability and stress-related psychiatric disorders. Frontiers in Cellular Neuroscience, 9, 392. https://doi.org/10.3389/fncel.2015.00392
30. Perez-Pardo P, Dodiya HB, Engen PA, *et al*., 2019. Role of TLR4 in the gut-brain axis in Parkinson's disease: A translational study from men to mice. Gut, 68(5), 829-843. https://doi.org/10.1136/gutjnl-2018-316844PMid:30554160
31. Pellegrini C, Antonioli L, Colucci R, *et al*., 2023. Enteric glia at the crossroads between intestinal immune system and epithelial barrier: Implications for Parkinson disease. Handb. Clin. Neurol, 191, 195-213. https://doi.org/10.1016/B978-0-323-96178-1.00012-6
32. Schwiertz A, Spiegel J, Dillmann KU, *et al*., 2018. Fecal markers of intestinal inflammation and intestinal permeability are elevated in Parkinson's disease. Parkinsonism andrelated disorders, 50, 104-107. https://doi.org/10.1016/j.parkreldis.2018.02.023PMid:29475591 PMCid:PMC6319386
33. Barichella M, Severgnini M, Cilia R, *et al*., 2019. Unraveling gut microbiota in Parkinson's disease and atypical parkinsonism. Movement Disorders, 34(3), 396-405. https://doi.org/10.1002/mds.27581PMid:30576008
34. Mulak A, Bonaz B; 2015. Brain-gut-microbiota axis in Parkinson's disease. World J Gastroenterol, 21(37), 10609-10620. https://doi.org/10.3748/wjg.v21.i37.10609 PMid:26457021 PMCid:PMC4588083
35. KimS, Kwon SH, KamTI, *et al*., 2019. Transneuronal propagation of pathologic α-synuclein from the gut to the brain models Parkinson's disease. Neuron, 103(4), 627-641.e7. https://doi.org/10.1016/j.neuron.2019.05.035 PMid:31255487 PMCid:PMC6706297
36. FriedlandRP,Chapman MR; 2017. The role of microbial amyloid in neurodegeneration. PLoS Pathogens, 13(12), e1006654. https://doi.org/10.1371/journal.ppat.1006654PMid:29267402 PMCid:PMC5739464
37. Svensson E, Horváth-Puhó E, Thomsen RW, *et al*., 2015. Vagotomy and subsequent risk of Parkinson's disease. Ann. Neurol, 78(4), 522-529. https://doi.org/10.1002/ana.24448PMid:26031848
38. BedarfJR, Hildebrand F, Coelho LP,*et al*., 2017. Functional implications of microbial and viral gut metagenome changes in early-stage L-DOPA-naïve Parkinson's disease patients. Genome Medicine, 9, 39. https://doi.org/10.1186/s13073-017-0428-yPMid:28449715 PMCid:PMC5408370
39. Zhu F, Ju Y, Wang W, *et al*., 2020. Metagenome-wide association of gut microbiome features for schizophrenia. Nature communications, 11, 1612. https://doi.org/10.1038/s41467-019-14241-1PMid:32235826 PMCid:PMC7109134
40. Yano JM, Yu K, DonaldsonGP, *et al*., 2015. Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. Cell, 161(2), 264-276. https://doi.org/10.1016/j.cell.2015.02.047PMid:25860609 PMCid:PMC4393509
41. Sampson TR, Debelius JW, Thron T, *et al*., 2016. Gut microbiota regulate motor deficits and neuroinflammation in a model of Parkinson's disease. Cell, 167(6), 1469-1480.e12. https://doi.org/10.1016/j.cell.2016.11.018PMid:27912057 PMCid:PMC5718049
42. Sampson,TR, Challis C, Jain N, *et al.,*2020. A gut bacterial amyloid promotes α-synuclein aggregation and motor impairment in mice. eLife, 9, e53111. https://doi.org/10.7554/eLife.53111PMid:32043464 PMCid:PMC7012599
43. Choi JG, Kim N, JuIG, *et al*., (2018). Oral administration of proteus mirabilis damages dopaminergic neurons and motor functions in mice. Scientific reports, 8, 1275. https://doi.org/10.1038/s41598-017-18835-2PMid:29352191 PMCid:PMC5775305

44. Keshavarzian A, GreenSJ, Engen PA, *et al.*,(2015. Colonic bacterial composition in Parkinson's disease. Movement disorders, 30(10), 1351-1360. https://doi.org/10.1002/mds.26307PMid:26179554
45. Aho VTE, Houser MC, Pereira PAB, *et al.*, 2021. Relationships of gut microbiota, short-chain fatty acids, inflammation, and the gut barrier in Parkinson's disease. Molecular neurodegeneration, 16, 6. https://doi.org/10.1186/s13024-021-00427-6PMid:33557896 PMCid:PMC7869249
46. Shen T, Yue Y, He T, *et al.*, 2021. The association between the gut microbiota and Parkinson's disease, a meta-analysis. Frontiers in Aging Neuroscience, 13, 636545. https://doi.org/10.3389/fnagi.2021.636545PMid:33643026 PMCid:PMC7907649
47. Elfil M, Kamel S,Kandil M2020. Implications of the gut microbiome in Parkinson's disease. Movement Disorders, 35(3), 377-385. https://doi.org/10.1002/mds.28004PMid:32092186
48. Palacios N, Molsberry SA, Shah RD,*et al.*, 2023. Metagenomics of the gut microbiome in Parkinson's disease: Prodromal changes. Annals of Neurology, 93(3), 450-461.https://doi.org/10.1002/ana.26719PMid:37314861 PMCid:PMC10538421
49. AhoVTE, Pereira PAB, Voutilainen S, *et al.*, 2019. Gut microbiota in Parkinson's disease: Temporal stability and relations to disease progression. EbioMedicine, 44, 691-707. https://doi.org/10.1016/j.ebiom.2019.05.064PMid:31221587 PMCid:PMC6606744
50. Gerhardt S, Mohajeri MH; 2018. Changes of colonic bacterial composition in Parkinson's disease and other neurodegenerative diseases. Nutrients, 10(6), 708. https://doi.org/10.3390/nu10060708PMid:29857583 PMCid:PMC6024871
51. Fitzgerald E, Murphy S, MartinsonHA 2019. Alpha-synuclein pathology and the role of the microbiota in Parkinson's disease. Frontiers in Neuroscience, 13, 369. https://doi.org/10.3389/fnins.2019.00369PMid:31068777 PMCid:PMC6491838
52. Palacios N, Gao X, McCullough ML, *et al.*, 2018. Caffeinated coffee, caffeine intake, and risk of Parkinson's disease in men and women. Movement disorders, 33(10), 1480-1485. https://doi.org/10.1002/mds.27435
53. Gubert, C., GasparottoJ, Ribeiro CT, *et al.*, 2022. Probiotics prevent cognitive, behavioural and molecular alterations induced by chronic unpredictable stress in mice. J. Psychiatr. Res, 148, 43-56. https://doi.org/10.1016/j.jpsychires.2022.01.029PMid:35091357 PMCid:PMC8764617
54. Nishiwaki H, Ito M, Ishida T, *et al.*, 2020. Meta-analysis of gut dysbiosis in Parkinson's disease. Movement disorders, 35(9), 1626-1635. https://doi.org/10.1002/mds.28193PMid:32725640
55. Lin CH, Chen CC, Chiang HL, *et al.*, 2019. Altered gut microbiota and inflammatory cytokine responses in patients with Parkinson's disease. J. Neuroinflammation, 16, 129. https://doi.org/10.1186/s12974-019-1528-yPMid:31248424 PMCid:PMC6598278
56. Quigley, EMM; 2017. Microbiota-brain-gut axis and neurodegenerative diseases. Current neurology and neuroscience reports, 17, 94. https://doi.org/10.1007/s11910-017-0802-6PMid:29039142
57. Singh V, Roth S, Llovera G, *et al.*, 2016. Microbiota dysbiosis controls the neuroinflammatory response after stroke. J. Neurosci, 36(28), 7428-7440. https://doi.org/10.1523/JNEUROSCI.1114-16.2016PMid:27413153 PMCid:PMC6705544
58. Cryan JF, Dinan TG 2012; Mind-altering microorganisms: The impact of the gut microbiota on brain and behaviour. Nature Reviews Neuroscience, 13, 701-712. https://doi.org/10.1038/nrn3346PMid:22968153
59. Ochoa-Repáraz J, Kasper LH; 2014. The second brain: Is the gut microbiota a link between obesity and central nervous system disorders? Current obesity reports, 3, 404-413. https://doi.org/10.1007/s13679-014-0121-5
60. Obata Y, Pachnis V; 2016. The effect of microbiota and the immune system on the development and organization of the enteric nervous system. Gastroenterology, 151(5), 836-844. https://doi.org/10.1053/j.gastro.2016.07.044PMid:27521479 PMCid:PMC5102499
61. Fuentes TC, Schellekens H, Dinan TG,CryanJF ;2017. The microbiota-gut-brain axis in obesity. The Lancet Gastroenterology and Hepatology, 2(10), 747-756. https://doi.org/10.1016/S2468-1253(17)30147-4PMid:28844808
62. Grenham, S, Clarke G, Cryan JF, Dinan TG; 2011. Brain-gut-microbe communication in health and disease. Frontiers in Physiology, 2, 94. https://doi.org/10.3389/fphys.2011.00094PMid:22162969 PMCid:PMC3232439
63. Needham BD, Funabashi M, Adame MD, *et al.*, 2022. A gut-derived metabolite alters brain activity and anxiety behaviour in mice. Nature, 602, 647-653. https://doi.org/10.1038/s41586-022-04396-8PMid:35165440 PMCid:PMC9170029
64. Jangi S, Gandhi R, Cox LM, *et al.*, 2016. Alterations of the human gut microbiome in multiple sclerosis. Nature Communications, 7, 12015. https://doi.org/10.1038/ncomms12015PMid:27352007 PMCid:PMC4931233
65. Tremlett H, Bauer KC, Cresswell AS, *et al.*, 2017. The gut microbiome in human neurological disease: A review. Ann. Neurol, 81(3), 369-382. https://doi.org/10.1002/ana.24901PMid:28220542
66. Cryan JF, O'Riordan KJ, Sandhu K, *et al.*, 2020. The microbiota-gut-brain axis. Physiological Reviews, 99(4), 1877-2013. https://doi.org/10.1152/physrev.00018.2018 PMid:31460832

67. Erny D, Angelis HAL, Jaitin D, *et al*., 2015. Host microbiota constantly control maturation and function of microglia in the CNS. Nature Neuroscience, 18, 965-977. https://doi.org/10.1038/nn.4030PMid:26030851 PMCid:PMC5528863
68. Fung TC, Olson CA, Hsiao EY2017. Interactions between the microbiota, immune and nervous systems in health and disease. Nature Neuroscience, 20, 145-155. https://doi.org/10.1038/nn.4476PMid:28092661 PMCid:PMC6960010
69. Valdes AM, Walter J, Segal E, Spector TD 2018. Role of the gut microbiota in nutrition and health. BMJ, 361, k2179. https://doi.org/10.1136/bmj.k2179PMid:29899036 PMCid:PMC6000740
70. RutschA, Kantsjö J B, RonchiF 2020. The gut-brain axis: How microbiota and host inflammasome influence brain physiology and pathology. Frontiers in Immunology, 11, 604179. https://doi.org/10.3389/fimmu.2020.604179PMid:33362788 PMCid:PMC7758428
71. Marin I A, Goertz JE, Ren T, *et al*., 2017. Microbiota alteration is associated with the development of stress-induced despair behavior. Scientific Reports, 7, 43859. https://doi.org/10.1038/srep43859PMid:28266612 PMCid:PMC5339726
72. Minter MR, Zhang C, Leone V, *et al*., 2016. Antibiotic-induced perturbations in gut microbial diversity influences neuro-inflammation and amyloidosis in a murine model of Alzheimer's disease. Scientific reports, 6, 30028 https://doi.org/10.1038/srep30028PMid:27443609 PMCid:PMC4956742
73. Ogbonnaya ES, Clarke G, Shanahan F, *et al*., 2015. Adult hippocampal neurogenesis is regulated by the microbiome. Biological psychiatry, 78(4), e7-e9. https://doi.org/10.1016/j.biopsych.2014.12.023PMid:25700599
74. Lu J, Lu L, Yu Y, *et al*., 2021. Gut microbiota influence immunosuppressive function of bone marrow-derived mesenchymal stem cells via modulating serotonin levels. J. Transl. Med, 19, 99. https://doi.org/10.1186/s12967-021-02747-2
75. Pan R, Zhang H, Yu Y, *et al*., 2022. The role of gut-brain axis in regulating neuroinflammation in Alzheimer's disease. Front. Aging Neurosci. 14, 825180. https://doi.org/10.3389/fnagi.2022.825180