

Article History

Received:
January 10, 2024

Revised:
February 28, 2024

Accepted:
March 01, 2024

Available Online:
June 30, 2024

THE ROLE OF GUT MICROBIOTA IN THE PATHOGENESIS OF PARKINSON'S DISEASE: IMPLICATIONS FOR EARLY DIAGNOSIS AND TARGETED THERAPEUTIC INTERVENTIONS

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Abstract

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms. Considerable evidence now implicates the gut microbiota (GM) as being very important in its causation. The gut-brain axis-the bidirectional communication between the gut and the central nervous system-is said to be involved in the neuroinflammation, α -synuclein aggregation, and intestinal permeability that facilitate PD onset and progression. Studies establish that gut dysbiosis-the change in the composition of the gut microbiota that is likely to be less favorable to the health of the person-due to a decrease in the number of beneficial SCFA-producing bacteria, with compensatory increase in those whose action is more pro-inflammatory-is related to the severity of PD. Changes in the composition of gut microbiota may also qualify as important biomarkers in early diagnosis of PD, while other interventions aimed at enhancing the composition of the microbiota through probiotics, prebiotics, dietary changes, and fecal microbiota transplantation are promising in their utility in modulating the course of the disease. Our understanding of the complex interplay of the gut microbiota and PD pathophysiology may enable us to develop new diagnostic products and microbiota-targeted therapeutic strategies.

Keywords: Parkinson's Disease, Gut Microbiota, Neuroinflammation, Microbiota-Based Therapy

INTRODUCTION

Parkinson's disease (PD) is one of the progressive neurodegenerative diseases manifested by the loss of dopaminergic neurons in the substantia nigra with the resultant motor dysfunction and non-motor symptoms [1]. The prevalence of PD has been on the rise across countries, with studies providing epidemiological evidence of an increasingly mounting disease burden on aging populations [2]. Although the exact etiology of PD remains obscure, recent developments point to the involvement of gut

microbiota (GM) in PD pathogenesis through their interactions with the gut-brain axis [3]. Dysbiosis or microbial imbalance may lead to neuroinflammation, α -synuclein aggregation, and increased intestinal permeability, thereby inducing further disease progression [4]. By producing less SCFA and conversely increasing levels of pro-inflammatory taxa, PD has been associated with additional gut microbiota alterations, thereby aggravating neurodegenerative processes [5,6].

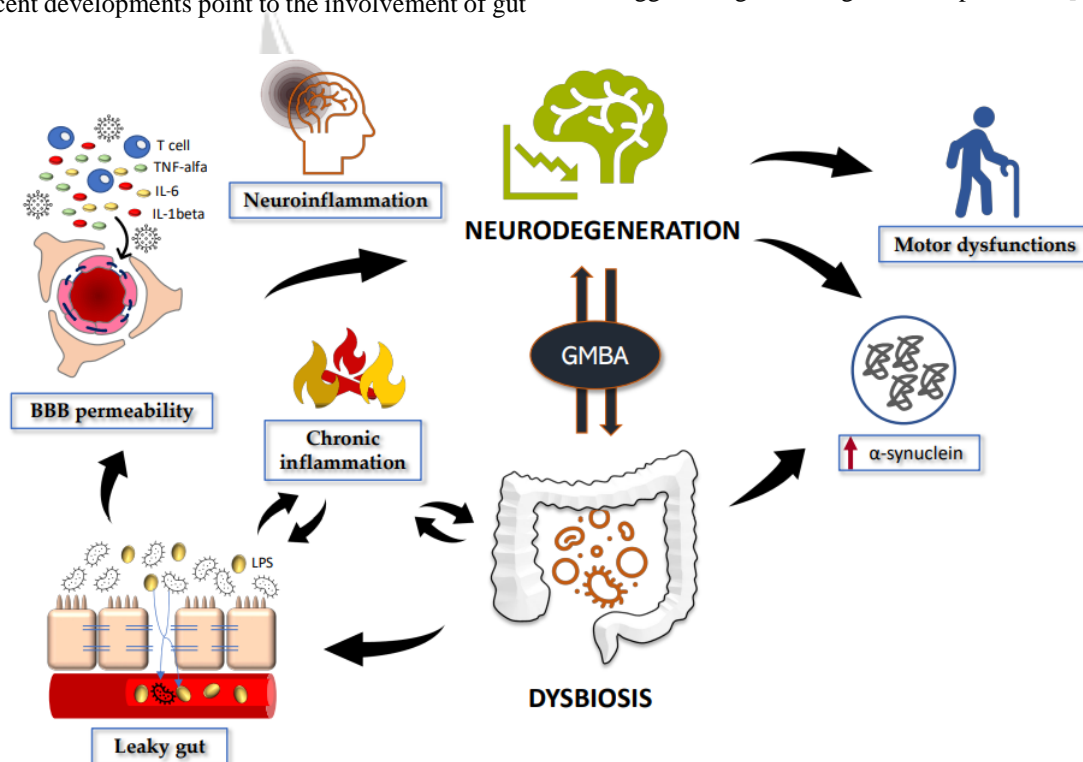


Figure 1. Parkinson's disease (PD) suffers from effects due to the gut microbiota brain axis (GMBA).

The aggregation of α -synuclein occurs in both dopaminergic substantia nigra neurons alongside the human gut where it commonly develops alongside intestinal dysbiosis. The abnormal structure of gut microbiota leads to sustained inflammation and blood brain barrier (BBB) dysfunction caused by the intestinal system becoming permeable (leaky gut). Neuroinflammation directly or indirectly causes

cognitive decline together with motor dysfunction that typical PD shows.

The pathogenesis of PD depends heavily on the gut-brain axis which uses neuroimmune modulation together with microbial metabolites [7,8]. Research reveals that bacterial amyloid and lipopolysaccharide inflammation together create systemic immune responses which damage blood-

brain barrier integrity and lead to dopaminergic neuron destruction[9,10]. This effect adds to the misfolding of α -synuclein that represents a PD diagnostic hallmark by finding evidence firstly in the enteric nervous system before CNS spread [11,12]. Research now suggests gut microbiota functions as viable biomarkers for making PD diagnoses at an early stage because scientists discovered specific microbial patterns linked to disease stages [13,14].

Current therapeutic strategies are still ongoing and include probiotics, prebiotics, dietary manipulations, and fecal microbiota transplantation; all of these host an idea of restoring microbial balance, alleviating neuroinflammation, and improving gut-barrier functions to bring about possible alterations in disease outcomes [37-38]. Studies have accumulated evidence that such gut microbiota changes will be related to PD

pathophysiology and could influence the responses to dopaminergic therapies. Some neuroimaging studies examined gut-derived inflammatory markers as indicators of early neurodegenerative changes in PD patients [39]. The complexity of this situation demands multidisciplinary teams such as neuroscientists, microbiologists, and clinicians who would be involved in developing targeted gut-microbiota-based therapies. Again, much has to be invested in long-term cohort studies that determine causality and the long-term effects of microbiota-based interventions. Deciphering the neurodegeneration-gut microbiota nexus may lead precision medicine approaches to offer new diagnostic and perhaps therapeutic avenues for PD, thereby improving outcomes and quality of life for individuals with this condition [40].

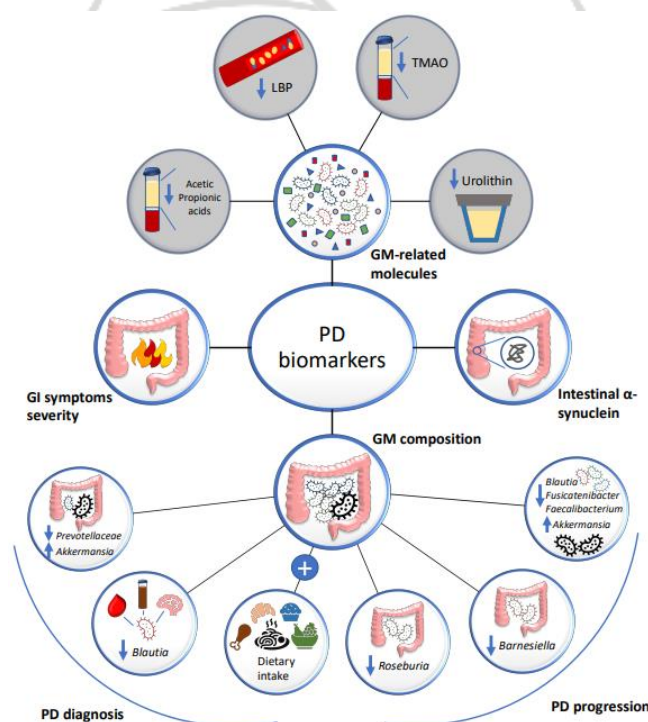


Figure 2. Medical tests that examine Parkinson's disease (PD) biomarkers through the analysis of Gut microbiota (GM).

Scientists proposed intestinal α -synuclein as well as GI symptom severity together with GM-related molecules and GM composition for potential use as PD biomarkers. The PD biomarkers related to GM-associated molecules include reduced levels of urolithin in urine samples as well as decreased plasma TMAO concentrations and decreased plasma-acetic and propionic acid levels and low LPS binding protein (LBP) concentration. PD progression may lead to PD diagnoses when combined with dietary intake data and dysbiosis assessment because it causes a relative reduction in Roseburia, Barnesiella, Blautia, Fusicatenibacter, Faecalibacterium abundance yet an increase in Akkermansia abundance. \uparrow : increase; \downarrow : decrease.

METHODOLOGY

Based on a comprehensive literature review, this study attempted to look into the peer-reviewed journal articles and clinical studies in which gut microbiota was most commonly considered relevant to the role in Parkinson's disease. Relevant articles published over the last 20 years were looked at through the databases of PubMed, Web of Science, and Google Scholar. The keywords used to get relevant studies were: "gut microbiota and Parkinson's disease," "gut-brain axis and neurodegeneration," "microbiota-based therapies," and "dysbiosis and neuroinflammation."

The selection criteria included studies that had some clinical preclinical or in vitro evidence linking alterations in gut microbiota to PD pathogenesis, progression, and therapeutic interventions. Data extraction focused on changes in microbial composition in PD patients, mechanisms of neurodegeneration driven by microbiota, and managerial interventions targeting the microbiome. The studies were also evaluated for quality, relevance, and contribution to knowledge regarding

gut microbiota's role in PD pathophysiology. Meta-analyses and systematic reviews were also checked to present a comprehensive evaluation of the current research landscape [26,27].

FUTURE DIRECTIONS

Further studies are needed to explore the role of gut microbiota in Parkinson's, focusing on longitudinal cohort studies to establish a causative relationship between gut dysbiosis and neurodegeneration [28]. Advanced multi-omic tools integrating metagenomic, transcriptomic, and metabolomic technologies may provide deeper mechanistic insight through delineation of microbiota-driven molecular pathways towards the pathology of PD [29]. In addition, the standardization of microbiota biomarkers for early PD diagnosis might improve early intervention when neurodegeneration is still minimal [30].

Personalized therapies based on the microbiome: such as precision probiotics, engineered bacterial strains, and targeted dietary interventions-have the potential to slow down disease progression [31]. Long-term assessment of FMT for PD should include its effectiveness and safety and its effect on neurologic outcomes [32]. Lifestyle factors, including diet and exercise, influence gut microbiota composition in PD and may inform future noninvasive preventive strategies [33].

The synergy of neurologists, microbiologists, and computational biologists will be critical for the transition from microbiome research to clinical applications. A global biobank for microbiota samples from PD patients would support large-scale studies to identify universal versus population-specific microbial signatures [34]. By addressing these research gaps, microbiota-targeted strategies will an important role in the future management of

PD and will ultimately enhance patients' outcomes and quality of life [35,36,41].

CONCLUSION

The research has been important in understanding the pathophysiology, diagnosis, and treatment of the disease. It examines the role of gut microbiota in Parkinson's disease. Gut dysbiosis is evidence for neuroinflammation, α -synuclein aggregation, and dysfunction of the blood-brain barrier—principally degrading factors in the progression of PD. The gut-microbiome axis would be the link between alterations due to microbes and neurodegenerative processes; this emphasizes the importance of microbial biomarkers for the detection and management of the early disease states. Microbial-targeted therapies such as probiotics, dietary changes, or even fecal microbiota transplants thus offer much promise to influence the composition of gut flora and, thus, influence the symptoms of PD; further research is needed to back these therapeutic interventions and examine their long-term effectiveness and safety in the clinic. Moving forward, multi-omics approaches and large longitudinal studies would be instrumental in improving the understanding of the role of gut microbiota in PD with subsequent translation into precision medicine. As research progresses, interdisciplinary inclusion of neuroscientists, microbiologists, and clinicians would be important in developing effective interventions based on microbiota. Mindful of current limitations and prising on the gut-brain connection, future innovations in microbiome-targeted therapies could dramatically change PD's management and functionality.

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