



Do All Roads Lead to Rome? - Rethinking Parkinson's Disease Through the Gut-Brain Axis

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Introduction

Parkinson's disease (PD) is a chronic, progressive, and disabling neurodegenerative disorder that affects the middle-aged and elderly population. It has been ranked second neurodegenerative disorders worldwide just after Alzheimer's disease (AD), with a prevalence and incidence that was observed in 1–2% of the population with age over 60 years. Emerging research suggests that the gut–brain axis plays a critical role in the pathogenesis of Parkinson's disease (PD), with the gut microbiota increasingly implicated as a key player. The hypothesis that PD may begin in the gastrointestinal tract—supported by early non-motor symptoms such as constipation and the presence of alpha-synuclein pathology in enteric neurons—has led to a paradigm shift in how the disease is understood. This review explores current evidence linking gut dysbiosis to neuroinflammation, alpha-synuclein aggregation, and disease progression in PD.

Materials and Methods

This review is based on 11 articles from the PubMed and Clinical Key databases, including reviews and meta-analyses published between 2017 - 2014, analyzing a total of 542 patients. The therapeutic strategies explored were centered on modulation of the gut microbiota, including the use of probiotics, prebiotics, dietary interventions, and fecal microbiota transplantation (FMT), aimed at restoring microbial balance and reducing neuroinflammation. Inclusion criteria for the clinical studies typically

involved patients with a confirmed diagnosis of Parkinson's disease, stable medication regimens, and gastrointestinal symptoms such as constipation or bloating. Exclusion criteria included the presence of other neurodegenerative or gastrointestinal diseases, recent antibiotic use, immunosuppressive therapy, or cognitive impairment interfering with participation.

Results

Gut dysbiosis was consistently observed in PD patients, with a significant reduction in short-chain fatty acid (SCFA)-producing bacteria like *Faecalibacterium* (down by 40%) and an increase in pro-inflammatory species such as *Enterobacteriaceae* (up by 30%). These microbial shifts were associated with increased intestinal permeability and worsened motor and non-motor symptoms, including constipation and higher Unified Parkinson's Disease Rating Scale (UPDRS)-III scores. Therapeutic interventions targeting the gut microbiota showed promise. Probiotic supplementation led to gastrointestinal improvements in 60%, with reductions in inflammatory markers like TNF- α and IL-6. Non-motor symptoms improved by 10-15% after 12 weeks. FMT, though experimental, improved motor symptoms and gut function in 11 patients. Preclinical studies also supported the gut-brain axis, showing microbiota from PD patients induced alpha-synuclein aggregation and neuroinflammation, reinforcing its potential role in disease progression.

Conclusion

Gut microbiota modulation shows promise as a therapeutic strategy in Parkinson's disease, with interventions like probiotics and fecal microbiota transplantation showing potential in improving symptoms and reducing inflammation. However, further large-scale studies are needed to confirm efficacy and long-term safety.

Keywords: Parkinson's disease, Gut microbiota, Gut-brain axis, disease-modifying therapy