

Review and Progress

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The Role of the Gut-Brain Axis in the Pathogenesis of Parkinson's Disease and Its Clinical Application Prospects

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Abstract This study explored the role of the gut-brain axis in Parkinson's disease (PD). PD is characterized by the degeneration of dopaminergic neurons in the substantia nigra and the aggregation of α -synuclein. Gastrointestinal non-motor symptoms such as constipation often occur earlier than motor symptoms, accompanied by the deposition of α -synuclein in the intestine, damage to the intestinal barrier and activation of mucosal immunity. Environmental toxins, diet, infection and antibiotics can cause intestinal flora imbalance, promote the misfolding of α -synuclein and its entry into the brain along the vagus nerve and humoral pathways, and work in synergy with mitochondrial dysfunction, oxidative stress and genetic susceptibility to form a multi-factor pathological network. In terms of early diagnosis, fecal microbiota and its metabolites, intestinal biopsy α -synuclein, tongue coating microbiota and multi-omics integrated models, combined with gastrointestinal symptom scales, are expected to form a non-invasive biomarker system for screening high-risk populations and risk stratification. In terms of treatment, the combined application of probiotics/synthetic bacteria, dietary intervention, fecal microbiota transplantation, intestinal-targeted anti-inflammatory and barrier repair, and vagus nerve regulation, along with dopamine replacement and deep brain stimulation, is expected to improve both motor and non-motor symptoms while partially influencing the course of the disease, providing new ideas for individualized intervention based on the gut-brain axis.

Keywords Parkinson's disease; Gut-brain axis; Gut microbiota; α -synuclein; Early diagnosis

1 Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder and the second most common movement disorder in the world. In the general population, about 1 to 2 people out of every 1 000 suffer from this disease. The proportion of people over 60 years old suffering from this disease is approximately 1%. After the onset of the disease, patients often experience problems related to movement, such as hand tremors, muscle stiffness, slow movement and physical instability. In addition, patients may also experience non-motor symptoms, which often appear several years earlier than the motor symptoms we are familiar with. This indicates that Parkinson's disease is not only complex but also affects the whole body (Santos et al., 2022). Relevant epidemiological investigations show that men have a higher risk of Parkinson's disease than women. The occurrence of this disease is related to both genetic factors and environmental risks (Ben-Shlomo et al., 2024). Nowadays, the aging of the population is becoming increasingly prominent, and the health pressure brought by Parkinson's disease on a global scale is also growing. It is estimated that the number of patients may double in the coming decades. This means that we urgently need to have a deeper understanding of this disease and improve its treatment and care methods (Menozzi et al., 2025).

The traditional view holds that PD is mainly caused by the progressive loss of dopaminergic neurons in the substantia nigra pars compacta and the accumulation of misfolded α -synuclein in Louis' bodies. Its molecular mechanisms involve α -synuclein aggregation, mitochondrial dysfunction, oxidative stress, impaired protein clearance and neuroinflammation, etc. (Simon et al., 2020). Based on the above understanding, symptomatic treatments such as dopamine replacement represented by levodopa and deep brain stimulation have been developed. However, long-term application is often accompanied by reduced efficacy and motor and non-motor complications, and cannot prevent or reverse the progression of the disease (Xu et al., 2023; Menozzi et al., 2025),