immune cells constantly detect substances in the intestine. After interacting with microbial antigens, they produce signal molecules such as cytokines, thereby regulating the local and overall immune responses of the body. These substances can cross the blood-brain barrier or affect brain function through neural pathways, participating in the occurrence and development of neuroinflammation and neurological diseases (Hattori and Yamashiro, 2021). Meanwhile, humoral factors such as intestinal hormones and neuropeptides, as well as microbial metabolic products like short-chain fatty acids, further regulate the activities of the nervous and immune systems, which also reflects the complexity and integrity of the gut-brain axis regulatory network (Suganya and Koo, 2020).

2.3 Regulation of the nervous system by gut microbiota and its metabolites

The gut microbiota, composed of trillions of microorganisms, settles in the human gastrointestinal tract and is now regarded as the core regulatory part of the gut-brain axis (Suganya and Koo, 2020). They are involved in various metabolic processes and can produce many bioactive substances, such as neurotransmitters like serotonin and gamma-aminobutyric acid, as well as metabolites like short-chain fatty acids that have an impact on the nervous system. These substances can act directly or indirectly on the enteric nervous system, change its function, and also regulate the activities of the autonomic and central nervous systems (Zheng et al., 2023; Bakshi et al., 2024).

From the initial development of the nervous system to the aging process of human beings, various factors such as diet, antibiotic use, high mental stress, and infection may all change the composition and metabolic characteristics of the intestinal microbiota, thereby affecting the generation of important metabolites and the overall situation of signal transmission between the intestine and the brain (Suganya and Koo, 2020). Researchers are actively studying methods such as probiotics, prebiotics, and dietary adjustments to restore or regulate the gut microbiota, and taking this as a potential direction for the treatment of neurodegenerative diseases and neuropsychiatric disorders (Zheng et al., 2023; Bakshi et al., 2024). This type of research further demonstrates that the gut microbiota is of great significance for maintaining the health of the nervous system and developing new clinical intervention methods.

3 Evidence for the Role of the Gut and Gut Microbiota in Parkinson's Disease

3.1 The relationship between gastrointestinal non-motor symptoms and the occurrence and development of parkinson's disease

Gastrointestinal (GI) symptoms are now regarded as the most common and earliest group of non-motor manifestations in Parkinson's disease (PD), often emerging many years or even decades earlier than classical motor symptoms (Chiang and Lin, 2025). Constipation, drooling, dysphagia and urinary dysfunction are particularly common. About 60%~80% of PD patients have at least one GI symptom. These manifestations not only significantly impair the quality of life, but are also related to the duration and progression of the disease. It is suggested that GI dysfunction is closely related to the potential pathophysiology of PD (Montalban-Rodriguez et al., 2024). Among them, constipation and defecation dysfunction often occur before motor symptoms and are regarded as potential early clinical markers of PD, which are expected to provide clues for early identification and intervention (Khalaf et al., 2025).

Some studies have shown that Parkinson's disease patients with poor gastrointestinal function tend to have more severe motor symptoms and more obvious cognitive decline, which further indicates that gastrointestinal problems are associated with the progression of Parkinson's disease (Jones et al., 2020). Patients with Parkinson's disease often have changes in gut microbiota, that is, microbiota imbalance. This change is related to their gastrointestinal symptoms and neurological symptoms (Chiang and Lin, 2025). The gut-brain axis enables bidirectional signal transmission between the gut and the central nervous system, allowing signals from the gut to influence the processes of neuroinflammation and neurodegeneration. So, gastrointestinal symptoms may not only be incidental manifestations of Parkinson's disease, but an important part involved in the occurrence and development of the disease (Montalban-Rodriguez et al., 2024).

3.2 Deposition of α -synuclein in intestinal mucosa and enteric nervous system and braak hypothesis

One of the most core pathological features of Parkinson's disease (PD) is the accumulation of misfolded α -synuclein in nerve cells, forming Lewy bodies. This pathological change not only occurs in the brain, but also