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**Gastrointestinal syndromes preceding a diagnosis of Parkinson’s disease: testing Braak’s hypothesis using a nationwide database for comparison with Alzheimer’s disease and cerebrovascular diseases. - Konings B, Villatoro L, Van den Eynde J, et al.**

Konings B, Villatoro L, Van den Eynde J, et al. [*Gastrointestinal syndromes preceding a diagnosis of Parkinson’s disease: testing Braak’s hypothesis using a nationwide database for comparison with Alzheimer’s disease and cerebrovascular diseases.*](https://gut.bmj.com/content/72/11/2103) Gut 2023; 72: 2103-2111. doi: 10.1136/gutjnl-2023-329685.

Parkinson’s disease (PD) is a neurodegenerative condition characterised by bradykinesia, tremor, rigidity, and postural instability. Lewy bodies are the pathological hallmark, which contain alpha-synuclein. Braak famously postulated that the gastrointestinal (GI) tract is implicated in the development of PD through accumulation of misfolded alpha-synuclein in the enteric nervous system. This may manifest as early-onset GI symptoms before neurological features develop.

To further challenge this hypothesis, Konings et al., looked at the association between GI conditions and new-onset PD using a large US-based electronic research database (TriNetX) that consists of >80 million patients. They conducted a case-control study to look at the association between PD and a previous diagnosis of 18 GI conditions using ICD-10 (International Classification of Diseases 10th Revision) coding. Contemporary assessment of Alzheimer’s and cerebrovascular disease allowed them to establish specificity to PD. A subsequent cohort study was conducted to validate their findings and see whether these GI conditions influenced the risk of developing PD five years after diagnosis.

Konings et al., identified that ten GI conditions were significantly increased among 24,624 patients with PD compared to matched controls (OR (odds ratio) >1, p<0.05). However, only dysphagia, gastroparesis, IBS (irritable bowel syndrome) without diarrhoea, and constipation were specific to PD. Across these four conditions, the relative risk of developing PD versus controls was 2.43, 2.27, 1.17, and 2.38, respectively (all p<0.05). Therefore, using a large US-based research database, Konings et al., demonstrated that dysphagia, gastroparesis, IBS without diarrhoea, and constipation may predict the subsequent onset of PD. These findings add weight to Braak’s original hypothesis and suggest certain GI syndromes may be risk factors for a cohort of patients with GI-onset PD.