Pan-Gut Dysmotility in Parkinson Disease

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Abstract: Parkinson disease (PD) is a rapidly growing neurologic disorder affecting millions of people worldwide. While bradykinesia, rigidity, and tremor define its motor phenotype, gastrointestinal (GI) symptoms are highly prevalent and significantly impact quality of life. These symptoms often persist or worsen despite dopaminergic therapy and result from dysmotility involving the entire GI tract. Notably, many patients exhibit substantial objective motility disturbances despite minimal or no reported symptoms. This mismatch reflects impaired gut-brain communication and profound gut hyposensitivity, which dampen symptom perception and awareness. As such, reliance solely on patient-reported symptoms risks overlooking clinically significant dysmotility that can impair drug absorption, promote malnutrition, and increase the risk of complications such as bacterial overgrowth or aspiration. In response, diagnostic strategies are evolving to incorporate objective assessments, including videofluoroscopy, cough reflex testing, high-resolution manometry, and transit studies. These tools enhance the detection and characterization of unrecognized GI dysfunction in PD. A more nuanced, mechanism-based approach to evaluation is critical, as improved recognition of pan-gut dysmotility can guide individualized management strategies. This article reviews the underlying mechanisms of GI dysfunction in PD and provides a framework for its clinical assessment and care, emphasizing the need for proactive, objective evaluation beyond symptom reporting alone.

Keywords
Parkinson disease, gut-brain axis, gastrointestinal motility, dysphagia, constipation, gastroparesis, enteric nervous system

Parkinson disease (PD) is the fastest-growing neurologic disorder globally, affecting more than 6 million individuals, with its prevalence projected to double every 25 years.[1] Although bradykinesia, cogwheel rigidity, and resting tremor define PD's motor phenotype, nonmotor gastrointestinal (GI) symptoms are highly prevalent and contribute substantially to morbidity and diminished quality of life.[2-4] Notably, longitudinal studies reveal that even after 18 months of dopaminergic therapy, GI symptoms persist, with constipation worsening over time.[5] These symptoms arise from dysmotility that spans the entire GI tract.

Table. Summary of GI Symptoms and GI Dysmotility in Parkinson Disease

GI symptoms	GI dysmotility	Clinical assessments	Clinical physiologic tests	Complications
Dysphagia	Oropharyngeal dysmotility Esophageal dysmotility	MDT-PD SDQ SCAS-PD ROMP	FEES VFSS High-resolution esophageal manometry Functional luminal impedance planimetry	Aspiration pneumonia Malnutrition
Nausea, vomiting, early satiety, post-prandial fullness, epigastric abdominal pain	Delayed gastric emptying	ANMS GCSI-DD GIDS PD	Gastric emptying scintigraphy Gastric emptying breath test Wireless motility capsule Body surface gastric mapping	Erratic medication absorption
Abdominal cramping/ distension, bloating	Intestinal dysmotility	Visual analog scale GIDS PD	Wireless motility capsule	Erratic medication absorption Malabsorption
Constipation	Increased colonic transit time Anorectal dysfunction Colonic sensory dysfunction	Prospective stool diary GIDS PD	High-resolution anorectal manometry Rectal sensation and tone testing Defecography Colonic transit testing Wireless motility capsule	Fecal impaction Anal fissure Pseudo-obstruction Rectal prolapse Hemorrhoids

ANMS GCSI-DD, American Neurogastroenterology and Motility Society Gastroparesis Cardinal Symptom Index Daily Diary; FEES, fiberoptic endoscopic evaluation of swallowing; GI, gastrointestinal; GIDS PD, Gastrointestinal Dysfunction Scale for Parkinson's Disease; MDT-PD, Munich Dysphagia Test–Parkinson's Disease; ROMP, Radboud Oral Motor Inventory for Parkinson's Disease; SCAS-PD, Swallowing Clinical Assessment Score in Parkinson's Disease; SDQ, Swallowing Disturbance Questionnaire; VFSS, videofluoroscopic swallowing study.

Yet, many patients with PD demonstrate severe objective motility disturbances while reporting few or no GI complaints. This mismatch in GI sensorimotor dysfunction can be attributed to profound gut hyposensitivity and disruption of bidirectional gut-brain signaling, which impair symptom perception and diminish the conscious awareness of dysfunction.[6]

As a result, health care providers cannot rely solely on patient-reported symptoms to assess GI involvement in PD. Conventional patient-reported, symptom-based assessments risk missing significant dysmotility, which may contribute to complications such as malnutrition, bacterial overgrowth, and impaired drug absorption. In response, diagnostic strategies are evolving to incorporate objective assessments such as videofluoroscopy, cough reflex testing, high-resolution manometry, and GI transit testing to better detect and characterize unrecognized GI dysfunction. This article examines the neurogastroenterology and motility underpinnings of GI dysfunction in PD and provides direction for its evaluation and management in clinical practice.

Pathophysiologic Framework of Gut Dysmotility in Parkinson Disease

GI dysmotility in PD reflects complex multifocal disruptions across neural, muscular, and sensory pathways of the gut. Pathologically, α-synuclein deposition within the enteric nervous system, dorsal motor nucleus of the vagus, and myenteric plexus is a consistent early feature of PD and may precede motor symptom onset by years.[7] These aggregates interfere with cholinergic excitatory signaling and disrupt reflexive peristalsis and sphincter coordination throughout the GI tract. Neuroinflammatory changes, oxidative stress, and loss of enteric dopaminergic and serotonergic neurons further impair gut neuromuscular control.[8]

Beyond motor disturbances, PD-associated gut hyposensitivity compounds the clinical challenge of diagnosis by rendering patients asymptomatic despite substantial underlying dysmotility. Reduced rectal sensitivity has been demonstrated in multiple studies of PD patients via manometric and balloon distension tests[9-11]

and via electrical stimulation.[6] This disconnect is amplified by the deterioration of bidirectional signaling along the gut-brain axis, which not only attenuates symptom perception but may also promote central maladaptive processing that further impairs motility.

Vagal nerve degeneration may contribute to delayed gastric emptying, esophageal transit disorders, and altered colonic motility. Myogenic contributions such as reduced contractility owing to smooth muscle fibrosis and loss of connection with interstitial cells of Cajal have been observed in both clinical and preclinical studies, although data remain preliminary.[12] Moreover, gut dysbiosis, increased intestinal permeability, and gut inflammation may drive neuroinflammation and α-synuclein aggregation.[13] The interaction between pharmacologic therapy and gut function is bidirectional, as dopaminergic therapy may improve or exacerbate gastric and colonic transit depending on receptor selectivity, regional effects, and disease stage.

Critically, skeletal muscle dysfunction involving the oropharyngeal and anorectal regions further complicates the clinical landscape but must be interpreted separately from pure autonomic or enteric nervous system–related dysfunction.[14,15] These voluntary muscles are under central pattern generator control and can be impaired in PD via basal ganglia and cortical mechanisms, contributing to dysphagia and dyssynergic defecation.

Altogether, gut dysmotility in PD is neither uniform nor solely attributable to a single pathogenic driver. Rather, it represents a spectrum of dysfunction influenced by neurodegeneration, neurotransmitter imbalances, smooth and skeletal muscle impairment, and loss of sensory feedback. Given this multifactorial framework, diagnostic and therapeutic approaches must evolve beyond symptom-driven strategies to incorporate objective motility testing and mechanistically guided interventions.

Oropharyngeal Dysfunction in Parkinson Disease

Sialorrhea, or excessive drooling, and dysphagia are prevalent oropharyngeal manifestations of PD and contribute significantly to morbidity. Sialorrhea affects 70% to 80% of patients and correlates with disease severity.[16] Although initially attributed to excessive salivary production, studies have shown reduced salivary output in PD, suggesting that impaired oropharyngeal clearance owing to diminished effective bolus transfer and decreased tongue pressure are major contributors.[17,18]

Dysphagia is another major concern and is often underreported despite affecting up to 80% of patients.[19] Self-report screening tools have been developed to facilitate detection. The Munich Dysphagia Test–Parkinson's Disease is a 26-item questionnaire with a 90% sensitivity and 86% specificity (Table).[20] The Swallowing Disturbance Questionnaire and the Swallowing Clinical Assessment Score in Parkinson's Disease also demonstrate high accuracy.[21,22] This latter questionnaire was validated against the videofluoroscopic swallowing study. The Radboud Oral Motor Inventory for Parkinson's Disease further assesses speech, swallowing, and salivation control with strong internal consistency and test-retest reliability.[23] Additionally, handheld cough testing has shown promise by evaluating voluntary cough airflow, cough reflex sensitivity, and reflex cough airflow to identify dysphagia with 90.9% sensitivity and 80% specificity.[24]

The gold standard diagnostic tools for dysphagia remain fiberoptic endoscopic evaluation of swallowing or videofluoroscopic swallowing study. In a systematic review, fiberoptic endoscopic evaluation of swallowing demonstrated superior sensitivity for detecting aspiration (88% vs 77%) and laryngopharyngeal residue (97% vs 80%), whereas both modalities showed comparable sensitivity for premature pharyngeal spilling.[25]

Oropharyngeal dysfunction is one of the multifactorial contributors leading to serious complications, including aspiration pneumonia. Patients with PD have a 3-fold higher incidence of aspiration pneumonia compared with non-PD populations (3.6% vs 1.0%).[26] Other contributors to aspiration pneumonia in PD include delayed gastric emptying, neurologic factors (brain stem and basal ganglia dysfunction leading to impaired cough reflex and cognitive impairment), pulmonary factors (diaphragmatic and intercostal muscle weakness leading to impaired inspiratory reserve), medication-related factors (sedatives, anticholinergics, and dopaminergic medications), immune suppression, and frailty.[19,27,28] Dysphagia severity independently predicts adverse outcomes, including death, institutionalization, or disease progression (hazard ratio, 2.3).[29] Nutritional deficits are common, and nutritional risk in PD can be independently associated with the number of symptoms present (sialorrhea, dysphagia to solids, dysphagia to liquids, and/or constipation) with a reported odds ratio of 1.39 (95% CI, 1.00-1.96; P=.048).[30]

Dysphagia also impacts quality of life, contributing to social withdrawal and mood disorders. Approximately 41% of patients reported anxiety or panic attacks during mealtimes, whereas other patients avoided eating socially and perceived their condition as untreatable.[31] Higher anxiety/depression scores have also been associated with greater dysphagia severity on the Swallowing Disturbance Questionnaire, suggesting a possible psychogenic overlay.[32]

Esophageal Dysmotility in Parkinson Disease

Beyond oropharyngeal dysfunction, PD also affects the esophageal phase of swallowing. Postmortem studies demonstrate that α-synuclein aggregates, pathologic hallmarks of Lewy body disorders, are more prevalent in the enteric nervous system of the esophagus and stomach than the colon.[33] These deposits may disrupt esophageal motility via degeneration of the myenteric plexus.

High-resolution esophageal manometry has identified esophageal motor abnormalities in a significant proportion of patients with PD. Distal esophageal spasms may occur more frequently in more advanced stages of PD, and up to three-quarters of patients can have findings of complete aperistalsis and diffuse esophageal spasm.[34,35]

These findings underscore the importance of evaluating esophageal symptoms in PD. If present, esophageal motor disorders may exacerbate oropharyngeal dysfunction and contribute to significant morbidity. High-resolution esophageal manometry should be considered in PD patients with persistent dysphasia, gastroesophageal reflux, or chest discomfort.

Gastric Dysmotility and Pharmacologic Implications in Parkinson Disease

Impaired gastric motility and delayed gastric emptying could impact motor fluctuations in PD. Electrogastrography in patients with PD reveals irregular slow-wave activity and gastric dysrhythmias, suggesting disturbance in the gastric pacemaker.[36] Nearly 90% of patients with PD have delayed gastric emptying of solid foods, whereas 38% show delays for liquids, with no significant differences based on sex or age (<65 years vs >65 years).[37] However, conventional electrogastrography used in these studies is limited, and slow-wave frequency alone is not a reliable discriminator of gastric dysrhythmia. Noninvasive body surface mapping with advances in bioinstrumentation, signal processing, and computational modeling may provide mechanistic insight through spatiotemporal gastric dysrhythmias.[38]

Multiple studies have evaluated rates of gastric emptying and the association of this symptom with PD. Significant variations in patient selection (eg, disease severity, on/off levodopa status), gastric emptying technique (liquid vs solid, breath test vs scintigraphy vs magnetic resonance imaging), and deviations in study interpretation introduce significant methodologic heterogeneity.[39] Nonetheless, delayed gastric emptying is estimated to be present in more than 70% of patients with PD seen in neurology clinics.[39] In treatment-naive patients with mild to moderate disease, observed gastric emptying time was significantly slower than in healthy controls. Interestingly, patients with PD treated for a short duration continued to exhibit delayed gastric emptying, whereas long-term levodopa use was associated with significantly improved gastric emptying.[40] These findings underscore the complex interplay between disease progression and dopaminergic therapy on gastric motility.

Delayed gastric emptying has important implications for the pharmacokinetics of levodopa. In patients with delayed gastric emptying, plasma levodopa concentrations often peak at 2 hours after dosing as opposed to 1 hour, contributing to delayed "on" periods and reduced symptom control.[41] Paradoxically, levodopa has also been implicated as a potential contributor to delayed gastric emptying.[39] Levodopa-carbidopa intestinal gel may be delivered continuously via a percutaneous gastrojejunostomy tube into the jejunum, reducing plasma level fluctuations and improving motor symptoms.[42] Continuous subcutaneous levodopa delivery is also an alternative to oral administration and is in development.[43]

Many PD patients with significant gastric emptying delay may not exhibit cardinal gastroparesis symptoms (nausea, vomiting, early satiety, postprandial fullness, upper abdominal pain, and bloating), similar to the lack of symptoms of oropharyngeal dysfunction.[44,45] Among gastroparesis experts, there is much debate about the relationship between gastroparesis symptoms and delayed gastric emptying.[46,47] Metoclopramide, the only medication approved by the US Food and Drug Administration for gastroparesis, is contraindicated in PD owing to its dopamine receptor antagonism. Multiple pharmacologic therapies have failed randomized controlled trials in gastroparesis.[48] At the current time, prioritized management of highly prevalent coexisting slow colon transit and constipation may be a useful strategy.[49] Promising nonpharmacologic, noninvasive neuromodulation strategies involving vagal nerve stimulation and magnetic stimulation of thoracic spinal nerves remain in development.[50-52]

Small Intestinal Dysmotility and Microbiome-Mediated Drug Interference in Parkinson Disease

Small case-control studies show intestinal permeability and whole gut transit can be impaired in PD.[53] Patients often report nonspecific GI symptoms such as abdominal discomfort, cramping, bloating, diarrhea, and constipation. One significant contributor to these symptoms is small intestinal bacterial overgrowth (SIBO), which has been reported in up to 54% of patients with PD.[54,55] However, smaller studies have failed to replicate this association,[53] and the lack of a standardized diagnostic test for SIBO contributes to this variability.

Delayed small bowel transit may predispose individuals to SIBO, as impaired motility facilitates bacterial accumulation.[56] SIBO may further disrupt intestinal motor function through the action of bacterial metabolites, including peptides, fatty acids, cytokines, and neuroendocrine mediators, thereby creating propagated effects on hyperalgesia and dysmotility.[57] Given the increased intestinal overgrowth and worsening nutritional status, SIBO itself may contribute to weight loss and independently predict worsening motor function; however, studies with large PD and control populations are lacking.[58]

Beyond SIBO, additional microbial species have been implicated in PD-related GI dysfunction. *Enterococcus faecalis*, for instance, expresses tyrosine decarboxylase, which converts levodopa to dopamine in the gut, a reaction that is not inhibited by carbidopa, thereby reducing the systemic availability of levodopa. Similarly, *Helicobacter pylori* has been shown to impair levodopa efficacy, likely through mechanisms involving delayed gastric emptying and altered intestinal transit.[59] Antibiotic therapy is the primary treatment for SIBO, with rifaximin commonly preferred owing to its oral route of administration and its minimal systemic absorption.

Colonic and Anorectal Dysfunction in Parkinson Disease

Constipation is one of the most common nonmotor symptoms in PD, often preceding the onset of characteristic motor symptoms.[60] Treatment-resistant constipation has been proposed as a risk for PD.[61] As PD progresses, constipation worsens or emerges in previously unaffected individuals.[62] Two principal mechanisms underlie constipation in PD: delayed colonic transit or anorectal dysfunction.

Similar to the workup in constipated individuals without PD, diagnostic evaluation includes anorectal manometry, defecography (barium or magnetic resonance imaging), and colonic transit tests with either radiopaque markers, scintigraphy, or wireless motility capsules.[63-66] Colonic transit time in patients with PD has been reported to be twice that of healthy controls, with the rectosigmoid segment showing the most significant delay.[66] Impaired rectoanal coordination, or dyssynergic defecation, is also highly prevalent—identified in up to 95% of PD patients with constipation.[67,68] These patients exhibited significantly lower resting rectal and anal pressures compared with non-PD individuals with functional constipation. During simulated defecation, rectal pressure and anal relaxation were also notably reduced in the PD cohort.

Pharmacologic therapies, especially dopaminergic and anticholinergic agents, can exacerbate constipation in PD. Management of PD-related constipation generally follows standard treatment algorithms for functional constipation. Initial approaches include adequate hydration, increased dietary fiber, physical activity, and avoiding or minimizing the use of constipating medications. Subsequent pharmacologic options include laxatives, secretagogues, and serotonergic promotility agents.[69] Linaclotide and prucalopride have demonstrated efficacy in PD and related neurodegenerative conditions.[70] Some patients with PD experience improved constipation symptoms after subthalamic nucleus deep brain stimulation.[71] For anorectal dysfunction, early studies suggest botulinum toxin injections may offer benefit, although further research is warranted.[72,73]

Conclusion

PD is widely recognized for its hallmark motor symptoms; however, GI dysfunction is highly prevalent. GI dysmotility in PD may not present as a primary complaint during routine clinical encounters, particularly in movement disorders clinics, and may therefore go underrecognized. The natural history of dysmotility in PD remains poorly defined, and findings of dysmotility in PD stem from heterogeneous and often selectively recruited cohorts, limiting generalizability. Nevertheless, when such disturbances impact medication absorption, nutritional status, and quality of life, their clinical relevance increases. Patients may exhibit substantial GI dysmotility in the absence of overt symptoms, reflecting gut sensory disturbance and disrupted gut-brain signaling that mask symptom perception. As such, clinicians should consider adopting diagnostic strategies in selected patients that extend beyond symptom-based assessments to identify clinically relevant yet unrecognized motility disturbances. An emerging body of evidence supports a central role for gut pathophysiology, not only in symptom burden but also potentially in the initiation and progression of PD. As our understanding of the gut-brain axis deepens, it may unlock new therapeutic opportunities targeting both motor and nonmotor manifestations of the disease.

Disclosures

Dr Sharma serves as a consultant for Atmo Biosciences. The other authors have no relevant conflicts of interest to disclose.

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