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Gastro-intestinal symptoms in early stage parkinson's disease

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Background: In Parkinson???s disease, here is growing evidence that the initial pathophysiological changes occur in the gastrointestinal tract before changes are seen within the brain. We aim to investigate the prevalence of GIT symptoms in early-stages PD and the association between GIT symptoms and the UPDRS.

Methods: 10 Early-Stage PD and 8 control patients were recruited from the Norfolk and Norwich University Hospital. UPDRS motor scores were completed at outpatient clinics with participants handed a PD-specific gastrointestinal questionnaire whereby both the severity and frequency was assessed. The symptoms assessed were abdominal pain, constipation, tenesmus, hard stools, reflux, dysphagia, early satiety and bloating.

Results: The frequency of symptoms within the PD group were tenesmus (80%), bloating (60%), reflux (60%), abdominal pain (50%), constipation (50%) and hard stools (50%), early satiety (20%) and dysphagia (10%). Tenesmus (p=0.02) was the only symptom to show a statistically significant difference between PD and control groups. The total median GIT symptoms score for PD and Control was 7.0 (IQR 2.0 to 9.0) and 1.0 (IQR 0.0 to 5.75), respectively with statistical signifcance (p=0.05). For total gastrointestinal and UPDRS motor scores, there was a positive correlation (r=0.239), although not significant (p=0.51).

Conclusions: Gastrointestinal symptoms were present in the majority of early-stage patients. Lower gastrointestinal symptoms were more prevalent that upper gastrointestinal symptoms which links in with Braak???s hypothesis. Further research into the timing of the symptoms in relation to diagnosis is cruicial and may lead to earlier diagnosis of PD.

Despite increased interest in the recent years in PD-associated NMS, there is still a paucity of knowledge on the GI features of PD. This is an unfortunate state of affairs since these features are more difficult to manage than motor symptoms and are therefore of great concern for parkinsonian patients. In addition to their adverse effects on quality of life, GI problems are even more relevant to the understanding of the etiology of PD, insofar as Braak's hypothesis holds true. Accordingly, by collecting more clinical data on peripheral symptoms in putative cases of PD, an early diagnosis and better preventive action, as well as more efficient management of this disorder at its critical initiation and development stages, might be possible. For the time being, such a therapeutic approach is still purely speculative since PD is diagnosed solely following the recurrent manifestation of motor symptoms. Therefore, inasmuch as the importance of the ENS is further confirmed by future PD research, it might become essential to target the earliest manifestations of the disease in order to delay or even prevent neurodegeneration and thus the apparition of motor symptoms in PD patients.

This review summarizes the range of effective as well as potential therapeutic approaches to the management of GI symptoms in PD patients. Unfortunately, all existing treatments for both motor and nonmotor symptoms are purely symptomatic and result in merely temporary relief of these manifestations. Furthermore, it is very difficult to adequately treat GI symptoms because the exact target remains often unknown due to the lack of basic knowledge on the pathophysiology of the ENS component in the etiology of PD. Indeed, the main objective of current therapeutic research on PD is still oriented towards its management within the limits of present knowledge, that is, mainly reducing the side effects of medication, rather towards the further investigation of PD pathogenesis.

To date, several hypotheses have been proposed to understand the GI aspects in the physiopathology of PD. The most promising among these hypotheses include neurodegeneration, α-syn overexpression, inflammation, intestinal hyperpermeability, and microbiota disturbance as likely mechanisms involved in GI dysfunction [83, 84, 99, 204–208]. Furthermore, some factors have been suggested to participate in the initiation of the PD process, namely, disruption of the lysosomal and proteasomal systems, abnormal autophagy, endoplasmic reticulum stress, mitochondrial dysfunction, and oxidative stress [209–215]. Unfortunately, none of the latter putative factors could be confirmed as a PD biomarker due to the lack of an animal or cellular model that faithfully reproduces all features of PD. In the current state of our basic knowledge on PD pathophysiology, more optimal therapeutic avenues might be obtained by targeting a subset of these elements, given the fact that PD is clearly a multifactorial disease. However, a better insight into the etiology and mechanisms of the disease is crucial in order to find more targeted and effective treatments.

As summarized in the present review, there are now several lines of evidence that clearly demonstrate that GI dysfunctions not only are painful symptoms whose treatment constantly challenges clinicians, but also are relevant to the very process that causes PD, likely as reflections of processes that are under control by the ENS. Thus, GI symptoms in PD definitely should deserve much closer attention and warrant more detailed investigation in order to grasp the causative mechanisms at the core of this complex disease, which is a necessary prelude to the proper management of the disease's symptoms and, ultimately, to an actual curative strategy. Undoubtedly, further critical aspects of the mechanism leading to PD remain to be discovered and should call for a reassessment of the whole medical approach to this devastating disorder. Thus, in view of the recent developments in PD research emphasized in the present coverage of the literature, the peripheral aspects of PD should remain a priority in order to improve the therapeutic approaches to the disease, which are clearly in need of major improvements.