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Occurrence of Crohn's disease with Parkinson's disease

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Author contributions

All authors contributed substantially to this research study: the conception and design of the study (Z.K.W.), acquisition of data (S.E.C.), and analysis and interpretation of data (S.F., S.E.C., M.G.H.); drafting of the article (S.F.) and revising the article critically for important intellectual content (S.E.C., K.D.K., P.T., M.G.H., Y.T., A.J.S., J.A.v.G., R.J.U., O.A.R., T.I., Z.K.W.); and final approval of the version to be submitted (S.F., S.E.C., K.D.K., P.T., M.G.H., Y.T., A.J.S., J.A.v.G., R.J.U., O.A.R., T.I., Z.K.W.).

Conflict of interest

None.

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Abstract

We retrospectively investigated the co-occurrence of Crohn's disease in a cohort of 876 patients with Parkinson's disease, based on the observation that *LRRK2* is a shared genetic risk factor. We identified 2 patients with Crohn's disease; this number was consistent with the number of cases expected in the general population.

Keywords

Co-occurrence; Crohn's disease; *LRRK2*; Parkinson's disease

Parkinson's disease (PD) is the most common neurodegenerative movement disorder, affecting 1% of those older than 60 years and up to 4% of those older than 80 years; approximately 15% of patients report a family history of disease. The leucine-rich repeat kinase 2 gene (*LRRK2*), encoding a protein highly expressed in immune cells, is the most commonly mutated gene in both familial and sporadic PD. The LRRK2 p.M2397T polymorphism has been linked to an increased risk of Crohn's disease [1], a common inflammatory bowel disorder that affects up to 600,000 people in North America [2]. Given the genetic overlap, the objective of this study was to explore the occurrence of Crohn's disease in patients with PD.

This study was approved by the Mayo Clinic Institutional Review Board, and all participants provided informed consent. We retrospectively reviewed the medical histories of 1146 patients with PD. Of these, 876 patients had sufficient clinical and genetic information for the study. The majority of patients were male (n = 564 [64.4%]), and all were white. None were carriers of known pathogenic *LRRK2* mutations, and no patients in the study were related.

We searched the patients' medical records for Crohn's disease (prior or current disease). Only 2 of the 876 patients (0.2%) had a diagnosis of Crohn's disease. This prevalence rate was consistent with the number of cases expected, given the sample size, in the general population (26.0–198.5 cases per 100,000 persons) [2]. Thus, our results do not suggest an increased occurrence of Crohn's disease in patients with PD. One possible reason for this finding could be due to differences in the pathobiology underlying the *LRRK2*-related risk for these different disorders. The 7 *LRRK2* mutations known to cause PD (N1437H, R1441C, R1441G, R1441H, Y1699C, G2019S, and I2020T) are located in the functional domains of the protein (Roc, COR, and kinase) [3], whereas the M2397T polymorphism associated with sporadic Crohn's disease is located in the *C*-terminus WD40 domain [4]. Interestingly, the LRRK2 p.M2397T mutation is not associated with PD, but the G2385R variant, also located in the WD40 domain, is established as a common risk factor for PD in Asian populations [5]. Given the proximity to LRRK2 p.M2397T and the relatively common

minor allele frequency of the G2385R polymorphism, further studies in Asian populations for the co-occurrence of Crohn's disease and PD are warranted.

The second caveat for consideration is the retrospective nature of the medical record review. We did not perform any confirmatory tests to detect the presence of Crohn's disease or related inflammatory disorders; these tests would have included physical examinations, blood tests, barium radiographs, abdominal computed tomographic scans, colonoscopies, sigmoidoscopies, or gastrointestinal endoscopies. Therefore, potentially more patients with PD in our series could be affected by Crohn's disease or other inflammatory disorders.

We acknowledge limitations to the study. The study cohort possibly was too small to detect a difference from the number of expected co-occurrences. The expected prevalence of Crohn's disease was based on previously published rates, which could be affected by factors such as race/ethnicity and age at study enrollment. Thus, neurologically normal controls matched for race/ethnicity and age are needed. In addition, a second arm with a large sample of patients with Crohn's disease may be needed to investigate the frequency of PD.

Prospective studies are warranted to investigate the prevalence of Crohn's disease and other inflammatory disorders in patients with PD and, specifically within PD, with *LRRK2* and other PD gene mutation carriers.

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Abbreviation:

PD	Parkinson's disease

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