Reply to: "Association between Microscopic Colitis and Parkinson's Disease in a Swedish Population"

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We appreciate the Letter to the Editor by Ong et al. and their interesting findings from the case series study.[1] Indeed, we noticed increased occurrence of microscopic colitis (MC) in our patients with Parkinson's disease (PD), but our study was not designed to investigate the specific role of anti-PD medications.[2] Thus, it is difficult for us to disentangle whether the excess MC occurrence may be explained by medications taken by patients with PD or pathological mechanisms underlying PD affecting the gut. We find the hypothesis that levodopa/dopa decarboxylase inhibitor might trigger onset of MC very interesting, but evidence is preliminary and further studies of the topic are needed. Although we hope that both our own and the findings by Ong et al. will increase awareness of this potential association among clinicians managing patients with PD, we also advocate for future large-scale pharmacoepidemiologic studies that carefully consider issues such as confounding by indication, lead time between start of drug treatment and MC onset, and dose–response relationships.

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Data Availability Statement

Not applicable. This is a Response to the Letter to the Editor and contains no additional data on top of those reported in the original publication.

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References

1. Ong TL, Dal S, Martin AJ, et al. Levodopa/dopa decarboxylase inhibitor associated microscopic colitis: an under-recognized drug reaction. Parkinsonism Relat Disord 2021;86:84–90.
2. Kang X, Ploner A, Roelstraete B, et al. Association between microscopic colitis and Parkinson's disease in a Swedish population. Mov Disord 2021. https://doi.org/10.1002/mds.28594

From VUS to AUS: The Connection and the Differences between Genetics and Immune-Mediated Disorders

Technological advances in DNA sequencing exponentially increased the detection of novel genetic variants. Five categories of variants are now accepted: (1) pathogenic, (2) likely pathogenic, (3) variant of uncertain significance (VUS), (4) likely benign, and (5) benign. The VUS classification was established to designate a variant that may or may not be the cause of the disorder.[1,2] In spite of recent genomic development, many genetic disorders are still undetermined because a VUS was detected. A strong work in clinical practice is necessary to define if a VUS is really pathogenic, and it may include functional studies, trio sequencing, and description of additional similar cases.[3]

On the contrary, along with the expanding field of neuroimmunology, several new antibodies related to autoimmune encephalitis were described, and many of them are available in the form of commercial autoimmune encephalitis "panel."

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