Association of Fecal and Plasma Levels of Short-Chain Fatty Acids With Gut Microbiota and Clinical Severity in Patients With Parkinson Disease

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Study Question
Can fecal and plasma levels of short chain fatty acids (SCFAs) distinguish patients with Parkinson disease (PD) from controls and do they correlate with disease severity in PD?

What Is Known and What This Paper Adds
SCFAs are gut microbial metabolites that promote the disease process in a rodent model of PD, but fecal levels of SCFAs in patients with PD are reduced. This study provides Class III evidence that gut metabolite SCFAs distinguish between patients with PD and controls and are associated with disease severity in patients with PD.

Methods
For this case–control study, the investigators measured fecal and plasma levels of SCFAs using chromatography and mass spectrometry from 96 patients with PD and 85 age-, sex-, and diet habit–matched healthy controls recruited from National Taiwan University Hospital. Gut microbiota was analyzed using metagenomic shotgun sequencing. The Movement Disorder Society–Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) and the Mini-Mental State Examination (MMSE) were used to assess motor and cognitive impairment in patients with PD. The area under the receiver operating characteristic curve was used to quantify the model’s diagnostic performance for exploring the ability of SCFAs to distinguish between patients with PD and controls. Multi-variable linear regression models with MDS-UPDRS part III and MMSE scores as dependent factors were applied to examine the associations between SCFAs and motor or cognitive symptom severity in patients with PD. Correlations between the relative abundance of gut microbiota and fecal or plasma levels of SCFAs and the functional profiling of the gut microbial community were performed.

Results and Study Limitations
Patients with PD (n = 96) had lower fecal but higher plasma levels of acetate, propionate, and butyrate compared to controls (n = 85). After adjustment for age, sex, disease duration, and anti-PD medication dosage, MDS-UPDRS part III scores correlated with reduced fecal levels of acetate, propionate, and butyrate and with increased plasma propionate levels in patients with PD. MMSE scores negatively correlated with plasma levels of butyrate and valerate. SCFAs-producing gut bacteria correlated positively with fecal levels of SCFAs in healthy controls but revealed no association in patients with PD. In patients with PD, the abundance of proinflammatory microbes significantly correlated with decreased fecal levels and increased plasma levels of SCFAs, especially propionic acid. The study’s limitations include lacking gut permeability assays and the need for longitudinal follow-up studies to delineate the causal relationship between SCFAs and the disease process in PD.

Study Funding and Competing Interests
This study was funded by the National Health Research Institutes, National Taiwan University, and National Taiwan University Hospital. The authors report no competing interests. Go to Neurology.org/N for full disclosures.
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