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Chronic fatigue syndrome linked to imbalanced microbiome

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Scientists at the Center for Infection and Immunity (CII) at Columbia University's Mailman School of Public Health have discovered abnormal levels of specific gut bacteria related to chronic fatigue syndrome/myalgic encephalomyelitis, or ME/CFS, in patients with and without concurrent irritable bowel syndrome, or IBS. Findings are published in the journal *Microbiome*.

The study is among the first to disentangle imbalances in the gut bacteria in individuals with ME/CFS and IBS. ME/CFS is a complex, debilitating disorder characterized by extreme fatigue after exertion and other symptoms including muscle and joint pain, cognitive dysfunction, sleep disturbance, and orthostatic intolerance. Up to 90 percent of ME/CFS patients also have IBS.

The researchers followed 50 patients and 50 matched healthy controls recruited at four ME/CFS clinical sites. They tested for bacterial species in fecal samples, and for immune molecules in blood samples.

They report:

- Levels of distinct intestinal bacterial species—*Faecalibacterium, Roseburia, Dorea, Coprococcus, Clostridium, Ruminococcus, Coprobacillus*—were strongly associated with ME/CFS; their combined relative abundance appeared to be predictive of diagnosis
- Increased abundance of unclassified Alistipes and decreased

Faecalibacterium were the top biomarkers of ME/CFS with IBS; while increased unclassified *Bacteroides* abundance and decreased *Bacteroides vulgatus* were the top biomarkers of ME/CFS without IBS

- An analysis of bacterial metabolic pathways associated with disturbances in gut bacteria revealed distinct differences between ME/CFS and ME/CFS subgroups relative to healthy controls
- In ME/CFS subgroups, symptom severity measures, including pain and fatigue, correlated with the abundance of distinct bacterial types and metabolic pathways
- No changes were observed in immune markers—a finding that may reflect the dearth of participants who had been ill for a short time; earlier research suggests immune changes may only be evident when comparing short and long duration cases

"Individuals with ME/CFS have a distinct mix of gut bacteria and related metabolic disturbances that may influence the severity of their disease," says co-lead investigator Dorottya Nagy-Szakal, postdoctoral research scientist at CII.

"Our analysis suggests that we may be able to subtype patients with ME/CFS by analyzing their fecal microbiome," says co-lead investigator Brent L. Williams, assistant professor of Pathology and Cell Biology at CII. "Subtyping may provide clues to understanding differences in manifestations of disease."

"Much like IBS, ME/CFS may involve a breakdown in the bidirectional communication between the brain and the gut mediated by bacteria, their metabolites, and the molecules they influence," says senior author W. Ian Lipkin, director of CII and John Snow Professor of Epidemiology at Columbia's Mailman School. "By identifying the specific bacteria involved, we are one step closer to more accurate diagnosis and targeted therapies."