

Indicator of chronic fatigue syndrome found in gut bacteria

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Colorized scanning electron micrograph of *E. coli*; some strains are common, beneficial gut bacteria. Credit: National Institute of Allergy and Infectious Diseases, National Institutes of Health

Physicians have been mystified by chronic fatigue syndrome, a condition where normal exertion leads to debilitating fatigue that isn't alleviated by rest. There are no known triggers, and diagnosis requires lengthy tests administered by an expert.

Due to this lack of information, some people have even suggested the [disease](#) may be psychosomatic.

Now, for the first time, Cornell researchers report they have identified biological markers of the disease in gut bacteria and inflammatory microbial agents in the blood.

In a study published June 23 in the journal *Microbiome*, the team describes how they correctly diagnosed myalgic encephalomyelitis/[chronic fatigue syndrome](#) (ME/CFS) in 83 percent of patients through stool samples and blood work, offering a noninvasive diagnosis and a step toward understanding the cause of the disease.

"Our work demonstrates that the gut bacterial microbiome in ME/CFS patients isn't normal, perhaps leading to gastrointestinal and inflammatory symptoms in victims of the disease," said Maureen Hanson, the Liberty Hyde Bailey Professor in the Department of Molecular Biology and Genetics and the paper's senior author.

"Furthermore, our detection of a biological abnormality provides further evidence against the ridiculous concept that the disease is psychological in origin."

Ruth Ley, associate professor in the Departments of Molecular Biology and Genetics and Microbiology, is a co-author.

"In the future, we could see this technique as a complement to other noninvasive diagnoses, but if we have a better idea of what is going on with these gut microbes and patients, maybe clinicians could consider

changing diets, using prebiotics such as dietary fibers or probiotics to help treat the disease," said Ludovic Giloteaux, a postdoctoral researcher in both Hanson's and Ley's labs and first author of the study.

Researchers have evidence that an overactive immune system plays a role in chronic fatigue. Symptoms include fatigue even after sleep, muscle and joint pain, migraines and gastrointestinal distress. One hallmark of the condition is post-exertional malaise, meaning patients may take weeks to recover from minor exertion. To test for ME/CFS, clinicians may give patients a cardio-pulmonary exercise test where they ride a bike until they become fatigued. If the test is repeated the following day, ME/CFS patients usually cannot reproduce their performance from the first day.

"That's very typical and specific of people with ME/CFS, because healthy people, or even people who have heart disease, can reproduce the exercise on the second day, but these people cannot," Giloteaux said.

In the study, Ithaca campus researchers collaborated with Dr. Susan Levine, an ME/CFS specialist in New York City, who recruited 48 people diagnosed with ME/CFS and 39 healthy controls to provide stool and blood samples.

The researchers sequenced regions of microbial DNA from the stool samples to identify different types of bacteria. Overall, the diversity of types of bacteria was greatly reduced and there were fewer bacterial species known to be anti-inflammatory in ME/CFS patients compared with healthy people, an observation also seen in people with Crohn's disease and ulcerative colitis.

At the same time, the researchers discovered specific markers of inflammation in the blood, likely due to a leaky gut from intestinal problems that allow bacteria to enter the blood, Giloteaux said.

Bacteria in the blood will trigger an immune response, which could worsen symptoms.

The researchers have no evidence to distinguish whether the altered gut microbiome is a cause or whether it is a consequence of disease, Giloteaux added.

In the future, the research team will look for evidence of viruses and fungi in the gut, to see whether one of these or an association of these along with bacteria may be causing or contributing to the illness.

More information: Ludovic Giloteaux et al. Reduced diversity and altered composition of the gut microbiome in individuals with myalgic encephalomyelitis/chronic fatigue syndrome, *Microbiome* (2016). [DOI: 10.1186/s40168-016-0171-4](https://doi.org/10.1186/s40168-016-0171-4)

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