Overactive Immune Responses in ME/CFS

Researchers found higher levels of molecules involved in inflammation in blood from people with ME/CFS than in healthy controls.

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At a Glance

- Researchers found signs of overactive immune responses in people with myalgic encephalomyelitis/chronic fatigue syndrome, or ME/CFS.
- The findings provide insights into the causes of ME/CFS and suggest new treatment approaches.

ME/CFS involves unexplained fatigue that may worsen after exertion and cause problems with thinking and memory that lasts at least six months. People with ME/CFS often report symptoms consistent with infection before developing ME/CFS. Yet no single microbe has been found to be responsible. This suggests that ME/CFS may be caused by a more general immune response to infection.

To test this idea, a research team from several institutions, led by Dr. W. Ian Lipkin at Columbia University Mailman School of Public Health, collected blood samples from 56 people with ME/CFS and 52 matched healthy people. The study appeared in npj Metabolic Health & Disease on September 3, 2025.

The team exposed the blood samples taken before and after exercise to elements from different microbes. They found higher levels of molecules involved in inflammation in blood from people with ME/CFS than in healthy controls. This suggests that the immune system in ME/CFS may be hypersensitive to infection. People with ME/CFS also had altered levels of certain proteins consistent with immune dysregulation.

The team found several molecular pathways that were disrupted in people with ME/CFS in ways that could lead to inflammation. People with ME/CFS had altered levels of proteins involved in maintaining the extracellular matrix, which provides structural support to tissues. They also showed signs of impairment in the urea cycle. This detoxifies ammonia, a waste product of metabolism. After exercise, people with ME/CFS had increased activity in antioxidant pathways.

This indicates increased cellular stress from oxidation, a type of molecular damage.

In addition, the team found evidence of impaired energy production in the people with ME/CFS, particularly after exercise. People with ME/CFS had higher levels of fats in their blood and lower levels of molecules involved in fat breakdown. These point to a reduced ability to use fats for energy. The resulting accumulation of fats could lead to inflammation.

Altered levels of metabolites from microbes were also found in people with ME/CFS. This suggests disruption of the gut microbiome, called dysbiosis. There were signs that the gut mucosal barrier was weakened in ME/CFS. The findings suggested that gut dysbiosis led to impaired metabolism of foreign compounds, such as drugs and toxins.

After exercise, people with ME/CFS also showed reduced conversion of the amino acid tryptophan to serotonin. Serotonin plays a role in many functions, including mood, sleep, and cognition. This finding suggests a link to cognitive problems in ME/CFS.

The molecular problems observed in the people with ME/CFS correlated with fatigue symptoms. This supports the view that these abnormalities are related to the illness. Overall, the enhanced inflammatory responses in ME/CFS were stronger in women than in men.

The findings provide additional support for the view that ME/CFS results from inflammation and altered immune responses. They also suggest candidate treatments for clinical trials. These include immune suppressing drugs, pre- and probiotics to restore the gut microbiome, dietary supplementation with compounds deficient in people with ME/CFS, and drugs to boost serotonin levels.

“While what gives rise to ME/CFS remains obscure, understanding the ways it disrupts the body’s various biological processes on the molecular level is revealing biomarkers for specific ME/CFS subtypes that may inform clinical research and lead to targeted interventions,” Lipkin says.

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