# Sulfur metabolites linked to neurodegenerative diseases

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Neurodegenerative diseases (NDDs), which have no known cures and elusive causes, result in irreversible damage to the brain and nervous system. Research into these diseases typically focuses on the brain, but

mouse studies from the last few years suggest that the microbiome plays a role in the onset and progression of some NDDs, as well.

"These findings suggest the gut microbiome plays an important role in the onset and progression of at least some neurodegenerative diseases," noted Chris Ellis, principal investigator of the multi-institution team of microbiologists from Netellis, the University of Tennessee at Knoxville and the University of North Carolina at Chapel Hill.

At ASM Microbe, the annual meeting of the American Society for Microbiology, those researchers report a new link in humans between a metabolite produced by gut microbes and three NDDs. Their analysis suggests that the metabolite DHPS (2,3-dihydroxypropane-1-sulfonate) may help answer critical questions about how sulfur metabolism pathways can connect the microbiome to these diseases.

DHPS has not previously been detected in people, and the researchers noted that metabolites produced by gut microbes in patients with NDDs might offer valuable clues to a better understanding, which could lead to improved diagnostic tools or even treatments.

In previous studies, researchers have found that fecal transplants can alleviate Alzheimer's disease-like progression in mouse models, and when fecal transplants from people with the disease are administered to mice, the animals experience impairments in memory function.

The researchers undertook the new study to identify distinct bacterial and metabolite profiles of the gut microbiome in people diagnosed with one of three NDDs: amyotrophic lateral sclerosis (ALS), Alzheimer's disease (AD), and Parkinson's disease (PD). To capture data on early-stage disease, they collected stool samples from diagnosed patients within the first two visits to a specialist, and they compared analyses of those samples to samples collected from healthy controls.

Their analysis revealed 19 metabolic biomarkers for neurodegeneration in all three NDD groups; they also found 20 unique ALS markers, 16 unique AD markers and nine unique PD markers. Those shared biomarkers included metabolites that have been connected to dyshomeostasis in sulfur metabolism pathways.

In addition, in all three disease groups, they found links to Bilophila and Desulfovibrio bacterial taxa, which play a role in synthesizing and degrading DHPS. Those increased levels of Bilophila corresponded to the observation that patients with AD, ALS and PD had lower abundance of DHPS in stool samples, compared to healthy subjects.

Bilophila can degrade DHPS into hydrogen sulfide, and the accumulation of hydrogen sulfide has been implicated in the dysfunction of mitochondria, which is known to contribute to NDDs. Hydrogen sulfide is linked to known NDD hallmarks, including inflammation, oxidative stress and gut dysbiosis.

The authors suggested that the new study flags DHPS as a "missing link" in our current understanding of the mechanisms of how NDDs are linked to sulfur metabolism, mitochondrial dysfunction and neuroinflammation.

**More information:** ASM Microbe is the annual meeting of the American Society for Microbiology, held June 13–17, 2024, in Atlanta, Ga.

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