

Bacteria-derived gut metabolites can affect brain's myelin content and induce depression-like symptoms

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Specific combinations of gut bacteria produce substances that affect myelin content and cause social avoidance behaviors in mice, according to a study conducted at the Icahn School of Medicine at Mount Sinai and published today in the medical journal *eLife*. This research suggests that targeting intestinal bacteria, or their metabolites, could be one way to treat debilitating psychiatric disorders and demyelinating diseases, like multiple sclerosis.

Multiple sclerosis is an autoimmune disorder characterized by damage to myelin, the insulating sheath around the axons of nerve cells that allows for faster electrical impulse conduction. Myelination is critical for everyday brain function. Damaged myelin results in altered synaptic transmission and clinical symptoms. Previous research from the Center of Excellence for Myelin Repair at The Friedman Brain Institute at the Icahn School of Medicine reported a thinning of myelin and a reduction of myelinated fibers in preclinical models of depression, thereby providing a biological insight for the high rate of depression in MS patients.

This current study led by Patrizia Casaccia, MD, PhD, Professor of Neuroscience, Genetics and Genomics, and Neurology, and Chief of the Center of Excellence for Myelin Repair, and post-doctoral fellow Mar Gacias, PhD, identifies bacteria-derived gut metabolites that can affect myelin content in the brains of mice and induce depression-like symptoms.

Researchers transferred fecal bacteria from the gut of depressed mice to genetically distinct mice exhibiting non-depressed behavior. The study showed that the transfer of microbiota was sufficient to induce social withdrawal behaviors and change the expression of myelin genes and myelin content in the brains of the recipient mice.

"Our findings will help in the understanding of microbiota in modulating multiple sclerosis," says Dr. Casaccia. "The study provides a proof of principle that gut metabolites have the ability to affect myelin content irrespective of the genetic makeup of mice. We are hopeful these metabolites can be targeted for potential future therapies."

In an effort to define the mechanism of gut-brain communication, researchers identified bacterial communities associated with increased levels of cresol, a substance that has the ability to pass the blood-brain barrier. When the precursors of myelin-forming cells were cultured in a dish and exposed to cresol, they lost their ability to form myelin, thereby suggesting that a gut-derived metabolite impacted myelin formation in the brain.

Further study is needed to translate these findings to humans and to identify bacterial populations with the potential to boost myelin production.

Source:

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