

Transplanting gut bacteria alters depression-related behavior, brain inflammation in animals

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Seema Bhatnagar, PhD, leads the Stress Neurobiology Program at Children's Hospital of Philadelphia. Credit: Children's Hospital of Philadelphia

Scientists have shown that transplanting gut bacteria, from an animal that is vulnerable to social stress to a non-stressed animal, can cause

vulnerable behavior in the recipient. The research reveals details of biological interactions between the brain and gut that may someday lead to probiotic treatments for human psychiatric disorders such as depression.

"In rats that show depressive-type [behavior](#) in a [laboratory test](#), we found that [stress](#) changes their [gut microbiome](#)—the population of bacteria in the gut," said study leader Seema Bhatnagar, Ph.D., a neuroscientist in Department of Anesthesiology and Critical Care at Children's Hospital of Philadelphia (CHOP). "Moreover, when we transplanted bacteria from those stress-vulnerable rats into rats that had not been stressed, the recipient animals showed similar behavior."

Bhatnagar added that stress also increased inflammation in the brains of vulnerable rats, and that this inflammation appeared in unstressed rats after they received transplants from vulnerable animals.

The study team published its findings online March 4, 2019 in *Molecular Psychiatry*.

Bhatnagar leads the Stress Neurobiology Program at CHOP, and many of her co-authors are members of the PennCHOP Microbiome Program, a collaboration between researchers at CHOP and the Perelman School of Medicine at the University of Pennsylvania. The program aims to better understand the communities of microbes inside our bodies and alter their properties to improve human health. Chunyu Zhao, Ph.D., of that program, performed microbiome data analysis and is a co-author of the paper.

Scientists already know that brain and gut influence each other. In humans, patients with psychiatric disorders have different populations of gut microbes compared to microbes in healthy individuals, with parallel findings also seen in animal models of psychiatric disease. This study

investigated mechanisms related to brain inflammation, microbiomes and stress.

"Humans do not all react identically to the same stresses—some are more vulnerable than others to developing psychiatric disorders, others are more resilient," said Bhatnagar. "Something similar happens in laboratory animals as well."

In rodents, social hierarchies and territoriality are major sources of stress. In the laboratory, researchers model stressors with validated behavioral tools such as a forced swim test or a social defeat test to examine how animals use coping strategies to deal with stress. Rats that cope more passively are more vulnerable to the effects of stress because they also exhibit more anxiety- and depressive-type behaviors, while rats that cope more actively are resilient to the effects of [social stress](#). Based on these assessments, the researchers classified the animals as either vulnerable or resilient.

The study team then analyzed the fecal microbiomes of vulnerable rats, resilient rats, a non-stressed [control group](#), and a placebo group. They found that vulnerable rats had higher proportions of certain bacteria, such as Clostridia, than the other groups.

They then performed fecal transplants from three donor groups—vulnerable rats, resilient rats or control non-stressed rats—into naïve rats, animals that had not been stressed. They found that different microbiomes changed depressive-like behavior. Rats receiving transplants from vulnerable rats were more likely to adopt depressive-like behaviors, whereas rats receiving transplants from resilient animals or non-stressed animals did not exhibit any changes in behavior or in neural measures. Patterns of brain inflammatory processes in recipients also resembled those seen in the brains of vulnerable [animals](#), suggesting that immune-modulating effects of [gut bacteria](#) such as Clostridia may

have promoted that inflammation. However, transplants did not significantly change anxiety-like behavior.

The finding that gut transplants from vulnerable [rats](#) increased depressive-type behavior but not anxiety-type behavior in non-stressed recipients may point to different mechanisms. The authors said this difference suggests that depressive-type behaviors are more regulated by the gut microbiome, whereas anxiety-type behaviors are primarily influenced by neural activity changes produced by stress experience.

"Although much more research remains to be done, we can envision future applications in which we could leverage knowledge of microbiome-brain interactions to treat human psychiatric disorders," said Bhatnagar. "People already are taking over-the-counter probiotics as supplements. If we can eventually validate beneficial behavioral effects from specific bacteria, we could set the stage for new psychiatric treatments."

More information: Jiah Pearson-Leary et al, The gut microbiome regulates the increases in depressive-type behaviors and in inflammatory processes in the ventral hippocampus of stress vulnerable rats, *Molecular Psychiatry* (2019). [DOI: 10.1038/s41380-019-0380-x](https://doi.org/10.1038/s41380-019-0380-x)

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