Gut(-Brain) Reaction

Do your gut bacteria contribute to or maybe even cause the shaking, stumbling, and overall deterioration of motor skills that are the hallmarks of Parkinson's disease?

by Lori Dajose

In December 2016, a team led by Sarkis Mazmanian, the Luis B. and Nelly Soux Professor of Microbiology and a Heritage Medical Research Institute Investigator, published a paper detailing the first demonstrated connection between the gut and this ravaging disorder.

How would such a link work?

It starts with the microbiome, "a diverse community of beneficial and sometimes harmful bacteria," Mazmanian says. In a series of experiments, he and his colleagues looked at mice whose guts harbored the usual complex collection of bacteria, and compared them to mice who were microbe-free.

Both sets of mice were engineered to overproduce a protein in the gut called alpha-synuclein that, in Parkinson's patients, also clusters in the brain's neurons, resulting in debilitating clumps and snarls. And that was indeed what happened in mice with a full complement of gut microbes. On the other hand, mice without a microbiome—the germ-free mice—tended to be almost or completely symptom-free.

What made the difference? Further experiments suggested it could be molecules called short-chain fatty acids (SCFAs)—produced by gut microbes when they break down fiber in the gut—interacting with the overabundance of alpha-synuclein. When the germ-free mice (who produced no SCFAs since they had no microbes) were fed SCFAs, they began to show Parkinson's symptoms again.

The researchers also confirmed that, in order to stay symptom-free, the mice need to stay free of germs ... but not of all germs. While mice given samples of the microbes found in the feces of human Parkinson's patients again began to show Parkinson's symptoms, microbe samples from healthy humans had no such effect.

"[T]he fact that you can transplant the microbiome from humans to mice and transfer symptoms suggests that bacteria are a major contributor to disease," Mazmanian says. Next up: trying to figure out which bacteria are a problem, and which are innocuous.

For more on the hows and whys of this intriguing gut-brain connection, check out the original story and its accompanying short video at **caltech.edu/news/parkinsons-disease-linked-microbiome-53109.**

This research was funded by the Larry L. Hillblom Foundation, the Knut and Alice Wallenberg Foundation, the Swedish Research Council, Mr. and Mrs. Larry Field, the Heritage Medical Research Institute, and the National Institutes of Health.