Stress wrecks intestinal bacteria, could keep immune system on idle

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Stress not only sends the human immune system into overdrive – it can also wreak havoc on the trillions of bacteria that work and thrive inside our digestive system.

New research suggests that this may be important because those bacteria play a significant role in triggering the innate immune system to stay slightly active, and thereby prepared to quickly spring into action in the face of an infection.

But exactly how stress makes these changes in these bacteria still isn't quite clear, researchers say.

"Since graduate school, I've been interested in how stress affects the bacteria naturally in our bodies,' explained Michael Bailey, an assistant professor of dentistry and member of the Institute for Behavioral Medicine Research at Ohio State University.

"Even though we've known that stress changes these bacteria, we didn't really understand what that meant or if there was any sort of biological function associated with effects on these bacteria."

The new study appears in the current issue of the journal *Brain, Behavior and Immunity*.

The human digestive tract is a universe filled with microbes. There are probably 100 trillion bacteria in the average human, 90 percent of which

live mainly in the intestine. They easily outnumber human cells 10-to-one in each person.

Bailey and colleagues turned to mice to better understand the roles that bacteria play in immune balance. They ran a series of experiments using a common stressor for these animals. For two hours daily for six days, an aggressive mouse was placed in a cage of a group of more docile mice.

At the end of the string of experiments, blood samples were taken from both stressed animals and matched mice from a control group, along with samples of material from inside each animal's intestine. The blood samples were analyzed to detect the levels of two biomarkers used to gauge stress – a cytokine called interleukin-6 (IL-6) and a protein called MCP-1 that summons macrophages, or scavenger cells, to the site of an infection.

From the intestinal samples, Bailey's team could determine the relative proportion of at least 30 types of bacteria residing there.

Compared to the control mice, the stressed animals showed two marked differences: The proportion of one important type of bacteria in the gut – Bacteroides – fell by 20 to 25 percent while another type – Clostridium – increased a similar amount. Also, levels of the two biomarkers, IL-6 and MCP-1, jumped 10-fold in the stressed mice, compared to controls.

The researchers then treated stressed mice with broad-spectrum antibiotics that could kill as much as 90 percent of the intestinal bacteria for a short period. When they again looked at the two immune biomarkers in the stressed mice, they saw only a doubling of IL-6 and MCP-1 – an increase only one-fifth as much.

"We know now that if we knock the population of bacteria down with antibiotics, we don't have the same innate immune response," Bailey

said. "That showed that the bacteria are involved in the ability of stress to prime the innate immune system."

He said that the research shows that some of the changes in systemic immunity in the body can be influenced by changes in these bacterial colonies, a result that reinforces the idea that they have a broader effect on the immune response.

The next step, the researchers say, is to better understand the roles that the bacteria play in activating the immune system, and to determine if other factors are playing a key role in the process.

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