

Study reveals role of spleen in prolonged anxiety after stress

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Credit: George Hodan/public domain

Scientists are uncovering clues to what might be unfolding in the relationship between the brain and immune system in those who suffer from long-term repercussions of stress.

New research details those connections, specifically that an abundance of [white blood cells](#) in the spleen could be sending messages to the brain

that result in behavioral changes long after [mice](#) experience repeated [stress](#).

"We found that [immune cells](#) in the spleen can contribute to chronic anxiety following psychological stress," said Daniel McKim, a [graduate student](#) at The Ohio State University and the lead author of the study.

"Our findings emphasize the possibility that the immune system represents a novel therapeutic target for the treatment of mental health conditions."

The research was part of a series of related studies presented Nov. 13 in San Diego at Neuroscience 2016, the annual meeting of the Society for Neuroscience.

McKim's co-authors and advisers, John Sheridan and Jonathan Godbout, are working toward explaining the complicated interplay between immunity and stress in animals that have experienced "repeated social defeat" in an effort to eventually improve the well-being of people who experience chronic [psychological stress](#). Sheridan is associate director of Ohio State's Institute for Behavioral Medicine Research and a professor of biosciences. Godbout is an associate professor of neuroscience.

In this study, the trio of scientists determined that the immune cell changes persisted for almost a month after the mice experienced the stress.

"Stress appears to prompt the release of stem cells from the bone marrow to the spleen, where they develop into white blood cells, or monocytes, and expand over time," Godbout said.

"Then the spleen becomes a reservoir of inflammatory cells."

Sheridan said the spleen is now understood to be integral to the sensitization that happens after prolonged stress in mice, leading to anxiety and other cognitive problems down the road.

"It's like a stress memory," Godbout said.

In their previous work, Ohio State researchers have documented an increased prevalence of long-term anxiety and depression in mice exposed to chronic stress, a model that has been compared to post-traumatic stress disorder in people.

"Maybe anxiety is a good thing for survival—it's beneficial evolutionarily—but the issue becomes what happens when that system is put into overdrive. That's when it gets problematic," Godbout said.

Added Sheridan, "We're beginning to piece together more details about the bi-directional communication between the brain and the body and the body and the brain."

The research was supported by the National Institutes of Health.

Other related Ohio State research shared Nov. 13, some of which was conducted under the leadership of Ning Quan, an Ohio State professor of biosciences, found that:

- Interleukin-1—one of several substances called cytokines that are central to regulation of immune and inflammatory responses—plays a critical role in the [stress response](#) in mice. In particular, expression of interleukin-1 activates the immune response by microglia in the brain and those cells call upon the immune system, leading to a subsequent surge of white blood cells to the brain. Graduate student Damon DiSabato led the research.

- During [chronic stress](#), activation of the brain's immune response in cells called microglia causes the brain's vascular system to recruit white blood cells. Those [blood cells](#), or monocytes, produce a robust signal that causes anxiety-like behavior in mice. Graduate student Anzela Niraula led the study.
- Specific types of interleukin-1 receptors serve a key role in cellular response to this cytokine, and one type in particular appears to prompt brain inflammation tied to anxiety in mice. Graduate student Xiaoyu Liu led the study.
- Drugs that mimic cannabis may lower anxiety and inflammation in mice that have undergone stress, a finding that could eventually have implications in the treatment of [post-traumatic stress disorder](#). Sabrina Lisboa, formerly of a visiting fellow at Ohio State and now a fellow at the University of Sao Paulo, led the study.

Provided by The Ohio State University

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