Acute stress may be detrimental to fighting off COVID-19 and influenza

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Acute stress can be detrimental to fighting off infection, especially COVID-19, and increases the chance of dying in mouse models.

This study, published in *Nature*, is the first to show how specific regions in the brain control the body's cellular immune response while under acute stress and infected with COVID-19 or influenza. More specifically, it demonstrated that acute stress prompts neurons from the region known as the paraventricular hypothalamus to instantly trigger a large-scale migration of white blood cells (immune cells, or leukocytes) from lymph nodes to the blood and bone marrow. This diminishes an immune response to viruses such as COVID-19 and influenza, making the body less resistant to fighting infection and putting it at greater risk of complications and death.

This fundamental discovery connecting the brain to the immune system provides a better understanding of how stress affects the body's response to a virus, and why some may be more susceptible to severe illness and worse outcomes.

First, researchers looked at groups of relaxed and stressed mouse models and analyzed their immune systems. Within minutes, mice experiencing acute stress showed big changes in their immune system when compared to the relaxed mouse group. Specifically, stress induced a major migration of immune cells in the body from one location to another. Investigators wanted to explain this phenomenon. Using sophisticated tools such as optogenetics and chemogenetics, the investigators discovered that neurons from the paraventricular hypothalamus were prompting immune cells to migrate from lymph nodes into the blood and bone marrow.

Then, researchers went further to analyze how mice in the relaxed and stressed models compared when infected with influenza and COVID-19. They noticed that mice in the relaxed group fared better when compared to the stressed group—they fought infection better and got rid of the virus more easily. Mice in the stressed group were sicker, had less immunity, and had a higher rate of death from the virus. The

investigators also explored how other regions of the brain related to motor function control different types of immune cells traveling from the bone marrow to the blood.

Distinct brain regions shape leukocyte distribution and function throughout the body during acute stress in miceThe effect of stress on white blood cells and how it may negatively impact fighting a virus is important to further understand outcomes and find ways to improve immunity. If white blood cells continually enter the bloodstream, this could have implications for cardiovascular health as well.

This study is an important example of how the brain controls inflammation and its link to diminishing an immune response during acute stress. This work may prompt physicians to further look into the mental state of patients, including sleep patterns and stress levels. It may prompt interventions to not just live a healthier and less stressful lifestyle, but help the body better fight infection and improve outcomes.

"This work tells us that stress has a major impact on our immune system and its ability to fight infections. It raises many questions about how socioeconomic factors, lifestyle, and environments we inhabit control how our bodies can defend themselves against infection," says Dr. Swirski. "Moving forward, we will need to better understand the long-term effects of stress. It will be particularly important to explore how we can build resilience to stress and whether resilience can diminish stress's negative effects on our immune systems."

More information: Brain motor and fear circuits regulate leukocytes during acute stress, *Nature* (2022). DOI: 10.1038/s41586-022-04890-z , www.nature.com/articles/s41586-022-04890-z

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