Exercise boosts brain health with chemical signals, study shows

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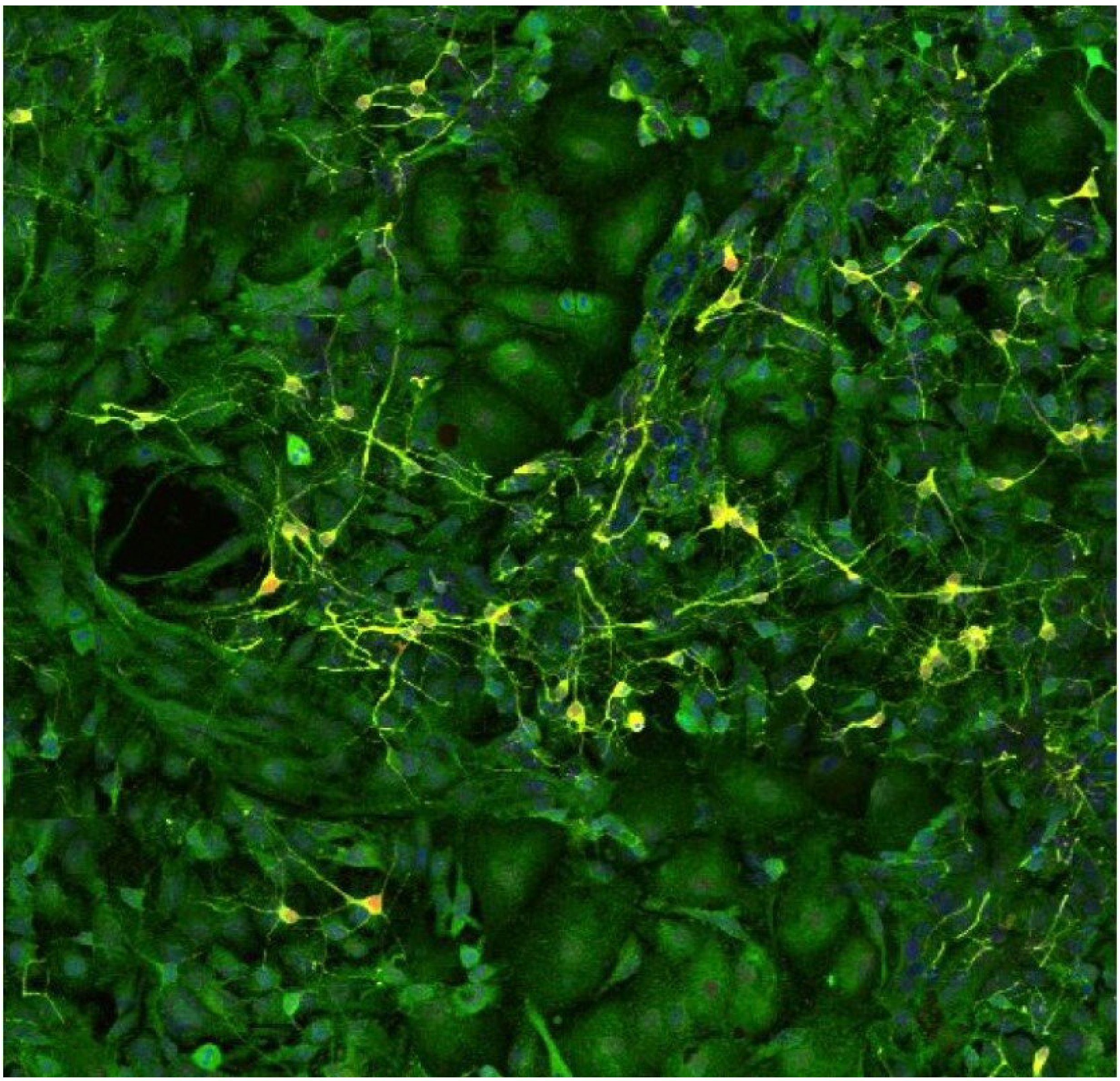

Hippocampal neurons (yellow) surrounded by astrocytes (green) in a cell culture from the study. Image provided by the authors. Credit: Taher Saif, Justin Rhodes, and Ki Yun Lee

Physical activity is frequently cited as a means of improving physical and mental health. Researchers at the Beckman Institute for Advanced Science and Technology have shown that it may also improve brain health more directly. They studied how the chemical signals released by exercising muscles promote neuronal development in the brain.

Their work appears in the journal *Neuroscience*.

When muscles contract during exercise, like the biceps working to lift a heavy weight, they release a variety of compounds into the bloodstream. These compounds can travel to different parts of the body, including the brain. The researchers were particularly interested in how exercise could benefit a particular part of the brain called the hippocampus.

"The hippocampus is a crucial area for learning and memory, and therefore cognitive health," said Ki Yun Lee, a Ph.D. student in mechanical science and engineering at the University of Illinois Urbana-Champaign and the study's lead author. Understanding how exercise benefits the hippocampus could therefore lead to exercise-based treatments for a variety of conditions including Alzheimer's disease.

To isolate the chemicals released by contracting muscles and test them on hippocampal neurons, the researchers collected small muscle cell samples from mice and grew them in cell culture dishes in the lab. When the muscle cells matured, they began to contract on their own, releasing their chemical signals into the cell culture.

The research team added the culture, which now contained the chemical signals from the mature muscle cells, to another culture containing hippocampal neurons and other support cells known as astrocytes. Using several measures, including immunofluorescent and calcium imaging to track cell growth and multi-electrode arrays to record neuronal electrical activity, they examined how exposure to these chemical signals affected the hippocampal cells.

The results were striking. Exposure to the chemical signals from contracting muscle cells caused hippocampal neurons to generate larger and more frequent electrical signals—a sign of robust growth and health. Within a few days, the neurons started firing these electrical signals more synchronously, suggesting that the neurons were forming a more mature network together and mimicking the organization of neurons in the brain.

However, the researchers still had questions about how these chemical signals led to growth and development of hippocampal neurons. To uncover more of the pathway linking exercise to better brain health, they next focused on the role of astrocytes in mediating this relationship.

"Astrocytes are the first responders in the brain before the compounds from muscles reach the neurons," Lee said. Perhaps, then, they played a role in helping neurons respond to these signals.

The researchers found that removing astrocytes from the cell cultures caused the neurons to fire even more electrical signals, suggesting that without the astrocytes, the neurons continued to grow—perhaps to a point where they might become unmanageable.

"Astrocytes play a critical role in mediating the effects of exercise," Lee said. "By regulating neuronal activity and preventing hyperexcitability of neurons, astrocytes contribute to the balance necessary for optimal brain function."

Understanding the chemical pathway between muscle contraction and the growth and regulation of hippocampal neurons is just the first step in understanding how exercise helps improve brain health.

"Ultimately, our research may contribute to the development of more effective exercise regimens for cognitive disorders such as Alzheimer's disease," Lee said.

In addition to Lee, the team also included Beckman faculty members Justin Rhodes, a professor of psychology; and Taher Saif, a professor of mechanical science and engineering.

More information: Ki Yun Lee et al, Astrocyte-mediated Transduction of Muscle Fiber Contractions Synchronizes Hippocampal Neuronal Network Development, *Neuroscience* (2023). DOI: 10.1016/j.neuroscience.2023.01.028

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