Exercise may create new neurons by making other brain cells contract

Physical activity causes a type of brain cell called astrocytes to contract, which then leads to the formation of new neurons, according to a study in mice

By Helen Thomson

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We know that being active is good for our brain, and scientists are starting to unpick why

Exercise may stimulate the growth of new neurons by making other brain cells contract. The discovery, which was in mice, could help explain how exercise boosts brain health and protects against cognitive decline.

Being physically active is one of the most important lifestyle factors for maintaining our mental health and guarding against cognitive decline. In animals, including humans, it is associated with neurogenesis – the growth of new neurons – in the hippocampus, a region involved in learning and memory.

Although many exercise-induced factors, such as signalling molecules and hormones, have been identified in the blood, how these benefit the brain is unclear. Justin Rhodes at

the University of Illinois Urbana-Champaign and his colleagues wondered whether astrocytes are involved. These star-shaped cells, present in the central nervous system, are among the first to detect circulating molecules and support neurogenesis by releasing substances that help neurons grow and repair.

To investigate, the researchers housed 20 mice for two or three days in cages with or without a running wheel. They then measured two molecular markers associated with astrocyte contraction in the hippocampus.

In exercising mice, one marker increased within 1 to 2 minutes of running, while the other was associated with exercise that occurred over the previous 27 to 38 minutes. “Together these two markers show that while the animal is exercising, astrocytes contract,” says Rhodes.

Next, the researchers placed mouse muscle cells in a dish and collected the substances they released upon spontaneous contraction. They then applied this “muscle medium” to mouse astrocytes to demonstrate that the contraction of muscle cells makes astrocytes contract. The researchers found that the astrocytes contracted slightly in a medium of ordinary stiffness, but adding the muscle medium increased their force.

Finally, the team collected the substances released by the contracting astrocytes and added them to cultures of mice hippocampal neurons. Liquid from astrocytes on stiffer gels, which contracted most strongly, produced the greatest abundance of immature neurons – a sign of neurogenesis. This suggests that the more astrocytes contract, the more neurogenesis occurs. Previous exposure to the muscle medium increased this further.

“The astrocytes are contracting in response to exercise, and the contraction is like a new force in the brain that is contributing to the function of the brain that we didn’t realise before,” says Rhodes.

It’s unclear why astrocyte contraction provokes neurogenesis, but Rhodes suggests it may make the cell membrane easier to cross. Alternatively, it might help facilitate the release of vesicles from within the cell that carry important chemicals, such as growth factors, to surrounding neurons.

“This is a fascinating and novel finding,” says Flaminia Ronca at University College London. “It is biologically plausible that some version of it operates in humans, because we share the broad cell types and cellular machinery involved.”

A better understanding of these mechanisms may lead to new therapies for cognitive decline and brain health more generally. “This is a major focus of my lab,” says Tara Walker at the Queensland Brain Institute in Australia. “We’re trying to understand the molecular mechanisms through which exercise enhances neurogenesis and other aspects of brain plasticity with the long-term goal of developing therapies that reproduce some of the beneficial effects of exercise for people who are unable to exercise.”

Walker’s team has already identified a molecule called PF4, which mimics some of the effects of exercise in older mice, like enhancing synaptic plasticity and cognitive function.

Rhodes is now developing technology to watch the mechanism in action in live mice. But for now, his take-home message is simple: “Exercise is the best thing you can do for your brain health.”

Reference:

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