The molecule that helps exercise protect the brain from Alzheimer’s

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Sometimes data behaves so nicely, lining up just the way you want it to. In 2012, irisin was identified as a molecular messenger induced by exercise. In 2013, irisin was found to stimulate genes in the hippocampus, a region of the brain essential for making and storing memories. In 2017, epidemiological studies indicated that exercise could slow the development of Alzheimer’s disease (AD) and other kinds of dementia. And this week—you guessed it—new research demonstrated that exercise alleviates AD and slows memory loss by sending irisin to the brain.

Irisin is sent from muscles to various tissues throughout the body during exercise. It was initially found to promote fat metabolism, turning white fat cells into brown ones, which burn more energy. It was only later recognized that it also plays a role in the brain.

More than muscle

This new study makes a pretty compelling case that exercise, working through irisin, can protect memories from the neurodegeneration that wreaks such havoc on the minds and

lives of Alzheimer's patients. The researchers first showed that irisin levels are lower in the brains of people and mice with AD than in age-matched healthy controls, a correlation that indicated a closer look was called for.

Amyloid β oligomers are toxic protein aggregates that accumulate in Alzheimer's brains and are associated with memory loss. Experiments with cultured rat brain cells, human brain slices, and live mice showed that these amyloid β oligomers are also associated with this decrease of irisin levels in the brain.

Next, the researchers showed that irisin is both necessary and sufficient for protecting memories from degradation. To show that it is necessary, the scientists artificially knocked it down in mouse brains. The mice could no longer recognize a familiar object. To show that it is sufficient, the scientists added extra irisin into the brains of mice and then added amyloid β aggregates. The irisin blocked the memory loss that was caused by the amyloid β aggregates.

Protection

So irisin saves memories from degradation, and irisin is induced by exercise. To fill in the missing step and demonstrate that exercise saves memories via irisin, the researchers put their mice on a strict exercise regimen: an hour of swimming a day, five days a week for five weeks. (Would *you* want to come into the lab on weekends to make your mice swim? Didn't think so.)

As expected, the mice that worked out had higher levels of irisin in their brains than sedentary controls, and their memories were protected from degradation when they got amyloid β oligomers infused into their brains. But the real kicker was that exercise did not help the memories of mice that were infused with an antibody that specifically blocks irisin. This antibody was administered to the circulatory system,

indicating that irisin can exert its effects by traveling to the brain during exercise.

The ramifications of these findings range from the coldly clinical to the more grandly philosophical. In the former camp, perhaps low circulating irisin can be used as a biomarker to diagnose and monitor AD, or perhaps the molecule can be administered as a drug to shore up the cognitive abilities of AD patients who are too physically debilitated to reap the other benefits of exercise. In the latter, this link between muscles and memories joins a number of links between the brain and other body parts—notably the gut and the microbiome it harbors. Reductionist views of brain science have not had much success treating Alzheimer's; maybe a more holistic one will.

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