

How Exercise Can Protect Against Alzheimer's

Researchers used a mouse model to gain insights.

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Exercise has well-known protective effects in Alzheimer's disease (AD). More exercise is associated with a lower risk for AD, better cognitive function and less cognitive decline in people with AD. How exercise leads to these effects at the cellular level remains unclear. Figuring this out could lead to novel ways to treat AD and other neurodegenerative diseases.

A research team led by Christiane Wrann, DVM, PhD, of Massachusetts General Hospital, looked for exercise-induced changes in gene activity in a mouse model of AD using a technique called single-nucleus RNA sequencing. This allows for analysis of gene activity at the single cell level.

They focused on the dentate gyrus region of the hippocampus. The hippocampus is essential for memory and learning, and the dentate gyrus is where new hippocampal neurons form. Past studies have found it to be particularly susceptible to changes during both exercise and AD. Results of the study, which was funded in part by the National Institutes of Health (NIH), appeared in *Nature Neuroscience* on June 12.

For exercise, mice were allowed to run freely on a wheel over a 60-day period. As expected, the AD mice who exercised had better cognitive function than the ones that were kept sedentary. Exercise led to changes in gene activity in both healthy mice and in the AD mice. The genes affected, however, differed between healthy and AD mice.

Certain gene activity changes were specific to AD mice across various cell types. Exercise restored some of these genes' activities to levels like those of healthy mice. Many of these recovered genes, the team noted, were found in immature neurons. This suggested that exercise has an impact on new neuron formation in the hippocampus. Further experiments showed that one exercise-recovered gene, *Atpif1*, was particularly important for neuron development and survival.

