

## Exercise, learning fight Alzheimer's

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Exercise and an enriched environment filled with challenging toys keep Alzheimer's disease at bay - and even help restore memories once thought to be lost - in mice destined for the devastating brain disease.

It's unclear whether a similar brain-sparing process can be coaxed in humans, but there is evidence that continued learning throughout middle and old age can strengthen the brain, just like physical exercise can make the body stronger.

Li-Huei Tsai, a scientist at the Massachusetts Institute of Technology and a Howard Hughes Medical Institute researcher, and her colleagues have restored memory in mice genetically engineered to develop the same neurodegenerative signs of Alzheimer's in humans.

This animal model allows these investigators for the first time to understand something very important about the disease process - that the animals seemed to lose the memories they acquired a long time ago, after the disease hit. Remarkably, the enriched environment - cages filled with toys and exercise wheels - was able to restore these memories, suggesting that they were still present, just inaccessible.

"Their memories were not erased," said Tsai, whose study appears in the latest issue of the journal *Nature*. "Those memories were recovered after four weeks of an enriched environment." Tsai speculated that the enriched environment induced a biochemical process that altered key proteins that are part of learning and memory.

Their animal model of severe neurodegeneration is unlike other models now used to study Alzheimer's. The animals are born normal, but at midlife researchers activated a protein that in large amounts is neurotoxic to the brain. This protein, p25, elevates brain diseases, including Alzheimer's, Lou Gehrig's disease and stroke. The animals have the same pathological problems as patients with Alzheimer's disease.

The researchers train the animals when they are normal and then turn on the gene that triggers the neurodegenerative process. And the memories of the events learned seem lost. But then those memories return after four weeks for those living in an enriched environment compared to the animals living in unadorned cages.

"We proposed that if memories can be recovered, then they are not erased," Tsai said. "It's not actually memory loss, but a loss of accessibility to the information." This is exciting, the scientist added, because it opens up the possibility that memories "can be brought back even in human patients."