SuperAger brains resist protein tangles that lead to Alzheimer's

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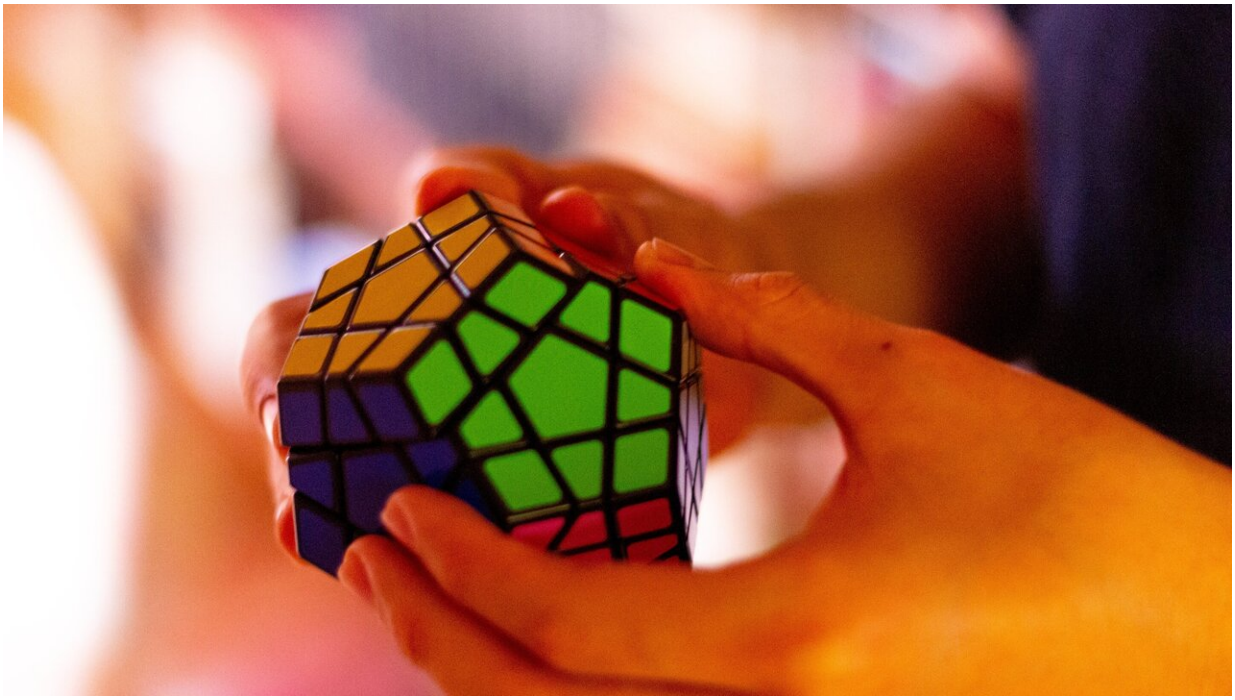

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A new Northwestern Medicine study showed cognitive SuperAgers have resistance to the development of fibrous tangles in a brain region related to memory and which are known to be markers of Alzheimer's disease.

The tangles are made of the tau protein which forms structures that transport nutrients within the nerve cell. These tangles disrupt the cell's

transport system, hampering communication within the neuron and preventing nutrients from performing their particular job within the cell. The end result of tangle formation is cell death.

"The results suggest resistance to age-related tau degeneration in the cortex may be one factor contributing to preserved memory in SuperAgers," said lead study author Tamar Gefen, an assistant professor of psychiatry and behavioral sciences at Northwestern University Feinberg School of Medicine.

"SuperAgers," a term coined by the Northwestern Mesulam Center for Cognitive Neurology and Alzheimer's Disease, are unique individuals over age 80 who show outstanding memory capacity at a level consistent with individuals 20 to 30 years younger. At the Center, SuperAgers are evaluated annually and may choose to donate their brains for post-mortem evaluation by Northwestern scientists.

This study quantified the amount of amyloid plaques and tau-containing neurofibrillary tangles in part of the brain that is heavily responsible for memory, known as the entorhinal cortex, in seven SuperAgers compared with six age-matched cognitively-healthy individuals. The findings showed significantly less tangles in the entorhinal cortex of SuperAgers than those of cognitively healthy controls by a difference of nearly three-fold.

"This finding helps us better identify the factors that may contribute to the preservation of memory in old age," Gefen said. "This research highlighted there are gradients of vulnerability to cell death in the brain."

"Individuals with significant memory impairment due to Alzheimer's disease showed nearly 100 times more tangles in the entorhinal cortex compared to SuperAgers," Gefen said. "There is a strong relationship between tau-tangles and memory loss, and these findings in a unique

SuperAging cohort could guide research in a new direction."

The study, "Paucity of Entorhinal Cortex Pathology of the Alzheimer's Type in SuperAgers with Superior Memory Performance", was published in *Cerebral Cortex* on Feb. 17.

The seminal characteristics of Alzheimer's disease are amyloid plaques and tau-containing neurofibrillary tangles found in the brains of individuals at death after autopsy. While these plaques and tangles are most commonly found in the brains of those with memory impairment, they are also found in cognitively healthy elderly individuals but in a more limited distribution.

Because advancing age is typically associated with declining memory abilities and increased risk of developing Alzheimer's disease, the Center studies SuperAgers to better understand what is going right in their brains.

The study also found there were no significant differences in amyloid plaque density in SuperAgers compared to cognitively healthy older persons.

"Many investigators have long thought that amyloid plaques are drivers of memory loss, which isn't what we found," Gefen said.

Gefen wants to explore the interaction of genetics and environment/lifestyle, and their collective impact, on the cellular level in post-mortem brains of SuperAgers.

"Why are memory cells selectively vulnerable to tangles in the first place?" she asked. "What is it about the cellular environment in the brains of SuperAgers that seem to protect them from tangles? Are the behaviors of SuperAgers somehow building up resistance in the brain?"

"To address these questions, we can study the molecular, biochemical, and genetic components of these specific memory cells, in SuperAgers, that are typically targeted by Alzheimer's. And, certainly, we must take their personal narratives (history, proclivities, behaviors, cultures) into account when making conclusions about their unique neuroanatomic profiles."

More information: Tamar Gefen et al, Paucity of Entorhinal Cortex Pathology of the Alzheimer's Type in SuperAgers with Superior Memory Performance, *Cerebral Cortex*, bhaa409, doi.org/10.1093/cercor/bhaa409

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