

WHY WOMEN TEND TO LIVE LONGER AND BE MORE RESILIENT TO COGNITIVE DECLINE THAN MEN

A recent study published in *Science Advances* (2025)¹ by Gadek et al. investigates how aging affects gene expression on the silent X chromosome (Xi) in the female mouse hippocampus. Using allele-specific single-nucleus RNA sequencing, the researchers found that aging alters transcription on both the active (Xa) and inactive (Xi) X chromosomes, with specific genes escaping inactivation as mice age.

One key finding is the increased expression of *Plp1*, a gene involved in myelination, which was also observed in the parahippocampus of aging women. The study suggests that reactivation of genes on Xi may contribute to cognitive resilience in aging females. The results highlight potential genetic mechanisms underlying sex differences in brain aging and open new avenues for therapeutic targets against cognitive decline. The paper warranted a comment in *Nature*².

1. <https://www.science.org/doi/10.1126/sciadv.ads8169>
2. <https://www.nature.com/articles/d41586-025-00723-x>