Who becomes a SuperAger Can Alzheimer's Genes Predict that

A new study published found that exceptional memory in SuperAgers, older adults who maintain unusually strong memory into their 80s and 90s, is not explained simply by lower inherited genetic risk for Alzheimer's disease (AD).

Study

The study included 142 SuperAgers and 89 cognitively average older adults (controls) recruited across five sites in the US and Canada. The groups were comparable in age and ancestry, although women made up a larger proportion of the SuperAger group. The statistical analyses adjusted for age, sex, and education.

The researchers examined the patterns of APOE as well as three PRSs that capture the combined effects of thousands of common genetic variants associated with Alzheimer's risk.

Findings and Conclusion

The findings show that APOE status (APOE ε2, ε3, and ε4 alleles) and PRSs were comparable between SuperAger and control subgroups.

For instance, approximately 16% of SuperAgers carried one or more ε4 alleles, compared with 19% of controls. Similarly, about 13% of both SuperAgers and controls carried at least one potentially protective ε2 allele. The mean PRS values were also comparable.

Moreover, the researchers found that the findings remained unchanged after accounting for genetic ancestry, with no evidence that ancestry modified the relationship between the genetic risk measures and SuperAger status.

Further exploratory analyses were performed to identify associations between the 768 variants common to the three PRSs. The findings showed no associations between any of the variants and SuperAger status after correcting for multiple testing.

The researchers also examined previously identified rare genetic variants that may offer protection against Alzheimer's disease. They found that one SuperAger carried the rare protective PLCG2 P522R variant, but there was no evidence that the protective variants examined were enriched among SuperAgers.

The study used rigorous methodologies to define SuperAgers and controls, model ancestry, and optimize PRS cut-offs. However, it had some limitations.

The sample was too small to detect small genetic effects or examine ancestry-specific effects within the groups. Because the study was cross-sectional, the authors could not determine how inherited genetic risk relates to changes in cognition over time.

Behavioral and vascular factors were not included, though they may influence the SuperAger phenotype. The authors also noted that polygenic risk scores developed largely from European-ancestry datasets may not perform equally well across different ancestral groups.

The findings suggest that SuperAging and Alzheimer's disease risk are not simply two ends of the AD risk spectrum. Specific biological and experiential factors may play a role in preserving exceptional cognitive function into late life.

To distinguish the effects of AD pathology from resilience and the interaction between the two factors, larger longitudinal studies with more diverse populations are required. They should incorporate genetic risk variants, lifestyle factors, and AD pathology markers.

Source:

https://www.news-medical.net/news/20260728/Can-Alzheimers-genes-predict-who-becomes-a-SuperAger.aspx