Molecular switches age-related memory decline? Genetic variant protect against brain aging

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Even among the healthiest individuals, memory and cognitive abilities decline with age. This aspect of normal aging can affect an individual's quality of life and capability to live independently but the rate of decline is variable across individuals. There are many factors that can influence this trajectory, but perhaps none more importantly than genetics.

Scientists are seeking to identify key molecular switches that control age-related memory impairment. When new molecules are identified as critical to the process of memory consolidation, they are then tested to determine whether they contribute to the memory problems of the elderly.

One of these proteins is called KIBRA and the gene responsible for its production is WWC1. KIBRA is known to play a role in human memory and so researchers at the Lieber Institute for Brain Development and the National Institute of Mental Health, led by senior author Dr. Venkata Mattay, conducted a study to determine the effects of genetic variants in WWC1 on memory. Their findings are published in the current issue of *Biological Psychiatry*.

"Identifying these genetic factors, while helping us better understand the neurobiology of cognitive aging, will also aid in identifying mechanisms that confer individuals with resilience to withstand the inevitable age-related changes in neural architecture and function," explained Mattay.

Using imaging genetics, a method that combines genetics with brain imaging technology, the team explored the effect of a variant in the WWC1 gene on age-related changes in memory function. The particular WWC1 variant under investigation has three potential forms – CC, TT, or CT.

They recruited 233 healthy volunteers, who ranged in age from 18-89 years. The volunteers completed a battery of cognitive tests, underwent genotyping, and completed a memory task during a brain imaging scan.

They found that individuals who carry the T allele, as either CT or TT, performed better on the memory task and showed more active engagement in the hippocampus, a vital brain region for memory, with increasing age.

"Our results show a dynamic relationship between this gene and increasing age on hippocampal function and episodic memory with the non-T allele group showing a significant decline across the adult life span," said Mattay. "A similar relationship was not observed in the T-allele carrying group suggesting that this variant of the gene may confer a protective effect."

Dr. John Krystal, Editor of *Biological Psychiatry*, commented, "The risk mechanisms for age-related memory impairment that we identify today may become the targets for the prevention and treatment of this problem in the future."

More information: The article is "WWC1 Genotype Modulates Age-Related Decline in Episodic Memory Function Across the Adult Life Span" by John Muse, Matthew Emery, Fabio Sambataro, Herve Lemaitre, Hao-Yang Tan, Qiang Chen, Bhaskar S. Kolachana, Saumitra Das, Joseph H. Callicott, Daniel R. Weinberger, and Venkata S. Mattay (DOI: 10.1016/j.biopsych.2013.09.036). The article appears in *Biological Psychiatry*, Volume 75, Issue 9 (May 1, 2014)

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