Researchers discover clues to memory performance in international genetic study

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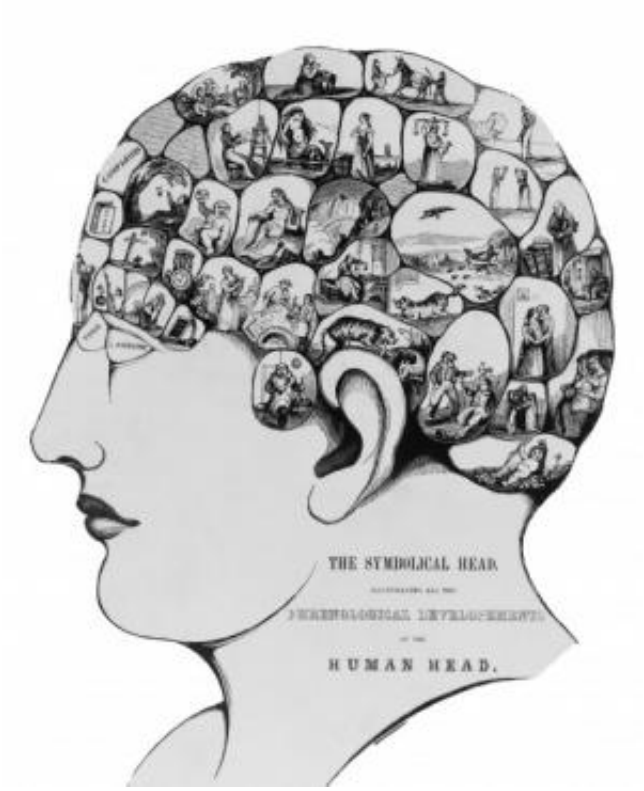

Credit: Karen Arnold/Public Domain

(Medical Xpress)— In the largest study of the genetics of memory ever undertaken, an international team of researchers, including scientists from the University of Mississippi Medical Center (UMMC), have associated two common genetic variants with memory performance.

The findings, which appeared Nov. 25, 2014, in the journal *Biological Psychiatry*, may provide clues to better understand memory loss in disorders such as Alzheimer's disease and during normal aging.

"Longer life spans and the growing prevalence of memory impairment and dementia worldwide have increased the urgency of efforts aimed at deciphering the underlying mechanisms of human memory," said Thomas Mosley, Ph.D., director of the MIND Center at UMMC and senior scientist on the study. "If memory loss can be slowed just a little bit, giving older adults even just a few additional years of functional independence, the population burden from dementia would be dramatically reduced, as would some of the burden on families and the nation's health care system."

The researchers analyzed genetic data from almost 30,000 dementia-free individuals of European descent who were 45 and over from collaborating research centers from around the world. In addition, data from nearly 11,000 participants of European descent, nearly 4,000 African-Americans and about 1,500 young adults were analyzed for comparison purposes.

Examining more than 2.5 million sites along each participants' genome, researchers associated genetic variants near the Apolipoprotein E gene with poor memory performance, mostly in the oldest individuals.

The same genetic variants are known to convey an increased risk of dementia, especially Alzheimer disease.

In a sub-study using postmortem brain samples, participants with more memory-risk variants also had more pathological features of Alzheimer's disease, perhaps reflecting some instances of early pre-clinical stages of the disease, the researchers said.

According to the researchers, two additional regions of the genome pointed to genes involved in immune response, providing new support for the role of immune system dysfunction in age-related memory decline.

"Interestingly genetic variants associated with memory performance also predicted altered levels of expression of certain genes in the hippocampus, a key region of the brain for the consolidation of information," said lead author Stéphanie Debette, M.D., Ph.D., an adjunct associate professor at Boston University School of Medicine. "These were mainly genes involved in the metabolism of ubiquitin that plays a pivotal role in protein degradation."

Mosley credits the genetic discovery to the large worldwide collaboration developed through the Cohorts for Heart and Aging Research in Genomic Epidemiology consortium, also known as CHARGE.

"Through CHARGE, we have brought together leading researchers from around the world who have agreed to pool data and analytic resources which has greatly enhanced our ability to identify genetic variations for complex phenotypes like memory and Alzheimer's," Mosley said.

The core CHARGE cohorts include five population-based studies, including the Atherosclerosis Risk in Communities study, AGES-Reykjavik Study, Framingham Heart Study, Cardiovascular Health Study, and the Rotterdam study.

For the memory analysis, 23 additional studies contributed data. Funding for the core CHARGE cohorts was provided by the National Institutes of Health.

More research is needed to confirm the findings before exploring treatments or the development of diagnostic genetic tests, researchers

said.

"The findings need to be carefully replicated and we need a much better understanding of the function of these genetic sites," said Mosley. "Identifying susceptibility regions is only a first step, but an important one, because understanding the mechanisms underlying susceptibility regions may ultimately lead to the development of new treatments for memory loss."

More information: Genome-wide studies of verbal declarative memory in non-demented older people: the CHARGE consortium, *Biological Psychiatry*, www.sciencedirect.com/science/ … ii/S0006322314008920

Provided by University of Mississippi