Study finds evidence for genetic influence on cognitive decline

A team led by researchers at Yale and Texas Biomedical Research Institute has shown that genetic factors play an important role in cognitive decline and reductions in cerebral white-matter integrity with normal aging. The study, reported in the Proceedings of the National Academy of Sciences, provides a path for the discovery of specific genes that influence successful brain aging.

Identification of genes associated with brain aging should improve our understanding of the biological processes that govern age-related decline in mental abilities.

The investigators used cognitive tests and MRI brain scans to study the effects of aging in 1,129 people aged 18-83 years from large extended families. The cognitive tests measured general intelligence, memory and processing speed. The scans were used to measure the structure of white matter which contains neural tracts that connect different parts of the brain. The study confirmed previous reports that aging is associated with decline in cognitive ability and in the integrity of the brain's white matter. In general, when white matter integrity was preserved cognitive abilities were also preserved. However, the study uncovered an intriguing new finding. The genetic factors that influence white matter integrity, as people grew older, were not the same as those that influence cognitive function. Applying an advanced statistical method termed gene-by-environment interaction analysis, the researchers demonstrated that cognitive decline with age was heritable and could be attributed to genetic factors. In contrast, reduction in white-matter integrity with age appeared to be non-genetic.

"One of the greatest societal challenges is to find ways to support and promote successful aging. The first step is to determine the processes connected to age-related declines in cognitive function and brain structure. Focusing on large extended families allowed us to disentangle the genetic from the non-genetic influences on the aging process," said David C Glahn, PhD, associate professor of psychiatry at Yale School of Medicine and lead author of the study. Glahn is affiliated with the Olin Neuropsychiatry Research Center at the Institute of Living, Hartford Hospital.

Identifying genetically influenced brain-aging traits is a critical first step in delineating the causal biological mechanisms of successful aging.

"The use of large human pedigrees provides a powerful resource for measuring how genetic factors change with age" said John Blangero, PhD, a scientist in the Department of Genetics at the Texas Biomedical Research Institute and senior author of the study. Blangero, a leader in statistical genetic methods, proposed the analyses implemented in this study in a groundbreaking article published in 1993.

In addition to Yale and the Texas Biomedical Research Institute, other researchers in the team were from the Department of

Psychiatry and the Research Imaging Institute at University of Texas Health Science Center at San Antonio, the Menzies Research Institute Tasmania at the University of Tasmania, and the Maryland Psychiatric Research Center at the University of Maryland School of Medicine.

The National Institutes of Mental Health provided financial support for this research.

Read the study: "Genetic basis of neurocognitive decline and reduced white-matter integrity in normal human brain aging"

Source: Yale University