# Study examines memory and effects on the aging brain

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A study of brain aging finds that being male was associated with worse memory and lower hippocampal volume in individuals who were cognitively normal at baseline, while the gene APOE ?4, a risk factor for Alzheimer disease, was not, according to an article published online by *JAMA Neurology*.

Typical cognitive aging may be defined as age-associated changes in cognitive performance in individuals free of dementia. To assess brain imaging findings associated with typical aging, the full adult age spectrum should be included, according to the study background.

Clifford R. Jack, Jr., M.D., of the Mayo Clinic and Foundation, Rochester, Minn., and coauthors compared age, sex and APOE ?4 effects on memory, brain structure (as measured by adjusted hippocampal volume, HVa) and amyloid [brain plaques associated with Alzheimer disease] positron emission tomography (PET) in 1,246 cognitively normal individuals between the ages of 30 and 95.

## The authors found:

- Overall memory worsened from age 30 through the 90s.
- HVa worsened gradually from age 30 to the mid-60s and more steeply after that with advancing age.
- Median amyloid accumulation seen on PET scans was low until age 70 but increased after that.

- Memory was worse in men than women overall, especially after 40.
- The HVa was lower in men than women overall, especially after 60.
- For both males and females, memory performance and HVa were not different by APOE ?4 carrier status at any age.
- From age 70 onward, APOE ?4 carriers had greater median amyloid accumulation seen on PET scans than noncarriers.
- The ages at which 10 percent of the population was "amyloid PET positive" were 57 years for APOE ?4 carriers and 64 years for noncarriers. Amyloid PET positive indicates individuals are accumulating amyloid in their brain as seen on PET scans and, while they may be asymptomatic, they are at risk for Alzheimer disease.

"We believe that this study of typical aging reveals interesting sex and APOE ?4 effects on age-related trends in brain structure, function and β-amyloidosis [buildup of plaque deposits in the brain]. To date, these effects have not been widely appreciated. Our findings are consistent with a model of late-onset AD [Alzheimer disease] in which β-amyloidosis arises later in life on a background of preexisting structural and cognitive decline that is associated with aging and not with β-amyloid deposits," the study concludes.

In a related editorial, Charles DeCarli, M.D., of the University of California at Davis, Sacramento, writes: "In their article, Jack et al present new information that challenges the notion that amyloid accumulation explains memory performance across the entire age range. Importantly, this work does not only address the likely highly significant impact of cerebral amyloid accumulation on dementia risk, but also extends current knowledge relating to the impact of the aging process across the spectrum of ages 30 to 95 years to brain structure, amyloid accumulation and memory performance among cognitively normal

individuals."

"Understanding the basic biology of these early processes are likely to substantially inform us about ways in which we can maintain cognitive health and optimize resistance to late-life dementia. However, such work requires the necessary motivation found by seminal work, such as that of Jack et al, which tell us where and when to investigate these processes. Establishing what is normal creates avenues for new research, increasing the likelihood of discovering novel therapeutics for late-life disease states, which is a laudable goal indeed," the editorial concludes.

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