

Abstract

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APOE epsilon4 genotype and longitudinal changes in cerebral blood flow in normal aging.

Thambisetty M, Beason-Held L, An Y, Kraut MA, Resnick SM.

Department of Radiology and Radiological Sciences, Laboratory of Personality and Cognition, National Institute on Aging, National Institutes of Health, Johns Hopkins University, Baltimore, Maryland 21224-6825, USA.

OBJECTIVE: To study differences in longitudinal changes in regional cerebral blood flow (rCBF) between apolipoprotein E (APOE) epsilon4 carriers and noncarriers in nondemented older adults from the Baltimore Longitudinal Study of Aging using positron emission tomography in order to determine whether there are regionally specific longitudinal changes in rCBF in APOE epsilon4 carriers that might be related to its well-established role as a genetic risk factor for Alzheimer disease.

DESIGN, SETTING AND PARTICIPANTS: Using oxygen 15 (^{15}O)-labeled water positron emission tomography and voxel-based analysis, we compared changes in rCBF over an 8-year period between 29 nondemented APOE epsilon4 carriers and 65 noncarriers older than 55 years. Serial neuropsychological data were collected for all participants.

RESULTS: Widespread differences were observed in longitudinal change in rCBF between epsilon4 carriers and noncarriers. The predominant pattern was greater rCBF decline in epsilon4 carriers. These differences were observed in the frontal, parietal, and temporal cortices. The affected brain regions were those especially vulnerable to pathological changes in Alzheimer disease. Both epsilon4 carriers and noncarriers remained free of clinical diagnoses of dementia or mild cognitive impairment during the course of the study.

CONCLUSIONS: Our findings suggest that APOE epsilon4-mediated risk for Alzheimer disease is associated with widespread decline in rCBF over time that precedes the onset of dementia. Accelerated rates of decline in brain function in APOE epsilon4 carriers may contribute to an increased risk for Alzheimer disease and a younger age at onset.

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