

# Severity of cerebral white matter lesions predicts rate of cognitive decline

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**BACKGROUND:** ApoE  $\epsilon$ 4 has been found to increase AD risk in genetically diverse populations although it is weaker in Africans and African-Americans. In a population based study we have screened all elderly residents of an Arab community (n = 821) located in Wadi Ara, northern Israel. An unusually high prevalence of AD was observed (20.5% of those >60, 60.5% of those >85 years), higher than observed in other countries even after adjustment for age, education and gender. The present study examined whether this is due to increased frequency of the ApoE  $\epsilon$ 4 allele in this population.

**DESIGN/METHODS:** DNA samples were collected randomly from 210 people from Wadi Ara study and their ApoE genotype was determined by a PCR based method.

**RESULTS:** Of the 210 cases examined, 18 carried an ApoE  $\epsilon$ 4 allele (all heterozygous), including 3/32 with AD (ApoE  $\epsilon$ 4 allele frequency 0.05), 6/103 non demented elderly subjects (ApoE  $\epsilon$ 4 allele frequency 0.03), 7/55 with age-associated memory impairment (AAMI; ApoE  $\epsilon$ 4 allele frequency 0.06) and 2/20 with vascular dementia (ApoE  $\epsilon$ 4 allele frequency 0.05).

**CONCLUSION:** These preliminary data suggest that the ApoE  $\epsilon$ 4 allele is relatively uncommon in Arabs in Wadi Ara. Therefore, although it was associated with cognitive decline, it does not explain the high AD prevalence in this population. It has been reported that 44% of all Arab marriages in Israel are consanguineous, with a mean inbreeding coefficient of 0.02. We speculate that recessive genes for AD exist, and are responsible for the high AD prevalence in Wadi Ara. Arab populations are ideal for the study of such genes because of the high family size and inbreeding.

S47.007

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### Severity of Cerebral White Matter Lesions Predicts Rate of Cognitive Decline

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**OBJECTIVE:** To assess the relation between the severity of cerebral white matter lesions and the rate of cognitive decline over time.

**BACKGROUND:** Cognitive decline occurs frequently in the elderly and is an established risk factor for dementia. White matter lesions have been associated with cognitive impairment, however few studies used longitudinal data to study the association between severity of white matter lesions and rate of cognitive decline over time.

**DESIGN/METHODS:** Non-demented subjects, 60-90 years of age were randomly sampled from the prospective population based Rotterdam Study. During 1995-96, 568 subjects (response = 68%) underwent 1.5T MRI scanning on which the severity of white matter lesions was assessed. White matter lesions in subcortical regions were scored according to number and size. White matter lesions in periventricular regions were scored according to size. Cognitive decline was measured as decline in mini mental state examination (MMSE) scores as measured 4 times during a maximal 8 years period. We calculated an individual rate of cognitive decline by means of the PROC MIX module of the SAS statistical program. The relation between severity of white matter lesions and rate of cognitive decline was analyzed separately for periventricular and subcortical regions using age and gender adjusted multivariate analyses (ANCOVA). Additional ad-

justments were made for level of education, presence of stroke, and cerebral atrophy. Next, the relation between periventricular white matter lesions and rate of cognitive decline was studied conditional on the severity of subcortical white matter lesions, and vice versa.

**RESULTS:** Mean age of participants was 73.6 years, 50% were women. Mean follow-up was 5.5 years (SD = 1.1). Mean rate of decline in MMSE scores was -0.10 per year (SD = 0.13). When both periventricular and subcortical white matter lesions were studied in quintiles of severity, periventricular white matter lesions had a significant relation with rate of cognitive decline (p-trend = 0.001), but subcortical white matter lesions had not (p-trend = 0.17). When studied in more detail, subjects with the most severe periventricular white matter lesions had a rate of cognitive decline that was up to 2.5 (95%CI 1.4-3.3) times faster than average. This association did not change after adjustment for possible confounders. When we studied the relation between severity of subcortical white matter lesions and rate of cognitive decline in more detail, we found no relation between severity of subcortical white matter lesions (in deciles) and rate of cognitive decline, maybe with the exception of subjects in the highest decile who had a 1.5 (95%CI 1.1-1.8) times faster rate of decline compared to the average decline. Adjusting for possible confounders did not change these results. When the relation between periventricular white matter lesions and rate of cognitive decline was studied conditional on the severity of subcortical white matter lesions, and vice versa, the relation between periventricular white matter lesions and rate of cognitive decline remained, whereas this relation disappeared for subcortical white matter lesions.

**CONCLUSION:** The severity of periventricular, rather than subcortical white matter lesions predicts the rate of cognitive decline.

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### Duration of Estrogen Use, Apolipoprotein E and Cognitive Decline: The Cardiovascular Health Study

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**OBJECTIVE:** To determine whether the lower rate of cognitive decline seen in women taking estrogen is modified by apolipoprotein E (ApoE) genotype and whether duration of estrogen use is associated with extent of cognitive decline.

**BACKGROUND:** Several studies have shown that cognitive function may be better in women taking estrogen; however, few have examined if duration of estrogen use is associated with cognition and whether ApoE  $\epsilon$ 4 modifies this association.

**DESIGN/METHODS:** We studied 2,429 women 65+ enrolled in the Cardiovascular Health Study. Baseline and annual visits included inventory of hormone prescription; at baseline, women were classified as current/past/never estrogen users. Cumulative estrogen use was obtained from prescription reports during the 9 years follow-up. The Modified Mini-Mental State exam (3MSE) was obtained for each follow-up year. Generalized estimation equations were used to analyze the association between estrogen and annual 3MSE change.

**RESULTS:** At baseline, 274 (11%) were current and 278 (11%) were past users; compared to never users, current users had less 3MSE annual change (-.51 vs. 0.20, p = 0.023).