

Abstract

Arch Neurol. 2004 Sep;61(9):1434-9.

APOE and APOC1 promoter polymorphisms and the risk of Alzheimer disease in African American and Caribbean Hispanic individuals.

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BACKGROUND: The APOE epsilon4 allele is a genetic risk factor for Alzheimer disease (AD), though the strength of the association varies by ethnic group. Polymorphisms in regulatory sequences of APOE have also been related to AD, but the effects are inconsistent across studies.

METHODS: We examined the association between AD and variants in 3 APOE promoters and in the promoter of the adjacent APOC1 gene in African American and Caribbean Hispanic individuals. Polymorphisms tested were the -491A/T, -427T/C, and -219G/T (Th1/E47cs) in the APOE promoter and the HpaI variant in the APOC1 promoter. Using standard research criteria for AD, overall odds ratios were computed and repeated stratified by presence or absence of APOE epsilon4.

RESULTS: The APOC1 HpaI+ variant was associated with AD in Caribbean Hispanic individuals, but strong linkage disequilibrium with the APOE epsilon4 allele indicated that this was not an independent effect. No promoter variant in APOE or APOC1 was associated with AD before or after adjusting for age, education, sex, and multiple comparisons. Estimated haplotypes including -219G/T, APOE, and APOC1 differed significantly in Caribbean Hispanic patients and controls but not in African American participants. This effect was primarily owing to the -219G/T-APOE haplotype, but we did not detect significant allele-specific differences in promoter activity comparing reporter constructs containing the APOE -219G and -219 T alleles.

CONCLUSION: These findings exclude a strong or independent influence of APOE or APOC1 promoter polymorphisms on the variation in APOE-related risk of AD in African American and Caribbean Hispanic individuals.

PMID: 15364690

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