To compare relative frequencies of apolipoprotein E (APOE) alleles in African-American and Caucasian populations and test associations with cognition, we studied two community-based samples: one of 253 African Americans and another of 466 Caucasians age 60–84 years. Logistic regression, adjusting for age, sex, education, and history of hypertension and diabetes was used to associate APOE with five cognitive measures. The APOE-ε4 allele frequency was 29.5% in African Americans and 12.1% in Caucasians. In the African Americans, no association was found between the presence of the APOE-ε4 allele and any of the cognitive measures. Among Caucasians, APOE-ε4 carriers performed more poorly on three of the five tests. We also report a considerably higher frequency of the APOE-ε4 allele in our African-American sample compared to other US-based studies. (Ethn Dis. 2006;16:9–15)

Key Words: Apolipoproteins E, Cognition, Gene Frequency, Racial Groups

INTRODUCTION

Recent studies of dementia and Alzheimer disease (AD) have reported higher prevalence and incidence rates among African-American compared with Caucasian populations.1,2 By contrast, lower rates have been reported among older African Blacks.3 The apolipoprotein E-ε4 (APOE-ε4) allele is a robust risk factor for AD among Caucasians.4,5 However, among African Americans and African Blacks, the evidence for this association is controversial. In a large prospective study of African Americans in Indianapolis, the ε4 allele was positively associated with the presence of AD,6 while in a methodologically standardized study of Africans in Nigeria, no association was present.7 In a multicenter case-control study, the APOE-ε4 allele was reported to confer increased risk among both African Americans and Caucasians.8 Different findings were reported in a prospective study in North Manhattan, where the relative risk for AD among African Americans associated with one or two ε4 alleles was 1.0 (95% CI 0.6–1.6), compared with 2.5 for Caucasians (95% CI 1.1–6.4).9 In that study, African Americans without an ε4 allele had cumulative risks of AD to age 90 that were four-fold higher than Caucasians, even when adjusted for education and sex. In addition, a large prospective study of community-dwelling African-American and Caucasian residents in Chicago reported no association between the ε4 allele and incident AD among African Americans.9

Some of the differences between studies may be due to differential associations between individuals who are homozygous vs heterozygous for the ε4 allele. In the Indianapolis cohort, for example, the risk for AD associated with the heterozygous form of APOE (specifically ε3/ε4) was 1.2 (95% CI 0.6–2.5), while that associated with the homozygous form was 4.8 (95% CI 1.7–13.6).6 This finding is consistent with a meta-analysis that showed that homozygosity for APOE-ε4 increased the risk for AD five-fold but that heterozygosity was not associated with the disease in African Americans.5

The association between APOE-ε4 and cognition has been studied cross-sectionally in 202 individuals in the United Kingdom of African Caribbean descent.10 In that study, ε4 increased the risk for cognitive impairment (OR=1.60, 95% CI 0.84–3.05), especially for those aged 70–75 (OR=6.2, 95% CI 1.3–29.8). In the Cardiovascular Health Study, Blacks with the ε4 allele were at a 50% higher risk (95% CI 0.9–2.5) for scoring low (<80/100) on the Modified Mini Mental State Examination (3MS) compared with those who did not carry an ε4 allele; among Whites, the magnitude of the association was similar but attained statistical significance.11 However, the risk of declining by five or more points on the 3MS over a two-year period was not elevated for Blacks with an ε4 allele.

In the present study, we report the frequencies of APOE genotypes in two methodologically standardized cross-sectional studies: the Hillsborough Elder African-American Life Study (HEALS), in which all of the participants were African-American, and the