

Letter to the Editor

The Use of Apolipoprotein E Genotype for Preclinical Detection of Risk's Group for Alzheimer's Disease

To the Editor:

The association between the apolipoprotein E (APOE) $\epsilon 4$ allele as a risk factor for early and late onset Alzheimer's Disease (AD), familial and sporadic, has been shown and replicated in several studies [Corder et al., 1993; Mayeaux et al., 1993; Noguchi et al., 1993; Strittmatter et al., 1993; Van Duijin et al., 1994; Clair et al., 1995].

Recently, in a community-based study, Jarvik et al. [1996] suggested that the APOE genotype, the family history, the gender, and age interactions should be relevant when making predictions about the effects of APOE on AD or age at onset.

Despite the widely confirmed characterization of the APOE $\epsilon 4$ allele as an important risk factor for AD, the value of using the APOE genotype as a predictive tool in a clinical practice as well as the social and ethical impact of genetic testing in AD have recently been questioned [Mihill et al., 1993; Riggs et al., 1994; Roses et al., 1994; Burgess et al., 1995; Corder et al., 1995; Karlinsky et al., 1995].

To further evaluate the possibility of APOE genotype application for symptomatic individuals, we verified the allelic frequencies of APOE in three groups:

1. A preclinical group ($n = 43$) characterized by subjects with memory deficit but without impairment of other cognitive functions or behaviour disturbances that composes the criteria for dementia syndrome.
2. A subgroup ($n = 20$) of the preclinical group with a positive family history of dementia.
3. A group of demented patients ($n = 57$) with probable/possible diagnosis of AD based on NINCDS-ADRDA [McKinnann et al., 1984].

The frequencies of APOE alleles in these three groups were compared with a normal control group of

TABLE 1. Frequencies of APOE $\epsilon 4$ Allele among Patients with AD, Normal Control Group, and the Preclinical Groups

Groups	Number of $\epsilon 4$ detected (%)	Mean age (range)	Total number of alleles analyzed
Control	17 (11.48%)	73 (37–92)	148
AD patients	34 (29.82%)	70 (55–92)	114
Preclinical	18 (20.92%)	58 (39–77)	86
Familial	10 (25.0%)	58 (40–77)	40
preclinical subgroup			

similar age ($n = 74$). The APOE genotype was analyzed according to the conditions described by Guo et al. [1993].

The $\epsilon 4$ allelic frequencies between AD patients and the normal control group was significantly greater ($\chi^2 = 13.8$; $P = 0.001$), confirming the APOE $\epsilon 4$ association with AD also in Brazilian patients (see Table I).

On the other hand the $\epsilon 4$ allelic frequency of the preclinical group is about 80% higher when compared with the normal control group, although this difference was not statistically significant. Interestingly, in the subgroup that in addition to the memory deficit has a positive family history for dementia, we verified an $\epsilon 4$ allele frequency of 25%, which is significantly different ($\chi^2 = 9.7$; $P = 0.008$) from the frequency observed in the normal control group.

Those results suggest that the utility of APOE genotype may be useful for screening of risk group for AD between subjects that have memory deficit and a positive family history for dementia even without the clinical or neuropsychological features characteristic of the NINCDS-ADRDA criteria for dementia syndrome.

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