

SHORT REPORT

Apolipoprotein E genotype in familial Parkinson's disease

The French Parkinson's Disease Genetics Study Group (see appendix)

Abstract

APOE genotypes were compared in 57 cases of familial Parkinson's disease, 46 cases of sporadic Parkinson's disease, and 387 controls. The frequency of the APOE allele $\epsilon 4$ was similar in patients with Parkinson's disease and controls, but the APOE allele $\epsilon 2$, thought to be protective for dementia, was significantly more frequent in patients with sporadic Parkinson's disease than in controls. This is the first study of Parkinson's disease to include familial cases. It confirms the absence of association between the APOE allele $\epsilon 4$ and this disease.

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Keywords: apolipoprotein E gene; Parkinson's disease;

The $\epsilon 4$ allele of apolipoprotein E gene (APOE) is associated with early and late onset Alzheimer's disease.¹ Because patients with Parkinson's disease occasionally become demented and the neuropathological hallmarks of Alzheimer's disease—neurofibrillary tangles and senile plaques—are found at postmortem in the brains of patients with Parkinson's disease, several studies of the APOE genotype in Parkinson's disease, with or without dementia, have been undertaken.^{2–7} Except in a small series of demented patients,⁴ no association was found between APOE allele $\epsilon 4$ and Parkinson's disease. There have been, however, no studies of patients with familial Parkinson's disease, the pathogenesis of which may differ from that of the "sporadic" form of the disease. We have, therefore, compared APOE genotype distributions in 57 index cases with familial Parkinson's disease with those from 46 patients with isolated Parkinson's disease and 387 age and sex matched subjects randomly selected from a control sample of non-demented subjects.

Patients and methods

All patients and controls were of French origin. The criteria for a definite diagnosis of Parkinson's disease were the presence of a pronounced response to levodopa and at least two of the following: bradykinesia, rigidity, rest tremor, or asymmetric onset. Exclusion criteria were the presence of at least one of the follow-

ing: ophthalmoplegia, pyramidal or cerebellar syndrome, apraxia, prominent and early postural instability, urinary incontinence, or dementia within the first two years of evolution. Familial cases, defined by the presence of definite Parkinson's disease in at least two examined first degree relatives, were selected through a French clinical network (The French Parkinson's Disease Genetics Study Group). Isolated cases with no family history of Parkinson's disease among first and second degree relatives, verified by structured interviews of the patient and spouse, were recruited successively at the Fédération de Neurologie of the Hôpital de la Salpêtrière in Paris, France. Controls were age and sex matched selected subjects from a non-demented control sample.⁸

APOE genotypes were determined by polymerase chain reaction/restriction on DNA extracted from the blood of consenting patients.⁹ APOE allele and genotype frequencies were compared by χ^2 test, with the Yates' correction when appropriate.

Results

Mean age at onset and at examination were similar in isolated and familial Parkinson's disease (table). The most frequent genotype in all groups was $\epsilon 3/\epsilon 3$. Only three patients were demented; they belonged to the familial Parkinson's disease group and had the $\epsilon 3/\epsilon 3$ APOE genotype. No $\epsilon 4$ homozygotes were found. The allele distribution was significantly different in patients with familial and sporadic Parkinson's disease compared with controls ($\chi^2=8.16$, $P=0.017$). The comparison was not significant between familial and sporadic Parkinson's disease groups. The $\epsilon 2$ allele was significantly more frequent in sporadic Parkinson's disease than in controls (odds ratio 2.45, 95% confidence interval 1.15–5.21), but did not differ between familial and sporadic patients.

Discussion

Thus in familial Parkinson's disease, as in sporadic cases, there is no association with the APOE $\epsilon 4$ allele. The lack of association between APOE $\epsilon 4$ allele and Parkinson's disease was already reported in previous studies that did not distinguish between sporadic and familial cases.^{2–3,6,7} Our data suggest that the APOE $\epsilon 2$ allele may be associated

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Table 1 General characteristics, APOE genotypes, and allele frequencies in patients with Parkinson's disease (PD) and controls

	Familial PD	Sporadic PD	Controls
Number	57	46	387
Mean (SD) age at onset (y)	57 (13)	56 (10)	
Mean (SD) age at examination (y)	65 (12)	65 (9)	67 (9)
Sex M/F	29/28	27/19	215/172
APOE genotype % (n):			
2/2	2 (1)	0	0.5 (2)
2/3	14 (8)	26 (12)	11 (43)
3/3	70 (40)	57 (26)	62 (239)
4/2	0	0	1.5 (6)
4/3	14 (8)	17 (8)	24 (92)
4/4	0	0	1 (5)
APOE allele frequency %:			
ε2	9	13	7
ε3	84	78	79
ε4	7	9	14

with patients with sporadic Parkinson's disease. The association cannot be explained by the exclusion of patients with early dementia, possibly related to APOE ε4 allele, as demented subjects were also excluded from the controls.

Although no conclusion can be drawn concerning the relation between familial and isolated Parkinson's disease, it is clear that an important risk factor for Alzheimer's disease, the APOE ε4 allele, is less frequent in Parkinson's disease, whether sporadic or familial.

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Appendix: The French Parkinson's Disease Genetics Study Group

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