Reply to Correspondence From Inzelberg et al.—“Onset age of Parkinson disease”

To the Editor:

The association between Parkinson disease (PD) and apolipoprotein E (APOE) gene has been the subject of several studies. We first reported the observation that $\varepsilon$4 carriers had on average four years earlier age at onset than those without $\varepsilon$4 [Zareparsi et al., 1997]. We had estimated that a minimum sample of 400 patients was needed to detect earlier age at onset of PD in $\varepsilon$4 carriers. In a study of 521 unrelated Caucasian PD patients, we found that $\varepsilon$3/$\varepsilon$4 patients had significantly earlier onset than $\varepsilon$3 patients [Zareparsi et al., 2002]. Inzelberg et al. [2002] have combined the samples from different studies and report that they do not detect a significant difference in onset among $\varepsilon$4 carriers and those without $\varepsilon$4.

One possible explanation is that the strength of the association between APOE and onset of PD may differ between samples collected at different sites. In our study, the difference in onset between $\varepsilon$3/$\varepsilon$4 versus $\varepsilon$3 patients ranged from 2.2 to 8.5 years among patient samples collected in Oregon and Washington, respectively [Zareparsi et al., 2002]. Furthermore, the two samples displayed different trends for effect of $\varepsilon$2 on PD onset [Zareparsi et al., 2002]. Thus, it may not be suitable to combine samples from different centers without performing tests of heterogeneity. In fact, in two of the studies, $\varepsilon$4 carriers had slightly earlier onset [Inzelberg et al., 1998; Oliveri et al., 1999]. In addition, the combined sample is based on samples from different ethnic backgrounds. It is possible that the effect of APOE on PD onset differs between ethnic groups as mentioned by Inzelberg et al.

Inzelberg et al. [2002] confirm our finding of earlier onset in patients with positive family history. They further suggest that earlier onset in $\varepsilon$4 carriers may be due to family history and patients with parkin mutations. It should be noted that the earlier onset in $\varepsilon$3/$\varepsilon$4 versus $\varepsilon$3, and in familial versus non-familial PD.

REFERENCES

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