Title
Apolipoprotein E Genotype and the Rate of Decline in Probable Alzheimer Disease-Reply

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In reply

We thank Corder and colleagues for their comments on our recent study[1] and we are pleased that they agree with our conclusion that ApoE genotype does not appear to significantly influence rate of cognitive decline in AD. In their letter, Corder et al also raised 2 other issues regarding our study.

The authors correctly note that the study by Corder et al[2] did not report "longer survival in ε4 carriers." In addition to the study by van Duijn et al,[3] those findings should have been correctly attributed to DeKosky et al[4] and not to Corder et al,[2] as indicated by the reference numbers in the text of our article. We apologize for the confusion this oversight created.

Corder et al state that we "argue against the existence of an ε4 gene-dose effect on the risk of becoming affected [with AD]." Our study on rate of decline in patients with AD did not address the issue of risk of AD associated with ApoE genotype. We did, however, describe the characteristics of the sample. We noted a trend for an inverted gene-dose effect of ε4 on age of symptom onset and, as stated in the discussion section of our article, this trend remained even after excluding subjects with symptom onset before age 60 years. We do not debate the existence of a gene-dose effect on the risk of becoming affected with AD. Other studies have also failed to find the expected difference in age of onset in relation to ApoE genotype (eg, Corder et al[2]), and the letter of Corder et al offers a clear explanation of the possible reasons. However, the most effective investigation of this issue, as also noted by Corder and colleagues, would be through population-based, prospective studies, some of which are currently in progress.

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