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ASSOCIATION OF APOLIPOPROTEIN E ALLELE $\epsilon 4$ WITH LATE-ONSET FAMILIAL AND SPORADIC ALZHEIMER'S DISEASE

A.M. Saunders, PhD; W.J. Strittmatter, MD; D. Schmechel, MD; P.H. St. George-Hyslop, MD; M.A. Pericak-Vance, PhD; S.H. Joo, BS; B.L. Rosi, BA; J.F. Gusella, PhD; D.R. Crapper-MacLachlan, MD; M.J. Alberts, MD; C. Hulette, MD; B. Crain, MD; D. Goldgaber, PhD; and A.D. Roses, MD

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Apolipoprotein E, type $\epsilon 4$ allele (APOE $\epsilon 4$), is associated with late-onset familial Alzheimer's disease (AD). There is high avidity and specific binding of amyloid β -peptide with the protein ApoE. To test the hypothesis that late-onset familial AD may represent the clustering of sporadic AD in families large enough to be studied, we extended the analyses of APOE alleles to several series of sporadic AD patients. APOE $\epsilon 4$ is significantly associated with a series of probable sporadic AD patients (0.36 ± 0.042 , AD, versus 0.16 ± 0.027 , controls [allele frequency estimate $\pm$ standard error], $p = 0.00031$). Spouse controls did not differ from CEPH grandparent controls from the Centre d'Etude du Polymorphisme Humain (CEPH) or from literature controls. A large combined series of autopsy-documented sporadic AD patients also demonstrated highly significant association with the APOE $\epsilon 4$ allele (0.40 ± 0.026 , $p \leq 0.00001$). These data support the involvement of ApoE $\epsilon 4$ in the pathogenesis of late-onset familial and sporadic AD. ApoE isoforms may play an important role in the metabolism of β -peptide, and APOE $\epsilon 4$ may operate as a susceptibility gene (risk factor) for the clinical expression of AD.

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Comment from David S. Knopman, MD, FAAN, Deputy Editor: Although this was not the very first report of APOE's role in AD, this article has been widely cited. Few realized at the time how much of an impact characterization of APOE would have on AD research.

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Association of apolipoprotein E allele ϵ 4 with late-onset familial and sporadic Alzheimer's disease

A.M. Saunders, W.J. Strittmatter, D. Schmechel, et al.

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