typical AD groups. Biparietal patients were younger at symptom onset (mean±SD age, 56.1±4.1 vs 65.6±6.9 years; $P<.001$), scored higher on the Mini-Mental State Examination (mean±SD score, 23.1±2.8 vs 19.2±4.3; $P=.01$) and were less likely to be *APOE* ε4–positive (2/10 vs 25/29, $P<.001$).

Comment. Possessing an *APOE* ε4 allele is the most important genetic risk factor yet identified for sporadic AD[3] and also significantly lowers onset age. It is therefore striking that despite their young age at onset, only 2 of our 10 biparietal patients were ε4-positive. While we believe that a lack of association between biparietal AD (or posterior cortical atrophy AD) and *APOE* ε4 genotype has not previously been reported, this observation is supported by supplementary online data from 1 study where only 1 of 6 patients with posterior cortical atrophy (mean age at onset, 58.5 years) with pathologically confirmed AD possessed an ε4 allele.[5]

We suggest that in biparietal AD, at least in part mediated by lack of *APOE* ε4, the pathological process is directed away from medial temporal structures and toward the parietal lobes. In support of this, decreased hippocampal pathologic abnormality has been reported in posterior cortical atrophy compared with typical AD[5] and increased hippocampal atrophy in AD has been shown to be related to *APOE* ε4 dose.[6] Other, as yet undetermined factors are likely to be responsible for early initiation of the pathological cascade in this distinctive phenotypic variant. This finding, if replicated in larger studies, may have implications for our understanding of the pathogenesis of AD and factors influencing the regional predilection of this and other neurodegenerative diseases. It may be important to consider biparietal and other AD variants[1,2] separately in studies seeking genetic associations in AD.

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Analysis of the *LRRK2* G2019S Mutation in Alzheimer Disease

Mutations in the leucine-rich repeat kinase 2 (*LRRK2*) gene result in typical late-onset Parkinson disease (PD).[1,2] Yet the neuropathological heterogeneity observed in such patients (eg, nigral degeneration alone or in combination with tau pathology, diffuse Lewy bodies, brainstem Lewy bodies, or anterior horn cell loss) suggests that *LRRK2* might be involved in the pathogenesis of several neurodegenerative diseases.[1,2] The potential role of *LRRK2* in Alzheimer disease (AD) is of particular interest because the gene resides within a region on chromosome 12 previously linked to late-onset AD.[3] The aim of this study was to screen a large sample of patients with AD for the presence of the *LRRK2* mutation most common in PD (G2019S).[4]

Methods. We studied 754 subjects who met the NINCDS-ADRDA criteria (National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association) for probable or definite AD. These individuals were participants in the National Cell Repository for Alzheimer's Disease at Indiana University, Indianapolis, or in ongoing studies at the Oregon Health and Science University Layton Aging and Alzheimer's Disease Center, Portland, and University of Washington Alzheimer's Disease Research Center, Seattle. All subjects (or their representatives) provided written informed consent according to procedures approved by the institutional review board at each participating site.

Standard methods were used to extract DNA, and genotyping was performed by TaqMan assay on an ABI PRISM 7900HT Sequence Detection system (Applied Biosystems, Foster City, Calif). The DNA from subjects known to be heterozygous for G2019S was included in all assays as a control. Power calculations were performed using Power and Precision software (Biostat, Englewood, NJ).

Results. The demographic and clinical characteristics of the study group are presented in the **Table**. Histopathologic data sufficient for a diagnosis of definite AD were available for 47.1% of the subjects. The mean±SD age at onset was 67.5±10.2 years (range, 30-95 years). Approximately two thirds of the subjects had a family history of dementia (in at least 1 first-degree relative) and 96% were Caucasian.

We did not detect the G2019S mutation in any of the 754 subjects genotyped. Our analysis of 1508 chromo-

Table. Characteristics of Subjects With Alzheimer Disease by Site

Site	Subjects, No.	Age at Onset, Mean ± SD, y*	Men, No. (%)	Autopsy Confirmed, No. (%)	Family History of Dementia, No. (%)†
OHSU LAADC	200	68.1 ± 9.9	103 (51.5)	72 (36.0)	102 (51.0)
NCRAD	305	67.8 ± 10.4	105 (34.4)	203 (66.6)	296 (97.0)
UW ADRC	249	66.8 ± 10.1	125 (50.2)	80 (32.1)	96 (38.6)
Total	754	67.5 ± 10.2	333 (44.2)	355 (47.1)	494 (65.5)

Abbreviations: OHSU LAADC, Oregon Health and Science University Layton Aging and Alzheimer's Disease Center, Portland; NCRAD, National Cell Repository for Alzheimer's Disease at Indiana University, Indianapolis; UW ADRC, University of Washington Alzheimer's Disease Research Center, Seattle.
*Age at onset was not known for 6 subjects.
†Defined as having 1 or more first-degree relatives with dementia.

somes provided greater than 95% power ($\alpha = .05$) to detect G2019 in the sample, assuming a frequency greater than or equal to 0.25% for the mutation in patients with AD in the population.

Comment. Our data suggest that G2019S, which occurs at a frequency of approximately 1% in sporadic[5] and 3% in familial[4,5] PD, is not a common cause of AD. We had adequate power to detect G2019S in our sample, which predominantly comprised cases with a family history of dementia, even if the true frequency of the mutation in AD was nearly 10-fold less than that in PD. Our findings are consistent with recent studies[6,7] and argue that the concomitant AD pathology observed in some mutation-positive patients[1] might simply be a chance occurrence rather than a direct result of dysfunction of the *LRRK2*-encoded product (dardarin) itself.

This study did not assess the frequency of less common PD-related *LRRK2* mutations in AD nor did it address the existence of pathogenic mutations specific to AD. Furthermore, the role of *LRRK2* in determining susceptibility to disorders other than AD and PD is not yet clear. Comprehensive studies of the gene in large samples of patients with other parkinsonian disorders, motor neuron disease, and non-AD dementing illnesses will be necessary to determine whether *LRRK2* truly represents a molecular link between neurodegenerative diseases.

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