MOLECULAR CHARACTERIZATION OF THE APP GENE IN ITALIAN PATIENTS WITH FAMILIAL ALZHEIMER DISEASE

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Introduction: Notably, the clinical presentation of familial forms of AD (FAD) is more complex, and mutations of APP gene have also been described in these patients. Only about 26 different missense mutations, located in exons 16 and 17 of APP, have been reported.

Aims: To better assess the genetic contribution of APP to FAD, we performed a systematic mutation analysis of this gene in a series of Italian patients with FAD.

Methods: Ninety-seven patients (age, 66.48 ± 10.1 years; mean ± SD) with FAD were recruited at the Institute of Neurology, University "Magna Graecia" in Catanzaro, and subsequently screened for mutations at the Institute of Neurological Sciences, National Research Council, in Cosenza, Italy. The exonic regions of APP (exons 16 and 17) gene were amplified and a mutational screening was done by DHPLC and direct sequencing.

Results: Within our FAD, a non-synonymous change in exon 16, previously described in a Japanese pedigree, was detected (D678N) in a proband with cognitive decline having had commenced at 58 years of age. We found five affected subjects of the same family, who showed cognitive disorders with the age at onset ranging from 50 to 65 years.

Conclusion: In this study, we found a D678N mutation in a patient showing a inheritance pattern consistent with EO-autosomal dominant transmission. Our data confirmed that APP is actually an EO-AD gene, in which onset occurs primarily prior to 65 years of age and often much younger; and for a given mutation, onset ages are tightly clustered.