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Neurodegenerative diseases: complexity of clinical phenotypes in genetic models of alzheimer's disease and frontotemporal dementia

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Background

Neurodegenerative diseases are a wide and complex group of disorders, age – associated, chronic and progressive whith unknown, and probably different, aetiologies. The complexity of the phenotype is probably due to the expression of a selective vulnerability of the different neuronal population and to the different pathogenetic mechanisms. This aetiopathogenetic complexity has been approached through the study of simple models constituted by the large Calabrian families in which Alzheimer's disease (AD) segregates associated to the Presenilin 1 (PS1) Met 146Leu mutation [1] and Frontotemporal dementia (FTD) is caused by the Progranulin (GRN) c1145insA mutation [2].

To investigate the phenotypic variability at onset in patients belonging to the two families for which all data (demographic, clinical and genetic) were available.

Materials and methods

The clinical presentations were studied in 50 out of 148 familial AD (FAD) patients (age at onset = 4 0.0±4.8; 38% women, 18 alive) and in 9 out of 34 patients (age at onset 65.1±17.1) belonging to the FTD family.

Results

Phenotypic variability at onset in AD is broad: four different clinical presentations may be recognized: 1) Amnestic (38%); 2) Disoriented (20%); 3) Dysexecutive (14%); 4) Apathetic (28 %). In the FTD, 89% of patients presented at onset with a memory deficit and 33% were spatially disoriented.

Conclusions

The study conducted on AD and FTD genetic models provides evidence that different genotypes present with a clinical overlapping at onset: symptoms classically associated with FTD are also present in AD and, conversely, FTD patients who are carriers of a PGRN mutation always show a memory deficit. Knowledge advancement calls for a steady upgrade and revision of the clinical criteria routinely used in the diagnostic processing.

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References

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