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MEETING ABSTRACT Open Access

Multidimensional evaluation in clinical diagnosis of Alzheimer's disease: genetic risk in Alzheimer's disease and neurodegenerative dementias

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Background

Late onset degenerative dementia is a growing, common and complex disorder in which the aetiological role played by environment and genes has not yet been established. A familial component is frequently ascertained in Alzheimer's disease (AD) (30% of first degree relatives affected) and also in Frontotemporal Dementia (FTD) (40-60%).

Early onset degenerative dementia has sometimes been recognized as caused by autosomal dominant genes, Presenilines (PS1 and PS2) and the Amyloid Precursor Protein (APP) in AD, whereas in Frontotemporal dementia, two major genes (Microtubule Associated Protein tau, MAPT and Progranulin, PGRN) have also been identified.

PS1 and MAPT mutations have been identified also in in very early onset patients (PS1 24 years [1], MAPT 22 years [2]), but also in late onset patients (PS1 78 years [3], MAPT 75 years [4] 87 years [5].

To evaluate whether FAD and PGRN gene mutations account for late onset dementia.

Materials and methods

Late onset familial dementia patients (onset >65 years) were regularly diagnosed in our centre.

Diagnosis of dementia was performed through a detailed clinical assessment. The NINCDS-ADRDA and Lund-Manchester group criteria were used for diagnosis of AD and FTD respectively.

Molecular screening of PS1, PS2, APP and PGRN genes was performed.

Results

A PS2 Ser130Leu [6] and a novel PS2 Val139Met [7] mutations have been found in two late onset AD cases with onset at 83 and 76.

Three more unrelated cases with an APP A713T mutation showed an onset age between 73 and 82 years [8]. A novel PGRN c1145insA has been identified in a FTD patient of 87 years belonging to a pedigree whose age at onset spans from 35 to 87 [5].

Conclusions

Several autosomal dominant genes, either in AD or in FTD show an impact on late onset dementia. Heritability in late onset forms is now more evident, probably due to longer life survival. It is possible that mutation frequency has been underestimated due to the lack of wide genetic epidemiology. Genetic screening of FAD and PGRN genes might be recommended in familial late onset dementia as a part of Multidimensional evaluation.

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