DEMENTIA WITH LEWY BODY: INVESTIGATION OF GENETIC FACTORS IN FOUR FAMILIES

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Introduction: Dementia with Lewy bodies (DLB) has been considered a late onset sporadic disease. More recently a limited number of DLB families have been described, suggesting that genetic factors may contribute to DLB pathogenesis. Moreover, several mutations identified in DLB patients have shown a large genetic heterogeneity and ε4 allele of the apolipoprotein E gene (APOE) and glucocerebrosidase (GBA) heterozygous variants revealed to be risk factors for DLB.

Aims: To investigate the association of leucine-rich repeat kinase 2 (LRRK2) and GBA with DLB in four Portuguese DLB.

Methods: Nine patients representative of four families with the clinical probable diagnosis of DLB (McKeith et al., 2005) were evaluated in the Dementia outpatient clinic of the University Hospitals of Coimbra. The exon 41 of LRRK2 and exons 9 and 10 of GBA genes were PCR amplified followed by direct sequenced on a capillary automated sequencer.

Results: Two families segregate the disease as an autosomal dominant trait, whereas the two remaining families are compatible with a recessive inheritance pattern with mixed phenotype of parkinsonism and dementia. Using direct sequence analysis, we excluded for all participating individuals the most common mutation in LRRK2 gene, G2019S and N370S and L444P mutations in GBA gene.

Conclusions: Familial aggregation in these cases is not explained by mutations in LRRK2 or GBA genes. Therefore, it is crucial to extend these studies to more familial clustering cases to further determine whether these genes have any role in DLB aetiology.