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Genetic screening for GBA mutations in parkinsonian patients from Campania

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Introduction: Mutations of the Glucocerebrosidase (GBA) gene are the most important genetic risk factor yet discovered for Parkinson's disease (PD), found in about 5-10% of Caucasian patients [1]. The most common mutations reported among PD patients are N370S and L444P. Both mutations are associated with a faster disease course and higher frequency of dementia than in the idiopathic form.

Objective: We assessed *GBA* gene variations frequency in a cohort of PD patients from Campania.

Methods: We studied 169 (108 M and 61 F) unrelated PD patients. At the time of screening, mean age ± SD of the patients was 67.7 ±8.9 years, and disease onset was 59.6 ± 10.7 years. GBA activity determination was performed by Dried blood spots (DBSs) on standard filter paper. Whole blood from DBSs was analyzed by fluorometric assay. The individuals with positive metabolic screening underwent genetic confirm by Sanger sequencing.

Results: Nine patients (3 M and 6 F) carried a heterozygous *GBA* mutation, with an overall prevalence of 5.3%. L444P was found in 4 subjects, three of whom presented with early dementia. We compared the whole sample of idiopathic PD(iPD) patients with the mutation carriers. We did not find any significant difference about age at exam, age at onset, subtype (tremor-dominant orakinetic-rigid), familial history for PD, presence of apathy, depression, hallucinations, self-reported olfaction, sleep and autonomic disorders, motor fluctuations, and dyskinesias. However, dementia and anxiety disorder were more significantly frequent among the carriers than iPD ($p=0.014$ and $p=0.039$, respectively).

Conclusions: Our results confirm that *GBA* mutations are common among PD patients. Furthermore, as previously described [1-2], the prevalence of cognitive impairment and anxiety resulted significantly higher among the carriers than iPD. We also confirmed that L444P represents the mutation most often associated with early onset of dementia.

References

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