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Non-motor symptoms assessment in Parkinson's disease patients carrying GBA gene mutations

Sandra Perillo[1], G.R. Palmieri[1], C. Pane[1], F.M. Di Canio[1], C.D.P. Dello Iacovo[1], S. Petrucci[2,3], E.M. Valente[4,5], F. Saccà[1], G. De Michele[1], G. De Michele[1], A. De Rosa[1]

[1]Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[2]Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy
[3]Department of Clinical and Molecular Medicine, S. Andrea University Hospital, Rome, Italy
[4]IRCCS Mondino Foundation, Pavia, Italy
[5]Department of Molecular Medicine, University of Pavia, Pavia, Italy

Introduction: Glucocerebrosidase (GBA) mutations are the most common genetic risk factor of Parkinson's disease (PD), present in about 5-10% of Caucasian patients.

Objective: We aimed to assess GBA mutations prevalence in a case series of PD patients from Campania (Southern Italy). We also attempted to characterize GBA-related PD in comparison to idiopathic PD (iPD), by assessing motor (MS) and non-motor symptoms (NMSS) through standardized scales.

Methods: We enrolled 207 (126 M and 81 F) unrelated PD patients. GCase activity was measured with fluorometric assay in 149 patients. Next Generation Sequencing was used to detect GBA mutations. MS were assessed in GBA carriers and iPD matched controls with Unified Parkinson's Disease Rating Scale (UPDRS)-section III, Freezing of Gait Questionnaire, and Wearing off questionnaire. NMSS were evaluated by Mini-Mental State Examination, SCOPA-AUT Questionnaire, Apathy Evaluation Scale, Non-Motor Symptoms Scale, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's disease, Beck Depression Inventory, Epworth Sleepiness Scale, Restless Legs Syndrom Rating Scale, Parkinson Psychosis Rating Scale.

Results: Fourteen patients (5 M and 9 F) carried a heterozygous GBA mutation (overall prevalence of 6.7%). L444P mutation was found in four subjects, three of whom had early dementia. Any significant differences were found in the presence and severity of apathy, depression, psychosis, self-reported olfaction, sleep, and autonomic disorders between 11 GBA-PD patients and 11 iPD controls. However, familial history for PD, dementia, dyskinesias, and higher UPDRS-III scores were more common in GBA carriers than iPD patients ($p=0.035$, $p=0.035$, $p=0.033$, and $p=0.035$, respectively).

Conclusions: Our results confirm that GBA gene mutations are common among PD patients and L444P mutation is associated with early-onset dementia. As previously described, the prevalence of cognitive impairment and familial history for PD is significantly higher in GBA carriers. Furthermore, GBA-PD patients had a more severe disease course and more dyskinesias than iPD controls. These findings suggest that GBA mutation carriers may have a more severe disease course.