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Longitudinal multicentric study on the impact of GBA variants on the clinical outcome of Parkinson's Disease patients with deep brain stimulation

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Introduction: GBA mutations are a well-known genetic risk factor for PD. We investigated the impact of GBA variants on the long-term outcome of deep brain stimulation (DBS) in a large cohort of Italian PD subjects who underwent DBS-surgery.

Methods: We retrospectively analysed clinical data from a multicentric Italian cohort of DBS-PD patients upon stratification for the presence/absence of GBA variants. Motor and non-motor features were recorded before surgery and after 1, 3 and 5 years.

Results: We recruited 294 DBS-PD patients, of whom 63 (22%) carried GBA variants (severe=29, mild=14, risk=12, unknown=8). In GBA-PD, mean age at onset was 44.1 ±1.1yrs, mean disease duration 9.0±0.5 yrs and age at DBS implant was 53.5±1.1. At pre-DBS evaluation, GBA-PD had earlier age at onset and shorter disease duration than non-mutated PD (NM-PD) but showed similar clinical features except dyskinesias (more prevalent in GBA-PD). At 3 to 5 years post-DBS, both groups showed motor improvement with satisfactory control of fluctuations and dyskinesias; all non-motor symptoms were also comparable except for cognitive scores, which worsened significantly faster in GBA-PD than NM-PD, already at 3 years from DBS. However a diagnosis of dementia were performed only in 25.81 % of GBA-PD after 5 years of follow-up. Analysis on GBA-PD stratified by mutation type are ongoing.

Conclusions: This is the first report addressing the impact of GBA variants on DBS clinical outcomes in a large well-characterized Italian PD cohort with a relatively long follow-up. Our data, although preliminary, suggest that GBA-PD patients benefit from DBS as much as NM-PD, as the frequency of motor complications is similar between the two groups. Cognitive performance, although progressively worsening in both groups, shows a more rapid deterioration in GBA-PD, however only a small percentage of them developed dementia after 5 years from DBS surgery.