P121

Impact of GBA variants on deep brain stimulation clinical outcome in Parkinson's disease patients

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Background: Deep brain stimulation (DBS) has become a routine treatment option for improving quality of life in Parkinson disease (PD). Although longstanding DBS in PD patients can impair cognition with a negative impact on verbal fluency, the occurrence of dementia is not higher compared to general PD population. GBA heterozygous variants are a well-known risk factor for PD and result in earlier disease onset and more malignant phenotype compared to non-carriers. Yet, how this genetic factor could influence the long-term outcome of DBS remains unclear.

Aims: To evaluate the prognostic role of GBA variants on the clinical outcome of DBS in PD patients.

Methods: We retrospectively analysed genetic and clinical data from our cohort of DBS-PD patients upon stratification for the presence/absence of *GBA*variants. All patients underwent pre-DBS evaluation and had a regular follow-up visit after surgery. Clinical assessment included: MDS-UPDRS in both ON and OFF state, cognitive evaluation and levodopa equivalent daily dose (LEDD).

Results: 84 DBS-PD patients were genotyped, of whom 16 carried GBA variants (9F/7M, disease duration 13,9±5.8 yrs; target DBS: 13 STN/3 GPI). Among GBA-PD, 7 had severe variants, 4 mild variants, 5 risk alleles. After surgery, all GBA-PD showed persistent motor improvement, with satisfactory control of motor fluctuations and dyskinesias. LEDD was also significantly reduced by 30%. Four patients developed postural instability; five patients, all with disease duration >10 years manifested dementia within 5 years from surgery.

Conclusion: This study addresses the impact of GBA variants on the clinical outcome of DBS. Although preliminary, our data suggest that GBA mutations do not seem to negatively influence the motor and non-motor outcome of DBS patients. Future studies on larger PD cohort are needed to clarify the impact of GBA mutations on DBS outcome, as this could open new perspectives for customized DBS implantation protocols and stimulation paradigms.