P122

Long-term subthalamic deep brain stimulation outcome in a Parkinson's disease patient associated with PRKN gene deletion

Anna Covolo[1,2], G. Imbalzano[1,2], C.A. Artusi[1,2], C. Ledda[1,2], M.M. Tangari[1,2], E. Montanaro[2], M.G. Rizzone[1,2], M. Bozzali[1,2,3], M. Zibetti[1,2], L. Lopiano[1,2], A. Romagnolo[1,2]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Torino, Turin, Italy [2]SC Neurologia 2U, AOU Città della Salute e della Scienza, Turin, Italy[3]Department of Neuroscience, Brighton & Sussex Medical School, University of Sussex, Brighton, East Sussex, U.K.

Introduction: Parkinson's disease (PD) patients with Parkin gene (*PRKN*) mutations show good response to subthalamic deep brain stimulation (STN-DBS)[1]. However, different *PRKN* mutations could lead to heterogeneous long-term outcomes. To date, no STN-DBS follow-up longer than 5 years are reported.

Objectives: To report the 15-year follow-up after STN-DBS of a PD patient presenting a compound heterozygous deletion of exons 3 and 11 of the *PRKN* gene.

Case report: In 1994, a 39 years-old male was diagnosed with PD after the onset of resting tremor; levodopa was started, and during the following ten years he reported good motor symptoms control, with only mild modification of levodopa intake and pramipexole introduction. In 2005 he developed disabling motor fluctuations and dyskinesia; entacapone was started, but immediately interrupted for visual hallucinations. The genetic diagnosis was made in 2006. In 2007 he underwent bilateral STN-DBS, with a marked improvement of motor symptoms and fluctuations. After six years, he reported mild motor fluctuations, improved after stimulation and treatment modifications. After ten years he showed diphasic dyskinesias, feet dystonia, postural instability, and gambling (disappeared after pramipexole discontinuation). Since 2018 he showed a single-domain MCI. In April 2022 (15 years after STN-DBS) motor symptoms/fluctuations are still well controlled with levodopa 1200 mg/day, and stimulation set at 3.3 V, 60 usec, 130 Hz bilaterally. MDS-UPDRS-I-II-III-IV scores are 21-18-30-8, respectively. He reports mild dysphagia, orthostatic hypotension; MoCA score is 26/30.

Conclusion: More than 40% of *PRKN* mutations result from structural variants,[2] with the deletion of exon 3 being the most frequent mutation. We described for the first time the STN-DBS outcomes of a compound heterozygous deletion of exons 3 and 11[3], along with the longest follow-up after STN-DBS in a *PRKN*-associated PD. We confirmed good long-lasting outcomes, with marked improvement in motor symptoms/fluctuations and no significant worsening of cognitive profile.

References:

[1] C. A. Artusi et al. Association of Subthalamic Deep Brain Stimulation With Motor, Functional, and Pharmacologic Outcomes in Patients With Monogenic Parkinson Disease: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2019 Feb 1;2(2):e187800.

[2] M. Kasten et al. Genotype-Phenotype Relations for the Parkinson's Disease Genes Parkin, PINK1, DJ1: MDSGene Systematic Review. *Mov Disord* 2018 May;33(5):730-741.

[3] S. Y. Kim et al. Phase analysis identifies compound heterozygous deletions of the PARK2 gene in patients with early-onset Parkinson disease. *Clin Genet* 2012 Jul;82(1):77-82.