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TRR 295 ReTune

Long-term outcomes on pallidal neurostimulation for dystonia: A controlled, prospective 10-year follow-up.

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Initiated between 07/2002 & 05/2004, the present study is the extension of a prospective multicenter trial involving 40 patients with isolated generalized or segmental dystonia and chronic bipallidal neurostimulation. 31 patients completed the 10-year follow-up (FU). Participants were assessed using the Burke-Fahn-Marsden dystonia rating scale (BFMDRS) for motor and disability scores, along with evaluations for depression, anxiety, and cognitive functions through the Beck Depression Inventory, Beck Anxiety Inventory, and Mattis Dementia Rating Scale.

The intention-to-treat analysis (incl. all 40 patients) showed significant group mean reductions in BFMDRS motor scores at 6 months, 5 and 10 years ($p<0.0001$) compared to baseline. In the per protocol cohort (n=31), a significant dystonia score reduction ($p<0.0001$) was sustained at FU, with a mean decrease of 25.3 points (SE±5.2) corresponding to 56% improvement after 10 years. There was no difference in the relative motor improvement between patients with generalized (n=24) and segmental (n=16) dystonia after 6 months, 5 or 10 years, although absolute score values were higher in generalized dystonia versus segmental dystonia because of more body regions affected. Improvements were also sustained in disability, mood, and anxiety scores, while cognitive functions remained stable. While 27 patients were classified as responders (≥ 25% improvement) with a mean improvement of 68.1±20.3% (range 31.5-98.0%) compared to baseline. Thirteen patients were classified as non-responders with a mean motor change of 8.5±27.3% at last available follow-up. Among these, three were primary non-responders (PNR) at 6 months, and another 10 patients became secondary non-responders (SNR) before the subsequent follow-ups at 1 year (n=1), 2 (n=1), five (n=3) and 10 years (n=5). A retrospective chart and video review revealed one or several potential causes of therapeutic non-response in 12/13 non-responders. Three patients had clinical signs not-compatible with isolated dystonia at baseline and must be considered selection failures. In further ten patients lead misplacement has to be assumed as reason for non-response.

Over the past two decades, significant advances have transformed the landscape of dystonia treatment, offering unprecedented opportunities that were not available when this study commenced. The key takeaways from this study are twofold: firstly, the remarkable safety and enduring clinical benefits of GPI-DBS in patients who were otherwise refractory to treatment even a decade post-surgery. Secondly, the urgent need for comprehensive (para-) clinical profiling both before surgery and throughout the postoperative treatment phase in order to reduce the high rate of therapeutic failures. Advances in imaging and gene-based diagnostics, in particular, offer promising avenues for more precise electrode placement, refined DBS programming, and improved identification of non-responders, enhancing the personalized effects of DBS. The study underscores the importance of ongoing advancements in diagnostics, such as genetic testing and enhancements in neurostimulation technology, which could potentially decrease the rates of non-response in the future. The study also points towards the need for better profiling and treatment planning to improve outcomes further and reduce therapeutic failures.

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