Pallidal Deep Brain Stimulation for dystonia

- Pallidal Deep Brain Stimulation Enhances Habitual Behavior in a Neuro-Computational Basal Ganglia Model During a Reward Reversal Learning Task
- Bi-pallidal deep brain stimulation as an effective therapy in atypical two-stage evolution adult-onset KMT2B-related dystonia
- Sweet spot for resting-state functional MRI effect of deep brain stimulation in dystonia lies in the lower pallidal area
- Long-Term Outcomes on Pallidal Neurostimulation for Dystonia: A Controlled, Prospective 10-Year Follow-Up
- Spiking Patterns in the Globus Pallidus Highlight Convergent Neural Dynamics across Diverse Genetic Dystonia Syndromes
- Prognostic factors for long-term outcomes of bilateral pallidal deep brain stimulation in the treatment of Meige syndrome
- Pallidal Spike-Train Variability and Randomness Are the Most Important Signatures to Classify Parkinson's Disease and Cervical Dystonia
- Network-wide effects of pallidal deep brain stimulation normalised abnormal cerebellar cortical activity in the dystonic animal model

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Pallidal Deep Brain Stimulation (GPi DBS) is one of the targets for dystonia treatment

Indications

The response is better for primary dystonias, e.g. tardive dystonias than for secondary dystonias such as postanoxic, postencephalitic, perinatal, and poststroke dystonias (other targets need to be assessed).

For primary dystonias, the globus pallidus internus (GPi) is the most common primary target

Good results have also been reported with STN DBS. Dyskinetic cerebral palsy in children may also be treated with pallidal stimulation.

Pallidal Deep Brain Stimulation is the primary surgical treatment. [1].

Deep brain stimulation (DBS) of the globus pallidus internus (GPi) has been established as an effective and safe dystonia treatment.

Pallidal Deep Brain Stimulation for the Treatment of Levodopa Responsive Juvenile Dystonia and Parkinsonism Secondary to SPG11 Mutation [2].

Response is better for primary dystonias, e.g. tardive dystonias than for secondary dystonias such as postanoxic, postencephalitic, perinatal, and poststroke dystonia [3]. (other targets need to be assessed). For primary dystonias, the globus pallidus internus (GPi) is the most common primary target.

Pallidal DBS can yield marked and long-lasting improvement in patients with Dystonia who underwent both pallidotomy and selective peripheral denervation earlier. Therefore, such patients, in general, should not be excluded from DBS [4].

Good results have also been reported with STN DBS. Dyskinetic cerebral palsy in children may also be treated with pallidal stimulation [5].

Stereotactic thalamotomy or dentatotomy: Useful for unilateral dystonia, but cannot be used for bilateral dystonia as bilateral lesions would be required which jeopardizes speech, cognition... Effective only for dystonia distal to shoulders or hips, and should not be used if the condition is rapidly progressive

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Evidence from case series or uncontrolled study suggests that it may lead in some patients to specific parkinsonian symptoms such as freezing of gait, micrographia, and bradykinesia.

Mahlknecht et al. investigated parkinsonian signs using the Movement Disorder Society Unified Parkinson's disease Rating Scale by means of observer-blinded video ratings in a group of 29 patients treated with pallidal Deep Brain Stimulation and a non-surgical control group of 22 patients, both with predominant cervical dystonia. Additional assessments included MRI-based models of volume of neural tissue activated to investigate areas of stimulation related to dystonic symptom control and those likely to induce parkinsonian signs as well as an EMG analysis to investigate functional vicinity of stimulation fields to the pyramidal tract. Compared with controls, stimulated patients had significantly higher motor scores (median, 25th-75th percentile: 14.0, 8.0-19.5 versus 3.0, 2.0-8.0; $P < 0.0001$), as well as bradykinesia (8.0, 6.0-14.0 versus 2.0, 0.0-3.0; $P < 0.0001$) and axial motor subscores (2.0, 1.0-4.0 versus 0.0, 0.0-1.0; $P = 0.0002$), while rigidity and tremor subscores were not different between groups. Parkinsonian signs were partially reversible upon switching stimulation off for a median of 90 min in a subset of 19 patients tolerating this condition. Furthermore, the stimulation group reported more features of freezing of gait on a questionnaire basis. Quality of life was better in stimulated patients compared with control patients, but parkinsonian signs were negatively associated with quality of life. In the descriptive imaging analysis maximum efficacy for dystonia improvement projected to the posteroventrolateral internal pallidum with overlapping clusters driving severity of bradykinesia and axial motor symptoms. The severities of parkinsonian signs were not correlated with functional vicinity to the pyramidal tract as assessed by EMG. In conclusion, parkinsonian signs, particularly bradykinesia and axial motor signs, due to pallidal stimulation in dystonic patients are frequent and negatively impact on motor functioning and quality of life. Therefore, patients with pallidal stimulation should be monitored closely for such signs both in clinical routine and future clinical trials. Spread of current outside the internal pallidum is an unlikely explanation for this phenomenon, which seems to be caused by stimulation of neural elements within the stimulation target volume [6].

Case series

Thirty-nine patients with dystonia treated with bilateral Pallidal Deep Brain Stimulation in Sweden at 2 Swedish DBS centers from 2005 to 2015 were included. Different pulse widths (PW) paradigms were used at the 2 centers, 60-90 µs (short PWs) and 450 µs (long PW), respectively. The frequency of IPG replacements, pulse effective voltage (PEV), IPG model, pre-/postoperative imaging, and clinical

outcome based on the clinical global impression (CGI) scale were collected from the medical charts and compared between the 2 groups.

Results: The average IPG longevity was extended for the short PWs (1,129 ± 50 days) compared to the long PW (925 ± 32 days; $\chi 2 = 12.31$, $p = 0.0005$, log-rank test). IPG longevity correlated inversely with PEV (Pearson's $r = -0.667$, $p < 0.0001$). IPG longevities did not differ between Kinetra® and Activa® PC in the short ($p = 0.319$) or long PW group ($p = 0.858$). Electrode distances to the central sensorimotor region of the GPi did not differ between the short or long PW groups ($p = 0.595$). Pre- and postoperative CGI did not differ between groups.

Short PWs were associated with decreased energy consumption and increased IPG longevity. These effects were not dependent on the IPG model or the anatomic location of the electrodes. PWs did not correlate with symptom severities or clinical outcomes. The results suggest that the use of short PWs might be more energy efficient and could therefore be preferred initially when programming patients with GPi DBS for dystonia [7].

Retrospective chart review of 22 consecutive PGD patients, ≤21 years of age treated by one DBS team over an 8-year period. The Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) was used to evaluate symptom severity and functional disability, pre- and post-operatively. Adverse events and medication changes were also noted.

Results: The median follow-up was 2 years (range, 1-8 years). All 22 patients reached 1-year follow-up; 14 reached 2 years, and 11 reached 3 years. The BFMDRS motor subscores were improved 84%, 93%, and 94% (median) at these time points. These motor responses were matched by equivalent improvements in function, and the response to DBS resulted in significant reductions in oral and intrathecal medication requirements after 12 and 24 months of stimulation. There were no hemorrhages or neurological complications related to surgery and no adverse effects from stimulation. Significant hardware-related complications were noted, in particular, infection (14%), which delayed clinical improvement.

Pallidal DBS is a safe and effective treatment for PGD in patients <21 years of age. The improvement appears durable. Improvement in device design should reduce hardware-related complications over time [8].

Indications

Deep Brain Stimulation (DBS) has been used as a therapeutic intervention for various movement disorders, including dystonia.

The Globus Pallidus Internus (GPi) is a structure within the brain that plays a role in regulating movement. In Pallidal Deep Brain Stimulation for dystonia, electrodes are implanted into the GPi, and these electrodes deliver electrical impulses to modulate abnormal neural activity, helping to alleviate symptoms. The exact mechanism of action is not entirely understood, but it is believed that DBS can influence and normalize dysfunctional neural circuits.

Indications for Pallidal Deep Brain Stimulation in dystonia may include:

Primary Dystonia: GPi DBS is often considered for individuals with primary dystonia, where dystonia is

the primary neurological condition without any other major underlying neurological disorder.

Generalized or Segmental Dystonia: Individuals with generalized or segmental dystonia, affecting multiple body regions, may be considered for GPi DBS.

Medication-Resistant Dystonia: GPi DBS is typically considered when dystonia symptoms do not respond adequately to medications or when the side effects of medications are significant.

Dystonia Associated with Genetic or Metabolic Disorders: In some cases, dystonia may be associated with specific genetic or metabolic disorders. GPi DBS may be considered in these cases after careful evaluation.

Dystonia with Functional Impairment: GPi DBS may be recommended for individuals whose dystonia significantly impairs their daily functioning and quality of life.

It's important to note that the decision to undergo Pallidal Deep Brain Stimulation is highly individualized. A thorough evaluation by a multidisciplinary team, including neurologists, neurosurgeons, and other specialists, is necessary to assess the appropriateness of DBS for a particular patient.

As with any surgical intervention, there are risks and potential side effects associated with Pallidal Deep Brain Stimulation, and patients should discuss these with their healthcare team to make informed decisions about their treatment options. The field of DBS for movement disorders, including dystonia, continues to evolve, and ongoing research contributes to refining the criteria for patient selection and optimizing the effectiveness of the procedur

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