



## OPEN ACCESS

### EDITED BY

Aasef Shaikh,  
 Case Western Reserve University,  
 United States

### \*CORRESPONDENCE

Sara Radmard,  
 ✉ sara.radmard@emory.edu

RECEIVED 28 June 2026

ACCEPTED 01 October 2026

PUBLISHED 19 October 2026

### CITATION

Je G, Miocinovic S, Huang V, Aia PG,  
 Tripathi R, Bueteftsch CM, Esper CD,  
 Higginbotham LA, Triche S, Factor SA and  
 Radmard S (2026) The long-term efficacy  
 of globus pallidus deep brain stimulation  
 in tardive dystonia and dyskinesia.

*Dystonia* 5:17246.

doi: 10.3389/dyst.2026.17246

### COPYRIGHT

© 2026 Je, Miocinovic, Huang, Aia,  
 Tripathi, Bueteftsch, Esper, Higginbotham,  
 Triche, Factor and Radmard. This is an  
 open-access article distributed under the  
 terms of the [Creative Commons  
 Attribution License \(CC BY\)](#). The use,  
 distribution or reproduction in other  
 forums is permitted, provided the original  
 author(s) and the copyright owner(s) are  
 credited and that the original publication  
 in this journal is cited, in accordance with  
 accepted academic practice. No use,  
 distribution or reproduction is permitted  
 which does not comply with these terms.

# The long-term efficacy of globus pallidus deep brain stimulation in tardive dystonia and dyskinesia

Goun Je<sup>1</sup>, Svjetlana Miocinovic<sup>1,2</sup>, Vicki Huang<sup>3</sup>, Pratibha G. Aia<sup>1</sup>,  
 Richa Tripathi<sup>1</sup>, Cathrin M. Bueteftsch<sup>1</sup>, Christine D. Esper<sup>1</sup>,  
 Lenora A. Higginbotham<sup>1</sup>, Shirley Triche<sup>1</sup>, Stewart A. Factor<sup>1</sup> and  
 Sara Radmard<sup>1\*</sup>

<sup>1</sup>Jean and Paul Amos Parkinson's Disease and Movement Disorders Program, Department of Neurology, Emory University School of Medicine, Atlanta, GA, United States, <sup>2</sup>Department of Biomedical Engineering, Georgia Tech, Atlanta, GA, United States, <sup>3</sup>Department of Neurosurgery, Emory University School of Medicine, Atlanta, GA, United States

**Introduction:** Tardive syndromes, including tardive dystonia (TDyst) and tardive dyskinesia (TDysk), are complications of exposure to dopamine receptor blocking agents (DRBAs) and remain common despite the use of second-generation antipsychotics. Approximately one-quarter of patients exposed to DRBAs may develop TDysk. Globus pallidus internus deep brain stimulation (GPI DBS) has emerged as a therapeutic option for medically refractory TDyst and TDysk, although data on long-term outcomes and effective stimulation sites remain limited.

**Methods:** We retrospectively reviewed clinical data for 18 patients with medically refractory TDyst/TDysk, who underwent GPI DBS at a single center. Clinical outcomes were assessed preoperatively and at 11.1 ± 3.2 months, 35.9 ± 5.1 months, and 62.5 ± 7.6 months follow-up using Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) in patients with TDyst, Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) in patients with prominent tardive cervical dystonia, and Abnormal Involuntary Movement Scale (AIMS) in patients with TDysk. Active electrode contact locations and stimulation parameters at the last follow-up were also evaluated.

**Results:** The mean duration of tardive symptoms before surgery was 9.0 ± 7.9 years. BFMDRS motor scores improved significantly after GPI DBS, decreasing from 27.5 ± 8.3 preoperatively to 9.1 ± 7.5, 5.0 ± 5.8, and 4.1 ± 7.6 at follow-up visits, respectively. Axial and extremity BFMDRS subscores showed significant improvement, whereas speech, swallowing and orofacial dystonia subscores showed numerical improvement without reaching statistical significance. TWSTRS and AIMS scores also demonstrated numerical improvement with limited statistical interpretation due to the small number of available scores.

**Conclusion:** GPI DBS resulted in robust and sustained long-term improvement in medically refractory TDyst, with potential benefit in TDysk. These findings support GPI DBS as a safe and effective therapeutic option for selected patients with severe treatment-refractory tardive syndromes. Earlier surgical intervention may be considered to facilitate timely symptomatic relief and durable long-term benefit.

### KEYWORDS

globus pallidus internus, GPI deep brain stimulation, tardive dyskinesia, tardive dystonia, tardive syndromes

## Introduction

Tardive syndromes including tardive dystonia (TDyst) and classical tardive dyskinesia (TDysk) are drug-induced movement disorders that are caused by dopamine receptor blocking agents (DRBAs), including antipsychotic drugs and certain antiemetics [1–4]. TDyst is characterized by sustained or intermittent involuntary posturing and torsional muscle contractions, most commonly involving the craniocervical region, although the trunk and limbs may also be affected [5]. The distribution of TDyst may be focal, segmental, multifocal, or generalized, similar to idiopathic dystonia, and symptoms often begin focally before spreading to additional body regions [4]. In contrast, TDysk is characterized by stereotyped, repetitive, involuntary movements, most commonly involving the oro-bucco-lingual region, followed by the upper limbs and, less commonly, the lower limbs and trunk. Both TDyst and TDysk can cause social distress and, in severe cases, significant physical disability.

One of the largest meta-analyses reported an average prevalence of TDysk of 25.3% among patients receiving DRBAs [6]. First-generation antipsychotics (30.0%) were associated with higher prevalence than second-generation antipsychotics (20.7%). The reported prevalence of TDyst varies widely, ranging from 0.5% to 21.6% [4, 7–9]. Tardive syndromes are generally irreversible once they develop [10]. In 2017, two vesicular monoamine transporter 2 (VMAT2) inhibitors were approved by the U.S. Food and Drug Administration (FDA) for the treatment of tardive dyskinesia and remain the only FDA-approved agents for this indication. Nevertheless, treatment of TDyst and TDysk remains challenging because of incomplete response, medication intolerance, limited access, and cost. Other treatments such as anticholinergics for TDyst, amantadine, benzodiazepines, and botulinum toxin injections with less evidence are often tried with limited effect [11, 12]; further, as TDyst and TDysk commonly co-occur, anticholinergics should be used with caution as this medication class can worsen TDysk. These therapeutic challenges have led to increasing interest in surgical interventions, including deep brain stimulation (DBS). Similar to idiopathic dystonia, the globus pallidus interna (GPi) is the most commonly targeted region, although a few reports have also described efficacy with subthalamic nucleus (STN) DBS [13].

Despite apparent increasing interest in DBS for the treatment of TDyst and TDysk, this therapeutic approach remains less extensively investigated than DBS for other movement disorders, including idiopathic or genetic dystonia. Currently, DBS is considered a Level C recommendation for the treatment of TDyst and TDysk [12]. To date, the available studies are largely small retrospective case series and cohort studies reporting improvements in disease-specific rating scales, including Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) and Abnormal Involuntary Movement Scale (AIMS), ranging from 30% to 100%, with most studies reporting improvements greater than 60% [14–17]. The only randomized, sham-controlled DBS trial in TDyst and TDysk demonstrated a reduction in hyperkinetic movements but did not reach statistical significance, possibly because of limited statistical power and the relatively short follow-up duration of 3–6 months [18].

Data on long-term clinical outcomes and effective stimulation sites remain limited, although such information is important for guiding patient selection, surgical targeting, and postoperative programming. In this study, we retrospectively evaluated long-term clinical outcomes

and effective stimulation sites in patients with medically refractory TDyst and TDysk treated with GPi DBS at a single center.

## Materials and methods

### Participants

Eighteen adult patients (9 male, 9 female) with a diagnosis of TDyst and/or TDysk who underwent GPi DBS surgery from 2008 to 2025 at Emory University Hospital, Atlanta, GA, USA were included in this retrospective review. Demographic information, medical history, clinical rating scales, and DBS programming parameters were obtained from patient electronic medical records. The Institutional Review Board of Emory University approved this study, and written consent was waived.

### Surgical procedure and DBS programming

Seventeen patients underwent bilateral GPi DBS surgery, and one patient underwent unilateral right-sided GPi DBS surgery. Quadripolar DBS electrodes were implanted using microelectrode recordings or intraoperative MRI guidance [19, 20]. Implanted DBS systems included commercially available DBS devices from Medtronic, Boston Scientific, and Abbott. Postoperative DBS programming was initiated approximately 4 weeks after surgery, and stimulation settings were adjusted over subsequent programming sessions as part of routine clinical care to optimize clinical benefit.

### Clinical assessment

Comprehensive clinical evaluations were performed preoperatively and at postoperative follow-up visits approximately 1-year (4–16 months; short-term follow-up), 3-year (27–45 months; mid-term follow-up), and 5-year (59–79 months; long-term follow-up) after surgery. Each patient underwent pre-operative psychiatric clearance prior to DBS surgery. Two patients underwent genetic testing of which one positive result revealed a mutation consistent with ataxia telangiectasia. The clinical outcomes were measured using BFMDRS in patients with TDyst, Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) in patients with prominent tardive cervical dystonia, and AIMS in patients with TDysk. Outcome measures were analyzed using available data at each time point.

### DBS lead coordinates

Postoperative DBS lead localization was performed using the Image Fusion and Lead Localization modules in Brainlab Origin Data Management software (Brainlab AG, Munich, Germany). Postoperative CT images were rigidly co-registered to preoperative MRI. DBS leads were localized based on the hyperdense postoperative CT artifact. The automated lead detection in the Lead Localization module was used to identify the lead trajectory, followed by manual refinement using inline and orthogonal image views to optimize lead position. The anterior commissure (AC), posterior commissure (PC), and mid-commissural point (MCP) were manually identified on preoperative T1-weighted MRI to

TABLE 1 Patient demographics.

| Patients | Sex (M/F) | Age at symptom onset (yr) | Tardive diagnosis | Distribution     | Symptom duration prior to DBS (yr) | Psychiatric diagnosis           | Causative medications         | Treatments before DBS                                                                                   | Follow-up at final assessment (months) |
|----------|-----------|---------------------------|-------------------|------------------|------------------------------------|---------------------------------|-------------------------------|---------------------------------------------------------------------------------------------------------|----------------------------------------|
| 1        | F         | 62                        | TDyst             | Focal (left leg) | 3                                  | -                               | Promethazine                  | Benzodiazepine, botulinum toxin                                                                         | 79                                     |
| 2        | F         | 39                        | TDyst             | Generalized      | 27                                 | Depression, anxiety             | Perphenazine                  | Clozapine, tetrabenazine, botulinum toxin                                                               | 27                                     |
| 3        | M         | 18                        | TDyst             | Generalized      | 13                                 | Bipolar disorder                | Olanzapine, quetiapine        | Benzodiazepine, botulinum toxin                                                                         | 38                                     |
| 4        | F         | 36                        | TDyst             | Generalized      | 3                                  | Schizophrenia, bipolar disorder | Lurasidone                    | Botulinum toxin                                                                                         | 43                                     |
| 5        | M         | 60                        | TDyst             | Generalized      | 3                                  | PTSD                            | Aripiprazole                  | Trihexyphenidyl, baclofen, benzodiazepine, botulinum toxin                                              | 53                                     |
| 6        | M         | 27                        | TDyst             | Generalized      | 3                                  | Depression, anxiety             | Prochlorperazine              | Trihexyphenidyl, carbidopa/levodopa, benzodiazepine, botulinum toxin                                    | 60                                     |
| 7        | F         | 47                        | TDyst             | Generalized      | 4                                  | -                               | Metoclopramide                | Propranolol, trihexyphenidyl                                                                            | 60                                     |
| 8        | F         | 35                        | TDyst             | Generalized      | 28                                 | Depression                      | Haloperidol, prochlorperazine | Trihexyphenidyl, botulinum toxin                                                                        | 62                                     |
| 9        | M         | 17                        | TDyst             | Generalized      | 10                                 | Bipolar disorder                | Risperidone, olanzapine       | Botulinum toxin                                                                                         | 66                                     |
| 10       | F         | -                         | TDysk             | -                | -                                  | Depression, anxiety             | Metoclopramide                | Valbenazine                                                                                             | 9                                      |
| 11       | M         | 59                        | TDysk             | -                | 8                                  | Bipolar disorder                | Quetiapine                    | Amantadine, tetrabenazine, deutetabenazine                                                              | 31                                     |
| 12       | M         | 62                        | TDyst, TDysk      | Generalized      | 8                                  | Bipolar disorder                | Aripiprazole                  | Valbenazine                                                                                             | 4                                      |
| 13       | F         | 39                        | TDyst, TDysk      | Generalized      | 6                                  | Depression                      | Aripiprazole                  | Propranolol, trihexyphenidyl, amantadine, benzodiazepine, deutetabenazine, valbenazine, botulinum toxin | 10                                     |
| 14       | F         | 53                        | TDyst, TDysk      | Generalized      | 17                                 | Depression, PTSD                | Prochlorperazine, quetiapine  | Amantadine, deutetabenazine, valbenazine, botulinum toxin                                               | 13                                     |
| 15       | M         | 36                        | TDyst, TDysk      | Generalized      | 6                                  | Autism spectrum disorder        | Risperidone                   | Propranolol, benzodiazepine, tetrabenazine, deutetabenazine, botulinum toxin                            | 35                                     |

(Continued)

TABLE 1 Continued

| Patients     | Sex (M/F) | Age at symptom onset (yr) | Tardive diagnosis | Distribution | Symptom duration prior to DBS (yr) | Psychiatric diagnosis    | Causative medications | Treatments before DBS                                    | Follow-up at final assessment (months) |
|--------------|-----------|---------------------------|-------------------|--------------|------------------------------------|--------------------------|-----------------------|----------------------------------------------------------|----------------------------------------|
| 16           | M         | 20                        | TDyst, TDysk      | Generalized  | 8                                  | Schizoaffective disorder | Ziprasidone           | Amantadine, benzodiazepine, deutetabenazine, valbenazine | 38                                     |
| 17           | F         | 51                        | TDyst, TDysk      | Generalized  | 5                                  | Bipolar disorder         | Thorazine, stelazine  | Benzodiazepine, trihexyphenidyl, clozapine               | 59                                     |
| 18           | M         | 52                        | TDyst, TDysk      | Generalized  | 5                                  | Depression               | Risperidone           | Amantadine, benzodiazepine                               | 61                                     |
| Average ± SD |           | 42.0 ± 15.4               |                   |              | 9.0 ± 7.9                          |                          |                       |                                                          | 41.6 ± 22.5                            |

Tardive dystonia (TDyst), tardive dyskinesia (TDysk). Post-traumatic stress disorder (PTSD).

establish the coordinate system. AC-PC based coordinates (relative to MCP) for all 4 contact levels were recorded using the center point of each contact.

## Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics, version 31.0.0.0 (IBM Corp., Armonk, NY, USA). Results are reported as mean ± standard deviation. Linear mixed model was utilized for BFMDRS and TWSTRS analysis due to missing patient data. AIMS evaluation was completed with analysis of variance (ANOVA). Post hoc pairwise comparisons were performed between preoperative scores and each follow-up time point with Bonferroni-adjustment for multiple comparisons. Statistical significance was set as Bonferroni-adjusted  $p < 0.05$ .

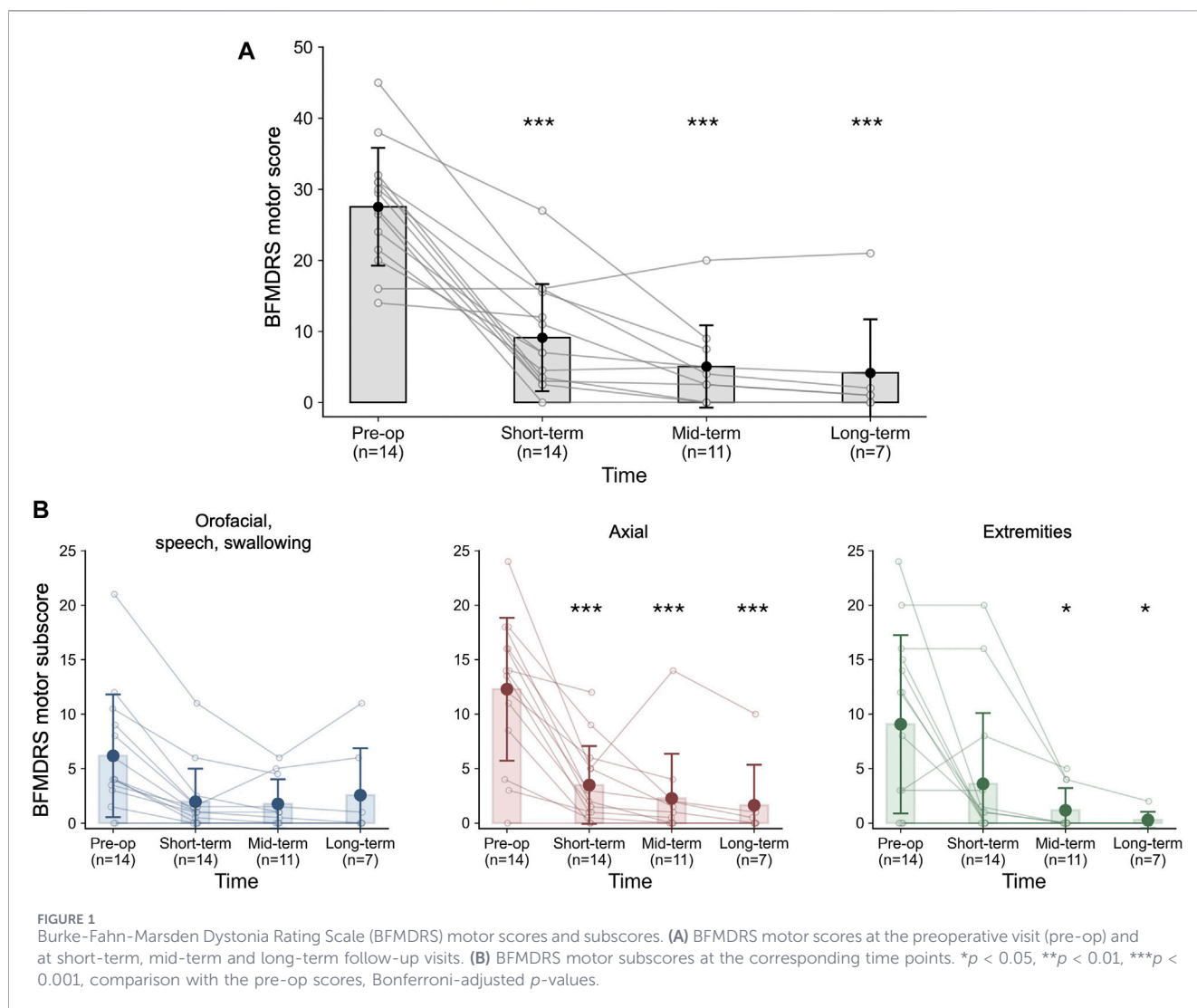
## Results

### Patient demographics

Detailed demographic and clinical information of the 18 patients with TDyst, TDysk, or both are shown in Table 1. Of these, nine patients were diagnosed with TDyst, two with TDysk, and seven with both. The mean age at onset of tardive symptoms was  $42.0 \pm 15.4$  years, and the mean duration of tardive symptoms prior to surgery was  $9.0 \pm 7.9$  years. Sixteen patients had psychiatric diagnoses. Fifteen patients had exposure to DRBAs for psychiatric indications, whereas three patients had exposure to DRBAs for nonpsychiatric indications, including promethazine in one patient and metoclopramide in two patients. Seventeen patients underwent bilateral GPi DBS surgery, and one patient had unilateral GPi DBS. One patient developed skin erosion and infection at the burr hole site that resolved without DBS lead explantation. Only one patient had both pre-operative and post-operative psychiatric scales for depression and anxiety. However, no patient had exacerbations of underlying psychiatric disorders based on chart review.

### Motor outcomes

The mean preoperative BFMDRS motor score was  $27.5 \pm 8.3$ . Compared with preoperative scores, BFMDRS motor scores improved significantly after GPi DBS (Figure 1A);  $9.1 \pm 7.5$  at short-term follow-up ( $11.1 \pm 3.2$  months;  $p < 0.001$ ),  $5.0 \pm 5.8$  at mid-term follow-up ( $35.9 \pm 5.1$  months;  $p < 0.001$ ), and  $4.1 \pm 7.6$  at long-term follow-up ( $62.5 \pm 7.6$  months;  $p < 0.001$ ). The corresponding mean percentage improvements from preoperative score were  $64.1 \pm 30.8\%$ ,  $83.8 \pm 14.1\%$ , and  $88.0 \pm 16.8\%$ , respectively. Three patients achieved complete resolution of motor symptoms, corresponding to 100% improvement, including one patient at short-term follow-up and two patients at mid-term follow-up; this response was maintained through their last follow-up visits. Improvement varied across BFMDRS motor subscores (Figure 1B). Axial dystonia, including neck and trunk involvement, showed significant improvement at all follow-up time points. The mean axial subscore improved from  $12.3 \pm 6.6$  preoperatively to  $3.5 \pm 3.6$  at short-term follow-up ( $p < 0.001$ ),  $2.3 \pm 4.1$  at mid-term follow-up ( $p < 0.001$ ), and  $1.6 \pm$



3.7 at long-term follow-up ( $p < 0.001$ ). Extremity dystonia also improved, with significant reductions at mid-term and long-term follow-up. The mean extremity subscore decreased from  $9.1 \pm 8.2$  preoperatively to  $3.6 \pm 6.5$  at short-term follow-up,  $1.2 \pm 2.0$  at mid-term follow-up ( $p = 0.01$ ), and  $0.3 \pm 0.8$  at long-term follow-up ( $p = 0.02$ ). Speech, swallowing and orofacial dystonia subscore showed numerical improvement but did not reach statistical significance, decreasing from  $6.2 \pm 5.6$  preoperatively to  $2.0 \pm 3.0$  at short-term follow-up,  $1.8 \pm 2.3$  at mid-term follow-up, and  $2.6 \pm 4.3$  at long-term follow-up.

A subset of patients with TDyst had available TWSTRS scores (Figure 2A). Although the change did not reach statistical significance, TWSTRS scores showed a sustained numerical improvement across all follow-up time points. The mean TWSTRS scores decreased from  $50.3 \pm 13.6$  preoperatively to  $25.6 \pm 12.8$  at short-term follow-up,  $20.4 \pm 19.6$  at mid-term follow-up, and  $21.7 \pm 31.5$  at long-term follow-up. TWSTRS subscores are shown in Figure 2B, with the most apparent improvements observed in the severity and disability subscores.

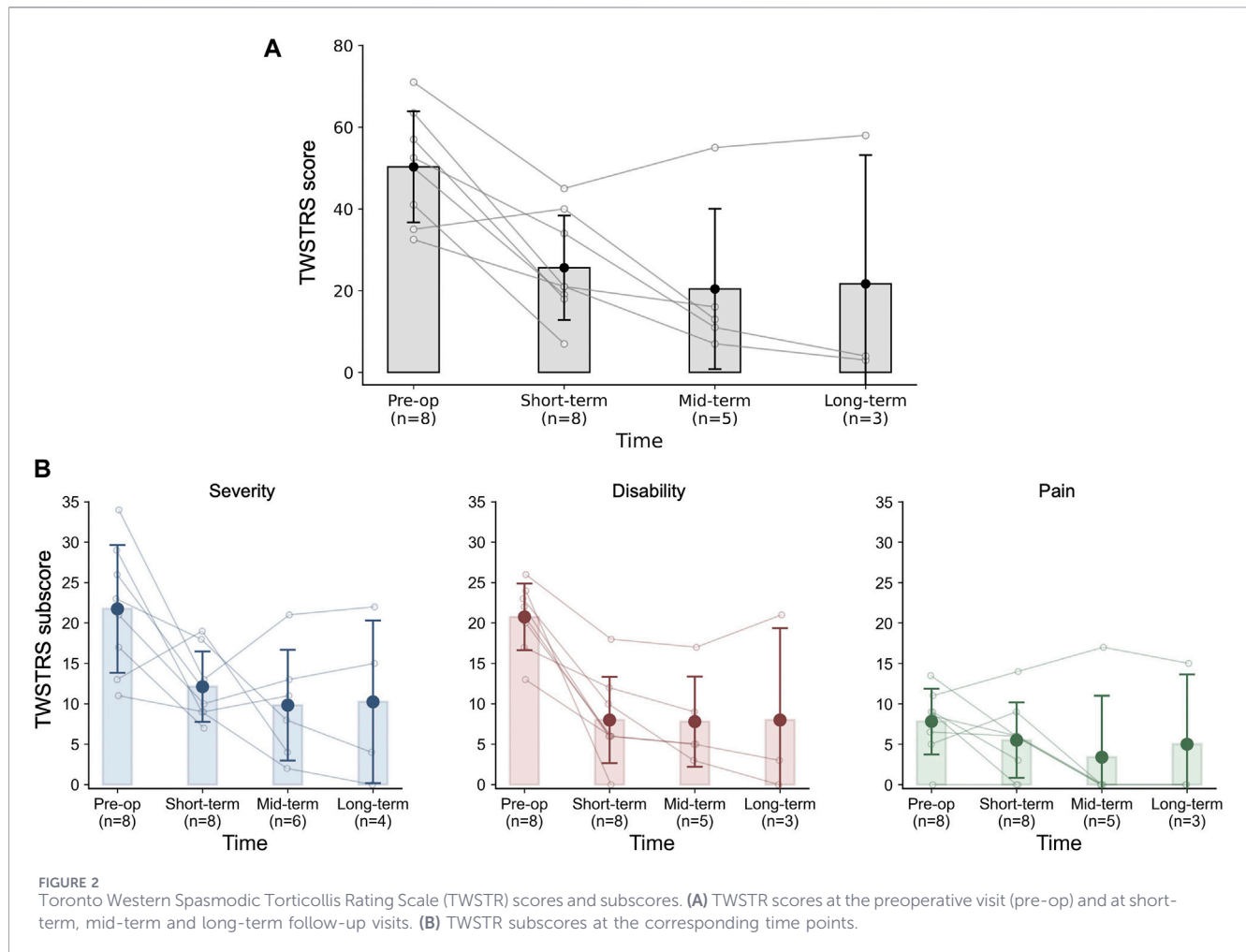
Among the nine patients with TDysk, four patients had available AIMS scores (Figure 3A). Although statistical significance was not reached, AIMS scores showed numerical improvement over time,

decreasing from  $15.8 \pm 5.4$  preoperatively to  $10.0 \pm 2.4$  at short-term follow-up, and  $5.0$  at mid-term follow-up. AIMS subscores are shown in Figure 3B, with the most apparent improvement observed in the orofacial and global judgement subscores.

## DBS contact locations and programming parameters

The coordinates of the active electrode contacts at the last follow-up visits were  $20.6 \pm 1.9$  mm lateral,  $2.5 \pm 1.7$  mm anterior, and  $1.1 \pm 1.3$  mm inferior relative to MCP. The stimulation parameters at the same timepoint are listed in Table 2. The mean stimulation amplitude was  $3.8 \pm 1.0$  mA, pulse width was  $95.1 \pm 36.1$   $\mu$ s, and frequency was  $119.4 \pm 38.5$  Hz.

Over time, stimulation parameters were adjusted as clinically indicated, whereas electrode configuration remained unchanged from short-term to last follow-up in all but one patient. In that patient, the configuration was changed from monopolar to double-monopolar stimulation to improve symptom control. From one to three years, the mean change in amplitude was  $0.7 \pm 0.7$  mA; from three to five years, the mean change amplitude was  $0.5 \pm 0.5$  mA. The



mean change in pulse width between time intervals was less than 6.5  $\mu$ s. Likewise, the mean change in frequency between time intervals was less than 10 Hz. No persistent stimulation-related adverse effects were reported.

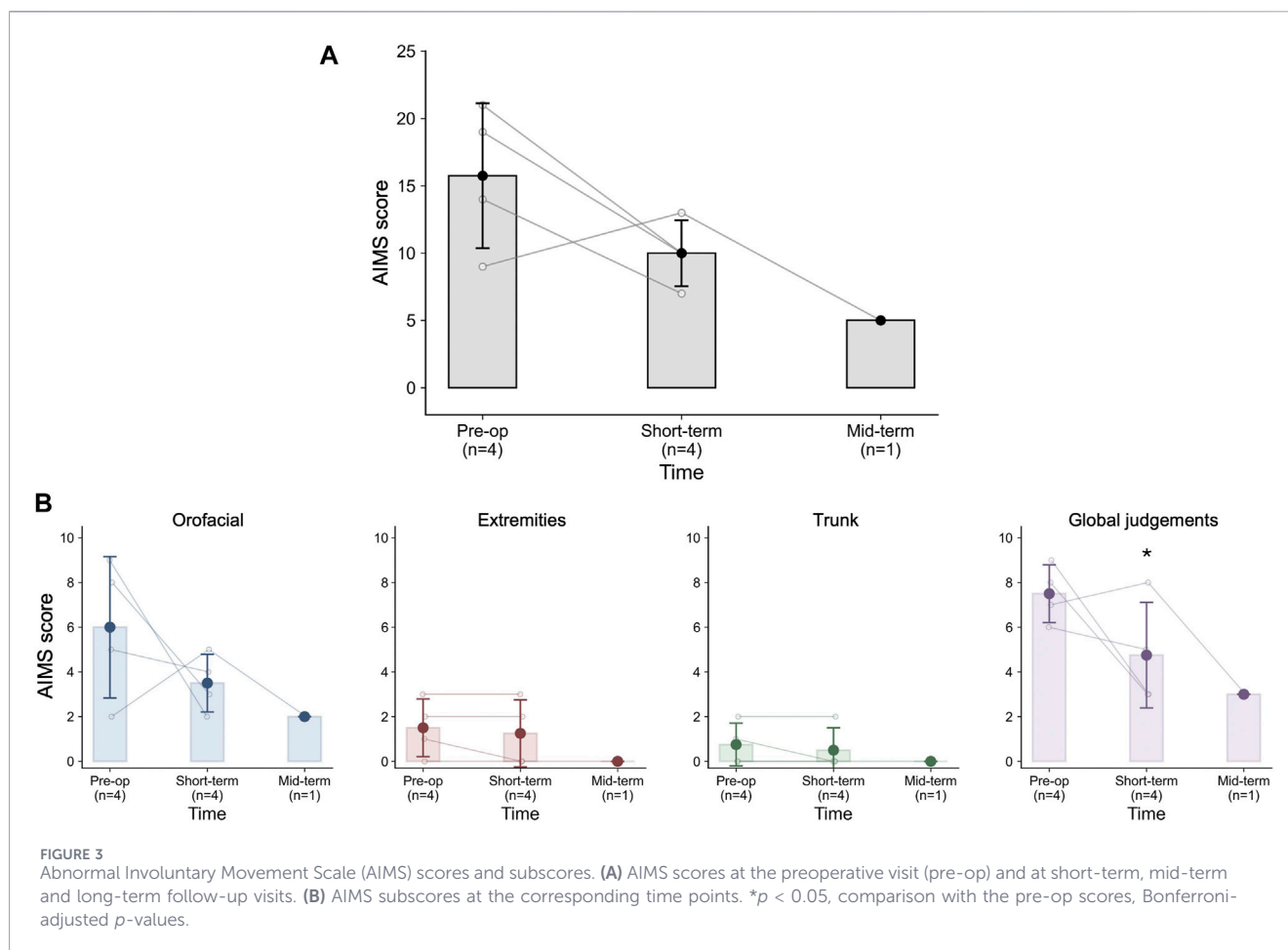
## Discussion

In this retrospective study, we evaluated the long-term clinical outcomes of GPi DBS in patients with medically refractory TDyst and TDysk. Our results demonstrate that GPi DBS provided robust and sustained improvement in TDyst, with significant reductions in BFMDRS motor scores at short-term, mid-term and long-term follow-up. The greatest improvement was observed within the first year after surgery and was maintained through 3- and 5-year follow-up among patients with available data. These findings are consistent with prior reports supporting GPi DBS as an effective treatment for refractory TDyst [14, 15, 17]. Notably, our cohort showed continued improvement from short-term to long-term follow-up, and 3 patients achieved complete resolution of motor symptoms that was maintained until their last follow-up visits. This pattern may reflect the delayed and cumulative therapeutic response to GPi stimulation previously described in dystonia [21]. Together, these findings support the long-term durability of GPi DBS benefit

in TDyst and suggest that clinically meaningful improvement can be sustained for several years after implantation.

Although BFMDRS motor scores improved significantly at all follow-up time points, the magnitude of improvement varied across BFMDRS motor subscores. Axial dystonia improved significantly at all follow-up time points, whereas extremity dystonia showed significant improvement at mid-term and long-term follow-up. In contrast, speech, swallowing and orofacial dystonia subscores showed numerical improvement but did not reach statistical significance. This lack of statistical significance should be interpreted cautiously, as the study was likely underpowered to detect changes within individual subscores, particularly given missing follow-up data and smaller sample sizes at later time points. Previous studies have reported that DBS efficacy may vary by dystonia distribution [22–25], which could potentially explain the differences observed across subscores in our cohort. However, craniofacial and cervical dystonia phenotypes, including Meige syndrome and cervical dystonia, have been shown to respond to GPi DBS in large study populations [26–29], suggesting that nonsignificant findings in selected subscores in this cohort may reflect limited statistical power rather than absence of clinical benefit.

Similarly, although BFMDRS axial subscores improved significantly at all follow-up time points, TWSTR scores, which were available only in a subset of patients with prominent cervical



TDyst, showed sustained numerical improvement without reaching statistical significance. This discrepancy may reflect several factors, including the smaller number of patients with available TWSTRS data, missing follow-up data, and differences in scale sensitivity.

AIMS scores in patients with TDysk also showed numerical improvement over time, but the small number of patients with available preoperative and postoperative AIMS scores limits interpretation and precludes definitive conclusions regarding DBS effectiveness for TDysk in this cohort. Nevertheless, the observed downward trend is consistent with prior studies reporting improvement in TDysk after GPi DBS [16, 18, 30]. Larger prospective studies are needed to better define DBS outcomes in patients with TDysk.

The coordinates of the active electrode contacts in our cohort were consistent with the GPi target region used for dystonia and aligned with previously reported GPi stimulation sites in tardive syndromes [24, 31–33]. In addition, stimulation parameters in this cohort were generally consistent with commonly used GPi DBS settings for dystonia [34].

One patient developed skin erosion and infection at the burr hole site, which did not require DBS lead explantation. Otherwise, no persistent stimulation-related adverse effects were reported. This low complication rate supports the overall safety of GPi DBS in appropriately selected patients with medically refractory TDyst and TDysk. The mean duration of tardive symptoms before surgery was 9 years, with a range of 3–28 years. Given the robust and sustained improvement and low

surgical complication rate observed in this cohort, earlier consideration of DBS may be reasonable in selected patients with severe, disabling, and treatment-refractory tardive syndromes.

Our study has several limitations. First, the retrospective design limited the uniformity of clinical assessments, and outcome assessments were not blinded, which may have introduced observer bias. Second, follow-up data were incomplete, particularly at later time points, which may have affected estimates of long-term treatment effect. Third, different rating scales were used depending on clinical phenotype, and not all patients had all outcome measures available. Fourth, the small number of patients with available TWSTRS and AIMS data limited statistical power for subgroup analyses.

Despite these limitations, this study adds to the growing evidence supporting GPi DBS as a safe and effective treatment for medically refractory TDyst, with sustained long-term benefit. The findings also suggest potential benefit for TDysk, although larger studies are needed to confirm this effect. Large, multicenter prospective studies with standardized outcome measures and long-term follow-up are needed to further define the efficacy, durability, and optimal stimulation parameters of DBS for tardive syndromes.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

TABLE 2 DBS stimulation parameters.

| Patients | Left GPi DBS  |                |                  |                | Right GPi DBS |                |                  |                |
|----------|---------------|----------------|------------------|----------------|---------------|----------------|------------------|----------------|
|          | Configuration | Amplitude (mA) | Pulse width (μs) | Frequency (Hz) | Configuration | Amplitude (mA) | Pulse width (μs) | Frequency (Hz) |
| 1        | -             | -              | -                | -              | M             | 5.2            | 120              | 130            |
| 2        | M             | 1.4            | 90               | 130            | M             | 1.6            | 90               | 130            |
| 3        | M             | 3.2            | 60               | 130            | M             | 3.3            | 60               | 130            |
| 4        | M             | 3.8            | 60               | 130            | DM            | 4.5            | 60               | 130            |
| 5        | M             | 4.7            | 120              | 120            | B             | 3.4            | 120              | 120            |
| 6        | DM            | 5.6            | 60               | 100            | M             | 5.8            | 90               | 100            |
| 7        | M             | 3.8            | 180              | 60             | B             | 3.1            | 210              | 70             |
| 8        | B             | 3.0            | 100              | 60             | B             | 3.3            | 100              | 60             |
| 9        | DM            | 5.1            | 120              | 60             | DM            | 4.7            | 150              | 60             |
| 10       | M             | 3.7            | 90               | 185            | M             | 3.3            | 90               | 185            |
| 11       | B             | 4.5            | 90               | 204            | B             | 4.5            | 80               | 204            |
| 12       | M             | 3.7            | 60               | 130            | M             | 3.7            | 60               | 130            |
| 13       | M             | 3.5            | 60               | 125            | M             | 2.5            | 60               | 125            |
| 14       | M             | 4.3            | 70               | 125            | M             | 4.1            | 70               | 125            |
| 15       | M             | 4.7            | 90               | 130            | M             | 4.7            | 90               | 130            |
| 16       | M             | 3.1            | 60               | 130            | M             | 4.4            | 150              | 130            |
| 17       | M             | 3.9            | 120              | 70             | M             | 4.0            | 90               | 70             |
| 18       | M             | 2.5            | 120              | 130            | B             | 3.3            | 90               | 130            |

Monopolar configuration (M), double monopolar configuration (DM), and bipolar configuration (B). For constant-voltage DBS, system, current was calculated using the programmed voltage and therapeutic impedance.

Ethics statement

The studies involving humans were approved by Emory University Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants’ legal guardians/next of kin because the study presents no more than minimal risk of harm as the participants underwent intervention outside of the research evaluation.

Author contributions

GJ, SM, SF, and SR participated in the design, interpretation of the studies and analysis of the data and review of the manuscript; GJ, SM, PA, RT, CB, CE, LH, and ST conducted patient evaluations. SR completed statistical analysis. GJ completed figure and table creation. GJ and SR wrote the manuscript, and SM and SF were involved in the editing process. All authors contributed to the article and approved the submitted version.

Funding

The author(s) declared that financial support was not received for this work and/or its publication.

Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The reviewer SP declared a shared affiliation with the author(s) SF at the time of review.

Generative AI statement

The author(s) declared that generative AI was not used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

## References

- Soares-Weiser K, Fernandez HH. Tardive dyskinesia. *Semin Neurol* (2007) 27(2): 159–69. doi: 10.1055/s-2007-971169
- Aquino CC, Lang AE. Tardive dyskinesia syndromes: current concepts. *Parkinsonism Relat Disord* (2014) 20(Suppl. 1):S113–7. doi: 10.1016/S1353-8020(13)70028-2
- Burke RE, Fahn S, Jankovic J, Marsden CD, Lang AE, Gollomp S, et al. Tardive dystonia: late-onset and persistent dystonia caused by antipsychotic drugs. *Neurology* (1982) 32(12):1335–46. doi: 10.1212/wnl.32.12.1335
- Kiriakakis V, Bhatia KP, Quinn NP, Marsden CD. The natural history of tardive dystonia. A long-term follow-up study of 107 cases. *Brain* (1998) 121(11):2053–66. doi: 10.1093/brain/121.11.2053
- Albanese A, Bhatia K, Bressman SB, Delong MR, Fahn S, Fung VS, et al. Phenomenology and classification of dystonia: a consensus update. *Mov Disord* (2013) 28(7):863–73. doi: 10.1002/mds.25475
- Carbon M, Hsieh CH, Kane JM, Correll CU. Tardive dyskinesia prevalence in the period of second-generation antipsychotic use: a meta-analysis. *J Clin Psychiatry* (2017) 78(3):e264–e78. doi: 10.4088/JCP.16r10832
- Raja M. Tardive dystonia. Prevalence, risk factors, and comparison with tardive dyskinesia in a population of 200 acute psychiatric inpatients. *Eur Arch Psychiatry Clin Neurosci* (1995) 245(3):145–51. doi: 10.1007/BF02193087
- van Harten PN, Matroos GE, Hoek HW, Kahn RS. The prevalence of tardive dystonia, tardive dyskinesia, parkinsonism and akathisia the Curacao extrapyramidal syndromes study: i. *Schizophr Res* (1996) 19(2-3):195–203. doi: 10.1016/0920-9964(95)00096-8
- Testini PFS, Factor SA. Treatment of tardive dystonia: a review. *Dystonia* (2023) 2: 10957. doi: 10.3389/dyst.2023.10957
- Zutshi D, Cloud LJ, Factor SA. Tardive syndromes are rarely reversible after discontinuing dopamine receptor blocking agents: experience from a university-based movement disorder clinic. *Tremor Other Hyperkinet Mov (N Y)* (2014) 4:266. doi: 10.7916/D8MS3R8C
- Bhidayasiri R, Fahn S, Weiner WJ, Gronseth GS, Sullivan KL, Zesiewicz TA, et al. Evidence-based guideline: treatment of tardive syndromes: report of the guideline development subcommittee of the American academy of neurology. *Neurology* (2013) 81(5):463–9. doi: 10.1212/WNL.0b013e31829d86b6
- Bhidayasiri R, Jitkritsakul O, Friedman JH, Fahn S. Updating the recommendations for treatment of tardive syndromes: a systematic review of new evidence and practical treatment algorithm. *J Neurol Sci* (2018) 389:67–75. doi: 10.1016/j.jns.2018.02.010
- Deng ZD, Li DY, Zhang CC, Pan YX, Zhang J, Jin H, et al. Long-term follow-up of bilateral subthalamic deep brain stimulation for refractory tardive dystonia. *Parkinsonism Relat Disord* (2017) 41:58–65. doi: 10.1016/j.parkreldis.2017.05.010
- Mentzel CL, Tenback DE, Tijssen MA, Visser-Vandewalle VE, van Harten PN. Efficacy and safety of deep brain stimulation in patients with medication-induced tardive dyskinesia and/or dystonia: a systematic review. *J Clin Psychiatry* (2012) 73(11): 1434–8. doi: 10.4088/JCP.12r07643
- Morigaki R, Mure H, Kaji R, Nagahiro S, Goto S. Therapeutic perspective on tardive syndrome with special reference to deep brain stimulation. *Front Psychiatry* (2016) 7: 207. doi: 10.3389/fpsy.2016.00207
- Poulet-Courtemanche H, Rouaud T, Thobois S, Nguyen JM, Brefel-Courbon C, Chereau I, et al. Long-term efficacy and tolerability of bilateral pallidal stimulation to treat tardive dyskinesia. *Neurology* (2016) 86(7):651–9. doi: 10.1212/WNL.0000000000002370
- Macerollo A, Deuschl G. Deep brain stimulation for tardive syndromes: systematic review and meta-analysis. *J Neurol Sci* (2018) 389:55–60. doi: 10.1016/j.jns.2018.02.013
- Gruber D, Sudmeyer M, Deuschl G, Falk D, Krauss JK, Mueller J, et al. Neurostimulation in tardive dystonia/dyskinesia: a delayed start, sham stimulation-controlled randomized trial. *Brain Stimul* (2018) 11(6):1368–77. doi: 10.1016/j.brs.2018.08.006
- Sharma VD, Bezchlibnyk YB, Isbaine F, Naik KB, Cheng J, Gale JT, et al. Clinical outcomes of pallidal deep brain stimulation for dystonia implanted using intraoperative MRI. *J Neurosurg* (2020) 133(5):1582–94. doi: 10.3171/2019.6.JNS19548
- Bezchlibnyk YB, Sharma VD, Naik KB, Isbaine F, Gale JT, Cheng J, et al. Clinical outcomes of globus pallidus deep brain stimulation for Parkinson disease: a comparison of intraoperative MRI- and MER-guided lead placement. *J Neurosurg* (2021) 134(3): 1072–82. doi: 10.3171/2019.12.JNS192010
- Ruge D, Tisch S, Hariz MI, Zrinzo L, Bhatia KP, Quinn NP, et al. Deep brain stimulation effects in dystonia: time course of electrophysiological changes in early treatment. *Mov Disord* (2011) 26(10):1913–21. doi: 10.1002/mds.23731
- Cersosimo MG, Raina GB, Piedimonte F, Antico J, Graff P, Micheli FE. Pallidal surgery for the treatment of primary generalized dystonia: long-term follow-up. *Clin Neurol Neurosurg* (2008) 110(2):145–50. doi: 10.1016/j.clineuro.2007.10.003
- Isaias IU, Alterman RL, Tagliati M. Deep brain stimulation for primary generalized dystonia: long-term outcomes. *Arch Neurol* (2009) 66(4):465–70. doi: 10.1001/archneurol.2009.20
- Shaikh AG, Mewes K, DeLong MR, Gross RE, Triche SD, Jinnah HA, et al. Temporal profile of improvement of tardive dystonia after globus pallidus deep brain stimulation. *Parkinsonism Relat Disord* (2015) 21(2):116–9. doi: 10.1016/j.parkreldis.2014.11.013
- Yarlagadda Sp M, Rajagopalan S, Jinnah HA, Factor SA, Miocinovic S, Scorr LM, et al. Pallidal deep brain stimulation in dystonia: investigating differential response by dystonia distribution. *Tremor and Other Hyperkinetic Movements* (2026) 16:42. doi: 10.5334/tohm.1175
- Wang X, Zhang Z, Mao Z, Yu X. Deep brain stimulation for Meige syndrome: a meta-analysis with individual patient data. *J Neurol* (2019) 266(11):2646–56. doi: 10.1007/s00415-019-09462-2
- Tsuboi T, Wong JK, Almeida L, Hess CW, Wagle Shukla A, Foote KD, et al. A pooled meta-analysis of GPi and STN deep brain stimulation outcomes for cervical dystonia. *J Neurol* (2020) 267(5):1278–90. doi: 10.1007/s00415-020-09703-9
- Jacksch C, Zeuner KE, Helmers AK, Witt K, Deuschl G, Paschen S. Long-term efficacy with deep brain stimulation of the globus pallidus internus in cervical dystonia: a retrospective monocentric study. *Neurol Res Pract* (2022) 4(1):48. doi: 10.1186/s42466-022-00214-8
- Wu G, Weng JC, Liu M, Shao X, Yu Y, Tian H. Globus pallidus internus versus subthalamic nucleus deep brain stimulation for Meige syndrome: a retrospective study on short- and long-term efficacy. *J Neurosurg* (2026) 144(5):1084–94. doi: 10.3171/2025.9.JNS251420
- Damier P, Thobois S, Witjas T, Cuny E, Derost P, Raoul S, et al. Bilateral deep brain stimulation of the globus pallidus to treat tardive dyskinesia. *Arch Gen Psychiatry* (2007) 64(2):170–6. doi: 10.1001/archpsyc.64.2.170
- Starr PA, Turner RS, Rau G, Lindsey N, Heath S, Volz M, et al. Microelectrode-guided implantation of deep brain stimulators into the globus pallidus internus for dystonia: techniques, electrode locations, and outcomes. *J Neurosurg* (2006) 104(4): 488–501. doi: 10.3171/jns.2006.104.4.488
- Tisch S, Zrinzo L, Limousin P, Bhatia KP, Quinn N, Ashkan K, et al. Effect of electrode contact location on clinical efficacy of pallidal deep brain stimulation in primary generalised dystonia. *J Neurol Neurosurg Psychiatry* (2007) 78(12):1314–9. doi: 10.1136/jnnp.2006.109694
- Nonaka T, Horisawa S, Kim K, Murakami M, Nishitani M, Kawamata T, et al. Optimal stimulation sites and long-term efficacy of pallidal deep-brain stimulation for patients with tardive dystonia. *J Mov Disord* (2026) 19(1):49–57. doi: 10.14802/jmd.25164
- Magown P, Andrade RA, Soroceanu A, Kiss ZHT. Deep brain stimulation parameters for dystonia: a systematic review. *Parkinsonism Relat Disord* (2018) 54: 9–16. doi: 10.1016/j.parkreldis.2018.04.017