Location of Active Contacts in Patients with Primary Dystonia Treated with Globus Pallidus Deep Brain Stimulation

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OBJECTIVE: Deep brain stimulation of the globus pallidus internus has been used for the treatment of various forms of dystonia, but the factors influencing postoperative outcomes remain unknown. We compared the location of the contacts being used for stimulation (active contacts) in patients with cervical dystonia, generalized dystonia, and Parkinson's disease and correlated the results with clinical outcome.

METHODS: Postoperative magnetic resonance scans of 13 patients with cervical dystonia, six patients with generalized dystonia, and five patients with Parkinson's disease who underwent globus pallidus internus deep brain stimulation were analyzed. We assessed the location of the active contacts relative to the midcommisural point and in relation to the anteroposterior and mediolateral boundaries of the pallidum. Postoperative outcome was measured with the Toronto Western Spasmodic Torticollis Rating Scale (for cervical dystonia) and the Burke-Fahn-Marsden Dystonia Rating Scale (for generalized dystonia) during the last follow-up.

RESULTS: We found that the location of the active contacts relative to the midcommisural point and the internal boundaries of the pallidum was similar across the groups. In our series, the contacts used for stimulation were clustered in the posterolateral region of the pallidum. Within that region, we found no correlation between the location of the contacts and postoperative outcome.

CONCLUSION: The location of the active contacts used for globus pallidus internus deep brain stimulation was similar in patients with cervical dystonia, generalized dystonia, and Parkinson's disease.

KEY WORDS: Deep brain stimulation, Dystonia, Electrode, Globus pallidus, Movement disorders

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Deep brain stimulation (DBS) of the globus pallidus internus (GPi) has gained acceptance in recent years as an effective therapy for the treatment of dystonia (2–12, 15–20, 22, 23, 25). With accumulation of experience, some of the factors influencing surgical outcome are now recognized. It seems, for example, that patients with primary forms of dystonia with predominantly phasic movements respond better to the procedure (2, 3, 7, 10, 17, 22, 25).

One aspect that has recently been explored, but not fully characterized, is the relationship between the location of the electrodes and clinical outcome. To date, only two studies have systematically addressed this issue (22, 24). They first examined patients with generalized dystonia and concluded that the active contacts were in the posterolateroventral portion of the GPi (24). A second study concluded that location of the contacts relative to the borders of the GPi had a significantly smaller variance in patients with more than 70% of improvement after GPi DBS, compared with patients who improved by less than 50% (22). In this context, the accuracy of lead placement with respect to the internal boundaries of the pallidum did affect outcome.

Other articles assessing the location of the electrodes in patients with dystonia have only provided coordinates relative to the midcommissural point but did not attempt to correlate these variables to postoperative outcome (2, 25). As a result, questions such as

TABLE 1. Demographics and outcomes in patients with cervical dystonia treated with bilateral GPi stimulation[a]

Patient	Age	Diagnosis	Preop TWSTR	Preop severity TWSTR	Postop TWSTR (%)	Postop severity TWSTR (%)	Follow-up (mo)	Active contact R/L
1	62	Cervical	70.7	29	31.7 (55)	5 (83)	24	1–/5–
2	25	Cervical	36	19	4 (89)	4 (79)	18	1–/5–
3	59	Cervical	45.2	24	6 (87)	6 (75)	18	1–/5–
4	39	Cervical	70.2	26	48.5 (31)	14 (46)	42	2–/5–
5	67	Cervical	45.7	20	12 (74)	9 (55)	60	1–/6–
6	37	Cervical	60.7	22	40 (34)	14 (36)	48	1–/5–
7	51	Cervical	51.7	15	35.5 (31)	12 (20)	12	2–3–/5–6–
8	67	Cervical	61.7	26	31 (50)	19 (27)	12	2–/6–
9	33	Cervical	74.5	21	20 (73)	9 (57)	36	1–/5–
10	63	Segmental[b]	55	17	23 (58)	14 (18)	6	1–/5–
11	62	Cervical	63	27	28.5 (55)	13 (52)	4	1–/5–
12	50	Cervical	22	17	6 (73)	4 (76)	67	2–3–/6–7–
13	55	Cervical	62	26	28.5 (54)	9 (65)	3	1–/5–
Mean ± SD	**51.5 ± 13.9**		**55.3 ± 15.0**	**22.2. ± 4.5**	**24.2 ± 14.0 (58.7 ± 19.6)**	**26.9 ± 19.6 (53.0 ± 22.5)**	**26.9 ± 21.6**	

[a] Preop, preoperative; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale; Postop, postoperative; %, percentage of improvement calculated as (1 − preop scores/postop scores) × 100; R/L, right and left electrodes. Results in bold represent mean ± standard deviation.
[b] Patient with segmental dystonia with a predominant cervical component.

whether different forms of dystonia respond to stimulation in different pallidal targets, or whether the location of the active contacts in patients with dystonia is similar to that previously used to treat patients with Parkinson's disease (PD) remain unanswered.

To further investigate these issues, we assessed the location of the electrodes in our series of patients with primary dystonia who were treated with bilateral GPi DBS. The coordinates of the contacts relative to standard anatomic landmarks, as well as their location within the boundaries of the pallidum, were calculated and compared among groups of patients with cervical dystonia, generalized dystonia, and PD.

PATIENTS AND METHODS

Patients

The following inclusion criteria were used in our study: 1) diagnosis of primary dystonia, 2) age older than 17 years, and 3) no previous intracranial surgical procedures. Nineteen of the 25 (76%) patients with primary dystonia treated with bilateral GPi DBS at the Toronto Western Hospital from October 1996 to August 2006 were included in our study. Five patients with primary generalized dystonia were excluded because they had previous pallidotomies. One patient with *DYT1*-generalized dystonia was excluded because she was 9 years old by the time of surgery. Of the 19 adult patients included, 12 had cervical dystonia, one had segmental dystonia with predominant neck involvement (these two groups were considered together as a primary cervical dystonia group), and six patients had primary generalized dystonia (two were positive and four were negative for the *DYT1* gene). Patients with cervical and generalized dystonia, respectively, were assessed before and after surgery (last follow-up) with the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and the Burke-Fahn-Marsden (BFM) Dystonia Rating Scale, respectively. For patients with generalized dystonia, we considered appendicular scores as the sum of the upper- and lower-extremity BFM scores for each hemibody. Demographics and the average pre- and postoperative TWSTRS and BFM scores are shown in *Tables 1* and 2.

In addition to patients with primary dystonia, a group of five patients with PD treated with unilateral pallidotomies and contralateral GPi DBS was also included in our analysis. We selected these patients on the basis of the availability of their magnetic resonance imaging (MRI) scans as electronic files in our system. The images of other patients with PD treated with bilateral GPi DBS were no longer accessible in electronic format and could not be sent to our imaging workstation. Postoperative improvement after unilateral GPi DBS in the five patients with PD included in our study was 25.5 ± 21.1%, as assessed with the Unified Parkinson Disease Rating Scale.

Programming of Patients with Dystonia

Programming of the stimulators was usually started 3 weeks after surgery. During the first session, each electrode contact was stimulated individually to establish the threshold for side effects (flashes of light with ventral contacts, and muscle contractions and dysarthria with other contacts). Stimulation was then started in a monopolar configuration with the lowest contacts serving as cathodes and the case as the anode. The voltage selected was 0.1 to 0.3 V lower than the threshold for side effects or 3.6 V or less. Two days to 2 weeks later (1 wk average), the patients returned for clinical reassessment. Improvement in dystonia was scored on the basis of their subjective impression as well as TWSTRS and BFM scores (recorded during each programming ses-

TABLE 2. Demographics and outcomes in patients with generalized dystonia treated with bilateral GPi stimulation[a]

Patient	Age	Diagnosis	Preop BFM	Postop BFM (%)	Follow-up (mo)	Active contact R/L
1	34	DYT1+	71.5	35 (51%)	50	1–/5–
2	46	DYT1+	65	25 (63%)	13	2–3–/6–7–
Mean ± SD	**40.0 ± 8.5**	**DYT1+**	**68.3 ± 4.6**	**30.0 ± 7.1 (57.0 ± 8.5%)**	**31.5 ± 26.2**	
3	26	DYT1–	40.5	3.5 (91%)	12	2–/5–
4	58	DYT1–	33	16 (51%)	7	1–/5–
5	53	DYT1–	65	17.5 (73%)	36	1–/5–
6	54	DYT1–	51	15 (71%)	3	2–/6–
Mean ± SD	**47.8 ± 14.7**	**DYT1–**	**47.3 ± 15.4**	**13.0 ± 10.6 (71.5 ± 15.2%)**	**14.5 ± 18.6**	
Mean ± SD	**45.2 ± 12.6**	**All**	**54.3 ± 15.4**	**18.7 ± 10.6 (66.7 ± 15.2%)**	**20.2 ± 18.6**	

[a] Preop, preoperative; BFM, Burke-Fahn-Marsden Dystonia Rating Scale; Postop, postoperative; %, percentage of improvement calculated as (1 − preop scores/postop scores) × 100; R/L, right and left electrodes. Results in bold represent mean ± standard deviation.

sion). In subsequent visits, homologous contacts (1 and 5; 2 and 6; 3 and 7) were tested in a similar way. After testing all contacts, the ones providing the most striking benefit on dystonia were selected for long-term stimulation. Additional adjustments included increases in voltage and/or pulse width and were made whenever clinical improvement was judged to be unsatisfactory. The most common settings for treating dystonia in our patients were monopolar stimulation at 2.5 to 3.5V, 60 to 90 μs, and 130 Hz.

Location of Active Contacts through MRI

Preoperative axial stereotactic T1-weighted or three-dimensional inversion recovery images (in patients operated on before and after 2002, respectively) and postoperative axial T2-weighted images were transferred to a workstation (StealthStation; Medtronic SNT, Louisville, CO). Using the FrameLink 4.1 software (Mach 4.1, StealthStation; Medtronic SNT) these two studies were fused, the fiducials of the frame were recognized, and the mean rod marking error was calculated and registered. Coronal and sagittal planes were reconstructed on the basis of the axial images. The anterior (AC) and posterior commissures (PC) were then targeted in the axial plane of the postoperative scan, and three additional points were plotted in the midline. Thereafter, the images were reformatted parallel to the AC-PC plane and orthogonal to the midline. Pitch, roll, and yaw were corrected in the StealthStation. DBS electrodes were visualized in all three planes, and their tips were targeted. For this study, we defined the tip of the electrode as the most distal portion of the electrode artifact. Although this does not represent the actual tip of the electrode, it was a standard measurement that could be compared across the studied groups.

After establishing the location of the tip of the electrodes, the trajectory angle was calculated and the distance between the MRI artifacts of each of the electrode contacts was assessed. For our study, we considered the center of the sphere-shaped artifacts correspondent to the electrode contacts as the center of the contacts (21, 22). The coordinates of the active contacts were then derived relative to the midcommissural point and lateral border of the third ventricle (*x*, mediolateral plane; *y*, anteroposterior plane; *z*, dorsoventral plane). The active contact was defined as the cathode in patients treated with mono- or bipolar stimulation. In patients using double monopolar stimulation, the location of the active contact was defined as the midpoint between the two cathodes.

The Euclidean distance from either the active contact or the tip of the electrodes to the center of the optic tract in the region closest to the projection of the electrode's tip was calculated. In a three-dimensional *xyz* system with p_1 being the optic tract (x_1, y_1, z_1) and p_2 being either the active contact or the tip of the electrode (x_2, y_2, z_2), the Euclidean distance between p_1 and p_2 was represented by

$$\sqrt{[(x_1 - x_2)^2 + (y_1 - y_2)^2 + (z_1 - z_2)^2]} \quad (1)$$

To evaluate the location of the active contacts relative to the pallidal boundaries, we used axial T2-weighted images containing the plane of the center of the active contacts. A straight line was drawn between the anteromedial and posterolateral corners of the GPi (*Fig. 1*). This was considered to be the anteroposterior (AP) extent of the pallidum in our study (APtotal). A second line was drawn parallel to APtotal from the projection of the anteromedial corner of the pallidum to the center of the active contact (APct) (*Fig. 1*). The percentage obtained when APct/APtotal × 100 was calculated denoted the relative distance of the center of the active contact from the anteromedial corner of the pallidum (%AP). A line perpendicular to APtotal that crossed the center of the active contact was then drawn and used to measure the mediolateral (ML) width of the pallidum (MLtotal) (*Fig. 1*). The distance from the most lateral point of this line to the center of the active contact was defined as the mediolateral location of the contact (MLct) (*Fig. 1*). The percentage obtained when MLct/MLtotal × 100 was calculated denoted the relative distance of the center of the active contact from the lateral aspect of the pallidum (%ML) (*Fig. 1*).

Note that most of the aforementioned variables assessed were obtained exclusively from postoperative images (*x*, *y*, *z* of the active contacts, Euclidean distances, and the location of the contacts relative to the internal anatomy of the pallidum). Fusion of pre- and postoperative scans was used only to calculate the arc and ring angles of the electrodes relative to the frame. Surgery was always performed in a similar way with burr holes placed approximately 1 to 2 cm anterior to the coronal suture and 2 to 2.5 cm lateral to the midline. In patients with cervical and generalized dystonia, arc angles were 71.7 ± 6.8

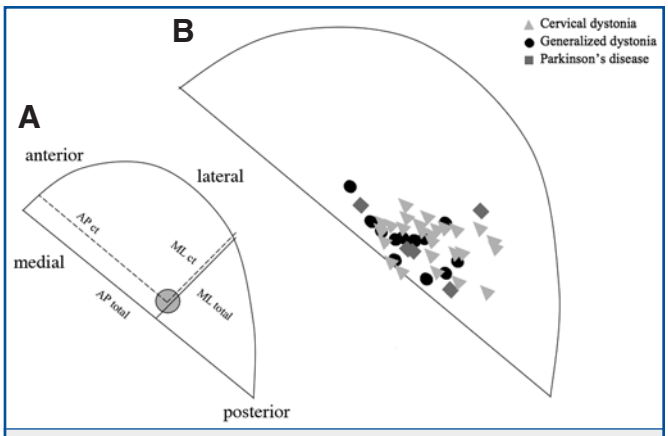

FIGURE 1. *Location of the active contacts relative to internal pallidal boundaries.* **A**, *schematic representation of a section of the GPi on a plane that crossed the center of the active contact* (gray circle). *A straight line was drawn between the anteromedial and posterolateral corners of the GPi* (APtotal). *A parallel line was drawn from the projection of the anteromedial corner of the pallidum to the center of the active contact* (APct). *Note that the actual lines representing MLtotal and MLct would superpose in a real case. These lines were separated in this figure for the sake of clarity.* **B**, *schematic representation of the location of the active contacts relative to the boundaries of the pallidum in patients with cervical dystonia, generalized dystonia, and Parkinson's disease (PD). In this figure, the dorsal ventral location of the contacts was not taken into consideration and all the plots were done in a schematic section corresponding to the level of the intercommissural plane.*

degrees and 76.7 ± 9.1 degrees, respectively. Ring angles were 89.0 ± 5.1 degrees and 89.2 ± 6.1 degrees, respectively.

Statistical Analysis

We used analysis of variance with a Tukey post-hoc analysis to compare the following: 1) the location of the active contacts and tip of the electrodes relative to midcommissural point (MCP), 2) the location of the active contacts relative to the third ventricular wall, 3) the Euclidean distances between the optic tract and either the active contacts or the tip of the electrodes, and 4) the percentage of AP and ML in groups of patients with cervical dystonia, generalized dystonia, and PD. We used the Student's *t* test to: 1) compare these same variables in patients with DYT1- and non-DYT1-generalized dystonia and 2) to compare the clinical outcome assessed in two independent groups. Correlation analysis was used to assess whether or not there was a relationship between the location of the active contacts and outcome.

For analysis of variance and Student's *t* test, a *P* value less than 0.05 was considered statistically significant. A correlation was considered to be strong when r ≥ 0.75, moderate when r ≥ 0.5, weak when r ≥ 0.25, and nonexistent when r < 0.25. All values in the text are expressed as mean ± standard deviation.

RESULTS

Location of Active Contacts in Different Clinical Conditions

A summary of our results can be found in *Table 3* and *Figure 2*. Because the location of the active contacts was similar in the right and left hemispheres, data from both sides were grouped for the analysis.

We found no significant differences in the location of the active contacts in patients with cervical dystonia, generalized dystonia, and PD (*Table 3*). Location of the active contacts was also similar in DYT1 and non-DYT1-generalized dystonia (*Table 4*). Although DYT1+ patients had their contacts placed closer to the midline ($P = 0.04$), this difference was not significant when the width of the third ventricle was taken into account.

When the location of the active contacts relative to the internal anatomy of the pallidum was considered, we also found no significant differences across groups (*Fig. 1*). Active contacts in patients with cervical dystonia, generalized dystonia, and PD were located within 49.0 to 75.6% (average, 59.3 ± 7.0%), 40.0 to 66.0% (average, 54.8 ± 8.8%), and 44.0 to 69.0% (average, 58.0 ± 9.1%) of the APtotal line ($P = 0.3$; 0% being the anteromedial corner and 100% the posterolateral corner of the pallidum), respectively (*Fig. 1*). In the mediolateral plane, the active contacts in patients with cervical dystonia, generalized dystonia, and PD were located within 54% to 100% (average, 76.0 ± 11.7%), 64% to 98% (average, 84.1 ± 10.7%), and 47% to 89% (average, 80.4 ± 18.7%) of the MLtotal line ($P = 0.2$; 0% being the lateral edge and 100% the medial edge of the pallidum over the line), respectively (*Fig. 1*). We did not explore

TABLE 3. Location of active contacts relative to the midcommissural point and third ventricular wall in patients with primary dystonia and Parkinson's disease treated with bilateral globus pallidus internus deep brain stimulation

	n	x	x (ventricle)	y	z	x (tip)	y (tip)	z (tip)	ED (tip-ot)	ED (ct-ot)
Cervical dystonia	26	20.3 ± 1.6	18.3 ± 1.9	3.0 ± 1.4	–1.0 ± 2.0	20.2 ± 2.0	0.8 ± 1.6	–6.4 ± 1.9	5.8 ± 2.3	7.3 ± 2.4
Generalized dystonia	12	19.5 ± 1.4	18.1 ± 1.3	3.4 ± 1.1	0 ± 2.2	18.9 ± 1.5	1.1 ± 1.2	–6.0 ± 1.5	6.1 ± 2.2	8.4 ± 2.1
Parkinson's disease	5	21.3 ± 2.2	18.5 ± 2.1	3.8 ± 0.6	–1.9 ± 1.7	20.6 ± 2.1	1.2 ± 2.4	–6.6 ± 2.5	5.3 ± 3.9	8.2 ± 2.6
P values		0.1	0.9	0.4	0.2	0.1	0.8	0.4	0.8	0.4

[a] n, number of electrodes implanted per group; x, mediolateral coordinate of the active contacts relative to MCP; x (ventricle), mediolateral coordinate of the active contacts relative to the lateral wall of the third ventricle; y, anteroposterior coordinate of the active contacts relative to MCP; z, dorsoventral coordinate of the active contacts relative to MCP; x, y, z (tip), coordinates of the tip of the electrodes relative to MCP; ED, Euclidean distance; tip-ot, from the tip of the electrodes to the optic tract; ct-ot, from the active contacts to the optic tract. Values represent mean ± standard deviation. *P* values were obtained with analysis of variance comparing the groups of patients with cervical dystonia, generalized dystonia (as a whole), and Parkinson's disease.

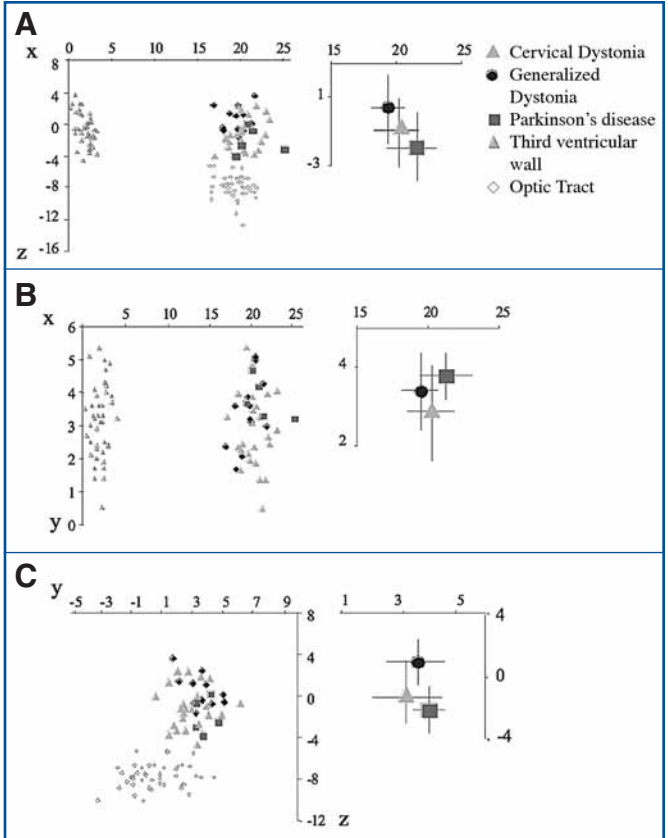

FIGURE 2. *Location of the active contacts relative to the midcommissural point in patients with generalized dystonia, cervical dystonia, and Parkinson's disease.* **A**, *schematic representation of a coronal view with the mediolateral* (x) *and dorsal-ventral* (z) *coordinates of the active contacts.* **B**, *schematic representation of an axial view with the mediolateral* (x) *and anteroposterior* (y) *coordinates of the active contacts.* **C**, *schematic representation of a sagittal view with the anteroposterior* (y) *and dorsoventral* (z) *coordinates of the active contacts. Graphs on the* right *side of the figure represent the correspondent means and standard deviations* (bars). *Numbers on the graphs represent mm from midcommissural point (MCP). Negative values are inferior and posterior to the MCP.*

the dorsoventral location of the active contacts relative to the internal pallidal anatomy because the border between the GPi and the globus pallidus externus could not be clearly delineated in our postoperative MRIs.

Correlation between the Location of the Active Contacts and Outcome

In patients with cervical dystonia, correlation analysis did not reveal a relationship between the location of the active contacts and outcome, as assessed with the TWSTRS scores (*Table 5*). In addition, the location of the active contacts was similar in patients with cervical dystonia that had more or less than 50% of improvement in TWSTRS severity scores (*Table 6*).

As for cervical dystonia, correlation analysis in patients with generalized dystonia has also revealed no relationship between the location of the active contacts and outcome (*Table 5*). Because all patients with generalized dystonia had a satisfactory outcome (> 50% of benefit), we did not subdivide them in groups according to clinical response.

Relationship between the Contact Being Used and Outcome

Most patients in our study were using contact 1 as the cathode (*Tables 1* and *2*). In cervical dystonia, upper contacts were only used when side effects were noticed with the lower ones. As a result, one could speculate that a better outcome might have been expected in patients using contact 1. In fact, TWSTRS scores in this group of patients improved by 63.1 ± 18.6%, whereas improvement in patients using upper contacts was in the order of 51.8 ± 21.3% ($P = 0.4$).

In contrast to these findings, although some patients with generalized dystonia were using upper contacts due to side effects with Contact 1, others had better clinical outcome when receiving stimulation through Contacts 2 and 3. Overall, BFM scores were reduced by 62.7 ± 11.1% in patients using Contact 1 and by 75 ± 14.4% in patients using upper contacts ($P = 0.3$).

DISCUSSION

We found that the location of the active contacts for DBS within the GPi was similar in patients with cervical dystonia,

TABLE 4. Location of active contacts relative to the MCP and third ventricular wall in patients with DYT1+ and DYT1- primary generalized dystonia treated with bilateral globus pallidus internus deep brain stimulation[a]

	n	x	x (ventricle)	y	z	ED
DYT1+	4	18.3 ± 1.1	17.4 ± 0.9	3.0 ± 1.1	–1.0 ± 2.8	7.3 ± 2.3
DYT1–	8	20.1 ± 1.1	18.4 ± 1.4	3.6 ± 1.1	0.5 ± 1.8	9.0 ± 1.9
P values		0.04[b]	0.2	0.4	0.4	0.3

[a] n, number of electrodes implanted per group; x, mediolateral coordinate of the active contacts relative to MCP; x (ventricle), mediolateral coordinate of the active contacts relative to the lateral wall of the third ventricle; y, anteroposterior coordinate of the active contacts relative to MCP; z, dorsoventral coordinate of the active contacts relative to MCP; ED, Euclidean distance. Values represent mean ± SD.
[b] Statistically significant.

TABLE 5. Correlation analysis of outcome and the location of active contacts relative to the MCP, third ventricular wall, and internal pallidal boundaries in patients with primary dystonia treated with bilateral globus pallidus internus deep brain stimulation[a]

	x	x (ventricle)	y	z	ED	%AP	%ML
TWSTRS scores	–0.01	–0.17	0.21	–0.15	–0.13	–0.23	–0.24
BFM scores	0.01	0.21	0.08	0.08	0.2	0.24	0.24
BFM appendicular scores	0.2	–0.07	0.3	0.03	0.07	–0.1	–0.1

Values represent the Pearson correlation coefficient (r).
BFM appendicular scores represent the sum of upper and lower extremity scores for the hemibody contralateral to stimulation.
[a] x, mediolateral coordinate of the active contacts relative to MCP; x (ventricle), mediolateral coordinate of the active contacts relative to the lateral wall of the third ventricle; y, anteroposterior coordinate of the active contacts relative to MCP; z, dorsoventral coordinate of the active contacts relative to MCP; ED, Euclidean distance; %AP, location of the active contact relative to the anteromedial and posterolateral corners of the pallidum as seen in postoperative MRI scans (see text for details); %ML, location of the active contact relative to the medial and lateral edges of the pallidum as seen in postoperative MRI scans (see text for details). TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale; BFM, Burke-Fahn-Marsden Dystonia Rating Scale.

TABLE 6. Location of active contacts relative to the midcommissural point and third ventricular wall in patients with cervical dystonia treated with bilateral globus pallidus internus deep brain stimulation[a]

	n	x	x (ventricle)	y	z	ED	%AP	%ML
>50%	16	20.5 ± 1.6	18.3 ± 1.9	3.0 ±1.5	–0.7 ± 1.6	7.4 ± 2.7	58.8 ± 7.2	74.8 ± 11.6
<50%	10	19.9 ± 1.7	18.1 ± 2.0	2.7 ± 0.9	–1.2 ± 2.6	7.3 ± 2.2	60.3 ± 7.1	77.5 ± 12.2
P values		0.4	0.8	0.6	0.6	0.9	0.6	0.6

[a] n, number of electrodes implanted per group; x, mediolateral coordinate of the active contacts relative to MCP; x (ventricle), mediolateral coordinate of the active contacts relative to the lateral wall of the third ventricle; y, anteroposterior coordinate of the active contacts relative to MCP; z, dorsoventral coordinate of the active contacts relative to MCP; ED, Euclidean distance; %AP, location of the active contact relative to the anteromedial and posterolateral corners of the pallidum as seen in postoperative MRI scans (see text for details); %ML, location of the active contact relative to the medial and lateral edges of the pallidum as seen in postoperative MRI scans (see text for details). Values represent mean ± standard deviation.

generalized dystonia, and PD. In addition, we found no correlation between the location of the active contacts and postoperative outcome in these patients.

The initial reason that led us to investigate the location of the active contacts in dystonia was our clinical impression that patients with cervical dystonia using upper contacts were doing slightly poorer than those using Contact 1. In this later group, improvement in TWSTRS scores was approximately 20% higher (although not statistically significant) than in patients using upper contacts. In contrast, BFM scores in patients with generalized dystonia using Contact 1 were approximately 15% lower (although also not statistically significant) than in patients being stimulated through upper contacts. Considering this, we initially thought that the pallidal region more suitable for stimulation in cervical dystonia would be ventral to the one for generalized dystonia. Our result, however, did not confirm this hypothesis.

A second aspect of our study was to evaluate whether or not part of the variability in postoperative results in patients with dystonia could be related to differences in the location of the active contacts within the pallidum. We found no correlation between the pallidal region being stimulated and outcome. This suggests that other factors, such as the clinical characteristics of the dystonic movements (tonic versus phasic), for example, are probably playing a more influential role in postoperative clinical results. However, we have only explored a small region of the pallidum. Our active contacts were relatively clustered in the posteroventral portion of the GPi, and we could not test the effects of stimulation in significantly more anterior or lateral regions of the nucleus. In this sense, the only thing we might conclude is that within that region of the pallidum, location of the active contacts did not determine the outcome. In contrast to our findings, Gross et al. (14), for example, have shown that differences in the location of lesions in PD patients treated with pallidotomy correlated with postoperative improvements in specific motor symptoms. In that series, variability in the location of lesions in the anteroposterior and mediolateral planes was much greater than in our study (location of the center of the lesions varied from 8.3 mm anterior to 0.5 mm posterior to MCP and 10.8–19.5 mm lateral to the third ventricular wall) (13).

As the target for the placement of the electrodes in dystonia is the posteroventral aspect of the GPi, the location of the electrodes in our series was similar to that reported in the literature (2, 24, 25). Yet, when our results are compared with those published by individual reports, small differences could be observed. For instance, compared with our data, the active contacts in the study by Starr et al. (22) were slightly more anterior relative to the MCP and a little more lateral when the borders of the pallidum were considered. When evaluating the results by Vayssiere et al. (24), however, one can appreciate the variability in the location of active contacts leading to

an excellent clinical outcome, particularly in the mediolateral plane. Considering these results and the variable clinical presentation of the patients, the meaning of small discrepancies in the location of the electrodes observed by different groups is difficult to interpret.

Most patients with dystonia in our study were receiving stimulation at 2.5 to 3.5V, 60 to 90 μs, and 130 Hz. Because of the proximity of the active contacts to the internal capsular border, motor contractions were often observed at 2.8 to 4V. Despite this, we continue to place the electrodes in the same way because our patients are having a significant postoperative improvement.

In summary, our results showed that the location of the active contacts was similar in patients with generalized and cervical dystonia. Future studies with a greater number of patients are certainly needed to confirm these findings and investigate the relationship between the clinical outcome and best location for electrical stimulation within the pallidum in patients with dystonia.

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COMMENTS

In this study of globus pallidus deep brain stimulation (DBS) for primary dystonia, the authors have carefully measured active contact locations using postoperative MRI scans. The active contact locations reported were associated with major improvements in most patients. They show that there was not a systematic difference in optimal active contact locations for cervical versus primary dystonia. They also show that, within the small region of the posterior globus pallidus internus (GPi) covered by their electrodes, lead location did not predict outcome.

The study helps to define the region of the GPi that should be targeted to achieve significant clinical benefit in primary dystonia. The active contacts in this study are slightly closer to the pallidocapsular border than those in our own series and were programmed at lower pulse widths but were associated with similar benefits.

In some patients with cervical dystonia, we have observed a side effect of pallidal stimulation: a mild bradykinesia in body parts (legs and arms) that are not affected by the dystonia. This has been very

annoying to some patients. Such a side effect has not been noticed in generalized dystonia, perhaps because the improvement in dystonia masks any subtle side effects of stimulation on movement times. It is possible that only some subregions of the posterior GPi are associated with this side effect, but this theory remains to be proven.

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The GPi is the favored target for DBS in the treatment of patients with dystonia (2, 4, 5, 11, 12). There is promising evidence for a striking efficacy of pallidal stimulation in dystonia. The most dramatic results have been obtained with pallidal stimulation to treat primary dystonia linked to genetic mutations, in particular, DYT1, other primary dystonias, and tardive dystonic syndromes. Conflicting results were reported for secondary dystonias. Long-term double-blind studies and a careful assessment of the efficacy are needed. But, first, there is a requirement for a consensus about the precise anatomic position of the optimal lead. Analyses of the intrapallidal localization of the quadripolar contacts associated with optimal benefit have been published infrequently. In fact, there has been a deficiency in much of the DSB literature in this regard. More recent publications have included computationally reformatted postoperative magnetic resonance images and the approximate locations of the contacts being used. These data should be essential in any future publications in the field so as to further delineate the optimal target. In this regard, Hamani et al. add to the literature.

In this article, the target is the sensorimotor area of GPi in all cases regardless of indication. This is a large area and the real question is whether there is an optimal target in that area. They did not find a "sweet spot," but the number of subgroups precluded meaningful statistical power. Although patients with Parkinson's disease in whom pallidotomy failed but who showed minimal improvement with DBS were included, the comparison of the patients with generalized dystonia and those with cervical dystonia were the focus of the article. Here, comparisons with the literature may shed some light.

In a study of 23 adult and pediatric patients with mixed forms of dystonia, Starr et al. (7) implanted DBS leads using MRI-based stereotactic, microelectrode recording, and intraoperative test stimulation to determine thresholds for stimulation-induced adverse effects. Lead locations were measured on computationally reformatted postoperative MRI scans. The active lead locations associated with robust improvement (>50% decrease in the Burke-Fahn-Marsden Dystonia Rating Scale score) were located near the intercommissural plane, at a mean distance of 3.7 mm from the pallidocapsular border. This result is consistent with our finding that the target is more lateral (physiological 21.5 mm rather than 20 mm for pallidotomy) but allows for greater current spread while avoiding capsular side effects (8). Hamani et al. place their lead closer to the capsule, and this placement might explain some of the differences in the two studies.

Starr et al. (7) also observed that the spontaneous discharge rates of GPi neurons in dystonia are similar to those of globus pallidus externus (GPe) neurons and the two nuclei must be distinguished by neuronal discharge patterns rather than by rates, verifying a previous report (15). The early models of dystonia suggested that reduced mean discharge rates in GPi lead to disinhibition and increases in activity in the thalamocortical circuit that precipitated the development of dystonia. The clinical improvement in dystonia after pallidotomy was difficult to reconcile with this "rate" hypothesis as the procedure results in a further reduction in pallidal output. This quickly led to the development of an alternative model that, in addition to rate, incorporates changes in pattern and degree of synchronization of neuronal activity (13, 15). Multiple groups have confirmed that the mean GPi neuronal firing rate in dystonic patients is lower than that in Parkinson's disease, whereas there is little to no difference in firing rate observed in GPe between the two disorders. This finding has recently been confirmed in cervical dystonia compared with Parkinson's disease in Toronto (9).

In the other referenced manuscript, Vayssiere et al. (11) found that all activated contacts were in the posterolateroventral portion of the GPi. A correlation between the active contact location and the part of the body in which the highest improvement was observed demonstrated that a location more anterior for the inferior limb and one more posterior for the superior limb were delineated for the right side, but not for the left side. Why there are left to right side differences is not clear, but probably this is a sampling error. An optimal cervical stimulation location was not defined. These results may be explained by the somatotopic anatomy of GPi, which is well established (1). There is preservation of GPi somatotopic organization in dystonia (9, 14, 15). When patients with generalized dystonia were compared with patients with segmental craniocervical dystonia, there was no difference in the volumes or separations of leg and arm related territories (14). Hamani et al. similarly did not find a specific area wherein cervical dystonia was maximally improved. This most likely relates to the somatotopic anatomy in which cervical kinestatic cells are diffusely and infrequently found along the posteroventral GPi.

Two other studies continue this theme. In a consecutive series of 15 patients with mixed forms of dystonia, the analysis by Tisch et al. (10) of the optimal stimulating contact coordinates with clinical improvement in the Burke-Fahn-Marsden Dystonia Rating Scale score identified two subgroups, distributed along an anterodorsal to posteroventral axis (10). Clinical improvement was greater for posteroventral than for anterodorsal stimulation for the arm and trunk and inversely correlated with the y coordinate. For the leg, posteroventral and anterodorsal stimulation were of equivalent efficacy. Overall clinical improvement was maximal with posteroventral stimulation and inversely correlated with the y (anterior-posterior) coordinate. Similarly, Houeto et al. (3), using a three-dimensional atlas magnetic resonance imaging coregistration method, demonstrated that acute ventral stimulation of the globus pallidus significantly improved the Burke-Fahn-Marsden Dystonia Rating Scale score when the stimulating contact was located in the GPi or medullary lamina in 18 of 21 patients (3). Bilateral acute dorsal pallidal stimulation, primarily localized within the GPe, had variable effects across patients, with half demonstrating slight or no improvement or even aggravation of dystonia compared with baseline. Stimulation of GPe can induce dyskinesias (6). So you do not want to locate the contact too laterally.

Undeniably, additional research in this arena is warranted. A larger number of patients are essential but, without more accurate diagnosis and subcategory partition, the patients can not be properly grouped. Multiple problems with inaccuracies in postoperative magnetic resonance localization still remain to be resolved. The irregularities of the nucleus and dissimilar programming philosophies add subtitle problems not yet addressed. So, although the target is the sensorimotor area of GPi, whether the optimal target within that area varies with the explicit type and anatomical localization of the dystonia remains to be resolved.

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This carefully performed study shows no difference in electrode position within the globus pallidus in patients with good outcomes after DBS performed for the treatment of cervical dystonia, generalized dystonia, and Parkinson's disease. The authors are properly cautious about generalizing from their data, pointing out the need for further studies with larger numbers of patients, even though the movement disorders group at the University of Toronto has one of the largest experiences with DBS for motor disease.

A further conclusion can, perhaps, be drawn from their data. The spatial distribution of effective DBS points extended within the globus pallidus 8 mm in the dorsal-ventral (z) axis and 6 mm in the anterior-posterior (y) axis. It would seem that the critical factor for efficacy of DBS is the total volume of the pallidum that is stimulated, a volume that can be reached from a number of points within the pallidum.

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