Thalamic Deep Brain Stimulation for Refractory Tourette Syndrome

Received: June 16, 2016 Revised: September 24, 2016 Accepted: October 11, 2016

(onlinelibrary.wiley.com) DOI: 10.1111/ner.12556

Thalamic Deep Brain Stimulation for Refractory Tourette Syndrome: Clinical Evidence for Increasing Disbalance of Therapeutic Effects and Side Effects at Long-Term Follow-Up

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Objective: Thalamic deep brain stimulation (DBS) is effective in reducing tics in patients with refractory Tourette syndrome at the short-term. Here, we report on the long-term outcome.

Materials and Methods: Seven patients underwent bilateral DBS between 2001 and 2008. The target was the centromedian nucleus, substantia periventricularis and nucleus ventro-oralis internus cross point of the thalamus. The effect on tics and side effects were evaluated with a variable follow-up duration of 12 to 78 months.

Results: Patient 1 and 2 showed good tic improvements of 81.6% (60 months) and 50% (36 months), respectively. However, side effects like reducing levels of energy and visual disturbances increased. In patient 1, the target was changed to the anterior part of the internal pallidum and patient 2 switched the stimulator permanently off. Patient 3 experiences still satisfying results with a tic improvement of 88.9% (78 months). Patient 4 and 7 showed minor tic improvements of 34% (16 months) and 9% (60 months), respectively. In both patients side effects became more severe and the target was changed to the anterior part of the internal pallidum. Patient 5 showed a tic improvement of 27.5% (12 months) and went abroad for stimulation of the external globus pallidus. Patient 6 developed cerebellar atrophy. He experienced several nonstimulation related side effects and turned the stimulator off.

Conclusions: There seems to be an increasing disbalance of therapeutic effects and side effects at long-term follow-up, often leading to either switching the stimulator off or new surgery with a different neuro-anatomic target.

Keywords: Deep brain stimulation, long-term outcome, thalamus, tics, Tourette syndrome

Conflict of Interest: The authors reported no conflict of interest.

INTRODUCTION

Tourette syndrome (TS) is a chronic childhood-onset neurodevelopmental disorder characterized by multiple motor and vocal tics (1,2). Although symptoms usually subside by adulthood, a significant proportion of patients fail to respond to standard medical and behavioral therapies (3–5). For these patients, deep brain stimulation (DBS) has emerged as a therapeutic escalation. At present, six different targets have been stimulated (6,7); the medial part of the thalamus, the globus pallidus internus (GPi), the globus pallidus externus (GPe), the nucleus accumbens (NA), the anterior limb of internal capsule (ALIC), and the subthalamic nucleus (STN). Most of the TS patients have shown beneficial short-term effects following DBS. Overall, DBS resulted in a significant short-term improvement of 52.68% on the Yale Global Tic Severity Scale (YGTSS) (7,8). In general, the degree of tic improvement appeared to be most robust for the thalamic and the GPi targets (7).

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For more information on author guidelines, an explanation of our peer review process, and conflict of interest informed consent policies, please go to www.wiley.com/WileyCDA/Section/id-301854.html

Source(s) of financial support: No sources of financial support.

So far, long-term follow-up data are sparse. Porta et al. (9) described their six years follow-up of thalamic DBS in 18 TS patients and showed a significant improvement on tics and comorbid behavioral disorders. However, long-term complications and difficulties such as noncompliance and differences in opinions between the medical team and the patients as to their satisfaction with the outcome were reported (9,10). Motlagh et al. (11) reported their experiences with DBS of the medial thalamus ($n = 5$) or the GPi ($n = 3$) in eight TS patients over seven years. Only three patients experienced more than 50% tic reduction (thalamic target in all three patients) and two patients had their DBS leads removed, one due to an infection and one to due lack of effect (thalamic target in both patients).

Given the small amount of published data, it is difficult to consider the gain for future individual TS patients. Therefore, rigorous reporting of all available data, and especially long-term follow-up data, is highly needed. The present paper reports on the long-term outcome of seven refractory TS patients treated with DBS of the medial thalamus between 2001 and 2008. The initial one year outcome of six patients (12) and the six years outcome of the seventh patient (13) have been reported previously.

METHODS

Patient Selection

Seven patients with refractory TS were referred to the Maastricht University Medical Centre (MUMC) and selected for bilateral DBS of the medial thalamus between 2001 and 2008. One other patient underwent thalamic DBS during that period. This was a 20 year old institutionalized female patient with intractable TS and severe comorbidity, including life-threatening self-injurious behavior. She underwent surgery for clinical urgency in 2006. Postoperative she experienced abrupt onset hypertonia, inconsistent and incongruent with organic disorders, bizarre movements and concomitant somatizations, suggesting a psychogenic nature. In 2009, she passed away in a nursing home. No follow-up data are available and the details have been described in a case report (14).

Inclusion criteria for surgery were: 1) a primary diagnosis of TS according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders criteria (fourth edition) (DSM-IV) (15), 2) minimum age of 25 years, 3) a minimum score of 80 on the Diagnostic Confidence Index (16), 4) a minimum score of 25 on the YGTSS (17), 5) failure to respond to, or intolerable side effects of three-months trials of adequately dosed classical (e.g., haloperidol) or atypical (e.g., risperidone, olanzapine, quetiapine) antipsychotic medication or clonidine, and 6) completed at least ten sessions of behavioral therapy. Exclusion criteria included: 1) tics not related to TS, 2) major psychiatric disorders, 3) current substance abuse or dependence (except for nicotine), 4) severe cognitive impairment, 5) structural abnormalities on brain magnetic resonance imaging, and 6) general contraindications for surgery or anaesthesia. All patients were evaluated by members of the Dutch-Flemish Tourette Surgery Study Group, a collaboration of neurologists, neurosurgeons, psychiatrists and neuropsychologists with special interest in TS, to ensure appropriate selection. These results represent a systematic audit of routine outcome measurements and formal approval by a medical ethics committee was therefore not required. The results of all patients have been published previously (12,13), after all patients gave written informed consent to report the results and to retrieve data from their medical records. To retrieve these long-term follow-up data, all patients gave oral informed consent.

Surgery

Stereotactic bilateral DBS of the medial thalamus was performed under local anaesthesia and sedation in all seven patients. Target was the centromedian nucleus, substantia periventricularis, and nucleus ventro-oralis internus (Cm-Spv-Voi) cross point of the thalamus, using the following standard coordinates; $x = 5$ mm lateral of the anterior commissure—posterior commissure (AC-PC) midline, $y = 4$ mm posterior to the mid-commissural point at the level of the AC-PC plane, $z =$ at the level of the AC-PC plane. Target coordinates were adapted according to the width of the third ventricle and the AC-PC length (Table 1). The trajectory with the best clinical outcome and no stimulation-induced side effects was determined using extracellular single-unit microelectrode recordings and test stimulation. Full details of our neurosurgical procedure are published previously (12).

Postoperative Management

Outpatient visits and programming sessions were performed as frequently as needed and wanted. Patients received a patient-programmer, which allowed them to change the stimulation voltage between individually assigned ranges. The initial goal was to evaluate all patients once a year, but due to noncompliance we were not able to collect data on a yearly basis. During visits to the outpatient clinic the effect on tics, side effects, complications and stimulations parameters were evaluated. At some moments the YGTSS was

Table 1. Stereotactic Coordinates and Stimulation Parameters.

Patient	Lead	Left electrode							Right electrode						
		x	*y*	*z*	Active contacts	Voltage (V)	Pulse (μsec)	Frequency (Hz)	*x*	*y*	*z*	Active contacts	Voltage (V)	Pulse (μsec)	Frequency (Hz)
1	3387	3	4.8	contact 1: target-4	0−, 1−, 2+, 3+	6	120	110	3	4.8	contact 1: target-2	4−, 5−, 6+, 7+	6	120	110
2	3387	5	4	contact 1: target	0+, 1−, 2−, 3+	1	60	70	5	6	contact 1: target +2	4−, 5−, 6+, 7+	2.1	60	70
3	3387	5	4	contact 1: target-3	1−, 2−, C+	1.7	210	100	5	6	contact 1: target-2	5−, 6−, C+	1.7	210	100
4	3387	7	4	contact 1: target-1	2−, C+	6.6	180	90	7	4	contact 1: target-1	5−, C+	6.6	150	90
5	3389	5	4	contact 1: target	1−,2−,C+	2.6	90	130	5	4	contact 1: target	5−,6−,C+	2.6	90	130
6	3387	9	4	contact 1: target-3	1−, C+	1	60	110	9	4	contact 1: target-3	5−, C+	1	60	110
7	3387	5	4	contact 1: target	1−, 2+, 3−	9.3	150	100	5	4	contact 1: target	5−, 6+, 7−	9.3	150	100

Active contacts and stimulation parameters are shown at final follow-up.
x, number of mm lateral of the anterior commissure – posterior commissure (AC-PC) midline; y, number of mm posterior to the mid-commissural point at the level of the AC-PC plane; z, number of mm deeper (+) or more superficial (−) than the AC-PC plane.

Table 2. Yale Global Tic Severity Scale.

	YGTSS total (motor/vocal)						
	Baseline	6–12 m	12–24 m	24–36 m	36–48 m	48–60 m	60–78 m
Patient 1	38 (19/19)	2 (0/2)	–	5 (0/5)	8 (4/4)	7 (4/3)	ND
Patient 2	44 (25/19)	19 (19/0)	11 (10/1)	22 (16/6)	22 (16/6)	ND	ND
Patient 3	45 (20/25)	19 (13/6)	22 (18/4)	–	12 (12/0)	–	5 (5/0)
Patient 4	46 (21/25)	34 (15/19)	30 (15/15)	ND	ND	ND	ND
Patient 5	40 (22/18)	29 (14/15)	ND	ND	ND	ND	ND
Patient 6	41 (16/25)	26 (10/16)	–	27 (13/14)	ND	ND	ND
Patient 7	43 (20/23)	26 (16/10)	–	–	44 (23/21)	35 (19/16)	39 (21/18)

ND, no data (because stimulator removed or switched off); YGTSS, Yale Global Tic Severity Scale.

completed by a neurosurgeon (LA), which provides an evaluation of number, frequency, intensity, complexity, and interference of motor and vocal tics. Total scores range from 0 to 50 with higher scores indicating higher severity (17).

RESULTS

Patient 1 (Male, 48 Years at Time of Surgery)

This patient developed his first tics at the age of 6. Motor tics consisted mainly of facial grimaces, eye blinking, and shoulders shrugs. Vocal tics were coughing and making uttering sounds. His tics were not responsive to medication or behavioral therapy. No comorbid disorders were present. In 2005, bilateral DBS of the thalamus was performed. After surgery, tics diminished and the YGTSS improved from 38 to 2 (94.7%) at one-year follow-up (Table 2). However, he experienced many psychosocial stressors since he lost his job a few months after surgery. He suffered from several periods of minor depression during the following years. At 60 months of follow-up, tic improvement was maintained with a score of 7 on the YGTSS (81.6%). However, from 2009 he needed higher voltage stimulation to obtain the same effect on his tics. As a consequence, more frequent battery changes were needed, including a rechargeable battery. He was admitted to the hospital several times to obtain the most effective stimulation parameters without success. Side effects like a reduced level of energy, sleeping disorders, and gaze disturbances became more severe, making stimulation at adequate parameters impossible. The active contacts and stimulation parameters at final follow-up are shown in Table 1. He was not satisfied with the effects of the stimulation anymore and bilateral DBS of the anterior GPi was carried out in 2012. The thalamic leads remained *in situ* but switched off. We were not able to reach a satisfying effect with pallidal stimulation on tics so far, even after rigorous adjusting of stimulation parameters. Finally, we decided to switch off the pallidal DBS and turn on the thalamic DBS again. No data, including the YGTSS, have been obtained during this period.

Patient 2 (Male, 39 Years at Time of Surgery)

This patient developed tics around the age of 6. He suffered from socially and physically debilitating motor and vocal tics, especially spitting and coprolalia. He also exhibited self-injurious behavior like banging his forehead against a wall. He did not suffer from comorbidities. Medication and cognitive behavior therapy were not effective. In 2005, he was selected for bilateral DBS of the thalamus. After surgery he developed a vertical gaze paralysis due to a small deep bleeding in the upper mesencephalon at the tip of the left electrode, which improved spontaneously (18). The YGTSS improved from 44 to 19 (56.8%) at 12 months of follow-up, and it improved even further at 24 months of follow-up (YGTSS of 11 (75%)). Coprolalia and self-injurious behavior disappeared after surgery. Although the vertical gaze palsy had resolved, he continued having visual disturbances and pressure behind his eyes during stimulation. He also experienced a reduction in his energy level. The YGTSS remained 22 (50%) at 36 months of follow-up. However, due to these side effects and the burden of visiting the outpatient clinic, he eventually decided to switch the stimulator permanently off.

Patient 3 (Male, 40 Years at Time of Surgery)

This patient developed tics at the age of 7. He suffered from several motor tics like shoulder shrugs and neck extensions; however, most debilitating were his vocal tics, mainly coprolalia. He had a history of substance abuse, but no other comorbidities. In 2005, bilateral DBS of the thalamus was carried out. Postoperative he developed an infection of his infraclavicular pulse generator (staphylococcus aureus), which was successfully treated with six weeks of intravenous antibiotics. Tics progressively diminished after surgery and the YGTSS decreased from 45 to 12 (73.3%) and further to 5 (88.9%) at respectively 45 and 78 months of follow-up. This patient still experiences some side effects like reduced levels of energy and minor visual disturbances, especially with higher voltage stimulation. However, with the current stimulation parameters these side effects are acceptable and he is still satisfied with the effect of the DBS.

Patient 4 (Male, 35 Years at Time of Surgery)

This patient experienced his first tics at the age of 7. Motor tics included flexion with both arms and jumping and vocal tics included shouting, coprolalia, and echolalia. Most debilitating were his vocal tics. He had a positive family history for TS and a history of depression and Attention Deficit Hyperactivity Disorder. In 2006, bilateral DBS of the thalamus was performed, with an improvement from 46 to 30 (34.8%) on the YGTSS at 16 months of follow-up. From 2009 he started to suffer from more serious side effects like reduced levels of energy and visual disturbances, making daily activities impossible. Due to these side effects and the burden of the disease, he did not tolerate the same voltage stimulation as before anymore and the positive effects of stimulation began to decrease. In September 2012, the whole system had to be removed due to a persisting hardware infection after a pulse generator replacement, not treatable with antibiotics. Tics increased to the preoperative level with a score of 48 on the YGTSS. In December 2012, DBS of the anterior GPi was carried out. An improvement from 48 to 17 (64.5%) was observed on the YGTSS after 12 months (19).

Patient 5 (Male, 40 Years at Time of Surgery)

This patient suffered from severe motor tics since the age of 12, most debilitating were forceful jerks of legs, arms and abdomen, facial grimaces, and jumping. No comorbidities were present. In 2008, he was selected for bilateral DBS of the thalamus. His YGTSS showed a minor improvement from 40 to 29 (27.5%) at 12 months after surgery. This patient was discontented with the results and went to Belgium for DBS of the external globus pallidus and was lost to follow-up.

Patient 6 (Male, 40 Years at Time of Surgery)

This patient developed tics at the age of 6, during childhood motor tics decreased but vocal tics became more pronounced. Most debilitating were coprolalia, echolalia, and uttering sounds. He had a history of substance abuse, but no other comorbidities. Bilateral DBS of the thalamus was carried out in 2008. Both motor and vocal tics diminished during stimulation, but almost all tics remained present to some extent. The YGTSS improved from 41 to 27 (34.1%) at 26 months of follow-up. Postoperative, he experienced several symptoms like binge eating, lethargy, dysarthria, gait disturbances, and apathy up to one year after surgery. These symptoms were not related to adjustments in stimulation settings and their interpretation was complicated by inconsistencies in his subjective report during the interviews and the complexity of his comorbidities. A CT-scan performed six months after surgery revealed cerebellar atrophy, not present at preoperative imaging. Due to all these other symptoms and the lack of effect we turned the stimulator off and as such he was lost to follow-up.

Patient 7 (Male, 45 Years at Time of Surgery)

This patient developed tics at the age of 8, which gradually worsened around adolescence. His most debilitating symptoms consisted of forceful head movements, leading to cervical myelopathy, and screaming. Moreover, sexual obsessions and compulsions such as breaking glasses were troublesome. In 2001, he was selected for bilateral DBS of the thalamus, which resulted in an improvement from 43 to 26 on the YGTSS (39.5%) at eight months of follow-up. During follow-up, major adjustments to the stimulation parameters were made with a progression of monopolar stimulation toward bilateral bipolar stimulation and an increase from 2.4 to 9.3V. However, this caused serious side effects including reduced levels of energy, gaze disturbances, and alteration of sexual function, making stimulation at adequate parameters impossible. After three to six years higher scores on the YGTSS were observed (44, 35, 39). Moreover, with lower voltage stimulation serious side effects remained. In 2010, a hardware defect in the left electrode was detected and, consequently, the whole DBS system was removed. Since a satisfying situation with thalamic DBS had not been reached in the last years, DBS of the anterior GPi was carried out in September 2010, at the age of 54. With pallidal DBS he experienced a large improvement on the YGTSS from 46 till 9 (80.4%), which was maintained after 38 months of follow-up (19).

DISCUSSION

These seven cases show that thalamic DBS in patients with severe TS can be effective in reducing tics at the short-term (12). However, at the long-term in only one patient (patient 3) the stimulator is still active. In three patients (patient 1, 4, and 7), the target has been changed to the anterior part of the internal pallidum due to side effects (i.e., reduced level of energy, sleeping disorders, gaze disturbances, and alteration of sexual function) In one of those patients (patient 1), a satisfying effect on tics during pallidal stimulation could not be reached and finally we switched off the pallidal DBS and turned on the thalamic DBS again. Three patients (patient 2, 5, and 6) were not satisfied with the result of the DBS and decided to switch off their stimulator. Two of them (patient 5 and 6) showed only minor improvement during stimulation, whereas the third patient (patient 2) had a good effect but suffered from the adverse effects. These results are partially in line with the results of Motlagh et al. (11), with an improvement of more than 50% in three out of eight cases vs. three out of seven cases in our sample. However, they did not report on side effects over the course of time, which appeared to increase in our sample and were often responsible for changing the target or switching off the stimulator. Porta et al. (9) reported a significant reduction in tic severity (pre-DBS 80.83 ± 11.98, post-DBS 22.11 ± 14.19, $p < 0.001$) at six years follow-up, but also difficulties like noncompliance and differences in the opinions between the patients and the medical team (9,10). In their sample side effects have been reported only as minor and not being a cause of the dissatisfaction, which is in contrast with our results.

At long-term follow-up, we also found differences in opinions between the medical team and the patients as to what a satisfactory outcome is. Whereas professionals mainly focus on tic reduction, a patients' wellbeing does not only depend on tic reduction (10,20). In our group, we noticed that patients with tic improvements between 9 and 34% generally were dissatisfied with results and end their stimulation. We also observed that patients who responded well in terms of tic reduction (>50%), but experienced increasing side effects were dissatisfied too. The YGTSS is a quantitative method to determine the effect on tics (17), but it does not necessarily represent the patient's satisfaction with the treatment. Satisfaction may concern many factors, which can be different for the individual patients. Besides, there will be a response shift with respect to expectations and ambitions, which may explain changes in satisfaction over time. Therefore, qualitative research concerning the perception of satisfaction, expectations, and ambitions in TS patients undergoing DBS is highly needed (20).

In the earlier years of DBS, professionals often mentioned the "burden of normality" as an explanation for dissatisfaction after surgery (21). On being rendered "disease" free, the process of successful adjustment primarily depends on the patient's ability to discard the roles associated with the disease and his capacity to adjust to leading a normal life. For TS patients this may be especially difficult since they suffer from a lifelong disabling condition, and the tics have played a major role in the development of their personality, education, and both social and professional life. In addition, DBS in TS improves the symptoms (tics), with a collateral improvement of comorbid behavioral disorders in only a minority of patients. In the early period after surgery, the relief of tic improvement may distract from essential other premorbid problems and side effects. However, these problems and side effects may become more obvious after a longer time, and at that time more difficult to accept. In general, one easily can get used to "success," but it is hard to accept "losses."

Saleh et al. (5) analyzed all reported complications and adverse events after DBS for TS and other psychiatric diseases. Long-term morbidity was reported in 16.5% of cases, in 6.2% this was related to the surgery or hardware and in 10.2% to chronic stimulation (5,12). Stimulation related side effects included; anxiety ($n = 7$), mood changes ($n = 2$), psychosis ($n = 1$), apathy ($n = 13$), and alteration of sexual function ($n = 6$). Notably, apathy was observed only in patients with thalamic DBS. The majority of reported side effects appeared to be transitory or resolved with adjustments of

stimulation settings. This is not in line with our experience during the long-term follow-up. The side effects in our group did most often not respond to adjustments in stimulation settings. Moreover, the side effects, though based on self-report, became more pronounced with increasing treatment duration.

Thoughtful programming of the stimulator is very important to achieve an optimal clinical outcome (11). Due to natural symptom fluctuations, variability in patients' responses to treatment and expectations adjustment in stimulation settings is often a temporary solution (9–11). In our experience TS patients tend to blame the stimulator for almost all negative symptoms and maybe professionals reinforce them to do so by adjusting the stimulation settings every time they report complaints. Given the experimental status of DBS in TS and their clinical responsibility to treat side effects, professionals might feel the pressure to intervene and as such maintain dissatisfaction. Intensive guidance, multidisciplinary, already early after surgery, is needed to differentiate between stimulation related changes and problems in coping with the postoperative situation. Standard postoperative psychoeducation for the patient and his system, either individual or in a group will be helpful to shift the focus from the stimulator to the person and his environment and as such reduce blaming the stimulator and unnecessary adjustment of the stimulation settings.

The main limitation of this case series is that we report on observational data of a small sample and case descriptions from routine clinical practice with variable follow-up duration. Specialized Tourette clinics have reported only a handful of appropriate DBS candidates each year, rendering it nearly impossible to draw critical conclusions about the effects. However, the importance of these data for our daily practice cannot be underestimated. Thorough reporting on small groups and long-term follow-up data is essential, particularly in dealing with a complex disease like TS. Our experience highlights the need for more qualitative studies and the incorporation of additional outcome parameters other than reduction of tics and comorbid symptoms. To overcome some of these problems, an International DBS Registry and Database for TS is being developed, with the idea that the statistical power necessary to refine and improve this procedure could only be achieved through the collection of a large worldwide community of cases (22).

CONCLUSION

In our group of patients receiving thalamic DBS for TS there seems to be an increasing disbalance of therapeutic effects and side effects at long-term follow-up, often leading to either switching off the stimulator or new surgery with a different neuro-anatomic target. The reported cases reflect the strong heterogeneity of the disease and comorbidity, the still underrated impact of individual expectations and ambitions and the caution of the professionals, all interfering with effects and side effects and the overall success of DBS.

Authorship Statements

Anouk Smeets, Annelien Duits, Albert Leentjens, Yasin Temel, and Veerle Visser-Vandewalle designed and conducted this retrospective study. Anouk Smeets, Linda Ackermans, Annelien Duits, Albert Leentjens, Koen Schruers, Vivianne van Kranen-Mastenbroek, Veerle Visser-Vandewalle, and Yasin Temel were involved in the treatment (including the surgery) and data collection (during standard outpatient clinic follow-up). Anouk Smeets prepared the manuscript with important input from Linda Ackermans, Annelien Duits, and Albert Leentjens. All authors have revised and approved the final manuscript. Anouk Smeets and Linda Ackermans had complete access to the study data.

How to Cite this Article:

Smeets A.Y.J.M., Duits A.A., Leentjens A.F.G., Schruers K., van Kranen-Mastenbroek V., Visser-Vandewalle V., Temel Y., Ackermans L. 2018. Thalamic Deep Brain Stimulation for Refractory Tourette Syndrome: Clinical Evidence for Increasing Disbalance of Therapeutic Effects and Side Effects at Long-Term Follow-Up.
Neuromodulation 2018; 21: 197–202

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COMMENTS

The authors of this article report long-term results of thalamic DBS in Tourette syndrome (TS) – and the results are rather disappointing. Not only less than half of all patients (3 out of 7) experienced long-term improvement, but due to side effects and complications only 1 out of 7 continues using thalamic DBS for his TS symptoms. Interestingly enough, we had very similar experience in our practice where one of our three patients had remarkable and lasting symptomatic improvement, while two others also improved but to a much lesser extent, and in one of them the device had to be removed and then reinserted due to hardware erosion.

I applaud the authors for meticulous follow up of their patient cohort. I also appreciate the authors' honesty and candor in describing unsatisfactory results and admitting inability to obtain reliable long-term success. In fact, one may only hope that the TS DBS Registry and Database answers the questions of best surgical candidacy and most effective intervention, so the thousands of treatment-refractory and disabled TS patients worldwide receive a hope for cure or, at least, palliation of their symptoms.

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It is important for practitioners engaged in refining DBS for Tourette syndrome to understand its shortcomings and to work to improve approaches and outcomes.

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The authors report long-term follow-up of 7 patients who underwent medial thalamic DBS for Tourette's syndrome. As they note, their data set is incomplete - what can be extracted from the data is the following: 2 of the 7 patients continued to use thalamic stimulation, 2 patients were switched to anterior GPi stimulation with benefit, 2 patients were no longer using the device, and one patient who underwent GPe stimulation at another institution was lost to follow-up.

As the authors note, it is difficult to draw any conclusions from this retrospective analysis of a small number of patients, and larger collaborative studies, such as the TS International DBS Registry and Database, will be the best way to obtain data going forward. In comparison with other series and the initially reported registry data, it appears that this cohort was older (mean age 41) – could this indicate that younger patients do better with DBS, or merely that those younger patients' symptoms would have naturally improved without surgical intervention?

I commend the authors on their willingness to report these less-than rosy outcomes from the earliest series of Tourette DBS patients, and I encourage all centers performing DBS for TS to publish their long-term outcomes and to contribute to the International Registry.

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Comments not included in the Early View version of this paper.

