Deep Brain Stimulation for Essential Tremor: Aligning Thalamic and Posterior Subthalamic Targets in 1 Surgical Trajectory

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BACKGROUND: Ventral intermediate nucleus (VIM) deep brain stimulation (DBS) and posterior subthalamic area (PSA) DBS suppress tremor in essential tremor (ET) patients, but it is not clear which target is optimal. Aligning both targets in 1 surgical trajectory would facilitate exploring stimulation of either target in a single patient.

OBJECTIVE: To evaluate aligning VIM and PSA in 1 surgical trajectory for DBS in ET.

METHODS: Technical aspects of trajectories, intraoperative stimulation findings, final electrode placement, target used for chronic stimulation, and adverse and beneficial effects were evaluated.

RESULTS: In 17 patients representing 33 trajectories, we successfully aligned VIM and PSA targets in 26 trajectories. Trajectory distance between targets averaged 7.2 (range 6-10) mm. In all but 4 aligned trajectories, optimal intraoperative tremor suppression was obtained in the PSA. During follow-up, active electrode contacts were located in PSA in the majority of cases. Overall, successful tremor control was achieved in 69% of patients. Stimulation-induced dysarthria or gait ataxia occurred in, respectively, 56% and 44% of patients. Neither difference in tremor suppression or side effects was noted between aligned and nonaligned leads nor between the different locations of chronic stimulation.

CONCLUSION: Alignment of VIM and PSA for DBS in ET is feasible and enables intraoperative exploration of both targets in 1 trajectory. This facilitates positioning of electrode contacts in both areas, where multiple effective points of stimulation can be found. In the majority of aligned leads, optimal intraoperative and chronic stimulation were located in the PSA.

KEY WORDS: Deep brain stimulation, Essential tremor, Ventral intermediate nucleus of the thalamus, Posterior subthalamic area, Target planning

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The ventral intermediate nucleus (VIM) of the thalamus is an effective deep brain stimulation (DBS) target for essential tremor (ET).[1-3] Over time, however, a significant decrease in tremor suppression is found.[4-8] Hence, other targets were considered for stimulation, including the posterior subthalamic area (PSA).[9] The PSA is situated medial and ventral to the VIM and surrounded by the red nucleus (medial), subthalamic nucleus (STN; anterolateral), and medial lemniscus (posterior). It corresponds largely to Hasslers prelemniscal radiations, to the prerubral field or field H of Forel, and to the caudal zona incerta and contains the dentato-rubro-thalamic tract (DRT). In small studies, PSA DBS has shown better tremor control than VIM DBS.[10,11]

VIM and PSA can be stereotactically explored serially but can also be aligned in 1 electrode trajectory (Figure 1). We evaluated the possibility of aligning VIM and PSA in a series of ET patients undergoing DBS surgery, and

ABBREVIATIONS: **AC-PC,** anterior–posterior commissure; **CT,** computed tomography; **DBS,** deep brain stimulation; **DRT,** dentato-rubro-thalamic tract; **ET,** essential tremor; **MCP,** midcommissural point; **MRI,** magnetic resonance imaging; **PC,** posterior commissure; **PSA,** posterior subthalamic area; **STN,** subthalamic nucleus; **VIM,** ventral intermediate nucleus

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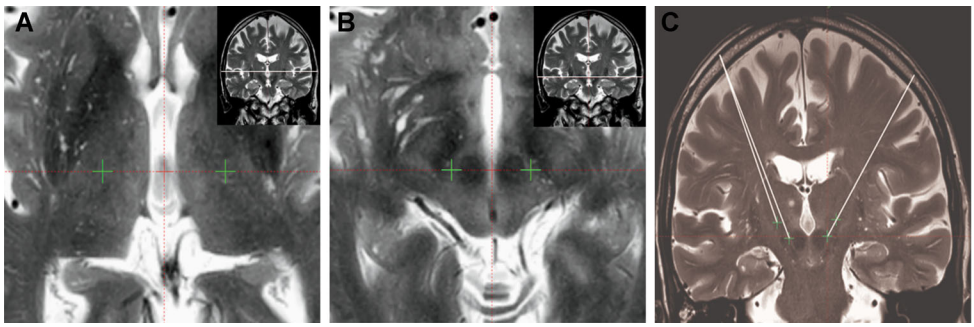

FIGURE 1. *VIM and PSA alignment in 1 patient.* **A** *shows an axial oriented 3-T T2-weighted image used for target planning. The 2 green crosses indicate left and right VIM targets (the right VIM target is represented by the left cross). Target coordinates (center of green cross) were 15 mm lateral, 8 mm anterior, and 2 mm superior, relative to the PC for both sides. In the right upper corner, a corresponding coronal oriented T2-weighted image is displayed; the white horizontal line indicates depth of the VIM targets.* **B** *Comparable design as shown in panel* **A**. *The 2 green crosses indicate left and right PSA targets. The PSA target was chosen medial to the posterior tail of the STN and lateral to the red nucleus at the level of the widest diameter of the red nucleus. Target coordinates (relative to the MCP) of the right PSA were 9.8 mm lateral, 5.2 mm posterior, and 4.6 mm inferior. Target coordinates of the left PSA were 10.9 mm lateral, 5.7 mm posterior, and 4.8 mm inferior. In the right upper corner, a corresponding coronal oriented T2-weighted image is displayed; the horizontal white line indicates depth of the PSA targets.* **C** *shows a coronal oriented 3-T T2-weighted image used for target planning. On the right hemisphere (left side of the brain) 2 separate trajectories are shown (white lines) using the same entry point to reach either VIM or PSA. The upper green cross indicates the VIM target, the lower the PSA target. On the left hemisphere, the VIM and PSA targets are aligned in a single trajectory. In order to achieve alignment, the entry point is situated more lateral compared to the separate trajectories displayed on the right hemisphere.*

analyzed the location of active contacts during long-term follow-up, concomitant tremor reduction, and side effects.

METHODS

Patients

Our center has performed VIM DBS since 1993.[4] Since 2000, we have applied intraoperative test stimulation below VIM when no tremor suppression is noted in VIM.[12] In 2010, we rationalized this approach by adding PSA exploration. We routinely inform patients about this step-wise operative DBS procedure. Up to 2012, this often resulted in performing 2 separate electrode trajectories. However, to minimize surgical risks and to prevent possible loss of satisfactory stimulation points determined in the previous trajectory, a single surgical trajectory for the exploration of both targets has preference. During the stereotactic planning of our 2010 to 2012 ET patients, we noted that both targets could be reached through 1 aligned trajectory when small angle adjustments were applied. The rationale for this technique was discussed with all ET patients undergoing DBS from August 2012, and all gave informed consent. Since we did not consider these angle adjustments as experimental, medical ethical committee approval was not sought.

Surgical Procedure

Patients underwent a preoperative frame-based 1.5-T magnetic resonance imaging (MRI; Siemens, Munich, Germany) or computed tomography (CT; Phillips, Best, The Netherlands). For MRI, axial T2-weighted and postgadolinium (Gd) volumetric axial T1-weighted sequences were acquired. In 5 patients additional preoperative axial 3-T T2-weighted MRI was available.

VIM target planning started with standard stereotactic coordinates relative to the posterior commissure (PC) on anterior–posterior commissure (AC-PC) aligned MRI: 15 mm lateral, 8 mm anterior, and 2 mm dorsal (Leksell Surgiplan, software version 10.0, Elekta Instrument AB, Stockholm, Sweden). The PSA target was chosen medial to the posterior tail of the STN and lateral to the red nucleus on AC-PC aligned axial T2-weigthed MRI at the level of the widest diameter of the red nucleus (Figure 1). Trajectory planning was done using the PSA as the primary target. We adjusted coronal and sagittal angles in order to accomplish a trajectory that traversed the VIM target. Planned trajectories were inspected to be precoronal, start on top of a gyrus, avoid ventricles, the caudate nucleus, and blood vessels. When alignment was judged not possible, VIM or PSA exploration was chosen based on the discretion of the neurosurgeon. Surgery was under local anesthesia. A macrostimulation electrode (Elekta) was used, except for 1 case with microelectrode recordings. Test stimulation was evaluated by applying monopolar stimulation in 2 mm steps, starting 6 to 8 mm above the VIM target. If effective tremor suppression was obtained in VIM, PSA was not explored. The DBS lead (model 3389 or 3387, Medtronic Inc, Dublin, Ireland or ActiveTip 0.5 mm interspace model St Jude Medical, St. Paul, Minnesota) was implanted so that trajectory points with the best therapeutic window were available. Lead placement was confirmed using fluoroscopy. Implantation of infraclavicular pulse generators was done under general anesthesia.

Patient Assessment and DBS Programming

Clinical notes were used and no additional visits were initiated. Initial programming was performed 10 to 14 d postoperatively, or postponed until tremor returned. The electrode contact with most

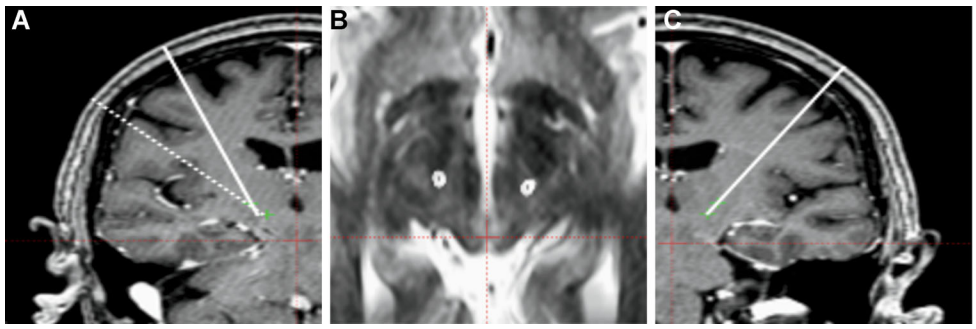

FIGURE 2. *Example of a patient in whom alignment of the VIM and PSA was not possible due to traversing of insular cortex.* **A** *shows a coronal oriented 1.5-T T1-weighted image of the right hemisphere used for target planning. The white line indicates the trajectory chosen for surgical exploration with the VIM as the target, and the white dotted line indicates the trajectory needed to align VIM and PSA target points. The entry point of the aligned trajectory is situated more lateral, which resulted in traversing the insular cortex and therefore was not chosen for surgical exploration. Intraoperative test stimulation in the VIM did not result in adequate tremor suppression, and test stimulation was therefore continued at multiples levels below VIM; the definitive electrode was implanted 8 mm deeper than VIM, ie in the posterior part of the STN.* **B** *Shows a midbrain section on axial oriented 1.5-T T2-weighted imaging and coregistered postoperative CT in the same patient. In the right midbrain (left midbrain section), the electrode artifact (white round dot) is located in the posterior STN region. Stereotactic coordinates of the electrode artifact were 11.1 mm lateral, 4 mm posterior, and 5.3 mm inferior relative to the MCP. This lateral position relative to the PSA resulted from the (more medial situated) entry point chosen for the VIM trajectory as shown in panel* **A**. **C** *Shows a comparable design to panel* **A** *for the left hemisphere. The white line indicates the trajectory chosen for surgical exploration with the VIM and PSA aligned in its course. Intraoperative test stimulation in the VIM did not result in adequate tremor suppression, and test stimulation was therefore continued at multiple levels below the VIM and into the tPSA; the definitive electrode was implanted 8 mm deeper than the VIM, ie in the PSA. Electrode implantation in the PSA is confirmed in panel* **B** *(right midbrain section). Stereotactic coordinates of the electrode artifact were 12.3 mm lateral, 4.5 mm posterior, and 5.1 mm inferior relative to MCP.*

optimal therapeutic window was chosen for chronic stimulation. The ET rating assessment scale was used to assess postural and intention tremor.[13] Tremor control was considered successful when complete tremor suppression (grade 0) or almost complete suppression (grade 1) was observed. Stimulation-induced side effects, including dysarthria and gait ataxia, were categorized into moderate or severe. Moderate side effects did not lead to disabilities in daily living, severe did. Most recent follow-up was used for evaluation.

Analysis of Neuroanatomical Location of Active Contacts

To categorize the neuroanatomical location of stimulation, we determined the location of the center of the active electrode contact (when multiple contacts were used, the interspace between active contacts was determined) on postoperative CT (1 or 2 mm slice thickness) coregistered with the preoperative magnetic resonance using Leksell Surgiplan (Elekta). The center of stimulation was classified as "VIM" when the active contact(s) were localized in or just below (=touching) the ventral thalamic border on T2-weighted coronal MRI, and as "PSA" when active contacts were localized deeper.

Data Analysis

Due to the exploratory nature of the study, data were analyzed descriptively. Numerical data are presented as mean ± standard deviation (range).

RESULTS

From 2012 until 2015, a total of 38 DBS leads were placed in 20 ET patients. There were 13 male and 7 female patients, age at surgery was 70 ± 10 (47-82) yr. In 3, we did not attempt VIM/PSA alignment due to sole availability of CT-imaging for the planning phase. Thus, we attempted aligning VIM and PSA targets in 1 surgical trajectory in 17 patients representing 33 planned trajectories (16 bilateral and 1 unilateral).

Alignment of VIM and PSA

Mean stereotactic coordinates of VIM were 15.0 ± 0.7 (14–17) mm lateral, 8.4 ± 0.5 (7.5–9.0) mm anterior, and 2.0 ± 0.1 (2.0–2.1) mm superior relative to the PC and 4.2 ± 0.9 (2.6–6.0) mm posterior relative to midcommissural point (MCP). Mean laterality from third ventricle was 11.6 ± 1.0 (10–13.5) mm. Mean stereotactic coordinates for PSA were 10.7 ± 0.9 (9.6–12.8) mm lateral, 6.7 ± 1.4 (4.9–10.9) mm posterior, and 4.0 ± 1.0 (2.0–6.7) mm inferior relative to MCP. Aligning PSA and VIM was achieved in 26 (79%) trajectories (15 patients). Average trajectory distance between VIM and PSA was 7.2 ± 1.0 (6.0–10.0) mm (Table). In 5 trajectories, alignment was not possible due to traversing of insular cortex (Figure 2), in 2 due to proximity of the entry point to a sulcus. In these 7 trajectories, VIM was

TABLE. Overview of Lead Placement, Tremor, and Stimulation Characteristics

Aligned	Hemisphere	Coronal/sagittal angle (degrees)	Delta VIM/PSA (mm)	Exploration	Intraoperative optimal target	Final target	Chronic stimulation	Postural tremor		Intention tremor		FU (mo)	Side effects dysarthria/gait ataxia
1	Left	26/70	8.5	VIM + PSA	PSA	PSA + 2	C1: PSA PSA –0.5 VIM + 8	4 →	0	3 →	0	43	–/–
	Right	39/78	8.5			PSA + 2	C2: PSA PSA –2.5 VIM + 6	3 →	0	3 →	0		
2	Left	29/57	9.5	VIM + PSA	PSA	PSA + 1	C3: PSA PSA –5.5 VIM + 4	2 →	0	2 →	1	38	–/M
	Right	30/66	10	PSA	PSA	PSA + 1	C3: PSA PSA –5.5 VIM + 4.5	3 →	0	3 →	2		
3	Left	40/74	7	VIM	VIM	VIM + 2	C1: VIM PSA –7.5 VIM + 0.5	1 →	0	1 →	0	35	–/–
	Right	–	6.5	VIM + PSA				0 →	1	0 →	1		
4	Left	34/70	7	VIM + PSA	PSA	PSA –3	C1: VIM PSA –5.5 VIM + 1.5	0 →	0	2 →	0	34	M/M
	Right	35/70	7	VIM + PSA	PSA	PSA –1	C1-C2: PSA PSA –4.5 VIM + 2.5	1 →	0	3 →	1		
5	Left	31/63	8.5	VIM + PSA	PSA	PSA –4	C0: PSA PSA –5.5 VIM + 3	0 →	0	1 →	1	32	–/–
	Right	30/59	8.5	VIM + PSA	PSA	PSA –4	C2-C3: VIM PSA –10.5 VIM –2	2 →	0	2 →	1		
6	Left	29/70	8.5	VIM + PSA	PSA	PSA + 0	C0: PSA PSA –1.5 VIM + 7	2 →	1	3 →	2	29	M/M
	Right	30/69	8.5	VIM + PSA	PSA	PSA –4	C1: VIM PSA –8 VIM + 0.5	3 →	2	4 →	3		
7	Left	25/63	8	VIM + PSA	PSA	PSA –4	C1: VIM PSA –6.5 VIM + 1.5	3 →	3	3 →	3	28	S/S
8	Left	35/67	6	VIM + PSA	PSA	PSA –2.5	C1: VIM PSA –5 VIM + 1	1 →	0	2 →	0	24	M/–
	Right	35/68	8	VIM + PSA	PSA	PSA –2	C1: PSA PSA –4.5 VIM + 3.5	0 →	0	3 →	1		
9	Left	30/66	7	VIM + PSA	PSA	PSA –2	C1: PSA PSA –4.5 VIM + 2.5	2 →	0	3 →	1	23	–/–
	Right	30/71	8	VIM + PSA	PSA	PSA –2	C1-C2: PSA PSA –5.5 VIM + 2.5	2 →	0	4 →	1		
10	Left	31/67	8	VIM + PSA	PSA	PSA + 2	C2: PSA PSA –2.5 VIM + 5.5	3 →	0	3 →	0	21	M/S
	Right	28/66	7.5	VIM + PSA	PSA	PSA + 1	C0: PSA PSA + 1.5 VIM + 8	3 →	0	3 →	2		
11	Left	31/74	6	VIM + PSA	PSA	PSA + 2	C3: VIM PSA –6 VIM + 0	2 →	0	2 →	2	17	–/S

TABLE. continued

Aligned	Hemisphere	Coronal/sagittal angle (degrees)	Delta VIM/PSA (mm)	Exploration	Intraoperative optimal target	Final target	Chronic stimulation	Postural tremor	Intention tremor	FU (mo)	Side effects dysarthria/gait ataxia
12	Left	40/75	8.5	VIM + PSA	PSA	PSA + 0	C1: PSA PSA –3.5 VIM + 5	2 → 0	2 → 0	13	M/–
13	Left	25/78	7	VIM + PSA	PSA	PSA –3	C1: VIM PSA –5.5 VIM + 1.5	1 → 0	2 → 0	11	– +/–
	Right	30/78	7	VIM + PSA	PSA	PSA –3	C2: VIM PSA –7.5 VIM + 0.5	1 → 0	2 → 1		
14	Left	23/81	6	VIM	VIM	VIM + 2	C0: VIM VIM + 1.5 PSA –4.5	3 → 0	4 → 0	5	–/–
	Right	27/80	7	VIM	VIM	VIM + 2	C2: VIM VIM –2.5 PSA –9.5	0 → 0	3 → 0		
15	Left	30/61	9.5	VIM + PSA	PSA	PSA + 2					

Not Aligned	Hemisphere	Coronal/sagittal angle (degrees)	Contraindication alignment	Exploration	Intraoperative optimal target	Final target	Stimulation	Postural tremor	Intention tremor	FU (mo)	Side effects dysarthria/gait ataxia
7	Right	25/62	Proximity to a sulcus	VIM	VIM	VIM + 2	C0: VIM VIM + 1.5	2 → 2	3 → 3	28	S/S
11	Right	22/61	Transinsular trajectory	VIM	Posterior STN	VIM + 8	C1: in between VIM/STN VIM + 4	3 → 0	4 → 2	17	–/S
12	Right	31/63	Proximity to a sulcus	PSA	PSA	PSA + 2	C1: PSA PSA –0.5	2 → 0	2 → 0	13	M/–
16	Left	31/69	Transinsular trajectory	PSA	PSA	PSA + 2	C1: PSA PSA –0.5	3 → 0	4 → 0	10	M/M
	Right	31/67		PSA	PSA	PSA + 3	C2: PSA PSA –1.5	3 → 0	4 → 1		
17	Left	21/66	Transinsular trajectory	VIM	VIM	VIM + 4	C2: VIM VIM + 0.5	3 → 0	4 → 1	5	M/–
	Right	22/68		VIM	VIM	VIM + 2	C2: VIM VIM –2.5	4 → 0	4 → 1		

The first column contains case numbers, divided as "aligned" (VIM and PSA aligned in 1 surgical trajectory) and "not aligned" (VIM and PSA were not aligned in 1 surgical trajectory) group. The second vertical column indicates the hemisphere of lead placement, "left" or "right." The third column indicates the coronal and sagittal trajectory angle. The fourth column indicates measured trajectory distance (dorsal–ventral plane, in millimeters) between VIM and PSA for the "aligned" group. For the "not aligned" group this column indicates contraindication for alignment. The fifth column indicates which area (VIM, PSA, or VIM + PSA) was explored during intraoperative stimulation. The sixth column indicates which area showed an optimal therapeutic window during intraoperative stimulation. The seventh column indicates at which depth the bottom contact point was placed with respect to either VIM or PSA coordinates. Numbers are expressed in millimeters, minus (–) meaning dorsal and plus (+) ventral to respective target. The eighth column indicates which contact point is used for stimulation during the most recent follow-up visit and its trajectory distance (dorsal–ventral plane, in millimeters) with respect to VIM and PSA coordinates. The ninth column indicates change in postural upper extremity tremor before surgery and during most recent follow-up visit. The tenth column indicates change in upper extremity intention tremor score. The left hemisphere corresponds with right upper extremity and vice versa. The "tremor research group ET rating assessment scale" (TETRAS) was used to assess pre- and postoperative postural and intention tremor. The eleventh column indicates number of months of follow-up. The twelfth column indicates whether stimulation induced dysarthria and/or gait ataxia were noted during most recent follow-up. Minus (–) meaning not present, "M" meaning moderate, and "S" severe.

#1 in the table: no test stimulation was performed in the second hemisphere because of exhaustion of the patient, and the second electrode was implanted in PSA mirroring the first electrode. #3 in the table: intraoperative right-sided test stimulation in 3 separate trajectories did not suppress tremor and only caused dysarthria and ataxia patient. Therefore, no definitive electrode was implanted on the right side. #15 in the table: surgery was aborted after left-sided electrode placement due to a hemorrhage in the area surrounding the electrode tip, causing intraoperative dysarthria and right-sided hemiparesis. It was decided not to implant the subcutaneous extension cable and pulse generator. C0 = contact point 0/bottom contact point, C1 = contact point 1, C2 = contact point 2, C3 = contact point 3, M = moderate, S = severe.

chosen as target in 4, and PSA in 3. Average coronal angle was 31 ± 4.7 (23–40) degrees for aligned trajectories, 23 ± 1.7 (21–25) degrees for nonaligned VIM trajectories, and 31 ± 0 (31–31) degrees for nonaligned PSA trajectories. Average sagittal angle was 70 ± 6.4 (57–81) degrees for aligned trajectories, 64 ± 3.3 (61–68) degrees for nonaligned VIM trajectories, and 66 ± 3.1 (63–69) degrees for nonaligned PSA trajectories.

Surgical Findings

In 3 aligned trajectories, tremor suppression in VIM was so successful that deeper exploration was not undertaken (Table). In 21 aligned trajectories, intraoperative tremor suppression obtained in PSA was better than in VIM. In 1 bilaterally aligned patient, no test stimulation was performed in the second hemisphere because of exhaustion, and the second electrode was implanted in PSA, mirroring the first electrode (#1 in the table). In another bilaterally aligned patient, no right-sided electrode was implanted because test stimulation only induced dysarthria and ataxia (#3). In 1 unilaterally left-sided aligned PSA-targeted patient, no pulse generator was implanted due to a hemorrhage. (#15).

In 3 out of 4 nonaligned trajectories targeted at VIM, successful intraoperative tremor suppression was observed. In 1, test stimulation was continued below VIM; the definitive electrode was implanted 8 mm deeper, in the posterior part of STN (Figure 2; #11). In all 3 nonaligned trajectories targeted at PSA, successful intraoperative tremor suppression was observed.

Neuroanatomical Location of Active Contacts

The center of chronic stimulation of the 21 PSA-targeted leads was in PSA for 13 leads, and in VIM for 8. Chronic stimulation of the single lead that ended up in the posterior part of the STN was located in between VIM and STN. For the 3 nonaligned leads targeted at PSA, chronic stimulation was in PSA. Chronic stimulation of the 6 leads targeted at VIM was in VIM.

Effectiveness of Tremor Alleviation and Side Effect Profiles

Tremor scores at baseline and during follow-up at 23 ± 12 (5-43) mo are listed in the Table. Successful tremor control was achieved in 24 out of 31 contralateral body sides (75%), or 11 of 16 patients (69%). Successful tremor control was comparable for aligned and nonaligned leads (75 vs 71%, respectively). For aligned leads, chronic stimulation in PSA resulted in slightly better tremor control than chronic stimulation in VIM (81% vs 69%, respectively). In 3 contralateral body sides (2 patients) of aligned PSA leads, successful tremor control was only achieved with stimulation during the first 3 to 6 postoperative months.

Stimulation-induced side effects are listed in the Table and **Supplemental Digital Content**. Seven patients (44%) experienced gait disturbances. Ten of their 14 leads were aligned leads. Eight active contacts of these 14 leads were located in the PSA. Nine patients (56%) experienced stimulation-induced dysarthria, preceded in 6 of them by intraoperative dysarthria during test stimulation. Twelve of their 18 leads were aligned leads. Active contacts of these 18 were equally distributed among VIM and PSA. We could not deduct whether side effects in bilaterally implanted patients were attributable to left- or right-sided stimulation. In 3 patients with leads covering both the VIM and PSA (1 patient bilateral and 2 unilateral), severe stimulation-induced dysarthria or gait ataxia could not be markedly reduced by switching between PSA and VIM.

Surgical Complications

In 4 patients, a subcortical hemorrhage occurred along the electrode trajectory. Three were localized in the left hemisphere and induced dysphasia in all and additional hemiparesis in 1. The 1 in the right hemisphere initially occurred subclinical, but induced left upper extremity weakness 1 wk after implantation due to a large area of edema surrounding the hemorrhage. All hemorrhages occurred in aligned trajectories. Complete recovery of symptoms was noted in 3 patients. No infection or malfunction of implanted material was noted.

DISCUSSION

Aligning VIM and PSA

Aligning VIM and PSA in 1 surgical trajectory during DBS for ET was implementable in the majority of cases. It enabled intraoperative exploration of both targets in order to determine which location offered the optimal therapeutic window, thereby preventing a second trajectory and possible loss of satisfactory stimulation points determined in the previous trajectory. In many cases, both VIM and PSA could be covered by the definitive electrode. This provides an advantage, as it is not yet clear which point in (or between) these areas provides the best point of stimulation for ET. Also, it potentially avoids the need for second surgery.[14,11,15]

Aligned trajectories are possibly in closer relationship with the DRT, which is considered an optimal target of stimulation, although this hypothesis remains to be verified by diffusion tensor imaging MRI.[16] Simply advancing an electrode trajectory when targeting VIM will make the electrode enter the subthalamic area in a more lateral position than the PSA/DRT, such as the posterior part of the STN (Figure 3).[17] This may results in side effects due to stimulation of nearby internal capsule fibers. Moreover, as individual trajectory angles differ, final electrode position in the PSA will be less predictable.[17,18]

Chang et al (2013)[15] inserted electrodes containing contacts in both VIM and PSA in 5 patients. No superiority of VIM or PSA was found. In accordance with our findings, they concluded that targeting both targets in one trajectory is useful as patients can have most benefit from either VIM or PSA stimulation.

Comparison Between VIM and PSA

Adequate tremor suppression without severe side effects was achieved in 69% of patients through stimulation of the VIM or

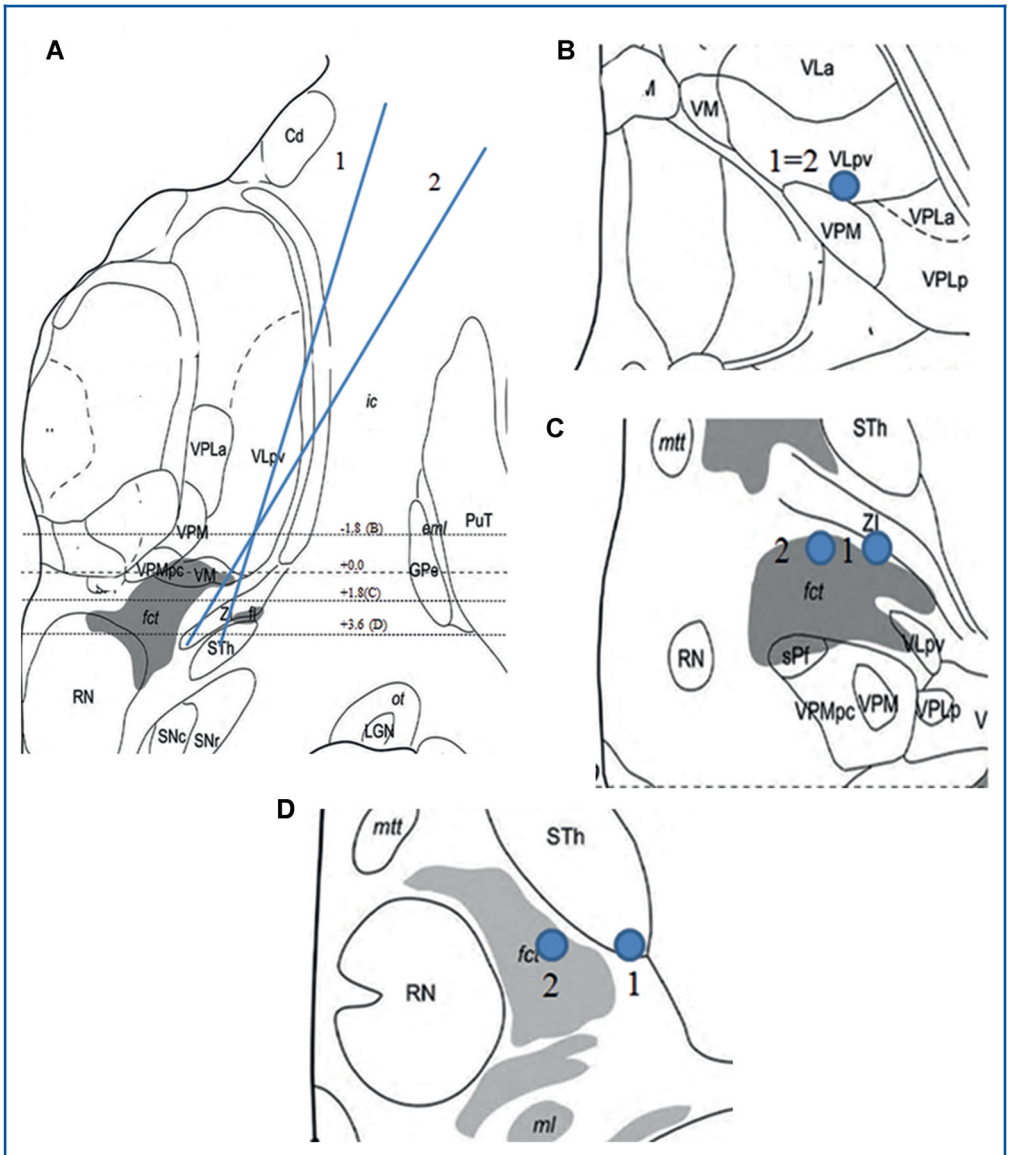

FIGURE 3. *Trajectory courses with VIM/PSA alignment and solely VIM targeting displayed on coronal and axial oriented sections of stereotactic brain atlas illustrations.* **A** *Shows a coronal oriented brain atlas section covering diencephalic, thalamic, and subthalamic structures with 2 trajectory courses displayed. Trajectory labeled 1 is planned with VIM as primary target, trajectory labeled 2 is planned with the VIM and PSA aligned. Alignment of the VIM and PSA results in a more lateral situated entry point, and in a more medial situated ending (target) point. Four horizontal dotted lines each represent an individual depth relative to the PC (represented by 0.0 line). Numbers above each line indicate the specific depth. Letters* **B, C,** *and* **D** *above individual lines correspond to* **B, C,** *and* **D** *section of the figure, respectively. These 3 panels each show an axial brain atlas section covering thalamic and/or subthalamic structures with both trajectory 1 and 2 displayed.* **B** *shows an axial section at 1.8 mm dorsal relative to the PC. The blue dot represents the electrode trajectory. Notice that 1 dot represents both trajectories, as at this depth trajectories coincide in their course (1 = 2). This occurs at the level of target depth for the VIM, and is 14.0 mm lateral and 7.0 mm anterior relative to the PC.* **C** *shows an axial slice at 1.8 mm ventral relative to the PC. Trajectory 2 follows a more medial course relative to trajectory 1, which brings it in closer relationship with (anterior area of) the faciculus cerebellothalamicus. This site is considered a better stimulation site for tremor control in ET than the more lateral area covered by trajectory 1. Trajectory 1 is situated 11.0 mm lateral and 8.0 mm anterior relative to the PC. Trajectory 2 is situated 13.0 mm lateral and 8.0 mm anterior relative to the PC.* **D** *shows an axial section at 3.6 mm ventral relative to the PC. More dorsal trajectory course increases the medial course of trajectory 1 relative to trajectory 2. Trajectory 1 is in close relationship with the fasciculus cerebellothalamicus and ventral ZI, which are considered optimal areas for tremor control. Trajectory 1 is in close relationship with posterolateral STN, which is known for tremor suppressing effects,*

FIGURE 3. *Continued.*
general not considered an optimal area of stimulation for ET. Trajectory 1 is in close relationship to the internal capsule fibers. Stimulation of these fibers could induce unwanted effects, for example muscle contractions. Trajectory 1 is situated 10.0 mm lateral and 6.5 mm anterior relative to the PC. Trajectory 2 is situated 12.5 mm lateral and 6.5 mm anterior relative to the PC. VPLa, ventral posteral lateral thalamus; Cd, caudate nucleus; VPM, ventro posterior median thalamus; VM, ventro median thalamus; fct, fasciculus cerebellothalamicus; ZI, zona incerta; Gpe, globus pallidus externus; RN, red nucleus; Pu, putamen; ic, internal capsule; mlt, medial longtidunal tract. Atlas illustrations adapted with permission from Stereotactic Atlas of the Human Thalamus and Basal Ganglia by A. Morel.[29]

PSA, comparable to the literature.[8,19-21] Intraoperatively, PSA stimulation offered superior tremor control compared to VIM in 88% of aligned trajectories. Chronic stimulation included the PSA or the area just above the PSA in the majority of cases, supporting the rationale of planning surgical trajectories that include the area below the VIM.

Dysarthria and gait ataxia were noted for both VIM and PSA stimulation. Differentiation between effects of test stimulation and edema due to electrode introduction was occasionally challenging. In 33% of patients, stimulation-induced dysarthria was not preceded by dysarthria during test stimulation, indicating that this is not a reliable predictor for chronic effects. Gait ataxia occurred as gradual decline, both with or without preexisting balance difficulties. Occurrence of stimulation-induced side effects are in line with recent reports.[14,22-24] When severe side effects occurred (in 3 of our patients), different stimulation settings offered no satisfactory therapeutic window. It is unclear how side effects are exactly induced and which patients are at risk.[25] A complex relation between stimulation, microlesion, edema, and disease-related factors is assumed.[22,26,27] Further exploration is essential in order to optimize VIM and/or PSA DBS in ET.

Surgical Complications

Coronal trajectory angles in our aligned leads were more lateral in comparison with VIM targeting described in literature.[15] One potential disadvantage is a possible closer relationship with frontal language and motor areas. Peri-electrode edema or hemorrhage could induce symptoms such as central facial palsy and dysphasia, as occurred (transiently) in 4 of our patients (24%). This percentage is higher than reported in the literature ,[9] and higher than our own previous experience: From 1994 until 2012, 2 symptomatic hemorrhages occurred among 55 ET patients (4%). Whether hematomas occurred during introducing/advancing the macrostimulation electrode or during definitive electrode placement is unclear. Postoperative reassessment of electrode trajectory did not reveal traversing blood vessels. Whether the high occurrence can be explained by the trajectory course remains speculative. Sagittal angles were comparable between groups.

Limitations

The current study has several limitations. First, we did not perform a (blinded) group comparison between VIM and PSA stimulation. Second, follow-up differed between cases. Third, the exact interrelationship between electrode contacts and DRT was not possible to determine due to the unavailability of diffusion tensor imaging MRI on Leksell Surgiplan (Elekta). Fourth, we chose to categorize the center of stimulation as "VIM" or "PSA," while recognizing that such dichotomous division may be arbitrary for such adjacent and interconnected areas. We considered adding an "in between area" for expressing contact localization between VIM and PSA, but we thought this to complicate the interpretation and applicability of the results.

CONCLUSION

Alignment of VIM and PSA for DBS in ET enables intraoperative exploration of both targets in 1 single trajectory. This facilitates optimal positioning of electrode contacts in these adjacent areas, where multiple optimal points of stimulation can be found. It allows for a clinical trial comparing the efficacy of tremor suppression between both targets employing 1 aligned electrode.[28] In the current series, optimal intraoperative and chronic stimulation were located in the PSA in the majority of aligned leads. It offered limited benefit when severe stimulation-induced side effects occurred. The more lateral entry of the aligned trajectory course could be situated closer to frontal language and motor areas, which are at risk when inducing peri-electrode edema or hematoma.

Disclosures

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COMMENT

The authors detail a technique for implantation of a DBS electrode for essential tremor targeting both the ventral intermediate nucleus (VIM) and the posterior subthalamic area (PSA), the goal of which is to improve the yield of successful implantation during a single procedure. For the trajectories that are possible (some were excluded due to anatomical barriers) this is an elegant technique to improve the yield and efficiency of implantation for essential tremor, mainly because there would be no need for a second trajectory and because there would be a reduction in operative time and possibly a repeat operation. There is controversy between the targets, because some studies report better efficacy of PSA DBS compared to VIM DBS while others do not. This small series seemed to suggest better efficacy of PSA over VIM (81% vs 69% tremor control). Unfortunately, the study suggested a higher rate of complications with 56% of patients experiencing dysphasia versus 33% in a series published by Blomstedt et al (reference 9 in the article). This could be related to the known complications associated with implantation in PSA and just a random upswing since the number of patients in the study is small. However, it could be related to the lateral entry angle used to align the 2 different targets. We agree with the authors that this should be studied further in a more controlled prospective study. If a larger controlled study shows no difference in complication rates this may become the preferred method for implantation in patients where aligned trajectories are feasible.

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