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Stimulation-induced side effects in the posterior subthalamic area: Distribution, characteristics and visualization

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ABSTRACT

Objective: The posterior subthalamic area (PSA) is an emerging but relatively unexplored target for DBS treatment of tremor. The aim of the study was to explore the area further by evaluating the spatial distribution and the characteristics of stimulation-induced side effects in this area.
Methods: Twenty-eight patients with essential tremor (ET) implanted with 33 DBS electrodes were evaluated concerning stimulation-induced side effects by testing each contact separately one year after surgery. The location of the side effects were plotted on axial slides of the Morel Stereotactic Atlas and a 3-dimensional model of the area for visualization was created.
Results: Visualization of the contacts eliciting stimulation-induced side effects demonstrated that identical responses can be elicited from various points in the PSA and its vicinity. The majority of contacts inducing muscular affection and cerebellar symptoms, including dysarthria, could not be attributed to an effect on the internal capsule. Paresthesias, affecting various body parts were elicited throughout the area without a clear somatotopic pattern.
Conclusion: Stimulation-induced side effects in the PSA and its vicinity were difficult to attribute to certain anatomical areas as the same response was induced from various locations. Therefore, this study could not provide a meaningful somatotopic map with regard to stimulation-induced side effects in the PSA.

1. Introduction

Deep brain stimulation (DBS) is an established treatment for essential tremor (ET), Parkinson's disease (PD), and other movement disorders. Currently, the subthalamic nucleus (STN) is the target of choice in PD and the ventral intermediate nucleus of the thalamus (Vim) in ET.

A number of publications have shown that many patients operated with Vim DBS actually achieve the best effect from contacts located below the thalamus in the posterior subthalamic area (PSA), including the zona incerta (Zi) and the prelemniscal radiation (Raprl) [1–4]. Several recent studies have further suggested that the PSA might be a more efficient target than the Vim in the treatment of ET [5–9] and promising results have been reported regarding PSA DBS in PD [9–13].

The PSA is really not a new target, but can be described more properly as a "forgotten" target, as thousands of patients were operated upon with subthalamotomies in this area during the lesional era. [5] It is, however, a new target for DBS, and further evaluation of the treatment and the area itself is needed. In this perspective it is important to investigate the panorama of stimulation-induced side-effects as this might differ from other targets in the proximity, such as VIM and the STN. It is further of importance to investigate the anatomical distribution of these side effects, in order to evaluate their possible localizing value for intraoperative macrostimulation. Considering the above, we evaluated the stimulation-induced side effects in relation to the anatomical location in patients with ET and PSA DBS.

2. Materials and methods

Twenty-eight consecutive patients with ET who underwent implantation of, in total, 33 DBS leads in the PSA from 2004 to 2009 were analyzed regarding stimulation-induced side effects. Twenty-four of the electrodes were on the left side and 9 on the right. Nineteen (67.9%) of the patients were men and the mean age at implantation was 60.5 (±15.3 years, range 25–79). The surgical technique has been described previously. [14] The operations were frame-based stereotactic implantations of the DBS electrode 3387 or 3389 (Medtronic, Minneapolis, MN, USA) in the PSA. Preoperative

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Table 1
Categorization and frequency of appearance of the encountered stimulation-induced side effects. The mean coordinates in the three stereotactic axis's are given. Values are mean (SD ±) (range).

Side-effect	No	*X*	*Y*	*Z*	Amplitude (V)
1.Paresthesias	219				
Hand	75	11.7 ± 1.5 (8.6–15.4)	−6.3 ± 1.6 (−9.8– −1.7)	−2.3 ± 2.7 (−7.1–3.8)	1.7 ± 0.9 (0.3–4)
Face	71	11.6 ± 1.6 (8.4–16.0)	−6.3 ± 1.9 (−1.2 to −10.2)	−2.5 ± 2.6 (−7.6–4.0)	2.2 ± 1.0 (0.8–4.5)
Arm	32	11.2 ± 1.4 (8.4–14.5)	−6.4 ± 1.8 (−9.4 to −1.8)	−3.1 (±2.2) (−6.0–1.4)	2.0 ± 0.8 (0.3–3.6)
Leg	39	11.8 ± 1.3 (9.2–15.0)	−6.5 ± 1.6 (−2.4 to −8.8)	−3.6 ± 2.5 (−7.9–3.4)	2.1 ± 1.1 (0.6–4.5)
2. Dizziness	32	11.8 ± 1.5 (9.5–15.4)	−6.0 ± 1.5 (−9.1 to −1.7)	−2.4 ± 2.6 (−7.9–3.8)	3.2 ± 0.8 (1.3–4.5)
3. Blurred vision	26	11.8 ± 1.8 (8.4–15.0)	−5.7 ± 1.7 (−8.8 to −2.3)	−1.3 ± 2.8 (−6.3–4.0)	3.2 ± 0.7 (1.5–4.2)
4.Muscular affection	19	12.7 ± 1.7 (10.3–16.0)	−6.0 ± 1.8 (−9.8 to −2.4)	−2.6 ± 2.6 (−7.9–2.0)	2.9 ± 0.8 (1.5–4.5)
5. Dysarthria	15	12.4 ± 2.1 (9.3–16.0)	−5.2 ± 1.5 (−7.1 to −1.9)	−0.9 ± 2.6 (−5.2–3.4)	3.2 ± 0.6 (1.8–4.1)
6.Ataxia/dysmetria	13	11.3 ± 1.2 (9.2–13.2)	−5.4 ± 1.8 (−7.2 to −1.7)	− 2.4 ± 3.0 (−6.8–3.8)	3.0 ± 0.9 (2–4.5)
7. Diplopia	4	9.4 ± 1.3 (8.4–11.3)	−5.1 ± 2.6 (−7.2 to −1.8)	−3.7 ± 2.2 (−1.5 to −6.3)	3.3 ± 0.2 (3–3.6)
8.Ptosis	2	12.5 (12.1–12.9)	−6.8 (−5 to −8.5)	−2.0 (−0.7 to −3.2)	3.6 (3.3–3.9)
9.Hyperhidrosis	1	11.6	−6.1	−4.4	3.0
Total	331				

stereotactic 1.5 Tesla MRI and postoperative CT were performed. The target was identified anatomically as slightly posterior and medial to the posterior tip of the subthalamic nucleus (STN) at the horizontal level of the maximal diameter of the red nucleus. The procedures were performed under local anesthesia and the effect and side effects were evaluated using macrostimulation through the permanent electrode. No microelectrode recording was made.

The total Essential Tremor Rating Scale (ETRS) score was improved from 43.9 ± 11.5 preoperatively to 18.4 ± 11.5 on stimulation 1 year postoperatively. As regards upper extremity tremor and hand function, ETRS items 5/6 and 11–14, the improvement in the group was 89% on the treated side. The clinical results have previously been presented in 21 of these patients [15].

2.1. Evaluation

Each contact of the implanted electrode was evaluated in a standardized fashion one year after surgery using monopolar stimulation, a pulse width of 60 μsec and a frequency of 145 Hz. The amplitude was gradually increased up to 4.5 V, or less if the patient experienced intolerable side effects. The side effects were recorded at the amplitude at which they first appeared and were categorized according to Table 1. The Framelink® planning station (Medtronic, Minneapolis, MN, USA) was used for target planning and evaluating the location of the electrodes. After fusion of the pre- and postoperative images, the coordinates were calculated for each contact in relation to the midcommisural point (MCP), and further in relation to the posterior tip of the STN at the level of the maximal diameter of the red nucleus (pSTN).

2.2. Visualization

All contacs were plotted on the stereotactic atlas of Morel and a 3D atlas was created based on the axial images of this atlas (Figs. 2 and 3) [16]. Each side effect was visualized with a spherical 3D object (radius 0.3 mm) which was color-coded according to the type of side effect (Figs. 1 and 2). Initially spheres with a diameter proportional to the voltage at which the side effect occurred were used. This did however prove to be of limited value,

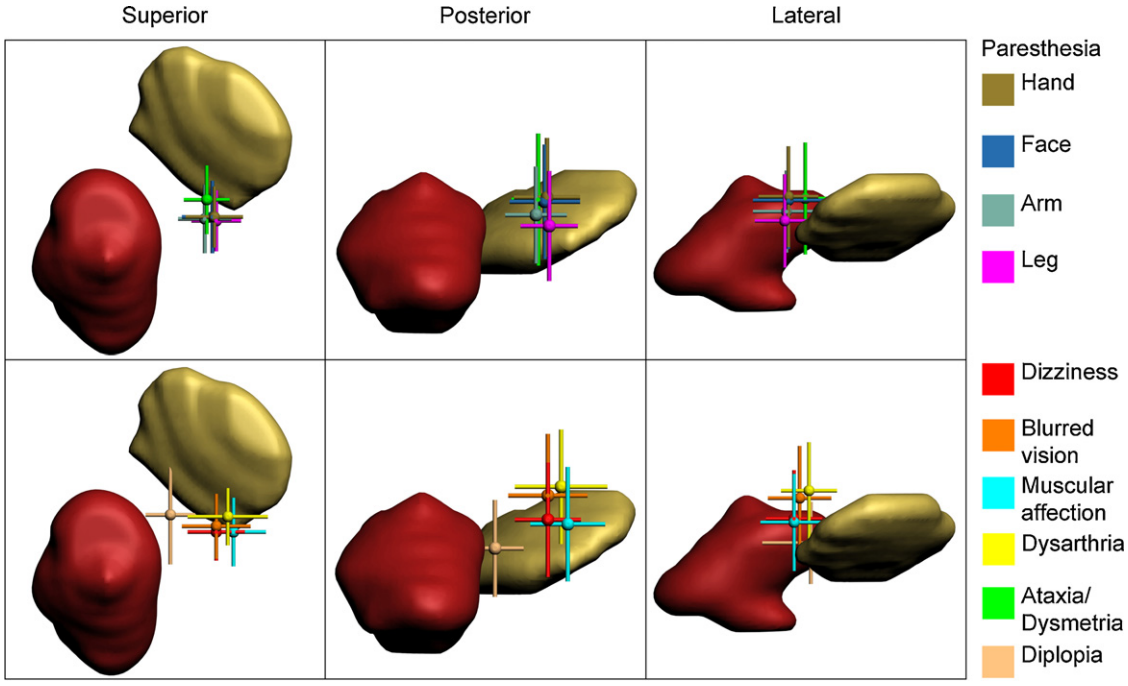

Fig. 1. A 3D reconstruction of the area outlined medially by the red nucleus (RN), and anterolaterally by the STN. The spheres demonstrate the mean location for each of the stimulation-induced side effects. The bars show one standard deviation for these locations in two axes in each view.