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LETTER TO THE EDITOR - FUNCTIONAL

Deep brain stimulation after previous gamma knife thalamotomy of the Vim for essential tremor is feasible! Clinical, electrophysiological and radiological findings

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Dear Editor,

We have read with great interest the recent paper by Oertel et al. [5], reporting the case of a patient with tremor-dominant Parkinson's disease, who benefited from double-site target [ventro-intermediate nucleus (Vim) and subthalamic nuleus] simultaneous stimulation after incomplete improvement from bilateral DBS of the Vim.

We also encountered an interesting case in our practice of a patient who had all possible remedies (medication, Gamma Knife thalamotomy and deep brain stimulation) for essential tremor (ET). We report the clinical, electrophysiological and neuro-imaging details.

A right-handed, 71-year-old male, suffering from familial ET since age 11, presented a drug-resistant hand tremor with right predominance and functional impairment. Initial Gamma Knife (GK) thalamotomy of the left Vim was performed. Before final target definition, fractional anisotropy was used to visualize the internal capsule (Fig. 1, A1). The target was the left Vim, defined using the quadrilate of Guiot, named after the physician who initially described the Vim as an electrophysiological concept together with Albe-Fessard [2] (Fig. 1, A2) [9]. Isodoses of 90 and 15 Gy were displayed, the former as a dose limit received by the internal capsule (Fig. 1, A3 and A4) after additional beam channel blocking [9]. We used a single 4-mm collimator and 130 Gy at the 100% isodose [3, 9]. Stereotactic radiosurgery was performed using the Leksell Gamma Knife Perfexion™ (Elekta Instruments, AB, Sweden).

The tremor improved dramatically 6 months later and further relapsed after 20 months. Magnetic resonance imaging (MRI) showed the presence of a small contrast enhancement (CE) surrounding a hypodense T1 necrotic core, corresponding to the GK targeting. When coregistred with the dosimetry planning data, this corresponded to a 90-Gy isodose line, as previously reported by Régis et al. [7] (Fig. 1, B to E). Compared to the previous follow-up MRI (when clinically alleviated), both the necrotic core and CE were diminished in size. Three-Tesla MRI diffusion imaging data displayed, after fully automated segmentation of the thalamic nuclei [1], that a ventro-lateral ventral cluster (corresponding to the Morel nomenclature [4]) was contained inside the CE area, in the ventral position, having anatomical relevance (Fig. 2).

A bilateral deep-brain stimulation (DBS) procedure was indicated after multidisciplinary discussion. For the left side,

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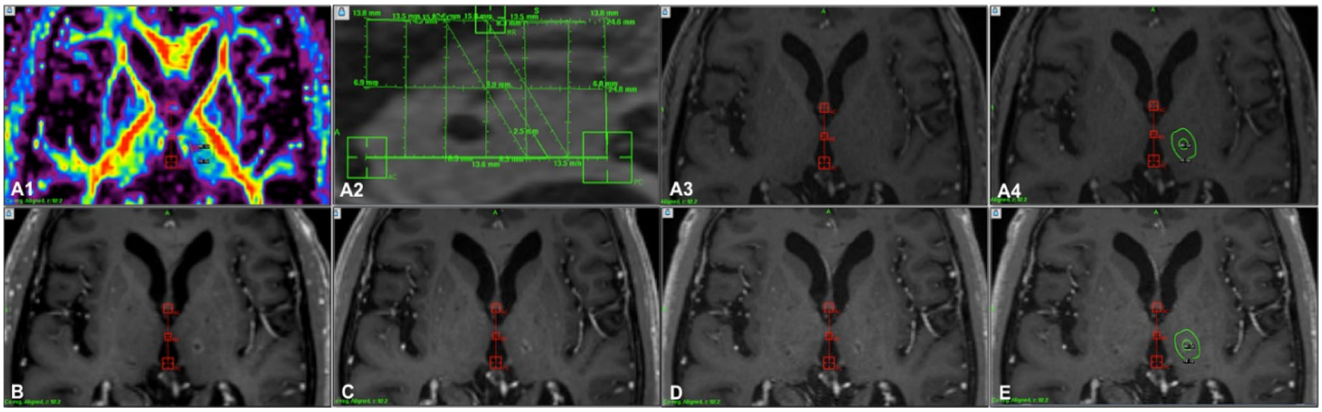

Fig. 1 Targeting of the Vim for the GKS procedure: diffusion tensor imaging (fractional anisotropy) for visualization of the internal capsule so as to adapt the dose gradient toward the pyramidal tract (A1), the quadrilatere of Guiot (A1), axial image without projection of dosimetry (A3) and with the former (A4), by displaying isodoses of 90 and 15 Gy. Follow-up images after GKS at 6 (B), 12 (C) and 20 months without (D) and with (E) the superposition of GKS dosimetry

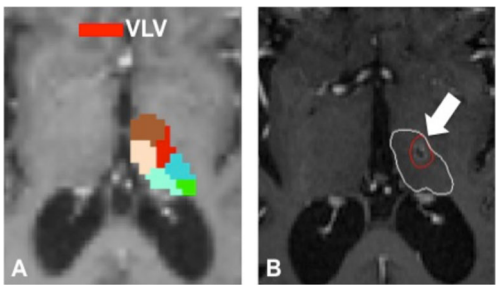

Fig. 2 Automated segmentation of seven clusters of thalamic nuclei by the methodology developed by Elena Najdenovska et al., with the ventro-lateral ventral (VLV) cluster displayed in red (A). The former contains the superimposed contrast-enhancement area, as corresponding to the GKS targeting and showing anatomical relevance

previously treated with GK, we aimed at stimulating the vicinity of the preexisting lesion. Intraoperative microrecording showed that when the left and right sides were compared, the signal root mean square signifying the neuronal noise (17.4 versus 42.0 μV, $p < 0.001$), single unit amplitude (120 versus 248 μV, $p < 0.001$) and single unit frequencies (10.6 versus 24.6 Hz, $p < 0.05$) were significantly higher on the right side (not treated by GK) compared to the combination of all left-side recordings (Fig. 3, A, B, C). In this sense, the center of the CE-visualized lesion on MRI was silent (no cells) and was surrounded by an area of normally active neurons. However, there was a clear difference in terms of potentials of action between the left (previous GK) and right (no previous GK) sides, raising the question whether new or surviving cells were present on the left. The final left target was centered on the antero-lateral side of the previously visible GK thalamotomy; the delta in x, y and z compared to the GK target position was 0.6, 0.2 and 2.5 mm, respectively. The delta between both the left and right DBS electrode tips in y and z was 0.3 and 6.8 mm, respectively (Fig. 4, B); for a trajectory of 3–4 mm, no cells were recorded on the left, corresponding to the necrotic area, as visualized on the follow-up MRI.

The patient had immediate and complete bilateral clinical alleviation after DBS. Three days after the procedure, he presented with dysarthria and left hemisyndrome due to right anterior choroidal artery stroke (Fig. 4, C). Therapeutic anticoagulation treatment was reintroduced with further disappearance of symptoms a few hours later. Left tremor did not recur, while right Vim DBS was turned off because of the described effects of right anterior choroidal artery stroke.

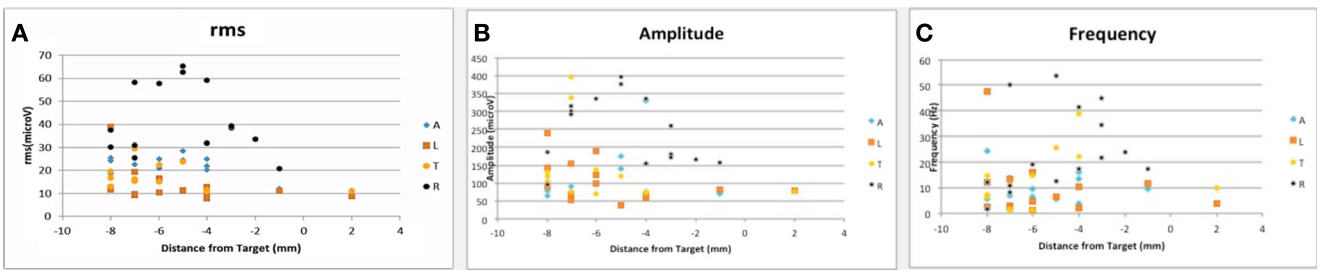

Fig. 3 (A) Signal root mean square recorded on the anterior, lateral and target tracks on the left side (colored) and the right side (black); please note that the signal rms was higher on the right side. (B) Single unit amplitude recorded on the anterior, lateral and target tracks on the left side (colored) and the right side (black); please note that no single units were recorded between 3 and 2 mm above the left target. (C) Single unit frequency recorded on the anterior, lateral and target tracks on the left side (colored) and the right side (black)

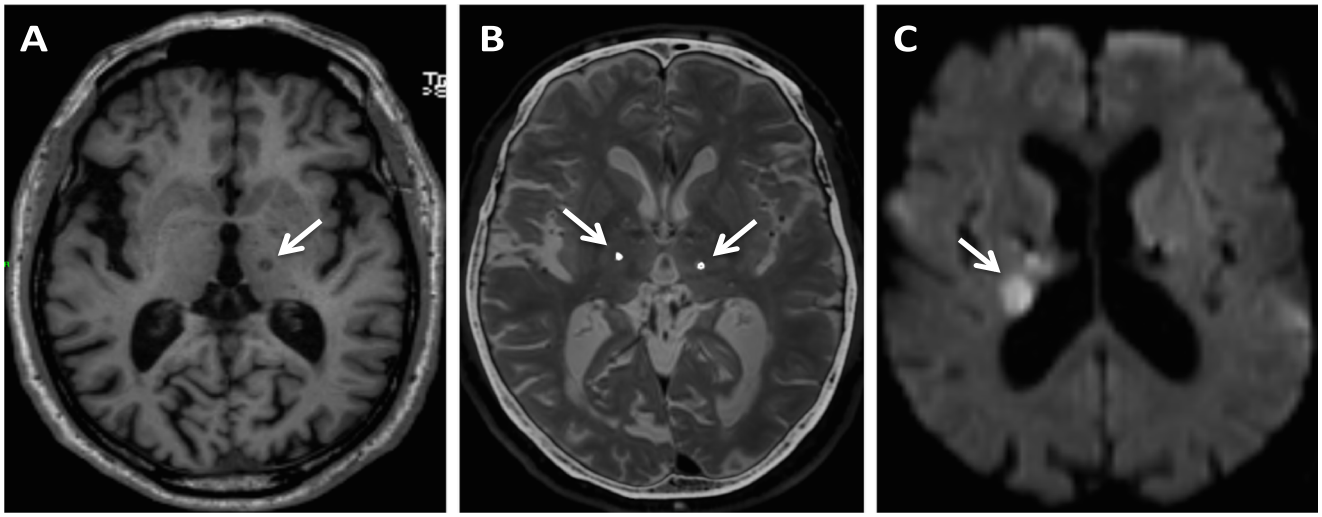

Fig. 4 (A) T1w brain MRI, displaying the left thalamotomy (arrow). (B) T2w brain after the DBS procedure, with the tip of both electrodes (arrows). (C) Diffusion brain MRI, with the right anterior choroidal artery stroke (arrow)

Complete disappearance of the right tremor was maintained 31 months after DBS.

In conclusion, electrophysiological findings suggested functional reorganization at the periphery of the necrotic core visualized on the follow-up MRI after GK. Consequently, this peripheral area containing neuronal activity most probably responds to DBS, although is not identical on both sides, but with a final identical clinical effect. Deep-brain stimulation after GK thalamotomy, aiming at a target close to the previous lesion, is possible and can lead to tremor suppression with a durable effect. The analysis of the electrophysiological findings in this unique case helps to better understand the functional neuronal reorganization after GK thalamotomy. The real cause of a delayed recurrence of tremor after a previously successful GK thalamotomy remains unknown. Both our data and those few from previously published reports [6, 8] suggest a clear reorganization of the neuronal system inside (accounting for the initial effect) and at the periphery of the necrotic lesion (probably accounting for the late relapse). Although incomplete knowledge exists on this subject, electrophysiology clearly confirms this functional reset of the connectivity patterns. Further cases need to be analyzed to clearly understand the intimate mechanism of these complex processes.

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Compliance with ethical standards

Conflict of interest None.

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