

Thalamic deep brain stimulation in the treatment of essential tremor

Leczenie drżenia samoistnego metodą głębokiej stymulacji wzgórza

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Abstract

Background and purpose: Quality of life can be severely impaired by essential tremor (ET) being the main cause of the patient's disability. The authors present a group of ET patients treated with deep brain stimulation of the ventral intermediate nucleus of the thalamus (Vim DBS). The aim of the study was to evaluate the efficacy and safety of Vim DBS in the treatment of ET.

Material and methods: Between 2006 and 2009, 8 female and 10 male ET patients were treated with Vim DBS. Mean age at implantation was 63 ± 15 years. ET lasted from 4 to 30 years (mean 12 years). Clinical condition of the group was evaluated before surgery and 3 months after implantation with spirometry (spiral drawings), the modified Fahn (Tremor Rating Scale, TRS) scale, and the modified ADL (Activity of Daily Living) scale. The Vim was localized with CT and MRI. The procedures of implantation were performed under local and general anaesthesia. A bilateral procedure was performed in 11 cases and a unilateral procedure was performed in 7 cases.

Results: The therapeutic effect of DBS was maintained at the follow-up in the third month following surgery. Mean contralateral limb tremor reduction was 79%. Head tremor reduction was reported by 75% of patients in the bilateral Vim DBS subgroup and 50% of patients in the unilateral Vim DBS subgroup. Mean ADL score improved by 61%.

Streszczenie

Wstęp i cel pracy: Drżenie samoistne (DS) może w znaczący sposób obniżyć jakość życia chorych, będąc niejednokrotnie przyczyną ich inwalidztwa. Autorzy przedstawiają grupę chorych na DS leczonych metodą głębokiej stymulacji jądra brzuszno-pośrodkowego wzgórza (*nucleus ventralis intermedius thalami deep brain stimulation* – Vim DBS). Celem pracy była ocena skuteczności i bezpieczeństwa leczenia DS metodą Vim DBS.

Materiał i metody: W latach 2006–2009 metodą Vim DBS leczono 8 kobiet i 10 mężczyzn chorych na DS. Średni wiek chorych w dniu operacji wynosił 63 ± 15 lat. Czas trwania choroby wahał się pomiędzy 4 a 30 lat (średnio 12 lat). Stan pacjentów oceniano przed zabiegiem chirurgicznym oraz 3 miesiące po zabiegu z wykorzystaniem spirometrii (rysowania spirali), zmodyfikowanej skali Fahna (*Tremor Rating Scale* – TRS) oraz zmodyfikowanej skali ADL (*Activity of Daily Living*). W celu lokalizacji jądra brzuszno-pośrodkowego wzgórza wykonywano tomografię komputerową oraz rezonans magnetyczny. Zabiegi przeprowadzono w znieczuleniu miejscowym i ogólnym. U 11 pacjentów elektrody wszczepiono obustronnie, a u 7 pacjentów – jednostronnie.

Wyniki: Efekt terapeutyczny utrzymywał się po inicjacji stymulacji głębokiej w trzymiesięcznej obserwacji u wszystkich chorych. Stwierdzano zmniejszenie drżenia przeciwstronnej kończyny średnio o 79%. Nasilenie drżenia głowy zmniejszyło się u 75% chorych leczonych stymulacją obustronną

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Conclusions: Vim DBS is a safe and effective method of ET treatment. Vim DBS improves activities of daily living of ET patients.

Key words: essential tremor, deep brain stimulation, thalamus.

Introduction

Essential tremor (ET) is one of the most common movement disorders. The first symptoms of ET appear at the age of 35-45. The tremor progresses with age, frequently being the main cause of the patient's disability. Tremor among ET patients is most often located in the upper limbs; the head and tongue or even lower limbs are involved less frequently. More than half of ET patients might benefit from pharmacotherapy. The group of patients with severe tremor who do not benefit from or who do not tolerate pharmacotherapy might be qualified for surgery – thalamotomy or thalamic deep brain stimulation (ventral intermediate nucleus of thalamus deep brain stimulation, Vim DBS). The efficacy of thalamotomy and Vim DBS is comparable. Thalamotomy carries a higher complication rate than Vim DBS. The risk of irreversible complications after thalamotomy, especially if performed bilaterally, led to the acceptance of Vim DBS as the treatment of choice for the majority of ET patients [1-16]. Longer surgical procedure, the need for general anaesthesia and frequent visits for programming and reprogramming of Vim DBS, and the need for future internal pulse generator exchange, explains why thalamotomy is still used in selected ET cases. The definitive, consensual decision about the type of treatment should be made by the patient himself with the help of a movement disorders team. The authors present a group of patients treated with Vim DBS for ET. The aim of the study was to evaluate the efficacy and safety of Vim DBS in ET treatment.

Material and methods

Between 2006 and 2009, 8 female and 10 male ET patients were treated with Vim DBS. Mean age at implantation was 63 ± 15 . ET lasted from 4 to 30 years (mean 12). The clinical condition of the group was evaluated with spirometry (spiral drawings), the modified Fahn scale (Tremor Rating Scale, TRS), and the modi-

oraz u 50% chorych leczonych stymulacją jednostronną. Średnio poprawa w ADL wynosiła 61%.

Wnioski: Głęboka stymulacja jądra brzusznego-pośredniego wzgórza jest metodą bezpieczną i skuteczną w leczeniu DS, mającą wpływ na sprawność wykonywania codziennych czynności u chorych z DS.

Słowa kluczowe: drżenie samoistne, głęboka stymulacja mózgu, wzgórze.

fied ADL (Activity of Daily Living) scale [17]. After neurological, psychological and neurosurgical qualification patients were admitted to the department of neurosurgery. ET was the main cause of subjects' disability in the studied group. Tremor lasted for at least 6 hours/day with intensity of 3-4 on the TRS. The exclusion criteria included: psychiatric disorders, previous thalamotomy on the side of the planned DBS, coagulopathy or immunodeficiency. The procedures were performed under local and general anaesthesia. After placement of the stereotactic frame, computed tomography (CT) scanning with contrast injection and merging of CT and magnetic resonance images were performed to identify the target point according to the indirect method [6,18,19]. Macrostimulation was conducted in the whole group. Microrecording with 1 to 3 microelectrodes was performed in 3 patients [20]. After identification of the surgical target, a permanent electrode was implanted under fluoroscopic guidance. After dismantling of the stereotactic frame, the system was connected with the internal pulse generator and internalized. Bilateral procedures were performed in 11 cases and unilateral (left-sided) procedures were performed in 7 cases. The stimulation was initialized on the first day following surgery.

Results

Intraoperative contralateral limb tremor reduction was reported in the whole group of patients during stimulation. The therapeutic effect of DBS was maintained at the follow-up on the first day and 3 months following surgery. Initial parameters of the monopolar stimulation were set at the frequency of 130 Hz with pulse width of $80 \mu s$ and mean amplitude up to 1.0 V. The parameters were readjusted over time according to the clinical effect at the follow-up. If necessary, the stimulation was changed to bipolar and the amplitude was increased up to 2.5 V.

Mean contralateral tremor reduction measured with the modified Fahn scale was 79%. Three subjects reported 100% improvement in contralateral limb tremor

(from 4 to 0 on the Fahn scale). Twelve subjects reported 80% improvement in limb tremor (4 points on the Fahn scale). Two subjects reported 60% improvement (3 points on the Fahn Scale) and 1 subject reported 20% improvement (1 point on the Fahn scale). Head tremor was reduced at least by 1 point on the TRS in 75% (6/8) of patients treated with bilateral Vim DBS and in 50% (3/6) of those treated with unilateral Vim DBS. Reduction by 2 points on the TRS was reported in 25% of patients treated with bilateral Vim DBS (2/6). All studied subjects reported improvement of the functions evaluated by ADL. Mean improvement of ADL was 61% (Table 1). Improvement measured with spirometry was noted among the whole group.

Skin erosion over the cerebral electrode was reported in 1 case (1/29 implantations, 3%). Intracerebral haemorrhage at the electrode path at the left frontal lobe was noted in 1 case (as observed in control CT) and clinically manifested in mild disorientation. Clinical symptoms of haemorrhage had disappeared in 1-week follow-up. Haemorrhage was not visible in the 1-month control CT scan.

Discussion

Essential tremor is one of the most common movement disorders. Prevalence of ET depends on the age of the evaluated group and varies from 0.01 to 20.5% with new diagnoses of 23.7 patients/year/100 thousand population up to over 600 in the population of patients aged over 65. The aetiology of ET is unknown. The quality of life of over 70% of ET patients is impaired by tremor, but only 10% of them receive any treatment [1,5,18,19]. Modern pharmacology allows tremor to be controlled among the majority of ET patients. Surgical treatment can be considered only if the conservative treatment is not tolerated or if there is no response to treatment. Appropriate ET diagnosis at the surgical qualification level is a key factor for successful treatment. Neurological qualification and acceptance by the patient of the offered type of treatment will impact future patient satisfaction and compliance in the follow-up [1,3,5, 21-23].

In the mid twentieth century, the first attempts of neurosurgical treatment of tremor were made. In those years extensive neurosurgical procedures were performed which reduced tremor only with excessive costs of patients' motor skills [24,25]. Thalamotomy, elaborated by Guiot in the 1960s, was a breakthrough in ET

Table 1. ADL Scale* used for evaluation of the efficacy of ET treatment with Vim DBS. Pre-surgical and post-surgical (3 months after implantation) state and improvement in each task are listed

No.	Task	Before surgery	Three months after surgery	Improvement
1.	Feeding	2.2	0.7	-70%
2.	Drinking	2.6	0.7	-74%
3.	Pouring water	2.2	0.7	-70%
4.	Brushing teeth	1.6	0.4	-79%
5.	Face and hand hygiene	1.1	0.3	-72%
6.	Taking bath or shower	1.1	0.6	-50%
7.	Using toilet	1.0	0.3	-69%
8.	Tying shoelaces	1.8	0.8	-55%
9.	Fastening buttons	1.9	0.6	-67%
10.	Handwriting	2.5	1.5	-41%
11.	Book reading	1.6	0.4	-72%
12.	Hand drawing	2.2	1.2	-48%
13.	Phone dialling	1.6	0.9	-43%
14.	Sending letters	2.1	0.8	-61%
15.	Locking door with a key	1.9	0.8	-57%
Results (0-45)		27.5	10.2	-61%

*0 – able to perform independently, 1 – able to perform with effort and some help, 2 – able to perform with excessive effort, 3 – unable to perform independently

treatment, when efficacy and safety improved significantly [6,19]. Very good results of thalamotomy (tremor reduction up to 100% among ET patients) was followed by a relatively high complication rate, especially if thalamotomies were performed bilaterally. The introduction of Vim DBS in ET helped to reduce the complication rate and to maintain the high efficacy of treatment. Implantation of DBS is well tolerated but carries a risk related to the surgical procedure and adverse effects related to the stimulation itself. The surgical complication rate related to DBS implantation is estimated at 2-3%. Neurological morbidity related to the procedure is estimated at 1% with mortality of 0.4%. Adverse effects related to stimulation of the surrounding structures are usually not retained and are eliminated at the programming session [4-6,19,23-30].

Other, previously described anatomical targets such as the globus pallidus or other thalamic nuclei (VOP, VL) are not used nowadays because of the lower impact on tremor. Promising results in tremor reduction are

reported with stimulation of the posterior subthalamic area, especially among patients with tremor and Parkinson disease [31,32]. It seems that the leading role of Vim as a surgical target for ET treatment will remain, because of its simplicity, high efficacy for tremor, and low complication rate [6,11,19,31,32].

The efficacy of Vim DBS treatment in the group was evaluated with the modified Fahn scale, spirometry and ADL. Tremor reduction was reported in the whole group and was most significant in feeding and personal hygiene abilities. Handwriting ability improved less significantly than the other evaluated activities. The minor improvement of handwriting might suggest that the most commonly used test for tremor evaluation – spirometry – is not sufficiently sensitive for evaluation of Vim DBS treatment. Additionally performed ADL evaluation might supplement post-surgical evaluation of Vim DBS tremor treatment.

The progressive character of ET is one of the reasons why the efficacy of thalamotomy and Vim DBS diminishes over the years. Application of cyclic stimulation with stimulation off over night might prolong the treatment efficacy. Reprogramming of the internal pulse generator, which is possible with DBS, gives the possibility of prolonging Vim DBS efficacy in long-term observation among ET patients as well [1,2,4,30].

Conclusions

1. Vim DBS is a safe and effective method of ET treatment.
2. Vim DBS improves activities of daily living of ET patients.
3. If no contraindications are present and this type of treatment is accepted by patient, Vim DBS should be identified as the treatment of choice for ET, especially if bilateral procedures are planned.

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Disclosure

Authors report no conflict of interest.

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