Subthalamic deep brain stimulation for the treatment of Parkinson disease

Głęboka stymulacja jądra niskowzgórzowego w leczeniu choroby Parkinsona

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Abstract

Background and purpose: The role of subthalamic nucleus deep brain stimulation (STN DBS) in the treatment of Parkinson disease (PD) is well established. The authors present a group of patients diagnosed with PD who were treated with STN DBS.
Material and methods: Between 2008 and 2009, 32 female and 34 male patients with PD were treated with STN DBS. Mean age at implantation was 57 ± 12 years. PD lasted from 6 to 21 years (mean 10 years). Patients were qualified for the surgery according to the CAPSIT-PD criteria. The STN was identified with direct and indirect methods. Macrostimulation and microrecording for STN identification were used in all cases. A unilateral STN DBS system was implanted in two cases and bilateral implantation was performed among rest of the group. Outcome was assessed six months after implantation.
Results: The mean reduction of UPDRS III score among 51 patients who underwent follow-up was 45% (5-89%). Reduction of levodopa consumption varied from 15 to 100%. Infection forced the authors to remove the DBS system in one case four months after implantation. Skin erosion above the internal pulse generator was noted in four cases.
Conclusions: Cardinal symptoms of Parkinson's disease can be safely and effectively treated with STN DBS in selected group of patients.

Streszczenie

Wstęp i cel pracy: Rola głębokiej stymulacji jądra niskowzgórzowego (*subthalamic nucleus deep brain stimulation* – STN DBS) w leczeniu choroby Parkinsona (ChP) jest uznana. Autorzy przedstawiają grupę chorych na ChP, leczonych za pomocą STN DBS.
Materiał i metody: W latach 2008–2009 metodą STN DBS leczono 32 kobiety i 34 mężczyzn chorych na ChP. Średni wiek operowanych chorych wynosił 57 ± 12 lat, czas trwania choroby 6–21 lat (średnio 10 lat). Pacjenci byli kwalifikowani do operacji na podstawie kryteriów zawartych w CAPSIT-PD. Jądro niskowzgórzowe identyfikowano metodą bezpośrednią i pośrednią. Zabieg przeprowadzono w znieczuleniu miejscowym, wykorzystując mikrorejestrację oraz makrostymulację. U 2 pacjentów implantowano elektrody jednostronnie, u pozostałych etapowo, obustronnie. Skuteczność leczenia oceniano po 6 miesiącach od implantacji.
Wyniki: W grupie 51 chorych, u których przeprowadzono ocenę skuteczności leczenia, stwierdzono zmniejszenie punktacji w III części UPDRS średnio o 45% (5–89%). Zmniejszenie dawki lewodopy wahało się pomiędzy 15 a 100%. W badanej grupie stwierdzano powikłanie infekcyjne u jednego pacjenta oraz erozję skóry nad stymulatorem u 4 chorych.

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Key words: Parkinson disease, deep brain stimulation, subthalamic nucleus.

Wnioski: Stymulacja jądra niskowzgórzowego jest metodą bezpieczną i skuteczną w leczeniu objawów kardynalnych dla wybranej grupy chorych na ChP.

Słowa kluczowe: choroba Parkinsona, głęboka stymulacja mózgu, jądro niskowzgórzowe.

Introduction

At the beginning of the nineteenth century, James Parkinson described a disease characterized by bradykinesia, akinesia, rigidity and resting tremor. Parkinson disease (PD) is one of the most common diseases of the central nervous system. In the general population the incidence is 0.15%, and for individuals aged over 60 years the incidence increases tenfold. It is believed that the cause of PD is degeneration of the substantia nigra of the midbrain that results in a deficit of one of the neurotransmitters – dopamine. The pharmacological treatment consists mainly of its supplementation, specifically its precursor levodopa. Unfortunately, a group of patients after 5-10 years of treatment develops poor tolerance to pharmacotherapy, and in consequence on/off types of motor fluctuations appear. Along with progress of the disease suitable drug dosage application becomes impossible and then this group of patients might benefit from surgery. Deep brain stimulation (DBS), introduced in the 1990s, has become the method of choice for the neurosurgical treatment of PD. The subthalamic nucleus (STN) with its key role in the cortico-basal-thalamo-cortical loop is considered as an optimal target for surgical treatment of the cardinal symptoms of PD [1-10]. The authors present their experience in the STN DBS treatment of PD.

Material and methods

Thirty-two female and 34 male PD patients were surgically treated in 2008-2009 (131 STN DBS systems were implanted). The average age at surgery was 57 ± 12 years. The duration of the disease ranged between 6 and 21 years (mean 10 years). Mean age at the diagnosis of PD was 52 ± 9 years. Patients were qualified for surgery by a group of neurologists and neurosurgeons from dedicated movement disorder centres according to the CAPSIT-PD criteria.[11-13]. The mean scores of UPDRS part III in off state were 57 points and in on state –27 points. The difference between UPDRS part III scores in off and on states varied between 21% and 72% (mean 44%). The clinical state of patients in the group was evaluated as stage II-IV on the Hoehn-Yahr scale. After neurological, psychological and neurosurgical qualification, patients were admitted to the department of neurosurgery [14] 24 hours before surgery and antiparkinsonian drugs were withdrawn. Procedures were performed under local and general anaesthesia. After the stereotactic frame fixation and CT scanning, the CT and MRI scans were merged [15]. The target point was calculated using indirect (mid. AC-PC: 11, –2, –4) and direct methods that modified the position depending on the MRI image. Microrecording and macrostimulation were performed in all cases with two to five electrodes [16-18]. After the target point was identified, the permanent electrode was implanted and its location was verified with fluoroscopy. In a bilateral procedure, these steps were repeated for the opposite side. After removing the stereotactic frame, under general anaesthesia the connecting cable was conducted, assembled with the internal pulse generator, and the system was internalized. Programming the internal pulse generator took place six weeks after surgery [19,20]. In two cases electrodes were implanted unilaterally, and in the rest of the group the procedure was staged, bilateral. Follow-up was conducted six months after surgery.

Results

The follow-up was performed after 6 months among 51 patients (77%). Mean reduction of UPDRS part III score was 45% (5-89%). The best results (66% improvement) were achieved in bradykinesia and rigidity (items 22-27 and 31 in UPDRS). Poorer results (32% improvement) were achieved in speech, facial expression and tremor (items 18-21 in UPDRS). The poorest results (8%) were achieved in axial symptoms (28, 29 and 30 from UPDRS). Reduction of levodopa doses ranged from 15 to 100% (average 48%). In two cases, the levodopa daily dose was reduced to zero in 6-month follow-up. An infection was observed in 1 case (1/131 implantations, 0.7%), which forced the authors to remove the system. Three months after completion of targeted antibiotic therapy the system was reimplanted. In 4 cases (4/131 implantations, 3%) skin erosion was observed over the internal pulse generator, cerebral electrode or connector. In these patients, reconstructive surgery was performed without removal of the system. In 3 cases (3/131 implantations, 2.3%) clinically asymptomatic intracerebral haemorrhage located on the path of the electrode was found at control CT. In a further CT (1 month later) the haematoma had disappeared. A clinically asymptomatic intraventricular haemorrhage was reported in 1 case (1/131 implantations, 0.7%) on control CT, which disappeared within 1 week of observation (control CT). Motor, sensory or autonomic side effects of stimulation of the STN surrounding structures were eliminated during programming. Symptoms associated with the limbic STN stimulation appeared in 3 patients after the internal pulse generator was switched on in 1- to 4-week follow-up. The patient's relatives reported hypomanic or manic behaviour in 3 patients (3/66, 4.5%). Patients who presented manic or hypomanic symptoms denied any side effects.

Discussion

The history of functional neurosurgery, which aims at neuromodulation of the nervous system, begins in the nineteenth century. In the first half of the last century, spontaneous improvement was noticed among patients with extrapyramidal symptoms, which appeared after a stroke of specific brain regions. Lack of effective therapeutic methods contributed to experimental and often risky neurosurgical procedures. One of those methods was a procedure based on lesioning of certain brain structures using high or low temperatures, chemicals or radiation. The introduction of the modern stereotactic frame by Spiegel and Wycis in the mid-twentieth century was a breakthrough for functional neurosurgery. Procedures have become accurate and the high prevalence of surgery enabled larger groups of patients to be observed. Objective assessment of the effectiveness of ablative procedures was achieved as well. Another breakthrough in PD treatment was the introduction of an animal model of PD that helped to identify the neuronal loops. Alternation of those loops resulted in certain symptoms and enabled the identification of anatomical targets for neurosurgical treatment [3,4,8,21-24]. The idea of neuromodulation is to suppress the hyperactive elements or interrupt pathways between hyperactive and other elements of the loops. It is accepted that hyperactivity of the STN plays a key role in most PD symptoms, but attempts to lesion the STN (subthalamotomy) were associated with high risk of persistent dyskinesia, ballism or psychiatric symptoms. When performing ablative procedures for PD, most authors use test, intraoperative stimulation, which is aimed at determining the effectiveness and safety of the treatment. The main drawback of ablative surgery, even with intraoperative macrostimulation, is the irreversibility of its effects. The next natural step was the introduction of the internal pulse generator for constant and persistent brain stimulation. Due to technical difficulties, the use of neurostimulators until the early 1990s was very limited. The introduction of DBS with its reversible mechanism of action enabled safe bilateral suppression of the hyperactive STN. STN DBS has provided an improvement of cardinal symptoms of PD that included bradykinesia, rigidity and tremor [4,6,7,10,24-26].

The mechanism of action of DBS is not fully understood. Currently, the following main mechanisms of action of STN DBS are recognized: depolarization blockage (blockage of sodium channels), synaptic depolarization blockage, antidromic stimulation of the target nucleus with the topical release of GABA, masking of inhibitory coded information and activation of local inhibitory mechanisms in the target structure [3,8-10,27].

Complications associated with the introduction of DBS surgery are conditioned by the surgery and stimulation of the surrounding structures. Complications related to DBS implantation are primarily intracerebral haemorrhages, intracranial haematomas, infection, skin erosion over the implant, cerebrospinal fluid leakage or displacement of the implant. The incidence of surgical complications in DBS is estimated at 2-3%. Neurological morbidity is estimated at 1% and mortality at 0.4%. Adverse effects related to stimulation of the surrounding structures appear after initiation of the stimulation; they are usually eliminated during the programming session. Dyskinesias that appear after turning on the internal pulse generator are usually the result of a synergistic effect of medication and STN DBS, which should be interpreted as a favourable prognostic factor. Reduction of medication doses or reduction of the stimulation amplitude can eliminate dyskinesias. Hypomanic or manic behaviour, the symptoms of stimulation of the limbic part of the STN, are often denied by patients. During each programming session of the DBS, a careful medical history should be taken, from both the patients and their relatives [1,2,28-34].

To sum up, the introduction of the modern internal pulse generator, the consensus on qualifying for PD treatment, and standardization of the implantation process itself, are the main causes of the rapid development of functional neurosurgery in the last two decades, especially in the treatment of PD with STN DBS.

Conclusions

STN DBS is a safe and effective method of treatment of cardinal symptoms in a selected group of PD patients.

Acknowledgement

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Disclosure

Authors report no conflict of interest.

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