NEUROMODULATION OF THE CENTRAL NERVOUS SYSTEM: EXPERIENCE IN SURGICAL TREATMENT OF TOURETTE'S SYNDROME AND PARKINSON'S DISEASE

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Introduction.

Neuromodulation is the therapeutic process by which the activity of the central, peripheral or autonomic nervous system is regulated by means of electrical or pharmacological effects with the use of implantable devices. According to modern concepts, deep brain stimulation (DBS) produces electrical impulses that modify neurotransmission. This leads to suppression or exciting of neural groups activity (networks) and thus provides the therapeutic effect [7].

Tourette Syndrome (TS) is a progressive extrapyramidal system disease which is characterized by motor and vocal tics and behavior disorders varied by course and duration. Prevalence rate in the Moscow region is 1: 1000 [1]. The first case of DBS for TS was reported by Vandewalle in 1999 [10]. He used thalamic target point which was previously used by Hassler [6]. The number of DBS in TS performed by 11 years in 19 neurosurgical centers in 10 countries reached 55.

The modulation effect is confirmed by applying the DBS on the same subcortical structures of the brain (the internal segment of globus pallidus, GPi) at two diseases opposite in the pathogenesis - TS [9] and Parkinson's (PD) [5]. The most popular hypothesis now is the dopaminergic hypothesis of the pathogenesis of TS by which the cause of vocal and motor hyperkinesis is either an excess of a dopamine (presynaptic dysfunction) or increased sensitivity of dopamine receptors (postsynaptic dysfunction) caused by both increased number of receptors and their affinity ligand [4]. Dopaminergic hypothesis of the TS is confirmed by the positive effect of drug administration that blocks the synthesis of dopamine. This leads to motor and vocal tics suppression in TS while on the contrary a prescription of drugs increasing a production of dopamine or dopaminergic activity (such as amphetamines) leads to the hyperkinesis augmentation.

While in the PD pathogenesis, the dopamine in effectory areas of the brain decreases as a result of neuronal progressive degeneration in the compact part of the substantia nigra in the midbrain. Therefore, the regression of

PD symptoms is reached by increasing in functional activity of dopaminergic synapse compromised in PD [2, 3].

Methods

14 operations of electrodes implantation in the GPi area on both sides for chronic DBS in patients with akinetic-rigid PD were performed in Research Center of Neurology in the 2010-2015 period (Figure 1).

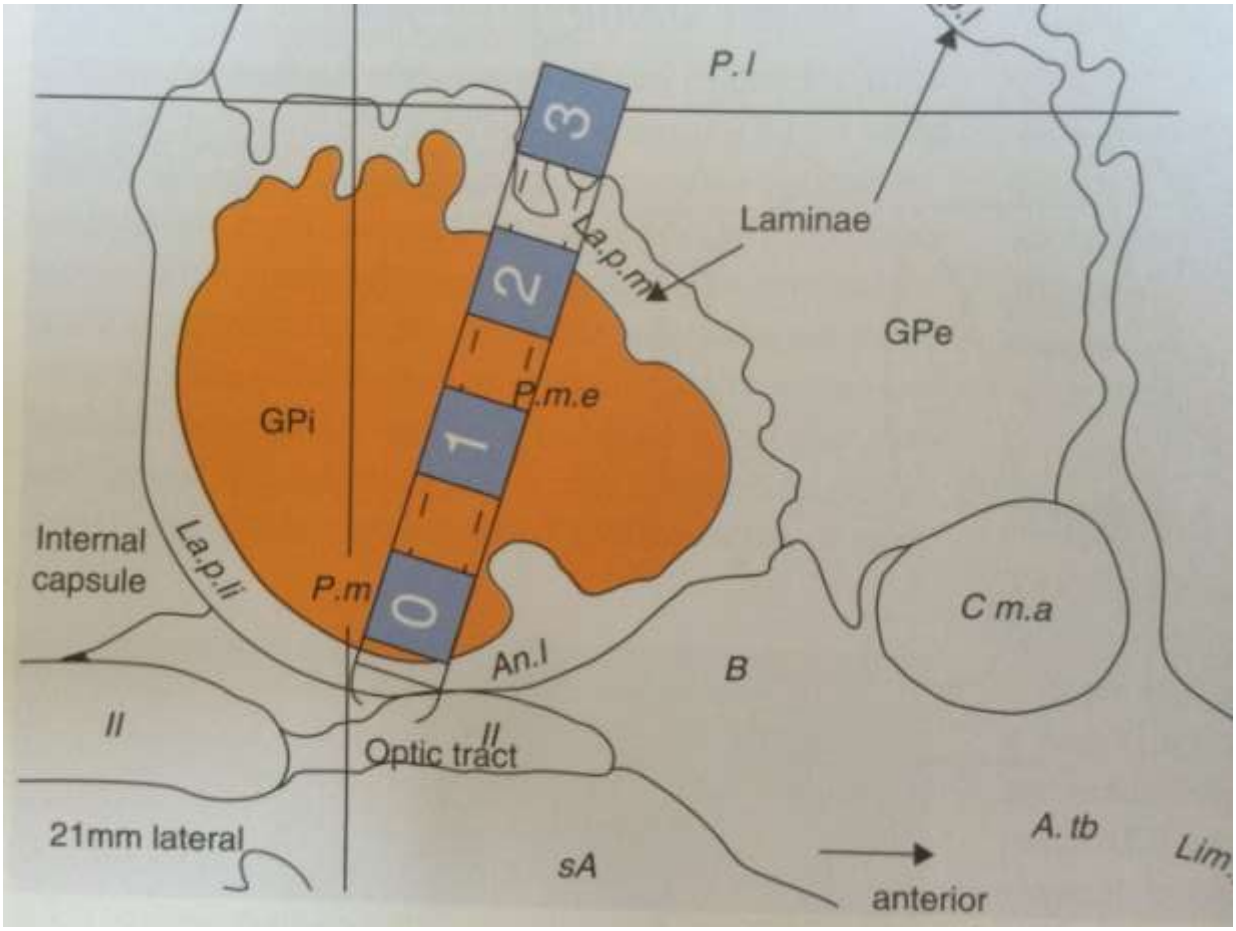

Figure 1. Location of the electrode in the GPi.

The average age of patients was 64 years. The average duration of the disease - 6.8 years. Patients were evaluated in OFF- and ON-states in 6 months after a surgery. All the patients underwent a complete neurological examination that included estimation by UPDRS (part II-III), the *Parkinson's*

disease questionnaire (*PDQ-39*), the *Hoehn* and *Yahr* and Schwab and England scales.

In TS, an implantation of DBS electrodes in the GPi was performed in one patient.

Case report

The 18-year old patient was admitted to the hospital with complaints on massive motor and vocal tics. Motor tics were characterized by short fast repetitive stereotyped actions (sniff, tongue protruding, shoulders twitching, hand twitching, head jerking and a sudden and quick head lag, kicking, body bending in prone position). In addition, the echopraixa was observed (another type of complex motor tics - imitation of gestures and movements of other people). Tics were uncontrolled and thus accompanied by psychological discomfort. The patient masked involuntary nature of ticks by adding a voluntary movement. Vocal tics were presented by senseless sounds and noises such as loud snort and inarticulate cries. Sometimes complex vocal tics were performed as phrases and sentences that had some meaning. Also vocal disturbances manifested as speech rituals (repeating the same phrase several times), echolalia (repetition of sounds, words, parts of words pronounced by others). Motor and vocal tics were combined with obsessive-compulsive syndrome presented by touching objects multiple times until the patient gets satisfied. Sometimes the patient was able to briefly slow down tics, especially in the presence of new people or during a visit to the doctor. But after a few minutes ticks became the "avalanche" character.

The onset of the disease was at the age of 6-7 years. The first symptoms were simple motor tics: shoulders twitching, sniff, quick head lag later. Vocal tics appeared during the first year of the disease: snort, incomprehensible sounds. The intensity and frequency of motor and vocal tics were increasing gradually. By the way, the patient's mother suffered in a childhood and adolescence by ticks like blepharospasm. At maternal aunt was diagnosed TS, at the second aunt - motor tics. During the past 12 years, the patient was under the care of neurologists. He took benzodiazepines (clonazepam), neuroleptics (pimozide, haloperidol - 10 mg 3 times a day, rispolept). During the last year of midication taking the weakness, memory loss, irritability, insomnia appeared. Nonetheless the drugs had no significant effect on tics.

Due to ineffective of medical treatment the patient underwent surgery - implantation of DBS electrodes in the medial segment of the globus pallidus on both sides (posterioventral GPi). Stimulation parameters were: current strength of 3,5 V, pulse width of 90 ms, the frequency of 180 Hz.

Results

After the surgery, the patient's condition improved significantly: frequency and severity of motor tics

decreased, the patient became increasingly control of them, vocal tics stopped. The patient continued to receive 2 mg rispolept per day.

Six months after the surgery the stimulation effect remains: motor tics are rare and mild, the patient can control the tics. There are no vocal tics. He continues to receive rispolept (2 mg per day). In assessing on a scale reduction in ticks reaches 85%.

Twenty months after the surgery the stimulation effect remains. 12 months after the surgery the patient enrolled at a university at the faculty of Mathematics and Physics. Successfully passed the first session. Motor tics are rare. There are no vocal tics.

4 years after surgery the stimulation effect remains. The patient continues to receive rispolept 2 mg per day, irregularly. He successfully completed the 4th study-year. In case of fatigue or agitation mild single vocal tics are observed, which the patient cleverly disguises.

At all patients with PD in 6 months after the DBS surgery (implantation of electrodes in posteroventral GPi) we observed a positive effect: rigidity in the OFF-period reduced by 62.6%, hypokinesia - by 36%. Also all 14 patients had a decrease in the severity of drug-dyskinesias - an average of 64.4%. Levodopa dose reduction was also reached - an average of 30.4%, quality of life improving - by 26,2% (PDQ-39).

Conclusion

GPi neurostimulation leads to regression of symptoms both in TS and in the akinetic-rigid form of PD. A similar effect can be achieved in dystonia and some other movement disorders [8]. That demonstrates the universal functional effect of the central nervous system modulation in various pathological conditions.

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