MODERN APPROACHES TO SURGICAL TREATMENT OF PARKINSON'S DISEASE

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Resume

Parkinson's disease (PD) is a progressive incurable degenerative disorder of the central nervous system, which significantly limits the functional status of patients. Modern medicine has various methods of drug and surgical treatment of this disease. The review considers all stages of surgical treatment of PD, starting with historically interesting descriptions of resection of the precentral gyrus to stereotactic destruction by various methods of exposure and electrical stimulation of deep brain structures. Indications for each method, their advantages and disadvantages, principles of patient selection are presented. Indications for neurosurgical treatment are determined taking into account the international CAPSIT-PD criteria. Stereotactic destructions lead to irreversible changes in the brain tissue, so their widespread use is limited. Stimulation with deep electrodes has advantages in disease progression due to the ability to change stimulation parameters and the possibility of bilateral influence on motor symptoms. Surgical treatment of PD does not mean the abolition of drug therapy, but it allows to reduce the dose of antiparkinsonian drugs and their possible adverse effects. The best result can be achieved with timely surgery and correct selection of patients by a multidisciplinary medical team, taking into account the characteristics of the course of the disease, the possibility of long-term postoperative observation of the patient and correction of stimulation parameters.

Key words: Parkinson's disease; deep brain stimulation; neurostimulation; implantation of electrodes into the brain; radiosurgery for Parkinson's disease; radiofrequency ablation; thalamotomy; subthalamotomy; pallidotomy.

Introduction. Parkinson's disease (PD) is a progressive brain disorder characterized by degeneration of dopaminergic neurons in the substantia nigra with accumulation of the α-synuclein protein and formation of Lewy bodies [1, 2]. Initially, surgical interventions for the treatment of PD included resection of the precentral gyrus of the cerebral cortex, then operations were developed on other parts of the pyramidal tract, including its spinal cord region, which were almost always accompanied by severe complications [3, 4]. In 1939, R. Meyers performed the first destruction of the caudate nucleus in hemiparkinsonism, based on the theory that hyperkinesia is a consequence of impaired influence of the neocortex on the basal ganglia [5, 6]. After successful treatment of unilateral postencephalitic tremor, a series of attempts followed to destroy individual sections of the basal ganglia using open approaches, and starting in 1947, using stereotaxis [7, 8]. The first thalamotomy was performed by chance. In 1952, I. Cooper was forced to clip the anterior choroidal artery, after which the patient's tremor stopped and bradykinesia decreased [8]. Later, this neurosurgeon worked with G. Bravo, performing stereotactic destructions of the ventrolateral nucleus of the thalamus to treat tremor in PD [9, 10]. After the invention of levodopa in the 1960s, the number of operations decreased sharply [11, 12]. And only after the description of the pronounced adverse effects of taking this drug, the gaze of contemporaries again turned to PD surgery. In modern medicine, several neurosurgical methods of symptomatic treatment of PD are used. They are distinguished by invasiveness, the ability to control and predict the size of the foci of destruction, the speed of onset of the clinical effect. There are two methods of surgical treatment of PD - destruction and neurostimulation. Among the destructive ones, cryodestruction, thermal and ultrasound ablation, stereotactic radiosurgery are distinguished. Deep brain stimulation (DBS) is used for neurostimulation. When selecting patients with PD for deep brain stimulation (DBS), the international CAPSIT-PD criteria are followed [13], similar rules are used in the Russian Federation [14 ,15]: 1) disease duration of at least 5 years; 2) disease stage according to Hoehn and Yahr not lower than 3rd; 3) high efficiency of levodopa during a pharmacological test (assessed in points according to the unified PD assessment scale (UPDRS)). The main criterion for performing thalamotomy is the presence of disabling tremor in the patient, for pallidotomy - disabling dyskinesia. Targets of surgical intervention in PD An important role in the development of PD belongs to degeneration of the nigrostriatal dopaminergic pathway, which leads to a decrease in the amount of dopamine produced and released from axon terminals. The connection between the striatum and the globus pallidus is carried out by direct and indirect pathways. The direct pathway connects the putamen and caudate nucleus with the internal segment of the globus pallidus and the reticular part of the substantia nigra. It functions via D1 dopamine receptors. The indirect pathway first goes to the external segment of the globus pallidus, then to the subthalamic nucleus, and only after that to the internal segment of the globus pallidus and the reticular part of the substantia nigra; it is regulated by D2 receptors. Activation of the direct pathway facilitates the formation of movements due to stimulation of the motor areas of the cortex. When the indirect pathway is activated, excitatory thalamocortical influences weaken, which leads to hypokinesia and rigidity. Dopamine inhibits the indirect pathway and activates the direct pathway, so its deficiency leads to an imbalance in the system, causing symptoms characteristic of PD [16, 17]. Surgical intervention methods in symptomatic treatment of PD are aimed at interrupting the pathological functioning of the connection between the striatum and the globus pallidus. The most studied are the ventral intermediate nucleus of the thalamus (VIM), the subthalamic nucleus (STN), and the internal segment of the globus pallidus (GPi). VIM is a part of the dentatothalamic tract involved in the formation of tremor. Therefore, this structure is universal for any tremor [18]. Impact on STN reduces all the main manifestations of PD [19, 20]. A distinction is made between subthalamotomy, which is the destruction of the subthalamic region, and subthalamic nucleotomy, which is the destruction of the subthalamic nucleus. STN is most often used for bilateral stimulation. Radiofrequency subthalamotomic nucleotomy is comparable in effectiveness to STN DBS, and therefore can be an alternative in the presence of contraindications to neurostimulation. It allows to reduce the dose of levodopa, the severity of motor fluctuations during the off period, but has a risk of developing hemichorea-hemiballismus [21]. Stimulation or destruction of GPi significantly reduces levodopa-induced dyskinesia [22], has a positive effect on the main motor manifestations of the disease - tremor, bradykinesia, rigidity, and improves the tolerance of the off state in patients with motor fluctuations [23, 24]. In 1963, A.-F. Denise proposed recording brain activity using a microelectrode to localize the target during stereotactic operations. Currently, the use of a microelectrode in invasive methods of treating PD, recording neuronal activity, test stimulation of nuclei allows us to determine the size of the nucleus, evaluate the effectiveness and side effects of test stimulation, and accurately establish coordinates for implantation of a permanent electrode or destruction. The widespread use of X-ray computed tomography and magnetic resonance imaging (MRI) contributed to the improvement of preoperative stereotactic planning of the trajectory and target of destruction, and made it possible to increase the safety and effectiveness of this type of exposure [25]. Most often, the target of destructive surgeries is VIM, which is associated with high efficiency, long-term effect, and low complication rate of thalamotomy [26]. Due to the effect on the entire spectrum of motor symptoms of PD, STN is the most common target for neurostimulation. Destructive surgeries for PD A feature of most destructive surgical methods is irreversibility and unilateral impact on the symptoms of the disease. Bilateral destruction of the basal ganglia can lead to the development of pseudobulbar syndrome, the severity of which can compete with the manifestations of the disease itself [27]. However, these complications are not applicable to destruction by focused ultrasound (FUS) ablation, which currently demonstrates good clinical outcomes with minimal complications, even with bilateral interventions [28, 29]. Complications of thalamotomy include transient gait disturbance, hemiparesis, dysarthria, and rarely paresthesia and ataxia in the contralateral side of the body [30, 31]. One of the factors for the lack of results is the variability of the VIM location [23]. Complications of subthalamotomy are usually transient, the most common of which is gait disturbance, while hemichorea-hemiballismus can be persistent [32]. Unilateral GPi destruction is comparable in effect to unilateral GPi neurostimulation [33], so it can be recommended for patients with unilateral dyskinesias [34]. Along with this, there are publications on the low efficiency and high frequency of radiosurgical complications of pallidotomy, so this type of intervention is practically not used [35]. Thus, cognitive impairment, dysphagia, dysarthria, transient hemiparesis and hemianopsia, and decreased sensitivity to levodopa in the late period have been described among the side effects of radiosurgical GPi destruction [36, 37]. If we talk about radiofrequency pallidotomy, complications include gait disturbance and a decrease in the effect of levodopa. The frequency of side effects in different types of unilateral destructions is variable. Complications after radiosurgical pallidotomy, according to various data, can be up to 50%, with persistent complications described in 4-5% of patients; these results are comparable with long-term effects after radiofrequency destruction of GPi [38]. There are several technical methods of destroying nuclei, which differ in controllability and the volume of the formed necrotic focus and invasiveness of the effect. Cryodestruction in neurosurgery is associated with the name of Irving Cooper, who in 1953 developed a cryoprobe for delivering liquid oxygen. The device provided an exposure temperature of up to -196 °C. The main disadvantage of the method was the impossibility of intraoperative control of the size of the necrotic area. In 1961, I. Cooper invented a modern cryosurgical apparatus, when working with which the size of the destruction focus was planned by setting a certain temperature of the coolant [39]. The model improved by E.I. Kandel and A.I. Shalnikov had a smaller needle diameter and vacuum thermal insulation of the body [40]. The advantages of the method include a low risk of hemorrhagic and infectious complications, reversibility of the procedure at a tip temperature of up to -10 °C, availability and simplicity of the method [41, 42]. However, the volume of the destruction focus is difficult to control even during unilateral operations, since it directly depends on the amount of liquid nitrogen, which is difficult to calculate in practice. Another disadvantage of the method is its invasiveness, which is the basis for the general risks of complications during open surgical interventions. Like other destructive operations, cryosurgery is not used for bilateral effects. Currently, cryodestruction of deep brain structures is a historical fact and has been replaced by a less traumatic and more controlled radiofrequency destruction technique. Radiofrequency ablation (RFA) is an effective and safe method. This is a stereotaxic method of destruction of the basal nuclei, implemented due to thermal action supplied to the "target" through a thermal electrode. When electric current passes through the brain tissue, a local increase in temperature develops, leading to the destruction of neural structures. The size of the necrotic focus is directly proportional to the size of the electrode tip, duration and temperature of action [43]. The advantages of RFA include the ability to predict and control the shape and volume of the necrotic focus. The destruction process can be quickly stopped, which simplifies the use of the method and increases its effectiveness. A disadvantage of the original technique was the "sticking" of coagulated tissue to the active end of the electrode, which, when it is removed, could lead to mechanical damage to brain tissue and the development of an intracerebral hematoma. A complication of RFA in the form of aneurysm formation at the site of local heating of the vessel wall with possible rupture and hemorrhage has also been described [44]. Another method of ablation of deep structures is high-intensity radiation from diode or neodymium lasers. High-intensity laser radiation is more effective and safe in stereotactic destructions, as it reduces perifocal edema of brain tissue and does not lead to the formation of coarse scars [45]. Using high-intensity laser radiation and choosing the appropriate temperature regime, it is possible to achieve an effect from tissue coagulation (60°–80°) to their ablation (over 300°). The disadvantage of the technique is its invasiveness. However, laser destruction is performed under MRI control, which allows for timely determination of the size and shape of the lesion. Stereotactic radiosurgery (SRS) is a non-invasive method for destruction of the basal ganglia. The method is based on a single high-dose effect of ionizing radiation of cobalt-60. The dose delivered to the center of the target averages 130–140 Gy, the prescribed dose is 65 Gy, the isodose is 30% [35]. In Fig. 1 shows an image of axial sections of a patient in the Leksell GammaPlan 10.1 planning program, performed at the Radiosurgery Center of the N.V. Sklifosovsky Research Institute of Emergency Care. The first changes in MRI of the brain are usually noted 3–4 months after exposure, their maximum severity develops by the 6th month, and clinical improvement develops 1–4 months after the operation [46]. According to MRI data, a necrotic area appears in the irradiation zone, with vascular changes and gliosis along the periphery [47]. A. Niranjan et al. suggested that it is the changes around the site of destruction that provide a long-term positive effect of SRS [48]. Radiosurgical thalamotomy is effective in approximately 90% of cases of treatment of unilateral tremor, and publications on stereotactic radiosurgical pallidotomy in cases of disabling levodopa-induced dyskinesias are few [49]. The disadvantages or limitations of the method include the lack of intraoperative clinical and neurophysiological control, delayed results, and variability in the size of the destruction focus when using standard irradiation parameters [50].

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