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DEEP BRAIN STIMULATION FOR MOVEMENT DISORDERS TREATMENT

Abstract. Deep brain stimulation (DBS) is the electrical stimulation of the deep nuclei. Electrodes implanted in the desired target and the stimulation parameters can be modified to enhance the positive and to reduce side effects. Mostly often such diseases as Parkinson's disease, essential tremor and dystonia are treated by DBS.

Tremor and rigidity in Parkinson's disease is treatable especially by stimulation of the subthalamic nucleus. Stimulation of the ventral nucleus of the thalamus is the most effective method of treatment of essential tremor. The stimulation of the globus pallidus showed to be effective in primary generalized dystonia, primary segmental dystonia, cervical dystonia, blepharospasm, Merge syndrome, tardive dystonia and certain forms of secondary dystonia.

128 patients with movement disorders were operated in the National Center for neurosurgery in the period from 2013 to 2015. 117 patients out of 128 were operated with the diagnosis of Parkinson's disease, 10 with dystonia, 1 with essential tremor. There were 57 men and 72 women. The average patient age was 51 year. A significant improvement in motor function in patients operated on Parkinson's disease increased by 65% in 2013 and 71% in 2014 to 92% in 2015. DBS treatment of patients with dystonia was significantly effective in spastic torticollis, but it is less effective in patients with secondary generalized and segmentary dystonia.

The National Center for Neurosurgery has been providing the movement disorders surgery program for 3 years.

Keywords: deep brain stimulation, Parkinson's disease, dystonia, tremor, surgical treatment.

Introduction. Surgical treatment of medically refractory forms of movement disorders lay in the destruction of neural structures involved in the process, usually the thalamus or pallidum. Thus small areas destruction is made by chemical degradation, freeze coagulation or electrical. Since a permanent hotbed of destruction developed after these procedures, if it is successful, the effect would be permanent, but if unsuccessful, the side effects would be very severe and irreversible.

Deep brain stimulation (DBS) is a high-frequency electrical stimulation of the underlying nuclei and causes the same therapeutic effect as with destruction. DBS method appeared in the 1960s. In the 1970s, a method was developed and began to be used in the treatment of pain syndromes, epilepsy, movement disorders and cerebral palsy [1, 2]. Currently, the method of DBS treats, in addition to movement disorders, Tourette's syndrome, depression, obsessive-convulsive disorders [3].

DBS has advantages over the destruction due to its adjustability and reversibility. Electrodes are implanted in the desired goal, but the stimulation parameters can be modified to enhance the positive effects and to reduce side. If the treatment is ineffective, the electrodes can be repositioned or removed altogether, without any consequences. In view of the above, the DBS has become the method of choice for the treatment of movement disorders, as compared to the currently used destructive operations [4]. Mostly often Parkinson's disease, essential tremor and dystonia are treated with DBS method.

Parkinson's disease. Parkinson's disease (PD) is the second most common neurodegenerative disease that affects between 1 and 3% of adults older than 65 years old [5]. The tremor, bradykinesia and rigidity - the main symptoms of Parkinson's disease. In spite of the therapy, in 40% of patients disease symptoms are saved and 28% experience levodopa-induced dyskinesia [6].

Traditional treatment with levodopa gives a positive effect, but long-term use develops side effects. Dyskinesia, a condition where the patient experiences a spontaneous involuntary movements are the most common side effect, and is also a limiting factor of levodopa therapy. DBS of subthalamic nucleus or globus pallidus cropped PD symptoms, leading to a reduction in the dose of levodopa, thereby reduce dyskinesia. The best candidates for DBS are patients with severe motor parkinsonian syndrome in the «off» stage, an improvement from the antiparkinsonian therapy, but with levodopa-induced movement disorders with a history of the disease for more than 5 years. Candidates for DBS should not have rude cognitive impairment or dementia [7-9].

Stimulation of the ventral nucleus of the thalamus (nucleus ventralis intermedius talami, VIM) is used in a limited number of patients with PD-tremor predominant because it has insufficient effect on rigidity and bradykinesia, the most common symptoms of PD [10,11]. The stimulation of the globus pallidus (globus pallidus interna, GPi) is also effective for the treatment of tremor, but also reduces symptoms of dyskinesia, rigidity and bradykinesia, postural stability somewhat improved [12]. Stimulation of the subthalamic nucleus (subthalamic nucleus, STN) is similar to GPi stimulation in terms of rigidity, bradykinesia and tremor treatment, and also results in reduction in the dose of antiparkinsonian drugs, which reduces dyskinesia pharmacological [13]. STN stimulation is fairly well studied and is therefore a more advanced procedure [14]. Tremor and rigidity is particularly amenable to treatment by STN stimulation, and bradykinesia, gait disturbances, and postural instability. Improvement by 50% motor UPDRS scale after STN stimulation was maintained for 5 years [15]. STN stimulation allows in 50-60% cases to reduce the dose of the dopaminergic agents, thereby reducing dyskinesia in 94% of cases after 12 months of treatment [14,16]. The results of 2 randomized studies comparing best medical therapy with STN and GPi stimulation showed that patients who received STN and GPi stimulation watched in addition more than 4 hours «on» period without medication dyskinesias [17]. Another study compared the stimulation of STN and GPi. They found that in the off-stage rigidity, bradykinesia and tremor were decreased during stimulation of both structures. Dyskinesia is also decreased for 12 months after surgery. However, bradykinesia was better treated by STN stimulation, and these patients have reduced the dose of antiparkinsonian drugs longer than patients who received GPi stimulation [19]. The comparison study of unilateral STN and GPi stimulation found no changes in mood or cognitive abilities [20]. Since PD - progressing disease, reducing of response of treatment may occur with the progression of the disease or as a result of adaptation to stimulation.

Essential tremor. Essential tremor (ET) is also known as benign tremor or familial tremor, is one of the most common movement disorders, affects more than 5% of the population over 60, but can occur at any age [21]. Over time, the ET can significantly reduce quality of life, leading to the fact that patients need help with eating and daily activities.

Drug ET treatment is usually with beta-blocking agent, such as propranolol. Anticonvulsants, ethanol and some benzodiazepines may be effective to reduce tremors. However, 50% of patients with ET do not respond to medical therapy [21]. With the recording microelectrodes it was revealed that cells in "VIM" light at the same frequency with which tremor occurs, and can be regarded as Targeted cells [26]. High frequency stimulation via electrode can suppress the abnormal activity, thereby reducing tremor. Unilateral and bilateral tremor of the extremities, face, vocal cords and tongue may be treated by VIM stimulation. Usually in practice, a bilateral VIM stimulation is used [23,24,25]. Many prospective studies have demonstrated the high efficiency of VIM stimulation in the treatment of ET [23,27,28,29]. Most patients report a significant reduction in tremor in the limbs from 50% to 80%. Although about 9% of patients with radiologically verified correct position of electrodes have no positive result [30,31].

Dystonia. Dystonia – is a movement disorder characterized by prolonged involuntary muscle contractions in the trunk or limbs. Neurophysiological studies indicate that the co-contraction of muscles of agonists and antagonists is responsible for dystonic position [32]. Primary dystonia has a hereditary nature and is associated with DYT genes [33]. Secondary dystonia appears after the well-known reasons. The prevalence of focal dystonia - 29.5 per 100,000 population, primary generalized dystonia 3.4 per 100,000 [34].

Drug treatment of dystonia is in the application of anticholinergic drugs, benzodiazepines and other preparations. However, the success of drug therapy varies from 20% to 40% [35,36]. Medication has a number of side effects such as sedation, Parkinsonism, cognitive dysfunction [37]. Treatment of focal

dystonia forms of botulinum toxin A, which has been the main treatment for dystonia to the 1980s, led to a good clinical effect. However, long-term use of botulinum toxin A is limited due to the follow immunoresistance thereto and reduce the effect of treatment [37, 38].

DBS for dystonia treatment showed to be effective in improving the symptoms of the disease. The main candidates for DBS - are patients with dystonia, the symptoms of which severely limit normal life, despite taking medication. The main criteria for inclusion in the DBS treatment group: age older than 7 years, primary dystonia, including generalized and segmental form, spasmodic torticollis [39]. The target of DBS is postventral lateral portion of GPi [40]. GPi stimulation showed to be effective in primary generalized dystonia, primary segmental dystonia, cervical dystonia, blepharospasm, Meige syndrome, tardive dystonia and certain forms of secondary dystonia [41].

Materials and methods of research. In the National center for neurosurgery there were operated 128 patients with movement disorders in the period from 2013 to 2015. Among them 117 patients were operated with the diagnosis of Parkinson's disease, 10 with dystonia, 1 with essential tremor. There were 57 men and 72 women. The average patient age was 51. In 116 cases, the aim was to stimulate the subthalamic nucleus (STN), in 12 cases - the globus pallidus (GPi) and in 1 case - the ventral thalamus (VIM). 73 operated patients were observed for more than 1 year.

We have used international criteria for the selection of patients with Parkinson's disease to the DBS. Their clinical status was assessed using the Unified Parkinson's Disease Rating Scale. The mean duration of disease was 10 years. Pronounced motor fluctuations and dyskinesias were in 75% of patients.

The main indication for DBS with a view to the globus pallidus was focal dystonia with spasmodic torticollis.

For the implantation of electrodes it was used multipurpose stereotactic frame and G-frame arch (Electa, Sweden) and SurgiPlan software (Elekta, Sweden) [42].

For implantation it was used Activa PC of the company Medtronic (USA, Minneapolis) system for deep brain stimulation, which consists of two electrodes, two extension cables and pulse generator.

The vast majority of implantations (90%) was carried out using the microelectrode recording of the LeadPoint Micro Electrode Recording (MER) system manufactured by Medtronic (USA, Minneapolis).

Results. Significant improvement of motor functions (more than 50% in the Unified Parkinson's Disease Rating Scale) in patients operated on for Parkinson's disease has increased from 65% in 2013 and from 71% in 2014 to 92% in 2015. Postural instability, gait problems and standalone symptoms regressed less. We reduced the dose of dopaminergic drugs by 30-50%, which allowed to neutralize levodopa-induced dyskinesia in all cases. 6 patients were to completely abandon the levodopa therapy.

DBS treatment of patients with dystonia was significantly effective in spastic torticollis, but was less effective in patients with secondary segementary and generalized dystonia.

Patient with essential tremor got rid of it, but not completely.

In 12 cases, we observed various surgical complications in patients with implanted devices. In 1 case it was symptomatic hemorrhage occurred during the installation of the electrode, which resulted in hemiparesis. In two cases there was asymptomatic hemorrhage. In 7 cases, there was infection contamination of the system that caused the complete removal of the system 4 and partially in 3 cases. Two patients developed a pulmonary embolism, which ended lethally in one patient. The number of complications was reduced as gaining experience and developing a protocol of diagnosis and treatment based on evidence-based medicine. Devices complications not observed.

Conclusion. In the National center for neurosurgery for 3 years it has been held the program of treatment of patients with movement disorders by DBS.

Deep brain stimulation has become an important part of the treatment of movement disorders including Parkinson's disease, essential tremor and dystonia. For patients whose symptoms are not amenable to drug therapy, DBS is the method of choice. The majority of patients who received DBS at the National center of neurosurgery, greatly stoped major disabling symptoms of diseases and increased quality of life. Of great importance is the correct patient selection, which allows to achieve the best outcomes.

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«Ұлттық нейрохирургия орталығы» АҚ, Астана, Қазақстан

ҚОЗҒАЛЫС БҰЗЫЛЫСТАРЫН ЕМДЕУДЕ МИДЫ ТЕРЕҢ СТИМУЛЯЦИЯЛАУ

Аннотация. Миды терең стимуляциялау (МТС) тереңде орналасқан ядроларды электр арқылы стимуляциялаудан тұрады. Электродтар қажетті нысанаға енділеді, алайда стимуляциялау параметрлері оң әсерлерді арттыру мен жанама әсерлерді азайту үшін өзгертілуі мүмкін. МТС әдісі көбіне Паркинсон ауруы, эссенциалды тремор және дистонияны емдеуде қолданылады. Паркинсон ауруы кезіндегі діріл мен сіреспе әсіресе субталамус ядросын стимуляциялау кезінде емдеуге келеді. Таламустың вентральды ядросын стимуляциялау эссенциалды треморды емдеудің айтарлықтай тиімді әдісі. Бозғылт шарды стимуляциялау өзінің тиімділігін жайылып кеткен бастапқы дистония, бастапқы-сегментарлық дистония, цервикальды дистония, блефароспазма, Мерж синдромы, тардивті дистониялар және екіншілікті дистонияның бірқатар формалары кезінде көрсетті.

Ұлттық нейрохирургия орталығында 2013–2015 жылдар аралығында қозғалыс бұзылыстары бар 128 пациентке операция жасалды. Оның ішінде 10 пациент Паркинсон ауруы, 10-ы дистония, 1-уі эссенциалды тремор диагнозымен операцияға алынды. Еркектер саны 57, әйелдер 72. Пациенттердің орта жасы 51 жасты құрады. Паркинсон ауруы бойынша операция жасалған пациенттердің қимыл – қозғалыс функцияларының айтарлықтай жақсаруы 2013 жылы 65%, 2014 жылы 71%, 2015 жылы 92% дейін артты.

Дистониясы бар пациенттерді МТС емдеу спазмдық қисықмойында айтарлықтай тиімдірек болды, алайда екіншілікті сегментарлық және жайылып кеткен дистонияда тиімділігі айтарлықтай аз болды.

Ұлттық нейрохирургия орталығында 3 жыл бойы МТС әдісімен қозғалыс бұзылыстары бар пациенттерді емдеу бағдарламасы жүргізіліп келеді.

Түйін сөздер: миды терең стимуляциялау, Паркинсон ауруы, дистония тремор, хирургиялық емдеу.

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ГЛУБИННАЯ СТИМУЛЯЦИЯ ГОЛОВНОГО МОЗГА В ЛЕЧЕНИИ ДВИГАТЕЛЬНЫХ РАССТРОЙСТВ

Аннотация. Глубинная стимуляция головного мозга (ГСГМ) заключается в электрической стимуляции глубинных ядер. Электроды вживляются в необходимую цель, однако параметры стимуляции могут изменяться для того, чтобы увеличить положительные эффекты и уменьшить побочные. Наиболее часто методом ГСГМ лечатся болезнь Паркинсона, эссенциальный тремор и дистония.

Тремор и ригидность при болезни Паркинсона особенно поддается лечению стимуляцией субталамического ядра. Стимуляция вентрального ядра таламуса – наиболее эффективный метод лечения эссенциального тремора. Стимуляция бледного шара показала свою эффективность при первично-генерализованной дистонии, первично-сегментарной дистонии, цервикальной дистонии, блефароспазме, синдроме Мержа, тардивной дистонии и некоторых формах вторичной дистонии.

В Национальном центре нейрохирургии были оперированы 128 пациентов с двигательными расстройствами в период с 2013 по 2015 годы. Из них 117 пациентов было оперировано с диагнозом болезнь Паркинсона, 10 - дистония, 1 - эссенциальный тремор. Мужчин было 57 и 72 женщины. Средний возраст пациента составил 51 год. Значительное улучшение моторных функций у пациентов, оперированных по поводу болезни Паркинсона, увеличилось 65% в 2013 и 71% в 2014 до 92% в 2015. Лечение ГСГМ пациентов с дистонией было значительно эффективно при спастической кривошеей, но менее эффективно у пациентов с вторичной сегментарной и генерализованной дистонией.

В Национальном центре нейрохирургии на протяжении 3 лет проводится программа лечения пациентов с двигательными расстройствами методом ГСГМ.

Ключевые слова: глубинная стимуляция головного мозга, болезнь Паркинсона, дистония, тремор, хирургическое лечение.