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CLINICAL FUNCTIONAL RESULTS OF THE CONTINUOUS ELECTROMAGNETIC STIMULATION IN PATIENTS WITH OPTIC NERVE PARTIAL ATROPHY

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✧ In this article, treatment analysis of 81 patients (98 eyes) with optic nerve pathologic conditions using an author-developed method of continuous optic nerve electromagnetic stimulation (neuromodulation) is compared to traditional in-patient therapy. Authors present an original method of electrode implantation and show the dynamics of visual functional changes, as a result of treatment including visual acuity, electrophysiology testing results, and visual fields. The neuromodulation method enables stimulation therapy to be performed in out-patients; continuous stimulation regimen use causes an important and longstanding therapeutic effect without any negative impact on surrounding tissues.

✧ ***Keywords:*** neuromodulation; partial optic nerve atrophy treatment; optic nerve stimulation.

КЛИНИКО-ФУНКЦИОНАЛЬНЫЕ РЕЗУЛЬТАТЫ ИСПОЛЬЗОВАНИЯ МЕТОДА НЕПРЕРЫВНОЙ ЭЛЕКТРОМАГНИТНОЙ СТИМУЛЯЦИИ В ЛЕЧЕНИИ ПАЦИЕНТОВ С ЧАСТИЧНОЙ АТРОФИЕЙ ЗРИТЕЛЬНОГО НЕРВА

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✧ В статье приведён анализ лечения 81 больного (98 глаз) с патологией зрительного нерва с использованием разработанного авторами метода непрерывной электростимуляции зрительного нерва (нейромодуляции) в сравнении с традиционным лечением. Авторами представлена оригинальная методика имплантации электродов, показана динамика изменений зрительных функций по группам в результате лечения: остроты зрения, результатов электрофизиологических исследований, полей зрения. В работе показано, что метод нейромодуляции позволяет управляемо проводить стимулирующее лечение в амбулаторных условиях, применение постоянного режима стимуляции вызывает значительный и продолжительный лечебный эффект без негативного воздействия на окружающие ткани.

✧ ***Ключевые слова:*** нейромодуляция; лечение частичной атрофии зрительного нерва; стимуляция зрительного нерва.

In the late 1980s, researchers first described a therapeutic method of direct electrical stimulation of the optic nerve through the orbit, which was widely used for the restoration of visual function in patients with residual vision due to partial atrophy of the optic nerve (PAON) [1–6].

The use of continuous electromagnetic stimulation (neuromodulation) ensures good treatment results in patients with pain syndromes, trigeminal neuralgia, other cranial neuralgias, and many other disorders [7–9]. These results encouraged us to use this method for the treatment of patients with PAON.

The aim of this study was to assess the performance of a novel neuromodulation method for the treatment of patients with PAON.

MATERIALS AND METHODS

The study included 81 patients (98 eyes) with optic nerve disorders recruited between 2014 and 2016.

The following methods were used for diagnosing PAON and monitoring treatment efficacy: refractometry, visual acuity testing, biomicroscopy, indirect ophthalmoscopy, fundus photography, tonometry, optical coherence tomography, and automated perimetry. The functional status and integrity of visual pathways were assessed through the registration of visual evoked potentials (VEPs). Electrophysiological examinations were conducted for all patients throughout treatment course (VEP-pattern) using the Roland Consult complex (Germany).

The experimental group comprised 39 patients (39 eyes) with PAON, whereas the control group included 42 (69 eyes). Patients in both groups were further divided into three subgroups based on disease etiology: subgroup I included patients with PAON developed due to certain disorders of the central nervous system (consequences of intoxication, traumatic brain injury, demyelinating processes, neurosurgical interventions, or congenital disorders); subgroup II included patients with PAON developed due to retinal disorders (central chorioretinal dystrophy or pigmentary retinal abiotrophy); and subgroup III included patients with optic nerve disorders developed due to acute circulatory disorders of the optic nerve and retina in the past (anterior ischemic optic neuropathy, posterior ischemic optic neuropathy, central retinal vein occlusion or occlusion of one of its branches, or occlusion of the central retinal artery or its branches).

The disease duration varied among the study participants; the mean duration of PAON in patients was calculated (Table 1). Patients in the control group received conventional treatment in accordance with the National Guidelines in Ophthalmology. It included daily intravenous and intramuscular injections of several drugs, including nootropics (Piracetam, dose of 3.0 g per 250 mL of 0.9% NaCl solution, intravenously administered), antioxidants (Emoxipin, dose of 3–5 mL of 3% solution, intramuscularly administered every day), neuroprotectors (Retinalamin, dose of 5 mg, intramuscularly administered every day), vitamins (B1 and B6, dose of 2.0 mL, intramuscularly administered on alternate days), and drugs for the improvement of microcirculation (Pentoxifylline, dose of 50 mg per 250 mL of 0.9% NaCl solution, intravenously administered). In addition to pharmacotherapy, patients received physiotherapeutic treatment (electrophoresis with calcium gluconate and magnetostimulation). The duration of in-patient treatment was approximately 8–10 days.

Continuous stimulation of the optic nerve was performed in accordance with the original method that consisted of two stages: surgical implantation of two 8-point electrodes in the optic nerve and temporal area (application for a Patent of the Russian Federation No. 2016125819, dated 06.28.2016); and physiotherapy, consisting of a continuous course of electrical stimulation for 8 days.

Table 1

Mean disease duration (months) according to case history

Таблица 1

Средняя продолжительность заболевания (в месяцах), по данным анамнеза

Group	Subgroup	Disease duration, months	Group	Subgroup	Disease duration, months
Experimental	I	84.1 ± 26.6	Control	I	76.5 ± 25.5
	II	76.3 ± 29.3		II	31.5 ± 15.7
	III	66.5 ± 15.7		III	59.4 ± 21.5

Electrode implantation was performed according to a specially developed protocol. After the standard disinfection of the eyelids and temporal area in the lower temporal quadrant of the orbit, a puncture site was marked on the skin, and 2 mL of 4% lidocaine solution was injected in the subcutaneous and retrobulbar regions. Next, a special needle guide with a mandren was introduced through the puncture toward the optic nerve. The mandren was then removed, followed by the placement of an electrode in the retrobulbar space.

The electrode was set in its final position under X-ray control (Figure 1), and the needle guide was removed. Similar procedures were performed on the skin in the temporal area on the same side where the second electrode was implanted. The sites of electrode insertion were covered with sterile adhesive strips. Both electrodes were led out through the area behind the ear to the back of the neck and further toward the back. The electrodes were fixed to the skin with sterile stickers and connected to an impulse generator (Figure 2).

Finally, a microprocessor was activated, and the neurostimulation mode was set according to patient comfort. A bipolar impulse current was used for stimulation. Specific parameters of stimulation were chosen together with the patient from the list of available stimulation modes of the device (Medtronic) (Reg. Certificate No. FSZ 2011/11151).

All participants were monitored on an outpatient basis during the entire course of wearing the

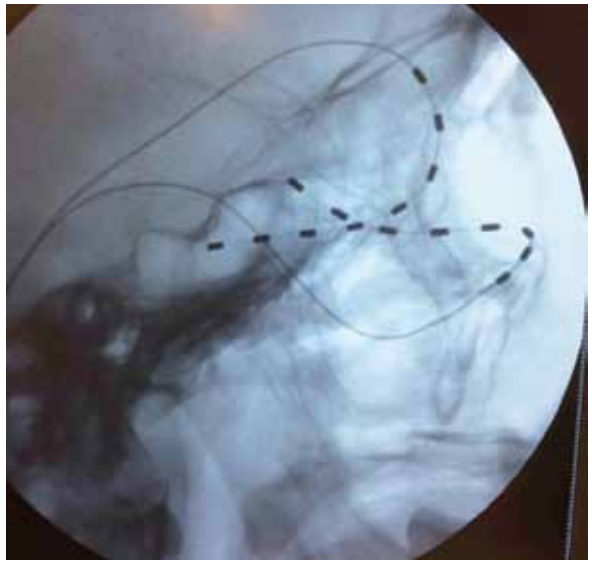

Fig. 1. Electrodes installed in the orbit and temporal region. X-ray monitoring of installed multipoint electrodes
Рис. 1. Электроды в орбите и височной области. Рентгенологический контроль установленных многоточечных электродов

Fig. 2. Electrodes connection to the microprocessor
Рис. 2. Подсоединение электродов к микропроцессору

implanted electrodes. Participants could switch off the signal generating device at any time. The session of continuous magnetic stimulation lasted for 8 days (around the clock), after which the electrodes were removed, puncture sites were disinfected, and the patients underwent ophthalmologic examination.

Statistical analysis was performed using StatSoft Statistica 6.0. Also, mean values and standard deviations were calculated. The significance of differences was tested using the Student's *t*-test ($p < 0.05$).

RESULTS AND DISCUSSION

During the specified period, 39 electrodes were implanted in outpatients; 42 patients underwent complex treatment for PAON in a hospital.

Participants in subgroups II and III of the experimental group demonstrated better visual acuity than those in the control group (Table 2). The improvement of visual acuity was 60% in patients with PAON associated with retinal pathological changes and 47% in patients with PAON developed due to circulatory disorders of the optic nerve and retina.

The reduction in the number of absolute and relative scotomas, as evaluated during automated perimetry, was used as a diagnostic criterion for the assessment of functional changes in visual function. Patients in subgroup III of the experimental group demonstrated the best results, with an average decrease of 25% in the number of absolute scotomas, and 58.4% in the number of relative scotomas.

The results of automated perimetry are presented in Table 3. The difference between the results obtained before and after treatment was significant ($p < 0.05$). Significant changes were observed in the values of latency and amplitude of the main peak estimated via electrophysiological examinations (Table 4).

Significant differences were found in P100 latency and amplitude before and after treatment in patients from the experimental group; however, the differences were not significant in the control group, which can probably be explained by the relatively small sample size.

The best functional results were achieved by subgroups II and III of the experimental group compared

Table 2

Dynamics of mean visual acuity ($N \pm n$)

Таблица 2

Динамика средних значений остроты зрения до и после лечения, 3 мес. ($N \pm n$)

Visual acuity	Experimental group			Control group		
	I	II	III	I	II	III
before treatment	0.17 ± 0.05*	0.25 ± 0.09*	0.17 ± 0.15*	0.16 ± 0.05	0.31 ± 0.15*	0.16 ± 0.03*
after treatment	0.23 ± 0.07*	0.4 ± 0.15*	0.25 ± 0.05*	0.19 ± 0.06	0.39 ± 0.02*	0.21 ± 0.02*
improvement gradient	0.06	0.15	0.08	0.03	0.08	0.05
% of improvement	35.3	60	47	18.7	25.8	31.2
*$p < 0.05$, significant differences before and after treatment						

Table 3

Dynamics of the mean number of scotomas according to perimetry results ($N \pm n$)

Таблица 3

Динамика среднего количества скотом различного порядка по данным периметрии ($N \pm n$)

Group		Relative scotomas of the 1st category		Relative scotomas of the 2nd category		Absolute scotomas		Reduction in the number of relative scotomas (both 1st and 2nd categories), %	Reduction in the number of absolute scotomas, %
		before treatment	after treatment	before treatment	after treatment	before treatment	after treatment		
Experimental	I	4.8 ± 1.1	4.4 ± 1.0	6.4 ± 1.1	5.6 ± 1.1	59.3 ± 5.1	41.5 ± 3.3	10.7	30
	II	23.8 ± 1.3	12.6 ± 0.3	36.7 ± 3.2	30.1 ± 4.1	84.4 ± 3.9	63.2 ± 2.7	32.4	25.1
	III	5.3 ± 0.1	1.9 ± 0.1	5.8 ± 0.2	2.7 ± 0.2	26.3 ± 0.3	19.7 ± 0.4	58.4	25.0
Control	I	6 ± 1.3	5 ± 1.2	7.1 ± 1.4	6.9 ± 1.3	48.5 ± 4.2	41.0 ± 3.2	9.2	15.4
	II	28.1 ± 2.2	24.9 ± 0.5	3.1 ± 0.1	2.4 ± 0.2	15.6 ± 1.7	13.3 ± 0.2	16.9	14.7
	III	7.1 ± 0.3	5.3 ± 0.2	19.4 ± 0.5	13.8 ± 0.4	44.5 ± 0.7	36.4 ± 0.5	27.0	18.2

Table 4

Dynamics of mean amplitude and latency of VEP ($N \pm n$)

Таблица 4

Динамика средних значений амплитуды и латентности зрительных вызванных потенциалов ($N \pm n$)

Group		Amplitude, μV			Latency, ms		
		before treatment	after treatment	improvement gradient, %	before treatment	after treatment	improvement gradient, %
Experimental	I	4.9 ± 0.5*	5.4 ± 0.3*	10.2	127 ± 3.6*	110.1 ± 1.8*	13.3
	II	3.2 ± 0.1*	5.0 ± 0.6*	56	118.5 ± 5.1*	113.8 ± 4.8*	4.0
	III	3.2 ± 0.1*	5.0 ± 0.6*	56	118.5 ± 5.1*	113.8 ± 4.8*	4.0
Control	I	4.9 ± 0.5	5.3 ± 0.3	8.2	117.8 ± 2.5	114.8 ± 2.8	2.5
	II	4.3 ± 0.3	4.5 ± 0.5	11.6	117.3 ± 4.7	113.3 ± 4.8	3.4
	III	4.3 ± 0.3	4.5 ± 0.5	11.6	117.3 ± 4.7	113.3 ± 4.8	3.4
*$p < 0.05$, significant differences before and after treatment							

Table 5

Dynamics of mean visual acuity ($N \pm n$)

Таблица 5

Динамика средних значений остроты зрения после лечения ($N \pm n$)

Visual acuity	Experimental group			Control group		
	I	II	III	I	II	III
at discharge	0.23 ± 0.03	0.4 ± 0.05	0.25 ± 0.03	0.19 ± 0.04	0.39 ± 0.02	0.21 ± 0.02
1 month post-treatment	0.21 ± 0.03	0.39 ± 0.04	0.25 ± 0.03	0.15 ± 0.02	0.3 ± 0.03	0.2 ± 0.01
3 months post-treatment	0.21 ± 0.03	0.37 ± 0.04	0.2 ± 0.03	0.13 ± 0.02	0.29 ± 0.03	0.15 ± 0.01

Table 6

Dynamics of the mean number of scotomas according to perimetry results ($N \pm n$)

Таблица 6

Динамика среднего количества скотом различного порядка по данным периметрии в различные сроки после лечения ($N \pm n$)

Group		Relative first order scotomas		Relative second order scotomas		Absolute scotomas	
		at discharge	3 months post-treatment	at discharge	3 months post-treatment	at discharge	3 months post-treatment
Experimental	I	4.4 ± 1.0	4.8 ± 1.1	5.6 ± 1.1	5.8 ± 1.1	41.5 ± 3.3	43.5 ± 3.7
	II	12.6 ± 0.3	23.8 ± 1.3	30.1 ± 4.1	32.7 ± 3.0	63.2 ± 2.7	65.7 ± 3.4
	III	1.9 ± 0.1	5.3 ± 0.1	2.7 ± 0.2	3.7 ± 0.3	19.7 ± 0.4	22.9 ± 1.1
Control	I	5 ± 1.2	6 ± 1.3	6.9 ± 1.3	7.0 ± 1.2	41.0 ± 3.2	48.4 ± 3.9
	II	24.9 ± 0.5	28.1 ± 2.2	2.4 ± 0.2	2.5 ± 0.1	13.3 ± 0.2	15.0 ± 1.4
	III	5.3 ± 0.2	7.1 ± 0.3	13.8 ± 0.4	15.2 ± 0.8	36.4 ± 0.5	41.7 ± 0.9

Table 7

Dynamics of mean amplitude and latency of VEP ($N \pm n$)

Таблица 7

Динамика средних значений амплитуды и латентности зрительных вызванных потенциалов в различные сроки после лечения ($N \pm n$)

Group		Amplitude, μV		Latency, ms	
		at discharge	3 months post-treatment	at discharge	3 months post-treatment
Experimental	I	5.4 ± 0.3	5.3 ± 0.5	110.1 ± 1.8	115 ± 3.0
	II	5.0 ± 0.6	4.7 ± 0.2	113.8 ± 4.8	117.2 ± 4.7
	III	5.0 ± 0.6	4.5 ± 0.2	113.8 ± 4.8	116.5 ± 3.7
Control	I	5.3 ± 0.3	4.7 ± 0.4	114.8 ± 2.8	114.8 ± 2.3
	II	4.5 ± 0.5	4.5 ± 0.3	113.3 ± 4.8	112.9 ± 4.5
	III	4.3 ± 0.3	4.5 ± 0.5	113.3 ± 4.8	115.3 ± 3.6

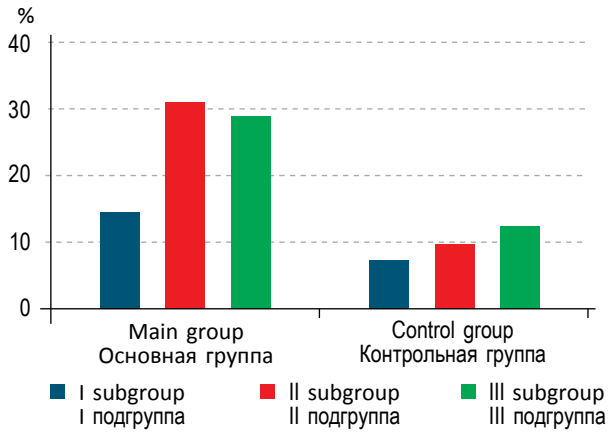

Fig. 3. Percentage ratio of improvement gradient of general functional indices by groups

Рис. 3. Процентное соотношение градиента улучшения общих функциональных показателей по группам

with the corresponding control subgroups. In subgroup II (patients with PAON due to retinal disorders), improvement of functional parameters was achieved in 35.5% of patients in the experimental group and 14.5% in the control group, whereas in subgroup III, this improvement was achieved in 32.9% of patients from the experimental group and in 19.5% in the control group. Patients in subgroup I of the experimental group (patients with PAON associated with central nervous system disorders) demonstrated poor results but achieved better outcomes than those in the control group. According to our data, 20.8% of patients in the experimental group and 10.8% in the control group demonstrated improved functional parameters (Figure 3).

Patients with PAON were followed up until 1 and 3 months post completion of the therapy (Tables 5–7). Patients in the experimental group had more stable results than those in the control group in terms of visual acuity, whereas the control group's functional parameters returned to baseline.

Our results suggest high efficacy of the proposed method for the treatment of patients with PAON. The technique is based on continuous electrical stimulation (neuromodulation) of the optic nerve, enabling controlled stimulatory treatment on an outpatient basis. The use of continuous stimulation ensures strong and long-term therapeutic effects, and the ability to maintain sensation during the procedure prevents a negative impact on the surrounding tissues. Our method provided favorable outcomes in the treatment of complicated cases of optic nerve and retina disorders, making particularly valuable and encouraging its implementation in routine clinical practice.

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