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The Effectiveness of the use of Transcranial Magnetic Stimulation in Ischemic Stroke

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ABSTRACT

To determine the rehabilitation potential in patients with ischemic stroke in the acute and early recovery periods with motor disorders, it is recommended to use functional transcranial magnetic stimulation. The preservation of motor evoked potentials from the affected hemisphere in the acute and early recovery periods indicates the prospect of restoring the motor functions of the affected limbs. The absence of a motor evoked potential from the affected hemisphere indicates a low rehabilitation potential for restoring motor functions. In post-stroke patients with new-onset hemispheric ischemic stroke with motor disorders and moderate neurological deficit, changes in the motor evoked potential were noted not only in the affected hemisphere, but also in the intact hemisphere, so rehabilitation interventions should also be directed to the conditionally intact hemisphere. Currently, a number of scientific literature sources provide information on the effectiveness of the method of synchronous use of transcranial magnetic stimulation and electrical myostimulation with preserved rehabilitation potential in patients with ischemic stroke with motor disorders. The application of the method improves the results of medical rehabilitation in the acute and early recovery periods of a stroke; the method of application, its duration and multiplicity have been developed and tested. This review analyzes data from a number of studies on the methods of rehabilitation of patients who have had a stroke.

Keywords: Transcranial magnetic stimulation, ischemic stroke, movement disorders, rehabilitation potential

INTRODUCTION

Cerebrovascular diseases and their most severe variant, cerebral stroke, are one of the main causes of disability in the world.

To date, it is known that the main mechanisms of neurorehabilitation include local processes of restitution (regression of edema, resolution of ischemic penumbra, reduction of delayed functional depression), reorganization of the central nervous system (CNS) (changes in the intensity of neurotransmitter production, restoration of suppressed ipsilateral corticospinal and accessory motor pathways, increased synaptogenesis, etc.). [6].

These mechanisms are implemented in different periods - from a few seconds to much longer periods of time (weeks, months and even years).

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Physical factors in the rehabilitation of patients with cerebral stroke

In the multidisciplinary system of rehabilitation of patients who have undergone ischemic stroke (IS), an important element is adequate, pathogenetically substantiated drug treatment in combination with physiotherapy methods.

That is why an active search for new approaches to improve the process of rehabilitation of stroke patients is impossible without knowledge of the features of the influence of physical factors. Known training programs (limiting the movement of a healthy limb, bilateral arm training, the use of robots, etc.) are designed to restructure the organization of the motor system. Significant assistance in this can be provided by invasive and non-invasive methods of brain stimulation (transcranial magnetic or electrical stimulation, stimulation of the primary motor cortex using epidural electrodes, etc.). The combination of transcranial influence with traditional training (exercise therapy, kinesitherapy, temporary restrictions on the use of healthy limbs, etc.) should activate the functional state of certain areas of the brain:

- zones adjacent to the lesion;
- secondary motor centers on the affected side;
- opposite hemisphere.

Such measures in patients after a stroke stimulate the formation of a growth factor and help reduce paresis in the long-term period of a stroke. Modern physical factors are promising for their implementation in the rehabilitation process. This is especially true for transcranial magnetic stimulation (TMS), which is increasingly being used in neurorehabilitation.

Functional Diagnosis of Movement Disorders by transcranial magnetic stimulation (TMS) in patients with IS

TMS is a modern neurophysiological method that allows you to study the functional state of the motor system in normal conditions and in various diseases of the central and peripheral nervous system, accompanied by motor disorders. [6].

Its essence lies in the generation of electric current in a high-intensity magnetic field (MF). The induced current causes membrane depolarization and the occurrence of an action potential in the nerve structures to which the MF was directed. In this case, the proximal part of the axons of fast-conducting motor neurons is excited at the level of the first three interceptions of Ranvier (D-wave - direct wave) and several intercalary ones, which transmit excitation to the motor neuron with different time delays (I-wave - indirect wave). In response to a one-time stimulus, a volley of descending excitation impulses arises in the motor centers of the cerebral cortex, the ultimate goal of which is spinal alpha motor neurons that transmit excitation to peripheral nerves. [11].

Registration of the motor evoked response (MVO) of the examined muscles is carried out by an electroneuromyograph synchronized with a magnetic stimulator.

It is important that with TMS of the motor centers of the brain, only those cortical neurons are excited that are the first to be activated during the implementation of voluntary movement.

Indications for the use of TMS are:

- diagnosis of pathology of the pyramidal tract in diseases of the central and peripheral nervous system;
- evaluation of the effectiveness of restoration of impaired functions after strokes, craniocerebral, spinal injuries, pathology of the peripheral nervous system;
- for the treatment of resistant forms of depression and epilepsy, assessment of the state of the CNS function in psychiatric pathology; for intraoperative monitoring of neurosurgical interventions.

The method also has a number of contraindications that must be taken into account when conducting treatment tactics:

- childbearing;
- the patient has an implanted pacemaker or other electronic devices that control the physiological functions of the body, metal objects that can heat up or move;
- acute disorders of cerebral circulation and other diseases accompanied by instability of vital functions, hyperthermia, etc.

According to V.P. Lyuseniuk 2012, the advantages of the TMS method are:

- the ability to assess the functional state of the parts of the brain and spinal cord, which are "hard to reach" for research by other methods;
- adjustable depth of impact on the structures of the central and peripheral nervous system;
- the method is painless, which is a significant advantage compared to, for example, electrical stimulation;
- does not cause adverse reactions when the intensity and frequency of the pulse are correctly selected, as evidenced by the absence of significant changes in heart rate, blood pressure, electroencephalography (EEG) parameters, prolactin and cortisol levels in the blood, as well as indicators of psychophysiological tests, etc.

Method of examination of patients with the use of TMS

Magnetic stimulation of the motor cortex is carried out using a ring or figure-eight coil (coil - a powerful electromagnetic coil) of various diameters.

Special magnetic stimulators are used, which are approved for medical use. Such stimulators provide the generation of very short duration (250 μs or less) magnetic pulses with a maximum induction of up to 2.5 Tl.

When using a ring coil, its center is placed above the vertex for cortical stimulation of the upper extremities or slightly in front of the vertex for stimulation of the lower extremities.

Motor evoked potentials (MEPs) are recorded bilaterally from symmetrically located muscles using a multichannel electro-neuromyograph. Examine two or more muscles on the upper and lower extremities on both the affected and unaffected side. Surface bipolar electrodes are used, which are fixed on the necessary muscles according to the motor point-tendon scheme. The study is performed with the patient sitting or lying down to ensure maximum muscle relaxation. Before the procedure, the patient is explained the purpose of the examination, its course and safety.

Evaluation of the results of the TMS study

To evaluate the results of the study of TMS, MEP indicators obtained from the proximal and distal muscles of the upper and lower extremities are used.

The following profit center parameters are analyzed:

1) MEP latency — time (in ms) from the beginning of stimulation of cortical motor zones to the moment of MEP occurrence in the corresponding muscle;

2) the duration of the central motor conduction (MCMP) - the difference in MEP latency during cortical and segmental stimulation (in ms); 3) the threshold of MEP occurrence - the minimum induction of the MP, which causes a motor response; percentage of the maximum induction of the magnetic stimulator;

4) MEP amplitude (from peak to peak of positive and negative deviations from the isoline), measured in mV;

5) MEP area (in mV ms);

6) difference in MEP latency between the left and right hemispheres (in ms);

7) amplitude coefficient (in %) — the ratio of the MEP amplitude during cortical stimulation to the M-response amplitude during electrical stimulation;

8) inter-amplitude coefficient (in %), calculated by dividing the amplitude of the MEP from the affected side by the amplitude of the MEP from the unaffected side;

9) area factor (in %), calculated by dividing the area of the MEP on the affected side by the area of the MEP on the unaffected side.

When assessing the functional state of the motor system in patients with IS in the acute and early recovery periods, we used the above-mentioned magnetic stimulator, which was synchronized with the Neuro-EMG-Micro electromyograph using the appropriate software.

For transcranial and transvertebral magnetic stimulation, a standard ring coil with a diameter of 125 mm with a maximum induction of 2.2 Tl was used.

To determine the threshold of MEP onset, stimulation was performed with single pulses, starting from a level of 30% of the maximum (2.2 Tl), with a further increase in intensity by 5% until the onset of MEP, the interpulse interval was 3 s. A series of 5-7 pulses was carried out with averaging of the obtained results.

Studies of other parameters were also carried out by single pulses with close to maximum intensity (2.2 Tl).

So - V.P. Lyusenyuk, V.A. Drought, A.P. Balitsky, N.I. Samosyuk - 2012 - studies were conducted using TMS in 202 patients, 40 of whom did not have neurological pathology (control group). TMS was carried out in them as part of the development of a methodology for determining the parameters of exposure - registration on the MEP myograph, synchronization of TMS of the brain motor centers and electrical myostimulation (EMS) of the muscles of the upper and lower extremities. This was the first stage of the study, which preceded the clinical one, in which 162 patients with new-onset hemispheric IS in the middle cerebral artery (MCA) basin, predominantly with movement disorders, were treated and rehabilitated. The condition of patients according to clinical standardized tests and scales (National Institutes of Health Stroke Scale (NIHSS), Barthel, Rankin) was defined as moderate.

The main goal of this study was to determine the effectiveness of the combined synchronous effect of TMS and electrical myostimulation (EMS) in motor disorders in patients with IS. V.P. Lyusenyuk, V.A.

The drought showed that in TMS of the motor centers of the affected and unaffected hemispheres of the brain, the presence of MEPs from the affected hemisphere has an important prognostic value in restoring movements in the paretic limbs. Absence of MEPSs in patients with IS from the affected hemisphere during the first 7 days. (sometimes up to 10-12 days, i.e., at a time when local

cerebral edema can persist) indicates a reduced rehabilitation potential for restoring movements in paretic limbs.

The authors [6] noted that the general condition of patients with low rehabilitation potential according to clinical signs (scales, tests, indices), CT data, MRI, etc. may not differ from the state of patients with IS with sufficient rehabilitation potential. Functional studies using TMS of the brain motor centers in the first 10–12 days after the development of IS make it possible to determine with a high probability (95% or more) the possibility of restoring movements in the paretic limbs. The main indicator, as emphasized, is the presence of MEPSs from the affected hemisphere of the brain. In the absence of MEPSs, according to MRI or CT data, the ischemic focus was localized mainly in the white matter of the brain. Such localization of the ischemic focus negatively affects the metabolic processes in the thalamus and in the structures that provide connections between the basal ganglia and the brain motor centers, and, therefore, negatively affects the recovery of motor functions.

The selection of patients to study the effectiveness of the developed method for the treatment of TMS with synchronized EMS of the muscles of the upper and lower extremities in IS was carried out according to the following inclusion criteria: clinical diagnosis - acute cerebrovascular accident in the MCA basin on the left or right, with motor disorders; the presence of CT or MRI results that do not contradict the clinical diagnosis; men and women aged 45 to 70; the possibility of carrying out physiotherapeutic procedures (TMS and EMS); the presence of MEPSs from the affected brain hemisphere in TMS of motor centers.

Assessment of the condition of patients before treatment was carried out according to the following scales:

• on the NIHSS scale — from 8 to 12 points (moderate impairment);

• additional determination of the degree of paresis in the affected limbs [special domains (5,6) of the NIHSS scale] - 2-3 points for one limb (moderate or severe hemiparesis, not reaching the level of hemiplegia);

• according to the Barthel index - from 21 to 70 points (moderate or significant dependence on others);

• on the Rankin scale - from 3 to 4 points (moderate or severe signs of disability). The exclusion criteria were: severe clinical condition of the patient (according to the NIHSS scale more than 12 points), hemiplegia, persistent bulbar disorders, urinary incontinence, severe concomitant diseases or complications that make it impossible to carry out full-fledged rehabilitation measures.

All patients of the main and control groups underwent basic rehabilitation measures with a certain individualization: the necessary medication, exercise therapy, breathing exercises, positional treatment, massage, early verticalization, periodic movement restrictions of healthy limbs, «mirror exercises», elements of occupational therapy, etc.

In the main groups of patients with IS with a positive rehabilitation potential (in terms of MEPSs and clinical scales), in addition to basic rehabilitation interventions, additional procedures were performed for the combined effect of TMS of the brain motor centers and EMS of the muscles of the upper and lower extremities according to the developed author's method. The number of procedures per course of treatment ranged from 5 to 10-15, which was determined individually.

Treatment efficacy was assessed according to the following clinical criteria:

• The therapy is effective if, according to the NIHSS scale, on the 10th day and subsequent days of treatment, compared with the 1st day, the dichotomous scale registers a decrease in the severity of neurological deficit by 1 point or more; therapy is ineffective (no changes) - 0 points; deterioration — 1 (by 1 point or more);

• changes in the Barthel index by 5 points or more in the same period of treatment;

• assessment of the degree of disability on the Rankin scale on the 30th and 90th days of treatment compared with the 1st day (changes of at least 0.5 points were taken into account);

• Dynamics of the severity of subjective complaints (headache, systemic and non-systemic dizziness, nausea and/or vomiting, inability to move, speech impairment, cognitive impairment);

• changes in functional parameters during TMS of the motor centers of the brain according to the main parameters (threshold of MEPS occurrence, latency, amplitude, MEPS area, etc.).

In another study [6], which included 162 patients aged 45-70 years (56.8 ± 3.5 years in patients who had a hemispheric stroke), the effectiveness of TMS therapy was also shown. with strokes). Among the examined patients, 94 (58%) were young and middle (up to 60 years old) age. IS was more common in men (61.1%) than in women (38.9%). The hemispheric localization of the ischemic focus in the MCA basin was as follows: in 87 (53.7%) patients it was left-sided, in 75 (46.3%) patients it was right-sided.

The clinical status of patients in all respects corresponded to a state of moderate severity, which was confirmed by assessment using standardized scales: 9.3±1.4 points according to the NIHSS scale, 55.0±2.1 points according to the Barthel index, 3.5±2.1 points according to the Rankin scale. 0.4 points. The leading clinical disorders were motor (100% of patients) and speech (53.7% of patients).

Before treatment, 32 (20%) patients had deep hemiparesis with a decrease in strength relative to healthy limbs by 80-85% - 7 points; in 96 (59%) - a decrease in strength by 60-80% - 5 points (severe hemiparesis), in 34 (21%) - a decrease in strength by 40-60% - 4 points (moderately pronounced hemiparesis).

The use of TMS for diagnostic purposes before the start of rehabilitation measures according to the developed method in the examined patients gave the following results. Of 162 patients with moderate IS, 22.8% had a low rehabilitation potential regarding the possibility of restoring motor functions in paretic limbs. The basis for this was the TMS indicators of the brain motor centers. Absence of MEPSs from the affected cerebral hemisphere in the first 10–12 days after the development of IS. As the results of studies have shown, it indicates a significant blockade of the corticospinal tracts and a low probability of their recovery. In such patients, the ischemic focus was localized in the deep structures of the brain with a fairly early formation of spasticity in the paretic extremities. These patients with low rehabilitation potential were not included in the program of rehabilitation activities according to the developed method.

With a preserved rehabilitation potential, an analysis was made of the MEPs parameters during TMS of the affected hemisphere of the brain and registered on the contralateral upper limb (m. abductor pollicis brevis) compared with similar indicators during stimulation of the intact hemisphere. The authors showed that the most significant difference was registered in the MEPs area from the affected hemisphere — a decrease by 62.5%, a decrease in MEPs amplitude from this hemisphere was 57.1%, and an increase in the latent period was 49.1%. MEPs threshold differed between the hemispheres by 14.8%. Almost all MEPs parameters from the muscles of the upper limbs during TMS of the intact and affected brain hemisphere significantly differed from each other ($p<0.001$).

The average MEPS values recorded from the lower limb (m. tibialis anterior) during magnetic stimulation of the affected and intact cerebral hemispheres significantly differed from each other, as noted above for the hands. MEPS threshold was increased by 16.9%, latency increased by 34.5%. The amplitude of the MEP was reduced by 50%, and the area of the MEP was reduced by 54.3%.

In other words, the difference in MEPS values recorded from the muscles of the lower limb corresponded to the established disorders (decrease in MEPs area and amplitude, increase in the latent period, etc.) for the upper limbs. Taking into account the length of the corticomuscular pathway, the MEPs latency for the muscles of the lower extremities was, on average, 10 ms greater than for the muscles of the arms.

The amplitude of the MEPSs when comparing the indicators on the lower and upper limbs differed by almost 2 times, which is explained by an increase in the phenomena of desynchronization with an elongation of the path of passage of nerve impulses from the cortical centers to the muscles of the legs. The difference in MEPs areas on the legs and arms was not as large as for the previous indicators, which confirms the effect of desynchronization. Also, the area coefficients did not differ significantly: on the lower limbs their value was 40.1±4.47%, and on the upper limbs — 37.3±4.61% ($p>0.1$).

When comparing MEPs parameters in the control group (without neurological pathology) with similar parameters in post-stroke patients (main group), the following differences were noted. The average values of the main parameters of the MEPs obtained during TMS of the motor centers of the intact hemisphere of both the arm and the leg significantly differed from similar indicators in healthy individuals by at least 15% ($p<0.05$). This indicates that the intactness of the hemisphere is relative, i.e., in the hemisphere without focal changes, according to MRI or axial computed tomography (ACT), there are significant functional changes in the corticospinal tract. The established facts justify the use of TMS in the rehabilitation process with the influence on the motor cortex not only of the affected hemisphere, but also of the intact one.

When comparing the main parameters in TMS of the motor centers of the arm and leg from the affected hemisphere, depending on the severity of paresis (assessment of signs on the NIHSS scale in a 4-point system separately for the arm and leg), the following data were obtained. In patients with mild motor disorders (paresis at the level of 1 point), a noticeable increase in the threshold and a decrease in the amplitude parameters of the MEPs were recorded compared with those on the

unaffected side. At the same time, the latency of the MEP did not change significantly. The same was true for the parameters of the peripheral M-response from the muscles of the paretic extremities ($p<0.05$).

In patients with more severe disorders (2 points on the NIHSS scale), corresponding to moderately pronounced paresis, an increase in the threshold and latency and a decrease in the amplitude of the MEPs on the side of the paresis were recorded compared to the unaffected side. In parallel, a decrease in the peripheral M-response from the muscles of the affected limbs was noted. In almost 30% of patients, MEPs was registered only with the patient's muscular effort, which may indicate a more significant pyramidal dysfunction.

The average MEPs values recorded from the lower limb (m. tibialis anterior) during stimulation of the contralateral affected and intact hemisphere significantly ($p<0.01$) differed from those in the control group.

In patients (n=37) with a general condition of moderate severity with paresis (3 points on the NIHSS scale), in most cases, TMS of the affected hemisphere did not cause MEPs, which was also accompanied by a decrease in the peripheral M-response from the muscles of the paretic limbs. Such changes (combination of pyramidal disorders and peripheral disorders) developed by the 5-6th week after the stroke and predictively indicated a severe motor deficit with the formation of severe spasticity.

Thus, the use of TMS in the complex of diagnostic methods in patients in acute and early recovery periods of hemispheric IS allows assessing the functional state of the corticospinal tract, objectifying the degree of paresis and, to a certain extent, predicting the possibility of restoring motor functions. The absence of any response from the muscles on the affected side indicates an unsatisfactory further recovery of motor functions. The method of conducting TMS is simple and does not require a significant investment of time, it is easily tolerated by patients. In the express examination of patients with IS in the acute and early recovery periods, it is sufficient to determine the presence or absence of MEPs from the affected hemisphere. Its absence indicates a reduced rehabilitation potential for restoring movements in paretic limbs. If more accurate prediction is needed, other parameters of the MEPs are determined, such as the threshold of occurrence, latency, amplitude, and their coefficients. These indicators can also serve as the basis for long-term monitoring of motor functions.

The use of TMS in the complex of treatment and rehabilitation measures for IS in the acute and early recovery periods.

A method was developed for the treatment of patients with IS with motor disorders in the acute and early recovery periods, aimed at improving the effectiveness of therapeutic and rehabilitation measures for this category of patients. The task was solved by the combined synchronous influence of TMS of the motor centers of both hemispheres of the brain (affected and unaffected) and EMS of the upper and lower extremities. We used standard equipment for TMS and multi-channel (4-, 6- or 8-channel) for EMS. Before TMS, the search for the necessary stimulation zones is carried out, the areas are determined, upon activation of which it is easiest to obtain the evoked response of the necessary muscles. The procedure is started by searching for the corresponding TMS zones for the intact (unaffected) side (ipsilateral to the paretic limbs), the EMS electrodes are fixed on the arm flexors. Next, determine the threshold intensity of magnetic pulses that cause contraction of the muscles of unaffected limbs. Current parameters are selected that cause muscle contraction in the elbow and wrist joints. TMS and EMS are carried out simultaneously. Stimulation parameters - sending 2-3 s, pause 4-6 s, (the duration of the procedures from 3 minutes is gradually increased to 5 minutes). Synchronization of transcranial and muscle stimulation makes it possible to reduce the power of magnetic impulses by 20–40%.

TMS of the corresponding zones of the motor cortex and EMS of the leg muscles, extensor of the unaffected limb, are carried out according to the same scheme (send 2–3 s, pause 4–6 s). Then, TMS of the cortical motor zones of the affected hemisphere and EMS of the muscles of the paretic limbs are performed. The scheme of action is similar, however, stimulation of other muscle groups (extensors on the arm, flexors on the leg), i.e., muscles are antagonists of spastic muscles.

Usually, an increase in the tone of the muscles of the extremities is recorded 1–2 months after a stroke, with complete formation of spasticity by the end of the 3rd month. TMS has an antispastic effect and in 67% of patients with hemispheric stroke who were followed up, the recovery of motor functions was significant with moderate spasticity.

It should be noted that in order to prevent the formation of spasticity in post-stroke patients, early rehabilitation interventions are necessary: proper styling, active and passive movements, elimination of pain syndrome, if any, etc. TMS has a significant antispastic effect when

used in the first 2–3 weeks after the onset of IS subject to the functional safety of the cortico-muscular pathway.

Transcranial sending of magnetic impulses synchronously with the stimulation of the muscular apparatus of the paretic limbs, which is under the appropriate control of the cerebral cortical centers, allows you to restore or improve the function of blocked pathways that are in a state of parabiosis after a stroke. Stimulation of the central and peripheral motor neurons makes it possible to close the functional circuit, since stimulation of the muscular apparatus also has an afferent effect. The impact on the affected hemisphere of the brain stimulates the restorative mechanisms of sanogenesis, helps to eliminate the phenomena of diaschisis and reduce the size of the ischemic penumbra. The impact on the unaffected hemisphere and healthy (non-paretic) limbs contributes to the activation of compensation mechanisms.

The developed technique uses an important rehabilitation principle: a combination of the afferent and efferent systems by stimulating the central and peripheral parts of the cortico-muscular tract, as well as the afferent structures of the neuromuscular apparatus.

TMS exposure parameters

A magnetic impulse (MIMP) is applied to the motor centers of the cerebral cortex, a magnetic induction field of 1–2.2 Tl, with a frequency of 1 Hz. First, the threshold value of the impulse is determined by registering the MEPs of the corresponding limb muscles on the screen of the electromyograph. The stimulation threshold is determined on each side for the motor centers of the arms and legs. The determination of the threshold begins with the minimum value of MImp - 0.8-0.9 T with its gradual increase until the registration of the MEPS. In different patients (depending on the severity of the condition) on the side of the affected or unaffected hemisphere, the threshold stimulation values vary within 0.9–2.1 Tl. Treatment began with MEPs of subthreshold strength (20–30% lower than the threshold VMPs) with their automatic delivery: sending 2–3 s, pause 4–6 s. At the same time, magnetic stimulation of the unaffected hemisphere was performed at a frequency of 1 Hz, and that of the affected hemisphere at a frequency of 5 Hz. Magnetic stimulation was synchronized with EMS. Subsequently, the parameters of TMS and EMS were selected in such a way as to cause visible contractions of the necessary muscles.

EMS was carried out according to the classical method: electrodes made of conductive rubber with wet pads or through a conductive gel were applied to the necessary muscles. A pulsed current with a frequency of 20–80 Hz was used, which was delivered in bursts rhythmically (send 2–3 s, pause 4–6 s). The current strength was regulated according to the found threshold in the range up to 40 mA (however, not exceeding the current density of 0.2 mA/cm2).

After the threshold values of MIMP were determined, stimulation was synchronized: simultaneous sending of MIMP and bursts of current to the muscles (sending 2–3 s, pause 4–6 s). The duration of exposure to each transcranial zone and the corresponding muscles is up to 5 minutes, in total up to 20 minutes. At the same time, the combined procedure made it possible to reduce the magnitude of MImp and current to 30% of the initial threshold values in the presence of contractions of the necessary muscles, which made the procedure more comfortable. The course of combined (TMS+EMS) exposure in the complex of rehabilitation treatment of patients with IS ranged from 3-5 to 10-15 procedures, depending on the individual rehabilitation program.

The use of the developed method in combination with other rehabilitation measures (exercise therapy, massage, breathing exercises, positional treatment, necessary drug therapy, etc.) was carried out in 50 patients with IS, 50 patients served as controls, who did not undergo TMS and EMS, but were prescribed the indicated above basic therapy.

The assessment of the condition of patients and the effectiveness of rehabilitation measures were determined by the authors using the most informative standardized scales and tests: the NIHSS scale, the modified Rankin scale, the Barthel index (scale).

Before the start of treatment in both groups (main and control), all patients needed outside help (the Barthel index was 52.0±3.8 and 53.1±1.9 points, respectively), and according to the clinical course (NIHSS scale) they corresponded to gradations "state of moderate severity" (fluctuations from 9 to 12 points; main group 10.1±1.8 points, control group 9.4±0.8 points). According to the Rankin scale before treatment, the patients could be regarded as invalids of groups I-II (3.6±0.3 and 3.5±0.4 points, respectively).

In the process of treatment and rehabilitation measures, positive changes were recorded in both groups, however, they were more significant when using the developed method in combination with the standard treatment regimen. So, already after 10 days of rehabilitation in the main group, the studied parameters changed by 28.7±2.3% (NIHSS scale) and 33.2±1.8% (Bartel index). In the control group of patients who received a

standard rehabilitation complex, these shifts were 11.7±1.2 and 13.8±1.7%, respectively (the difference between the groups was significant, $p<0.05$).

It is important that after an individually determined number of TMS and EMS procedures (from 3–5 to 15), the recovery processes continued. On the 90th day, a slight dependence remained (95.3±2.0 points with a norm of 100 points, $p>0.05$). In the control group, the indicators according to the Barthel index corresponded to the «moderate dependence» gradation (84.8±1.8 points), the difference between healthy individuals was significant ($p<0.05$).

The question of the duration and frequency of the course of treatment with TMS - therapy for stroke remains debatable.

There was a positive dynamics of the main indicators (Δ%) in the study of MEPSs in patients with IS under the influence of the treatment and rehabilitation complexes used. The latency of MEPs from the muscles of the upper limb upon stimulation of the intact hemisphere in patients with IS after treatment (19.9±0.48 ms) approached those in practically healthy individuals (19.3±0.2 ms; $p>0.05$). This also applied to the parameters from the lower limb — MEPs latency during stimulation of the intact hemisphere after treatment was 29.72±0.53 ms, in practically healthy people it was 28.01±2.4 ms ($p>0.05$). All other parameters of MEPs (amplitude, area, threshold of occurrence, etc.) differed from those in the control group ($p<0.01$), which indicated the preservation of pathological changes in both the affected and intact cerebral hemispheres.

In patients with IS who received basic therapy (without magnetic and electrical stimulation), the indices after treatment were inferior to those in the main group ($p<0.05$), although there was no difference between the groups in terms of MEPs before treatment ($p>0.05$). At the same time, in the group itself, changes in the MEPs were more significant during stimulation of the affected hemisphere (change in latency by 10%; $p<0.05$), while upon stimulation of the intact hemisphere after the course of treatment, only a tendency of the MEPs to increase was found ($p>0.05$).

When calculating the MEPs amplitude, it was revealed that it significantly ($p<0.05$) increased in the upper limbs during stimulation of the affected and intact hemisphere. Such data indicate that the use of TMS and EMS in medical rehabilitation had a very positive effect on the affected and intact cerebral hemispheres, while conventional rehabilitation methods mainly affected the affected hemisphere.

When comparing MEPS indicators in the acute and early recovery periods under the influence of the developed rehabilitation complex, the following features were revealed. In the acute period of IS (the first 10-12 days), the most significant positive dynamics was characterized by MEPSs from the affected hemisphere, the improvement of which was later, with some delay, accompanied by a decrease in motor disorders. Clinically, such results were manifested approximately by the 30th day after the stroke. Thus, according to the NIHSS scale, the average values of the indicator decreased by 2.1±0.9 points ($p<0.05$), which indicates a positive trend. Similar shifts were also found on other standardized scales: by 2.2±0.21 points on the Rankin scale ($p<0.05$), and by 34.3±1.95 points on the Barthel index ($p<0.05$).

This fact can be explained by restorative processes that are enhanced under the influence of TMS in the affected hemisphere of the brain. In the remaining viable neuronal and glial structures, the excitability and potential of cell membranes are apparently restored. This was consistent with the disappearance of concomitant cerebral tissue edema around the ischemic focus during MRI examination.

The dynamics of MEPs parameters after 3–4 weeks in patients after IS with preserved motor impairments differed significantly with early use of TMS (up to 2 weeks after the onset of IS). During these periods, the main mechanism of rehabilitation was determined by compensatory processes, positive MEPs dynamics was recorded from the intact hemisphere and the inclusion of an uncrossed corticospinal tract in the control of motor functions. The mechanism of neurological deficit correction due to stimulation (normally inhibited) of the downward control of the motor pathways of the unaffected hemisphere over the activity of ipsilateral motor neurons is an important component of recovery processes in motor disorders after hemispheric IS.

The conduction of EMS of a peripheral motor neuron synchronously with TMS creates a closed afferent-efferent circuit, contributes to the restoration of physiological connections disconnected as a result of the pathological process.

Thus, TMS of the brain in hemispheric IS is essential for determining the functional state of the motor centers of the brain and the motor system as a whole. Together with neuroimaging methods (MRI, CT), it makes it possible to objectively assess the condition of patients and, to a large extent, determine their rehabilitation potential. Comparison of the results of clinical observation, neuroimaging examination and TMS in patients with

hemispheric IS allows us to identify several possible moments in the restoration of impaired motor functions: activation and restoration of functionally inactive, but structurally preserved (including in the area of the ischemic penumbra) neurons and neuronal pathways (restorative mechanisms); stimulation of the formation of new functional connections due to retraining of other functional structures of the ipsi- and contralateral hemisphere (neuroplasticity and compensatory mechanisms).

Thus, the use of TMS in patients with hemispheric stroke with motor disorders is highly informative in determining the functional state of the cortico-muscular pathway (at the level of 95%) and, together with clinical scales (NIHSS, Barthel, Rankin) and neuroimaging methods, can serve as an objective modern method for examining post-stroke patients to determine the rehabilitation potential regarding the possibility of restoring motor functions.

Diagnostic TMS to determine the functional state of the corticospinal tract in patients with hemispheric IS should include the study of the MEPs not only from the affected hemisphere, but also from the intact one. The absence of MEPs in the acute and early recovery periods from the affected hemisphere indicates a low rehabilitation potential in restoring the motor functions of the affected limbs.

It has been established that in post-stroke patients with new-onset hemispheric IS with motor disorders and moderate neurological deficit, MEPs changes occur during magnetic stimulation of the motor cortex not only of the affected hemisphere, but also of the intact hemisphere (according to MRI and/or ACT), therefore, rehabilitation effects should be directed also to the conditionally intact hemisphere. TMS of the brain motor centers synchronously with EMS of the peripheral motor neuron in patients with hemispheric IS with preserved rehabilitation potential during course exposure (5-15 procedures) helps to restore the functional connections of the motor system (unblocking the corticospinal tract), inhibited due to stroke, and has a preventive effect against hypotrophic-dystrophic changes in the musculoskeletal system of paretic limbs.

It has been established that in case of motor disorders, in order to achieve the optimal result, magnetic stimulation of the affected hemisphere should be carried out with a frequency of magnetic impulses of 5 Hz, and of the unaffected hemisphere - 1 Hz with synchronous EMS according to the classical method. Such parameters enhance restorative and compensatory processes.

Treatment of patients with IS with a positive rehabilitation potential using TMS and EMS as part of a complex of rehabilitation measures made it possible to achieve positive results in terms of integrative indicators in 93% of cases, which manifested itself in patients after treatment with mild or moderate neurological deficits. In patients with preserved rehabilitation potential, who received a rehabilitation complex without TMS and EMS, the functional state improved after the course of treatment, but did not reach the level of the main group. A follow-up observation for 6 months showed the preservation of the achieved results with outpatient continuation of rehabilitation measures.

The developed method of synchronous use of TMS and EMS in patients with IS with motor disorders is different and can be used in patients in the acute and early recovery periods of a stroke.

To increase the effectiveness of treatment of patients in the acute and early recovery periods with a preserved rehabilitation potential, it is recommended to use TMS with the effect on the affected hemisphere of magnetic pulses with a frequency of 5 Hz, and on the unaffected hemisphere - 1 Hz in synchronous combination with EMS of the muscles of the extremities. The duration of the TMS and EMS procedures should be from 10 to 20 minutes, and the number of procedures should be from 5 to 10-15. TMS and EMS should be carried out against the background of other medical and rehabilitation measures: drug therapy, exercise therapy, massage, positional treatment, occupational therapy, verticalization. Diagnostic and therapeutic TMS procedures are optimally carried out from the first days of the disease with hemispheric IS after stabilization of hemodynamics, normalization of vital functions and in the absence of contraindications.

The need for repeated courses of TMS in combination with EMS for rehabilitation purposes in patients with IS is determined individually, however, it is optimal to conduct them within the first 6 months after a stroke. the period of the disease increases the rehabilitation potential of patients, contributes, according to many authors, to a faster recovery of impaired motor functions.

CONCLUSION

1. To increase the effectiveness of treatment of patients in the acute and early recovery periods with preserved rehabilitation potential, it is recommended to use TMS with exposure to magnetic pulses at a frequency of 5 Hz on the affected hemisphere, and 1 Hz on the unaf-

fected hemisphere with repeated courses of 10 days in synchronous combination with EMS of limb muscles.

2. The TMS therapy method is recommended for widespread implementation in the rehabilitation treatment of patients in the acute and early recovery periods of stroke to restore motor and sensory functions of the brain.

Conflict of interest: The authors declare that there is no conflict of interest as this article is a review of the scientific literature.

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ISHEMIK INSULTDA TRANSKRANIAL MAGNIT STIMULYATSIYASINING SAMARADORLIGI.

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ABSTRAKT

Ishemik insult bilan og'rigan bemorlarda motorli buzilishlar bilan o'tkir va erta tiklanish davrida reabilitatsiya salohiyatini aniqlash uchun funktsional transkranial magnit stimulyatordan foydalanish tavsiya etiladi. O'tkir va erta tiklanish davrida ta'sirlangan yarim shardan motorli qo'zg'atilgan potentsiallarning saqlanishi jabrlanganlarning motor funktsiyalarini tiklash istiqbollarini ko'rsatadi. Ta'sir qilingan yarim shardan vosita qo'zg'atilgan potentsialning yo'qligi vosita funktsiyalarini tiklash uchunreabilitatsiya salohiyatining pastligini ko'rsatadi. Harakat buzilishlari va o'rtacha nevrologik nuqsonlari bo'lgan birinchi marta yarim sharik ishemik insult bilan og'rigan bemorlarda nafaqat ta'sirlangan yarim sharda, balki butun yarim sharda ham motorning qo'zg'atilgan potentsialidagi o'zgarishlar qayd etilgan, shuning uchun reabilitatsiya tadbirlari ham shartli ravishda yo'naltirilishi kerak. Hozirgi vaqtda bir qator ilmiy adabiyot manbalarida transkranial magnit stimulyatsiya va elektromiyostimulyatsiyadan sinxron foydalanish usulining samaradorligi haqida ma'lumot berilgan. Motor buzilishlari bo'lgan ishemik insultli bemorlarda reabilitatsiya salohiyatini saqlab qolish. Usuldan foydalanish qon tomirlarining o'tkir va erta tiklanish davrida tibbiy reabilitatsiya natijalarini yaxshilaydi; Qo'llash usuli, uning davomiyligi va chastotasi ishlab chiqilgan va sinovdan o'tgan. Ushbu sharh insultga uchragan bemorlarni reabilitatsiya qilish usullari bo'yicha bir qator tadqiqotlar ma'lumotlarini tahlil qiladi.

Kalit so'zlar: transkranial magnit stimulyatsiya; ishemik insult; harakat buzilishi; reabilitatsiya salohiyati

ЭФФЕКТИВНОСТЬ ПРИМЕНЕНИЯ ТРАНСКРНИАЛЬНОЙ МАГНИТНОЙ СТИМУЛЯЦИИ ПРИ ИШЕМИЧЕСКОМ ИНСУЛЬТЕ

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АБСТРАКТ

Для определения реабилитационного потенциала у больных с ишемическим инсультом в остром и раннем восстановительном периодах с двигательными нарушениями рекомендуется использовать функциональный транскраниальный магнитный стимулятор. Сохранение двигательных вызванных потенциалов из пораженного полушария в остром и раннем восстановительном периодах свидетельствует о перспективе восстановления двигательных функций пострадавших. Отсутствие двигательного вызванного потенциала из пораженного полушария свидетельствует о низком реабилитационном потенциале для восстановления двигательных функций. У больных с впервые возникшим полушарным ишемическим инсультом с двигательными нарушениями и умеренным неврологическим дефицитом изменения двигательного вызванного потенциала отмечались не только в как в пораженном полушарии, так и в интактном полушарии, поэтому реабилитационные вмешательства также должны быть направлены на условно-целое полушарие. В настоящее время в ряде научных литературных источников приводятся сведения об эффективности метода синхронного применения транскраниальной магнитной стимуляции и электромиостимуляции на сохранение реабилитационного потенциала у больных с ишемическим инсультом с двигательными нарушениями. Применение метода улучшает результаты медицинской реабилитации в остром и раннем восстановительном периодах инсульта; Разработан и апробирован способ применения, его продолжительность и кратность. В данном обзоре анализируются данные ряда исследований, посвященных методам реабилитации пациентов, перенесших инсульт.

Ключевые слова: транскраниальная магнитная стимуляция; ишемический инсульт; двигательные расстройства; реабилитационный потенциал.