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ASPECTS OF CEREBRAL NEUROPLASTICITY INDUCED BY KINETOTHERAPY COMBINED WITH TRANSCRANIAL MAGNETIC STIMULATION IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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Abstract. *In this study the issue of early recovery in patients with acute ischemic stroke was addressed. The aim of the paper is to develop a phased recuperation algorithm by kinetotherapy and transcranial magnetic stimulation for patients with acute ischemic stroke. Research hypothesis is that: the association of these two types of therapies could induce a more pronounced plasticity in patients with motor deficit after ischemic stroke. Several methods, techniques and recovery concepts, such as rTMS, neuro-proprioceptive facilitators and other approaches by Bobath, Brunnstrom and Rood, have been used in the study.*

The study was randomized and performed on a group of 140 patients with acute ischemic stroke, selected according to strict inclusion and exclusion criteria. The results of this study, as well as other studies based on rTMS in stroke patients, indicate the possibility of reducing abnormal interhemispheric inhibition from the contraceptive hemisphere to the ipsilateral hemisphere by stimulation with high frequency aspiration to the ipsilateral hemisphere, as well as by low frequency stimulation of the contraceptive hemisphere, which has been shown to improve the functional performance of the hand affected by pathology.

Keywords. *repetitive transcranial magnetic stimulation, kinetotherapy, stroke, early neurorehabilitation.*

Introduction. Worldwide, stroke is manifested by increased incidence and prevalence of pathology, and most survivors require some assistance or depend on caretaker to carry out day-to-day activities. This pathology remains the main cause of adult disability so far, creating stressful situations and a great burden for patients, their families, and society, while imposing significant expenditure [7, 19]. In stroke patients the motor deficit is the most common neurological deficit and is manifested by contralateral hemiparesis of the ipsilateral hemisphere [16, p. 1349]. Hemiparesis occurs due to the pathological focus in one of the hemispheres, and the degree of impairment of the functions is closely correlated with the topographic location of the focus. At the same time, some research suggests that the degree of impairment of motor functions also depends on inter-spherical transcallosal inhibition processes [17, p. 1641-1659]. In the framework of research on healthy subjects, reciprocal inter-cerebral transcallosal inhibition processes were detected between the right and left hemisphere motor cortex [12, pp. 429-440]. In patients suffering from stroke, the inter-ispheric competition is deregulated by a decrease in the excitability of the ipsilateral hemisphere and at the same time by an abnormal increase in activation of the contraceptive hemisphere. Due to the hyperactivity of the contrallesional hemisphere, an abnormal inhibition of the ipsilateral hemisphere occurs, suppressing the lost function [17, p. 1641-1659].

Some authors such as Kakuda W. et al. [10, pp. 496-502] discusses its ability to regulate it, and considers that low-frequency TMSr applied counter-productively produces beneficial results in functional rehabilitation of stroke patients, while other authors such as Stagg C. J. et al. [9, p. 276-284] argue that high frequency TMSr on the ipsilateral hemisphere was the most effective option. At the same time, other authors combine TMSr low-frequency TMSr with ipsilesional high frequency TMSr [20, p. 323-9], also achieving significant results. The most commonly used rTMS protocols with bidirectional effects depending on the applied frequency are: low-frequency rTMS (most commonly used: 1 Hz) produces inhibition of cortical excitability, while high-frequency rTMS (most commonly used: 5 Hz) produces its facilitation [8, p. 187-199].

Recovery of stroke patients is a complex process in its nature, and rehabilitation approaches differ. Some specialists focus their treatment on a unique approach, while others combine several components from a range of different approaches, but to date there is no compelling evidence to support only a certain approach in rehabilitation treatment. The results achieved highlight the need for further elaboration, which will allow to minimize recurrence and to increase functional independence.

Research aim. Elaboration of a staged recovery algorithm by kinetotherapy and transcranial magnetic stimulation for patients with acute ischemic stroke.

Materials and methods. The research was conducted within the Cerebrovascular Diseases Department of the Institute of Emergency Medicine, on a sample of 140 patients that was divided into the control and experimental group, each of 70 patients. Patient selection and group homogeneity have been developed for strict inclusion and exclusion criteria in research. Inclusion criteria: 1) Adult patients diagnosed with ischemic stroke, confirmed by CT or MRI; 2) The age of the disease should be up to 72 hours from onset; 3) NIHSS exam less than or equal to 18 points; 4) Patient or family / legal representative agreement to participate in the study. Exclusion criteria: 1) Participation in another study of neuroplasticity; 2) The presence of metallic or electrical implants in the body; 3) Presence of neurosurgical intervention in anamnesis; 4) The presence of severe craniocerebral trauma in anamnesis; 5) The presence of metal objects on the face or head that cannot be removed during the experiment (e.g. piercing); 6) Using hearing aids; 7) Pregnancy and breast-feeding period; 8) The presence of an undetermined brain pathology; 9) Refusal of the patient or legal representative to take part in this study.

In the experimental group, recovery was initiated within the first 72 hours of onset, and the program included transcranial magnetic stimulation, respiratory gymnastics, postures, stretches, passive mobilizations, orthesis and at the same time elements of neuro-proprioceptive facilitation and other approaches to Bobath, Brunnstrom and Rood.

Transcranial magnetic stimulation was initiated within the first 72 hours and consisted of 5 procedures. Recognition of engine evoked potential (MEP) was performed bilaterally from the first dorsal intestinal muscle (FDI) using electrodes of 28 x 20 mm diameter and AgCl surface. The active electrode was placed on the pulp of the muscle, and the reference electrode on the metacarpophalangeal joint of the indicator finger. In the study we used a TMS "MagPro R30 + Option (MagVenture A / S, Denmark)" which has a biphasic pulse configuration with 280µs amplification time, connected to a MCF-B65 static cooling butterfly coil has an external diameter of 75mm. Initially, the M1 hand and M1 level left and right were determined as the point where stimulation evoked the largest MEP from the contralateral FDI muscle. The optimal position for FDI activation was found by moving the bobbin in steps of 0.5 cm around the motor area of the hand at the cortex motor for each hemisphere Figure 1.

Regions where light superpower intensities always produced the largest MEPs with the deepest where appropriate FDI muscle were marked with a marker. The ipsilenous hemisphere was stimulated with: 5 Hz, 100 pulses in block, 20 blocks, the interval between blocks 5 sec. Total-2000 pulses. 110% PMR and counter-polar hemisphere: 1 Hz, 60 pulses in block, 10 blocks, interval between blocks 5 sec. Total-600 pulses. 90% PMR.

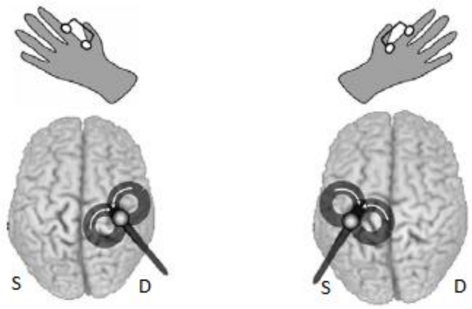

Fig.1. TMS of the corticospinal paths to the distal upper extremities, with the eight-figure coil

The point on the coil rings represents the optimal point of stimulation of the right-hand side of the cortex to the right (A) or to the left (B) [6, p. 858-882].

The kinetotherapy recovery program in the experimental group was divided into 5 phases: I Supporting vital functions, II Restoring the function of self-posturing in decubitus, III Lift at the edge of the bed, IV Orthostatism, V Walking.

For each rehabilitation stage the program is standard and has been selected depending on the patient's condition in: Breathing exercises; Exercises to promote the stability and controlled mobility of affected MS and MI; Exercises to promote the stability and controlled mobility of the trunk; Exercises to promote the stability and controlled mobility of the affected part as a whole; Exercises to develop the balance of the trunk from sitting; Techniques of initial acquisition, consolidation and improvement of control, equilibrium, coordination and correct paths in motor actions; Variations of walking.

The treatment cure in the experiment group included a total of 20 kinetotherapy sessions lasting 30 minutes each, and the sessions were performed two times a day during ten days.

Results. For this study it was proposed to find and then to highlight the evolution of neurological condition, functional independence, posture control capacity in space, motor recovery and disability in patients with ischemic stroke.

The lot established by us was evaluated through the international clinical assessment scales: NIHSS, Barthel, PASS, FMA AD and Rankin m. Through these assessment scales, patients were evaluated on the first, fifth and tenth days, which highlighted different degree of improvement in the studied lots (Table 1). The data obtained in the initial stage evaluations reveal the true homogeneity of the examined groups at the threshold P> 0.05 for all the tests we performed.

Table 1. Comparative statistical data of the tests of control lot (C) and experimental lot (E)

Clinical tests	Group	Evaluation phases								
		1st day			5th day			10th day		
		x ± m	t	P	x ± m	t	P	x ± m	t	P
NIHSS	M	9,43 ± 0,40	0,36	>0,05	8,50 ± 0,38	0,66	>0,05	6,90 ± 0,33	1,67	>0,05
	E	9,63 ± 0,38			8,17 ± 0,33			6,13 ± 0,33		
Barthel	M	31,71 ± 0,63	0,07	>0,05	36,36 ± 0,75	0,99	>0,05	46,07 ± 1,01	2,08	<0,05
	E	31,64 ± 0,75			37,50 ± 0,88			49,21 ± 1,13		
PASS	M	9,80 ± 0,58	0,89	>0,05	15,80 ± 0,53	2,14	<0,05	21,94 ± 0,50	2,91	<0,01
	E	9,07 ± 0,58			17,56 ± 0,63			23,96 ± 0,48		
FMA A-D	M	13,86 ± 0,68	1,37	>0,05	16,00 ± 0,70	0,64	>0,05	22,27 ± 0,90	0,98	>0,05
	E	12,59 ± 0,63			16,74 ± 0,93			23,66 ± 1,08		
Rankin	M	4,67 ± 0,05	0,25	>0,05	4,01 ± 0,05	2,01	<0,05	3,00 ± 0,05	2,61	<0,05
	E	4,69 ± 0,03			3,87 ± 0,05			2,81 ± 0,05		

Note: NIHSS-assesses neurological status by a score of 45-0, Barthel-appreciates functional independence by increasing score, from 0-100, PASS-appreciates posture control capacity in space by increasing score, from 0 to 36, FMA AD-appreciates the rhythm of hand rising from 0-66, and Rankin m.- appreciates the degree of disability by scoring from 5-0.

All patients showed a recovery of the tested parameters, but differently. Thus, the NIHSS score was improved by 0.93 points on day 5 and by 2.53 points on day 10 in the control group and in the 1.46 points on day 5 and 3.50 points on Day 10. In the evaluation with this scale, the "t" index is 0.66 on day 5 and 1.67 on day 10, which represents a significance threshold of P> 0.05. Changes in the Barthel Score show a more pronounced increase, which is also reflected by the significance threshold that was estimated to be P <0.05. This materiality threshold was obtained based on the differences between the data obtained from the group assessments. Thus, in the control group there was an increase of 4.64 on day 5 and 14.36 on day 10, and in the experimental group of 5.86 on day 5 and 17.57 on day 10.

More significant improvements are recorded in the PASS scale, where the statistical veracity at the threshold P <0.05 was obtained at the 5th assessment. On the 10 day of the valuation, the statistical verifiability threshold exceeds the "t" values of 2.66 for the significance threshold P <0.01. Thus, restoring posture control capacity in space was represented by an increase in the tested parameters in the control group of 6.00 on day 5 and 12.14 points on day 10 and the experimental group of 8.49 on day 5 and 14.89 points on day 10. It was more difficult to restore the hand, as it is well known that the hand is the segment that has a very complex structure and function, which makes it even more difficult to restore. Evaluation results with the FMA AD scale however show an increase in the results of 2.14 on day 5 and 8.41 points on day 10 in the control group and 4.16 on day 5 and 11.07 on day 10 in the experimental group. Outstanding results were also obtained in the Rankin scale evaluations, where an improvement of 0.66 on day 5 and 1.67 points was recorded on day 10 in the control group and 0.81 on day 5 and 1.87 points on day 10 in the experiment group.

The data obtained from the phased evaluations were statistically analyzed by the Student test, which made it possible to assess the level of authenticity of the obtained results.

Discussions. Initial growth of motor activity after stroke could result from solving reversible lesions in neurons and glia, such as changes in membrane potential, axonal conduction, or neurotransmission. The reorganization of the insecure assemblies of the neurons that represent motor actions in the sensory-motor cortex, as well as in the ascending and descending transortical pathways, seems to accompany further improvements in motor activities [5, p. 1677-1684].

Different sources of rehabilitation of stroke patients support the idea that kinetotherapy is an important mechanism for promoting functional recovery in these patients [19, p. 1482-1490]. However, the moment of kinetotherapeutic involvement is different and controversial, some sources support the initiation of the first 24 hours of diagnosis of stroke, considering this period to be a primary one in the recovery process, which will favor the achievement of therapeutic success even by the presence of the neurocitoprotective effects [19, pp. 1482-1490]. And it is well known that early initiation can minimize complications associated with stroke, which limits optimal recovery. At the same time, other sources disagree with this statement, for example the results of a randomized study [3, pp. 46-55] which at the initial stage highlighted that early mobilization seems to be safe [2, p. 390-396] This principle is also supported by some authors such as Bernhardt J. [1, pp. 88-98] and others claim that rehabilitation cannot be initiated at an early stage because the stroke patient should maintain the decubitus position for 72 hours from onset pathology, which would favor the maintenance of cerebral blood flow to ischemic tissue.

At the same time, studies were carried out aimed at exploring the opinion of different professionals that are related to the given problem. One of the most important was performed on 202 professionals, a group consisting of doctors, kinetotherapists, occupational therapists and nurses. Three quarters of them agreed that patients with ischemic stroke would be mobilized within 24 hours of onset, and one quarter of the professionals had concerns about mobilization during this period [15, p. 10-15].

Hence, although professionals' views on early mobilization after stroke have a different and controversial character, they have shown a prevalence largely aimed at initiating mobilization within the first 24 hours of onset of pathology.

Conclusions. According to the results obtained in the statistical processing of the data, significant improvements are revealed in all the tested functions, but mainly in the experimental group where the patients also benefited from rTMS.

The results of our study and other rTMS-based studies in stroke patients indicate the possibility of reducing abnormal interhemispheric inhibition from the contrallesional hemisphere to the ipsilateral hemisphere by high frequency stimulation with the ipsilateral hemisphere [9, p. 276-284] and by low-frequency stimulation on the contrallesional hemisphere [10, pp. 66-107] which has been shown to improve the functional performance of the hand affected by pathology.

These results assume that they were also influenced by early initiation by a program adapted to the rehabilitation stage, which appears to be safe and which may have influenced the minimization of central nervous system destruction processes, which, according to Cramer SC, [4, p. 272-287], suffers spontaneous processes at the molecular, cellular, systemic and behavioral levels.

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