# **Brain–Computer Interfaces in Poststroke Rehabilitation: a Clinical Neuropsychological Study**

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> **Objectives.** To assess the efficacy of using a brain–computer interface with a hand exoskeleton (BCI–exoskeleton) in the complex rehabilitation of patients with the sequelae of cerebrovascular accidents and to determine the minimally adequate reserves of cognitive functions required for the patient to carry out effective mental training using the movement imagination paradigm. **Materials and methods.** The study included 55 patients (median age 54.0 [44.0; 61.0] years, median time since stroke 6.0 [3.0; 13.0] months) in study and control (simulation of BCI) groups. The severity of paresis was evaluated on the Fugl–Meyer Assessment of Motor Recovery after Stroke (FMA) scale and the Action Research Arm Test (ARAT). Neuropsychological investigations to identify predictors for learning by movement imagination were carried out in 12 patients of the study group before training started. After investigations, patients received courses of movement imagination (hand extension) training using a BCI to control a hand exoskeleton. On average, patients received 10 30-min training sessions. After training, repeat assessments of parameters on motor scales were run, along with analysis of electroencephalography data obtained during training sessions; these results were compared with neuropsychological investigation data. **Results and conclusions.** Both groups showed improvements in upper limb motor function on the ARAT and Fugl–Meyer (sections A–D, H, I) scales. Only the BCI-exoskeleton group showed improvements in the ball grasp ( $p = 0.012$ ), finger pinch grip ( $p = 0.012$ ), and gross arm movements ( $p = 0.002$ ) scores on the ARAT scale. A significant correlation was found between BCI movement quality indicators with various neuropsychological test results: Taylor figures, Head test, reaction choice test. Thus, inclusion of the BCI-exoskeleton system into the complex rehabilitation of patients with poststroke upper limb paresis significantly improves a number of measures of grasping and movement functions in the proximal segments of the upper limb. Use of neuropsychological tests as screening to select patients may help with the personalized application of rehabilitation technologies.

**Keywords:** stroke, poststroke rehabilitation, central upper limb paresis, brain–computer interface, exoskeleton.

One priority area among studies in the field of neurorehabilitation is investigation of approaches to restoring upper limb function in poststroke hemiparesis [1–3]. Basic

motor rehabilitation methods for patients with poststroke motor impairments include physical training (therapeutic gymnastics, CI therapy, exercises with added loading and resistance), while adjunctive methods include robot therapy, physiotherapy, high-tech methods, and nonphysical motor rehabilitation methods (mirror therapy, mental training).

 So-called mental training, particularly imaginary movements (IM), constitute an adjunctive method significantly increasing the efficacy of complex motor rehabilitation [1, 2, 4]. During sessions, patients are asked to imagine

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carrying out a defined movement (for example, unclenching the hand, extending the wrist, forming a fist, lifting a cup from the table, etc.) from the first-person perspective  $[4-6]$ .

 Recent systematic reviews and clinical guidelines from professional societies indicate that mental training using IM is suitable for patients with poststroke upper limb paresis of any severity in the early and late recovery periods as an adjuvant rehabilitation method with the aim of increasing treatment efficacy in relation to restoring arm movements (evidence level 2a) [4–6].

However, it is difficult to monitor patients' correct performance of instructions for IM without using technical devices. Brain–computer interface (BCI) techniques can be used to make the process of IM objective and to generate feedback in different modalities [7–17]. During IM of the limb, a noninvasive BCI based on recording of the electroencephalogram (EEG) uses modulation of the sensorimotor rhythm in the corresponding cortical representations areas of the brain as signals indicating activity levels [11]. Recognized signals are converted into control commands for a hand orthosis or exoskeleton to generate kinesthetic feedback or the recognition result is presented graphically on a screen for presentation of visual feedback [12–17]. Kinesthetic feedback for improving arm movements is used more often than visual [15].

 The authors of the present study previously reported work at the Research Center of Neurology which demonstrated the fundamental possibility of using a BCI in patients with stroke of different durations and locations and different severities of arm paresis [16–19]. However, until the present study, the clinical efficacy of mental training using a hand exoskeleton in the BCI circuit in patients with poststroke upper limb paresis of different severities at different poststroke time points has not been addressed. There is also a lack of data on the minimally adequate reserve of cognitive functions required for patients to carry our effective mental training in the IM paradigm.

 It is also important to note that most robot devices used in motor rehabilitation have been shown to be effective in relation to restoring movements only in the proximal part of the upper limbs. Robot systems for restoring hand and finger functions have been introduced into practice relatively recently, such that there is a lack of clinical studies to confirm their efficacy  $[4, 6]$ . The exoskeleton used in the present studies is for the distal segments of the arm and is used for finger movements under control of the BCI.

The aims of the present work were to assess the efficacy of using a BCI with a hand exoskeleton (BCI-exoskeleton system) in the complex rehabilitation of patients with the sequelae of cerebrovascular accidents and to evaluate the minimally adequate reserve of cognitive functions required for patients to carry out effective mental training using the IM paradigm.

**Materials and Methods.** The design of the multicenter, blinded, randomized, controlled study was developed at the Research Center of Neurology. The present article reports the results of a study run at the Research Center of Neurology from December 2014 to June 2017 (the other two centers were the Vladimirskii Moscow Regional Research Clinical Institute and the Pirogov Russian National Medical Research University).

 Study participants were selected from December 2014 to June 2017 at the Research Center of Neurology in screening investigations of 385 patients. A total of 73 patients complied with the inclusion criteria, though 18 of these (three from the study group and 15 controls) dropped out after the first or second session. The study and ongoing analysis included 55 patients (39 men and 16 women) with median age 54.0 [44.0; 61.0] years and median poststroke period 6.0 [3.0; 13.0] months; stroke in 39 patients was ischemic and that in 16 hemorrhagic.

 Inclusion criteria were stroke with a single focus of ischemic or hemorrhagic type with supratentorial location (MRI or CT data) one month to two years before inclusion; upper limb paresis of different levels of severity (Medical Research Council (MRC) scale) [20].

 Criteria for refusal to take part/exclusion from the study were left-handedness (Edinburgh Handedness Inventory) [21]; severe cognitive dysfunction (<10 points on the Montreal Cognitive Assessment scale [22]); sensory or profound motor aphasia; severe visual impairment; contractures in the hands (4 points on the Ashworth scale, mAS) [23]; development of acute or decompensation of chronic disease with a risk of potential influences on the study results; administration of botulinum toxin formulations into the muscles of the paralyzed arm and/or prescription or dose correction of systemic myorelaxants after inclusion in the study.

 At the end of the screening study, patients were randomized to study and control groups at a ratio of 1:1 using software from Imagery Soft (Russia).

 Patients of both groups then underwent standardized rehabilitation methods: therapeutic exercises with an instructor (kinesiotherapy using classical methods directed to increasing range of movements and strength in the paralyzed muscles), neuromuscular electrical stimulation of the paralyzed arm and leg muscles, and therapeutic massage.

 Patients of the study group also underwent training using the BCI-exoskeleton system, while control patients underwent simulated use of this system. Patients of each group received a total of 12 daily procedures (except weekend days) each of duration 40 min.

 The study used a BCI based on Bayesian analysis of EEG patterns and recognition of sensorimotor synchronization/desynchronization reactions during IM [24, 25]. EEG signals were filtered in the band 5–30 Hz. The measure of classification accuracy was the percentage of correct classifier responses (recognition greater than the random at  $p > 33\%$ , as patients carried out three mental tasks following instructions). The components of the BCI-exoskeleton are shown in Fig. 1.

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Fig. 1. Diagram of the BCI-hand exoskeleton. *1*) 32-electrode electroencephalograph; 2) electroencephalograph, amplifier; *3*) computer with mental state classifier software; *4*) presentation monitor; *5*) hand exoskeleton.

 During the procedure, EEG recording electrodes were positioned using the 10–20 system. The exoskeleton was attached to the hand of the paralyzed arm and consisted of a

mobile plastic casing with pneumatic control designed to extend the fingers. During training, the patient carried out one of three instructions presented for 10 sec in random or-



Fig. 2. Graphical presentation of instructions. A change in the color of the arrow to green gives the instruction to start IM of the left hand; the marker at the center of the screen provides visual feedback; successful recognition by the classifier of the task corresponding to the instruction given is accompanied by a change in color to green. IM – imagination of movement.

der on a monitor screen : relax (upper arrow), kinesthetically imagine slow extension of the fingers of the right or left hand (change in the color of the arrow at right or left, respectively) (Fig. 2).

 Mental task recognition results were presented to the patient via visual and kinesthetic feedback: when recognition by the classifier was successful in terms of the task corresponding to the instructions, the marker in the center of the screen turned green (see Fig. 2) and the exoskeleton extended the fingers.

 During the simulation procedure, the control group used the BCI-exoskeleton system in the same conditions as the study group. Patients of the control group carried out the instruction "relax and watch the arrows change color." Arrow color was changed in random order, each change lasting 10 sec; the exoskeleton extended the fingers of the paralyzed hand on presentation of the corresponding arrow. Thus, patients of the control group were not presented with movements and did not try to control the exoskeleton but underwent passive mechanotherapy of the paralyzed hand.

 Hand motor function was assessed with analysis of changes in the Fugl–Meyer (FM) and Action Research Arm Test (ARAT) scales [26, 27] before and after training courses.

 The demographic and main initial data for patients of both groups are given in Table 1.

There were no statistically significant between-group differences in age, time since stroke, location and lateralization of foci, or severity of neurological deficit  $(p > 0.05)$ .

 The researcher conducting clinical assessment of patients' status was blinded to the patient's participation group. Only the specialists running rehabilitation procedures using the BCI-exoskeleton system or its simulation were aware of participation groups.

 Within the framework of the neuropsychological part of the study, patients of the study group underwent complex assessments using the Luriya method [28–31] adapted for the purposes of this study. Higher mental functions were an-

alyzed in terms of measures of "negative symptoms" using a three-point scale, where 1 point indicated the absence of the symptom, 2 indicated mild-moderate impairments or detectable compensatory approaches (for example, verbalization of shapes), and 3 indicated profound or severe impairments.

 One study was conducted including assessment of regulatory functions, memory, thinking, attention, gnosis, praxis, auditory-motor coordination, the optical-spatial domain, and the neurodynamic and energy components of mental activity. Tests for assessment of praxis were adapted for patients with hemiparesis: performance of tests such as the "fist–edge–palm" test, postural praxis, the Head test, and the reaction selection test with the healthy hand. Audioverbal memory was assessed by sounding out sequences of six words in two groups of three and remembering stories. Visual memory was assessed in a test for remembering five geometric figures which are difficult to verbalize [28–31]. Thought processes were studied by solution of arithmetic tasks, interpretation of proverbs and cards, and item exclusion [28–31]. The optical-spatial domain was assessed using a set of picture methods: independent drawing, copying, and reproduction of Taylor figures from memory, the clockface test, and the five figures test. Visual gnosis was evaluated using tests for simple visual gnosis (recognition of real images) and gnosis in sensitized conditions (crossed out and superimposed images, i.e., Poppelreiter figures). Acoustic nonverbal gnosis was analyzed by assessment and reproduction of rhythmic structures (single, serial, and accented). Regulatory functions were assessed using parameters such as the formation and retention of voluntary movement programs and actions, control of actions, levels of abstraction, and activity/inactivity during performance of various tests. The energy and neurodynamic components of mental activity were assessed in terms of the overall speed of operation during the study, fatigue, tiring, freezing, learning effectiveness and dynamics, micrography, volume of material remembered, and inertness.

Scale, points	Study group ( $n = 35$ )		Control group $(n = 20)$	
	<b>before</b>	after	before	after
ARAT. total	$1.0$ [0.0; 20.0]	$1.0$ [0.0; 34.0]**	7.0 [0.0; 30.0]	$9.5$ [0.0; 33.5]**
FM, total	71.0 [60.0; 92.0]	75.0 [62.0; 105.0]**	68.0 [60.0; 104.0]	75.0 [64.5; 110.0]**
ARAT, grasp	$0.0$ [0.0; 10.0]	$0.0$ [0.0; 12.0]*	$0.5$ [0.0; 12.0]	$1.5$ [0.0; 12.0]
ARAT, pinch grip	$0.0$ [0.0; 3.0]	$0.0$ [0.0; 11.0]*	$1.0$ [0.0; 4.5]	$1.0$ [0.0; 6.5]
ARAT, cylindrical grip	$0.0$ [0.0; 6.0]	$0.0$ [0.0; $8.0$ ]**	$1.0$ [0.0; 6.0]	$2.0$ [0.0; $7.5$ ]*
ARAT, proximal segments	$1.0$ [0.0; 4.0]	$1.0$ [0.0; 6.0]**	$1.5$ [0.0; 6.0]	$2.0$ [0.0; 6.0]

TABLE 2. Results of Assessments of the Motor Functions of the Arms Before and After Training Courses

Here and Tables 3–7:  $* p \le 0.05$ ;  $** p \le 0.005$  compare with baseline.

TABLE 3. Dynamics of Arm Motor Function in Patients in the Early Recovery Period of Stroke Before and After Training Courses

Scale, points	Study group ( $n = 18$ )		Control group $(n = 11)$	
	before	after	before	after
ARAT, total	$0.0$ [0.0; 7.0]	$1.0$ [0.0; 13.0]*	13.0 [0.0; 30.0]	13.0 [0.0; 31.0]*
ARAT, grasp	$0.0$ [0.0; 2.0]	$0.0$ [0.0; $3.0$ ]*	$4.0$ [0.0; 12.0]	$4.0$ [0.0; 14.0]
ARAT, proximal segments	$0.0$ [0.0; 3.0]	$1.0$ [0.0; $4.0$ ]*	$2.0$ [0.0; 6.0]	$3.0\,$ [0.0; 6.0]
FM, total	67.0 [60.0; 87.0]	74.5 [60.0; 96.0]*	68.0 [63.0; 107.0]	75.0 [66.0; 109.0]*

 The study protocol was approved by the Ethics Committee of the Research Center of Neurology. All participants signed informed consent to voluntarily take part in the clinical study.

 Data were analyzed statistically using the Mann–Whitney and  $χ²$  tests (for comparison of independent sets), the Wilcoxon test (for comparison of dependent sets), and the Spearman correlation coefficient run in Statistica 6.0  $(StatSoft, 2003)$ . Data are presented as medians with first and third quartiles. Differences were regarded as statistically significant at  $p < 0.05$ .

Results. *Clinical efficacy of use of the BCI-exoskeleton system.* Both groups showed improvements in hand motor function on the ARAT and FM scales (sections A–D, H, I). Only the BCI-exoskeleton group showed improvements on the grasp subscale  $(p = 0.012)$  and the pinch grip subscale  $(p = 0.012)$ , as well as on the gross movement subscale  $(p = 0.002)$  on the ARAT (Table 2).

Detailed analysis of efficacy in relation to individual hand movement parameters of the ARAT for the overall cohort of study participants revealed advantages from use of the BCI-exoskeleton system. However, despite the statistical significance, there were no changes in median values (improvements came from increases in points scores to greater than the 50th quartile). Given that the study included patients at different rehabilitation time points, further analysis in subgroups of patients in the early and late/residual recovery periods is appropriate, along with analysis stratified by initial severity of paresis.

*Early rehabilitation period (1–6 months after onset of stroke).* A total of 29 patients were studied during the early rehabilitation period: 18 in the study group and 11 in the control group.

Statistically significant improvements in grasp and improvements in movements in the proximal segments of the arms were seen only in the study group (Table 3).

 Patients with severe paresis of plegia (0–12 points on the ARAT) showed improvements in the proximal segments of the upper limbs on the ARAT scale, along with improvements in voluntary movements in both the proximal and distal segments of the arms on the FM scale (Fig. 3).

The control group showed no statistically significant recovery of motor functions in the arms among patients with initially severe paresis (Table 4).

 Patients with moderate or mild paresis (13–57 points on the ARAT) showed improvements in both the study and control groups, in both the proximal and distal segments of the upper limbs. However, improvements in the study group were greater than those in the control group; on average, improvements on the ARAT were by 39%  $(n=3)$  and 6%, respectively. These dynamics were not statistically significant  $(p > 0.05)$ , perhaps because of the small number of observations.

*Late rehabilitation period (more than six months after stroke).* A total of 26 patients were observed during the late

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TABLE 4. Dynamics of Arm Motor Function in Profound Paresis and Plegia in Patients in the Early Recovery Period of Stroke Before and After Training Courses

TABLE 5. Dynamics of FM Subscales in Profound Paresis and Plegia in Patients in the Late and Residual Recovery Periods of Stroke Before and After Training Courses

Scale, points	Study group $(n = 10)$		Control group $(n = 5)$	
	before	after	before	after
Voluntary movements	$12.5$ [10.0; 18.0]	$13.5$ [13.0; 20.0]*	$11.0$ [6.0; 12.0]	$13.0$ [7.0; 13.0]
Proximal segments	$10.0$ [9.0; 16.0]	$11.5$ [9.0; 19.0]*	$9.0$ [6.0; 11.0]	$10.0$ [7.0; 11.0]
Distal segments	$1.0$ [0.0; 2.0]	$2.0$ [1.0; 3.0]	$1.0$ [0.0; 2.0]	$2.0$ [1.0; 3.0]

 $**p* ≤ 0.05 compared with baseline.$ 



Fig. 3. Dynamics of voluntary movements on the FM scale in patients with profound paresis and plegia in the early rehabilitation period.

and residual period: 17 in the study group and nine in the control group.

 Among patients with initially severe paresis or plegia (0–12 points on the ARAT), only those in the study group showed significant improvements in voluntary movements on the FM scale due to the proximal segments; in addition, there was a tendency to improvement in the distal segments of the arm (Table 5).

 Patients of the study group with initially moderate or mild paresis (13–57 points on the ARAT) showed improvements in the characteristics of cylindrical and pinch grip, along with a tendency to improvements in the proximal segments of the arms on the ARAT. Data from the FM scale identified significant increases in measures of voluntary movements due to the distal segments of the arms. In the control group, there were no statistically significant differences in the recovery of the motor functions of the arms among patients assessed more than six months after stroke with initially moderate or mild paresis (Table 6).

 None of the groups showed any correlation in the dynamics of recovery of the motor functions of the arms on the ARAT and FM and time since stroke or age.

 Both the study and control groups showed a statistically significant ( $p = 0.0001$ ) correlation of moderate strength  $(Rs = 0.6)$  between the extent of improvements in arm function and initial severity of paresis on the ARAT.

**Assessment of reserve cognitive functions.** Before training, neuropsychological investigations to identify pre-

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Scale, points	Study group $(n = 7)$		Control group $(n = 4)$	
	before	after	before	after
ARAT, total	48.0 [37.0; 55.0]	51.0 [45.0; 55.0]*	35.5 [21.5; 39.0]	37.0 [25.5; 40.5]
ARAT, cylindrical grip	$10.0$ [8.0; 11.0]	$11.0$ [10.0; 11.0]*	$7.0$ [4.0; 8.0]	$9.0$ [5.5; 12.0]
ARAT, pinch grip	12.0 [12.0; 17.0]	14.0 [12.0; 18.0]*	$5.5$ [4.5; 8.5]	$8.5$ [6.0; 10.5]
ARAT, hand	40.0 [32.0; 46.0]	42.0 [37.0; 47.0]*	$27.5$ [16.5; 32.0]	$31.5$ [19.5; 35.0]
ARAT, proximal segments	$7.0$ [5.0; 9.0]	$8.0$ [ $8.0$ ; $9.0$ ]	$6.0$ [5.0; 7.0]	$6.0$ [5.5; 6.0]
FM, total	111.0 [110.0; 118.0]	$115.0$ [111.0; 121.0]*	104.5 [98.0; 107.0]	111.0 [103.0; 112.0]
FM, voluntary movements	53.0 [53.0; 61.0]	57.0 [56.0; 63.0]*	50.0 [44.0; 52.0]	54.5 [47.5; 56.0]
FM, proximal segments	35.0 [34.0; 39.0]	35.0 [30.0; 39.0]	28.5 [27.0; 32.5]	31.0 [27.5; 34.0]
FM, distal segments	19.0 [16.0; 22.0]	22.0 [19.0; 26.0]*	$17.5$ [14.0; 22.5]	$20.5$ [17.0; 25.0]

TABLE 7. Correlations of BCI Control Quality with Neuropsychological Test Performance Measures (Spearman correlation strength at  $p < 0.05$ )



dictors of effective training to control the BCI-exoskeleton system were performed in 12 patients of the study group (six men, median age 51.0 [37.0; 65.0] years, median time since stroke 7 [2; 12] months, with stroke foci in the left (four patients) or right (eight patients) hemispheres).

Statistically significant strong correlations between the mean achieved recognition quality by the BCI mental state classifier  $(P)$  with a number of measures on neuropsychological tests were found – Taylor figures, the Head test, and reaction choice (Table 7).

The finding of correlations between measures of classifier accuracy and neuropsychological test data allowed those cognitive difficulties whose presence decreases the effectiveness of controlling the BCI (an indirect indicator of low IM ability) to be identified. The results of this part of the study indicated that the following tests can be used for screening investigations of patients to assess the ability to assimilate the ability to control the BCI: Taylor figures, the Head test, and the reaction choice.

**Discussion.** The results obtained here indicate that use of a BCI-exoskeleton system in patients with profound paresis or plegia in the early recovery period is significantly more effective in increasing motor function on the ARAT and FM scales due to the proximal and distal segments of the arms in the study group than in the control group. In patients with paresis of comparable severity but in the late

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and residual recovery period, this training was significantly more effective in improving the motor function of the proximal segments of the arm on the FM scale. In patients with mild-moderate paresis and time since stroke of more than six months, use of the BCI-exoskeleton system was significantly more effective in improving cylindrical and pinch grips on the ARAT compared with the control group.

 Thus, use of the BCI-exoskeleton system in the complex rehabilitation of patients with poststroke arm paresis significantly improved a number of measures not only of grip (elements of which were acquired in the study group), but also movements in the proximal segments of the upper limb. Improvements in the function in those parts of the arm not involved in training in the IM paradigm can be explained in terms of the anatomical-physiological closeness of the motor cortical representation for the upper limbs and the wide propagation of arousal within it during training to IM of the hand.

Studies assessing the efficacy of the noninvasive BCI using external devices have also been performed in other countries. These studies have involved up to 30 patients with poststroke paresis of the arms and the external devices have been the Haptic Knob [14], the MIT-Manus [12, 13], or orthoses [15], not constructed as exoskeletons. Overall, the results of these studies are consistent despite differences in designs and training durations.

 BCI technology has transferred from the laboratory to clinical practice, though its wide use in the daily work of the rehabilitation services is limited by a number of factors [16–18, 32–34]. Apart from preparation for each procedure (the duration of which takes longer than the training itself) and the difficulty of maintaining hygiene at the end of training, the efficacy of learning IM in patients is often limited by their ability to perform mental training and to control the BCI, which is evidence of the importance of specific screening to identify predictors of the efficacy of IM. Processing of the results of neuropsychological investigations yielded a number of correlations between particular neuropsychological tests and BCI classification results. This allowed a prognostically unfavorable neuropsychological patient profile (presence of impairments to spatial and regulatory praxis) in the context of mental training to be identified. These results provide the first demonstration that the following tests can be used for screening: Taylor figures, the Head test, and the reaction choice test. This result is of great practical importance as it can be used to avoid providing this treatment method to unsuitable individual patients, i.e., it allows personalization of the use of the technology and more rational management of rehabilitation resources.

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