COGNITIVE REHABILITATION OF PATIENTS WITH ACUTE CEREBROVASCULAR ACCIDENT USING EEG-GUIDED ADAPTIVE NEUROSTIMULATION

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Abstract. The methodology of digital psychophysiological mapping was used in a group of 18 stroke patients and a matched group of healthy controls to reveal possible markers of acute cerebrovascular accident. The patients were found to have a number of indicators that were significantly different from the norm and could claim the role of stroke biomarkers. Among them there are lowered values of the power and peak frequency of the EEG alpha rhythm, significantly lowered HRV indices, as well as a significantly higher levels of emotional disadaptation. Stroke patients participated in a treatment session, in which they were exposed to EEG-based bimodal (light-musical) adaptive neurostimulation, in which some EEG characteristics (EEG oscillators) control sound (musical) stimulation, and other EEG characteristics (native EEG) simultaneously control light stimulation. As a result of the treatment, patients demonstrated a normalization of all the described indicators of the functional state: the values of a power and frequency of the EEG alpha rhythm significantly increased and approached the norm, as well as the parameters of the cardiovascular system and the cognitive-emotional sphere of stroke patients. The method of EEG-guided adaptive neurostimulation used in this work demonstrates the possibility of effective cognitive rehabilitation of stroke patients even with a single application.

Keywords: cognitive rehabilitation; digital psychophysiological mapping; stroke biomarkers; EEG-guided adaptive neurostimulation; normalization of the functional state.

List of Abbreviations

EEG – electroencephalogram
LED – level of emotional disadaptation
HRV – heart rate variability

Introduction

More than 400 thousand cases of acute cerebrovascular accident or stroke are registered in our country annually, and 95% of patients have a variety of cognitive disorders, leading to a decrease in the quality of life, disruption of everyday, social and professional activity of a person, often to disability and complete dependence on others (Bogolepova & Levin, 2020). Therefore a new promising area of medical care for patients with focal brain lesions, called cognitive rehabilitation, was formed more than 10 years ago (Grigorieva, 2010; Grigorieva & Nesterova, 2012).

To date, the methodology of cognitive rehabilitation is one of the most intensively developing areas of modern neurology. For cognitive rehabilitation in stroke a number of generally recognized approaches such as bioacoustic correction (Tereshin *et al.*, 2019) and neurofeedback (Renton *et al.*, 2017; Yoo, 2021) are successfully applied. New methods of cognitive rehabilitation have been developed, for example, cognitive training (Naumenko *et al.*, 2017), computerized stimulation programs (Prokopenko *et al.*, 2017: Draaisma *et al.*, 2020) and multimodal stimulation (Pohl *et al.*, 2018; Kotov *et al.*, 2020). Despite the abundance of already available therapeutic means, the search for new approaches to the cognitive rehabilitation of patients with stroke is actively continuing.

Cognitive rehabilitation can be carried out using non-invasive methods of adaptive neurostimulation based on the feedback from the patient's electroencephalogram (EEG). For example, in elderly patients, positive cognitive effects were noted under stimulation with music-like signals resembling flute sounds in

timbre, which smoothly vary in pitch and intensity directly depending on the current amplitude of the subject's dominant rhythmic EEG component – the alpha EEG oscillator (Fedotchev *et al.*, 2020). Even more pronounced cognitive effects were registered when applying a modification of the described approach, in which music-like stimuli controlled by alpha EEG oscillators are supplemented by rhythmic light stimuli controlled by the subject's total EEG (Fedotchev *et al.*, 2021). The positive results of such light-musical stimulation indicate the possibility of its application for effective correction of various unfavorable functional states of a person. However, it is still unknown whether the developed method can be used for cognitive rehabilitation in stroke.

The goal of this study was to examine the applicability and effectiveness of the developed method of EEG-based light-musical adaptive neurostimulation for the cognitive rehabilitation of stroke patients. The research was carried out in two stages. At the first stage, the methodology of digital psychophysiological mapping was used in stroke patients and healthy controls to reveal possible markers of acute cerebrovascular accident. At the second stage, stroke patients participated in a treatment session, in which they were exposed to EEG-based bimodal (light-musical) adaptive neurostimulation. To assess the effectiveness of treatment, the baseline values were compared with those after treatment.

Materials and Methods

The study involved two groups of subjects. The first group (experiment) consisted of 18 patients of the Volga Medical Center, aged 51.5 ± ± 2.7 years, 8 women, 10 men with a diagnosis of acute cerebrovascular accident. The second group (control) was formed from the university staff having no health complaints, and was equal to the group of patients in terms of the number of participants, age and gender.

The study was carried out in accordance with the Declaration of Helsinki (2013) and approved by the Ethics Committee of the Lobachevsky State University of Nizhny Novgorod. After clarifying the potential risks, benefits and nature of the upcoming study, each participant provided voluntary written informed consent to participate in the survey.

At the **first stage of the study**, the task was to compare the main indicators in the group of patients and in the control group in order to identify psychophysiological markers of acute cerebrovascular accident. For this purpose, the main elements of the previously developed methodology of digital psychophysiological mapping (Polevaya *et al.*, 2020) were used, including psychological testing of the level of emotional disadaptation (LED), registration of the parameters of heart rate variability (HRV), and analysis of electrical activity of the brain - electroencephalogram (EEG).

When testing *the level of emotional disadaptation* (LED test), the participant is asked to indicate the zone of his current state on the monitor screen. To do this, he uses a set of synonymous adjectives arranged in a circle, describing emotions in relation to four basic personal needs: a) in safety; b) in independence; c) in achievement; d) in unity (proximity). Depending on the position of the selected zone, the number of points scored by a person (from 0 to 3) for each need is determined. The total indicator of the degree of emotional disadaptation is equal to the sum of points scored for each need.

When *registering HRV parameters*, the previously described technology of event-related heart rate telemetry was used (Polevaya et al., 2019). For further analysis, the following HRV indicators were calculated: the total power of the HRV spectrum, the autonomic (sympathovagal) balance coefficient, and the stress index of regulatory systems.

Registration and analysis of electrical activity of the brain (EEG) was carried out according to the previously described method (Fedotchev *et al.*, 2021). When analyzing the obtained EEG records, the powers of the main EEG rhythms (theta, alpha and beta), as well as the peak frequency of the EEG alpha rhythm were taken into account.

At **the second stage of the study**, the task was to determine the possibility, conditions and effectiveness of the use of EEG-controlled

light-musical stimulation for the purpose of cognitive rehabilitation of stroke patients. To do this, they additionally wore stereo headphones (Philips SBC HL140) and tinted glasses, into which red light-emitting diodes with a power of no more than 100 μW were built. The subjects were not given any assignments, but were asked to sit quietly with their eyes closed throughout the examination. Then, during a 30-second registration of the background EEG, a dominant peak in the range of the alpha rhythm (alpha EEG oscillator) was determined for each patient. After that, the working mode was switched on, during which the patients were simultaneously presented with musical signals generated in real time on the basis of the EEG alpha oscillator, and two variants of rhythmic light stimulation. In the first variant, the frequency of photostimulation was controlled by a computer and gradually increased from 4 to 20 Hz, and in the second variant, photostimulation was automatically controlled by feedback signals from the total EEG of the subject. This was achieved by normalizing the digitized EEG values, at which the largest negative value of the EEG signal corresponds to the minimum, and the largest positive value corresponds to the maximum luminescence of the light-emitting diodes. After the end of the 15-minute light-musical stimulation, the recording of electrographic parameters was continued for 2 minutes to register the aftereffects. At the end of the survey, patients were interviewed about their subjective feelings during stimulation procedures. In addition, they underwent the LED test again.

Statistical processing of the results was carried out using the Sigma-Plot 11.0 software package. After passing the Shapiro-Wilk normality criterion, repeated measures ANOVA was used to assess the statistical significance of the post-treatment shifts from baseline for each parameter. The Mann-Whitney rank sum test was used to determine the differences between the indicators for two groups of subjects. Paired t-test was used to determine the mean values (M) and standard errors (m) for the parameters before and after treatment and to assess the significance levels p of the differences. Differences were considered statistically significant at $p \leq 0.05$.

Results

At the first stage, the results of digital psychophysiological mapping were compared in a group of patients and in a control group. The main indicators are presented in Table 1.

It can be seen that significant differences between groups are observed at all levels of analysis. When analyzing the EEG in patients with stroke, compared with controls, a significantly lower power of the EEG alpha rhythm was registered, as well as the peak frequency of the EEG alpha rhythm. Significant differences between the groups were also noted in terms of HRV indicators. In stroke patients the total

Table 1

Differences in main indicators of functional state between stroke patients and healthy controls

Level of assessment	Indicators	Patients	Controls	P value
EEG analysis	Theta-rhythm power, μV²	0.62±0.10	1.04±0.15	0.064
	Alpha-rhythm power, μV²	**0.44±0.11**	**0.95±0.21**	**0.036**
	Beta-rhythm power, μV²	0.21±0.06	0.35±0.04	0.090
	Peak alpha frequency, Hz	**8.1±0.2**	**9.5±0.2**	**0.001**
HRV analysis	Total spectral power, ms²	**896±177**	**2347±107**	**0.003**
	Autonomic balance coefficient, digits	**1.99±0.50**	**3.36±0.38**	**0.039**
	Stress index, relative units	**391±98**	**124±16**	**0.012**
EDL test	Average level of emotional disadaptation, scores	**5.9±0.7**	**3.4±0.6**	**0.016**

Note: the values with difference levels $P < 0.05$ are shown in bold

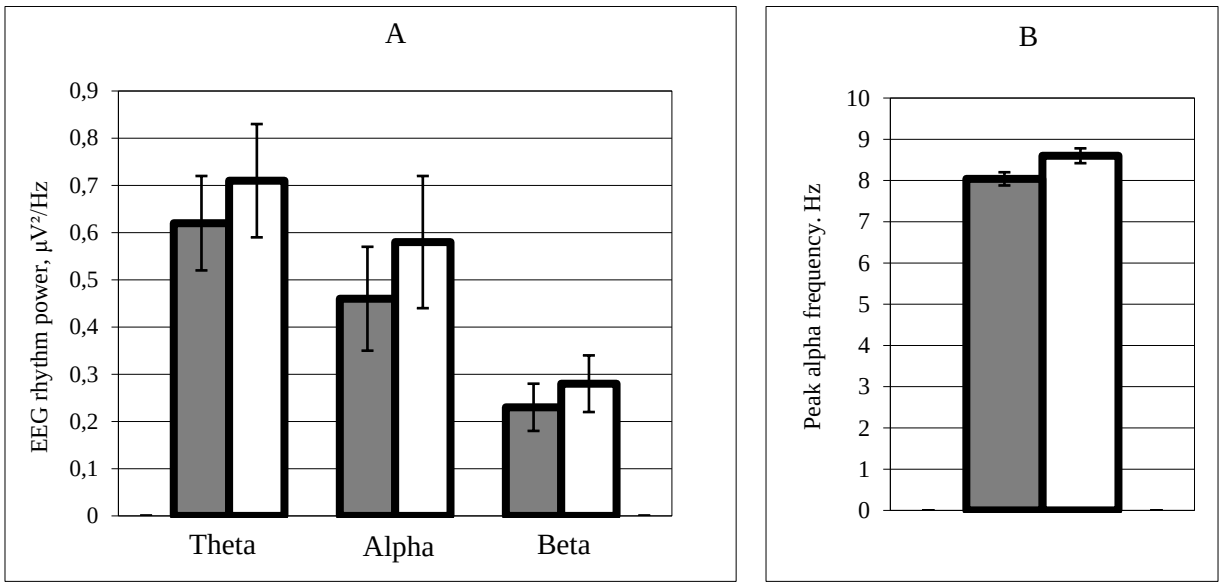

Fig. 1. EEG theta-, alpha-, beta-rhythm powers (A) and peak alpha-EEG frequency (B) in patients before (dark columns) and after (light columns) treatment.
Note: * – P < 0.05; ** – P < 0.01

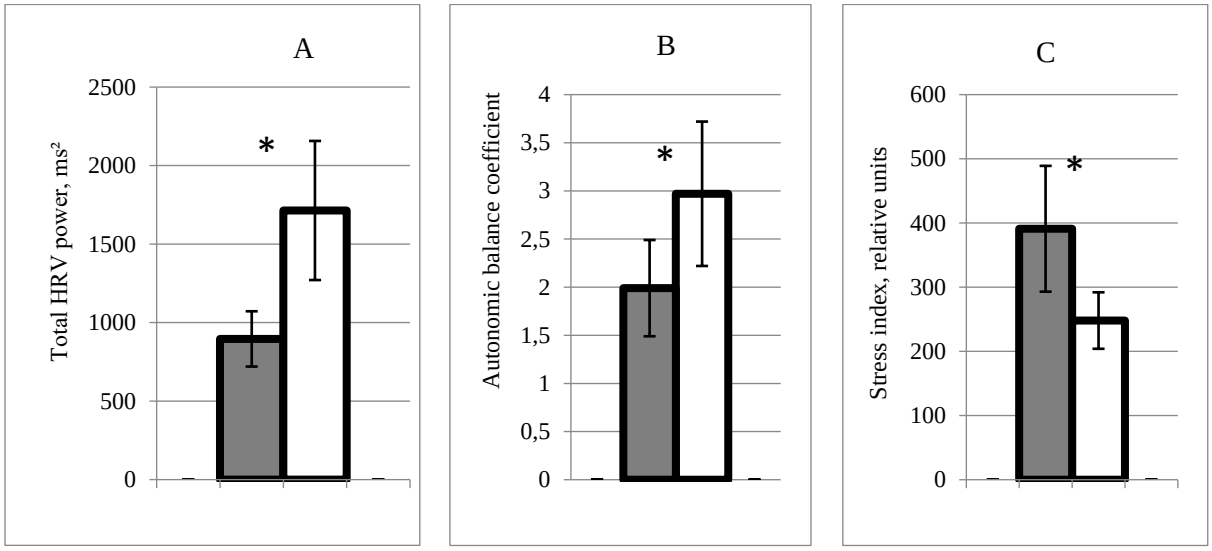

Fig. 2. Total heart rate variability (HRV) spectral power (A), coefficient of autonomic balance (B), and stress index (C) in patients before (dark columns) and after (light columns) treatment. *Note:* * – P < 0.05

power of the HRV spectrum and the coefficient of autonomic balance were significantly below the norm, while the stress index, on the contrary, was above the norm. In addition, stroke patients showed a significantly higher level of emotional disadaptation than normal subjects.

At the second stage, the results of the cognitive rehabilitation of stroke patients using the EEG-guided adaptive neurostimulation were analyzed.

When analyzing the EEG indicators (Fig. 1), it was found that under the influence of the treatment procedure, there is a significant increase in the power of the main EEG rhythms - theta, alpha and beta. The peak frequency of the EEG alpha rhythm also significantly increases.

Significant positive changes under the adaptive neurostimulation were also observed in stroke patients in the HRV indicators (Fig. 2). A significant increase after stimulation relative

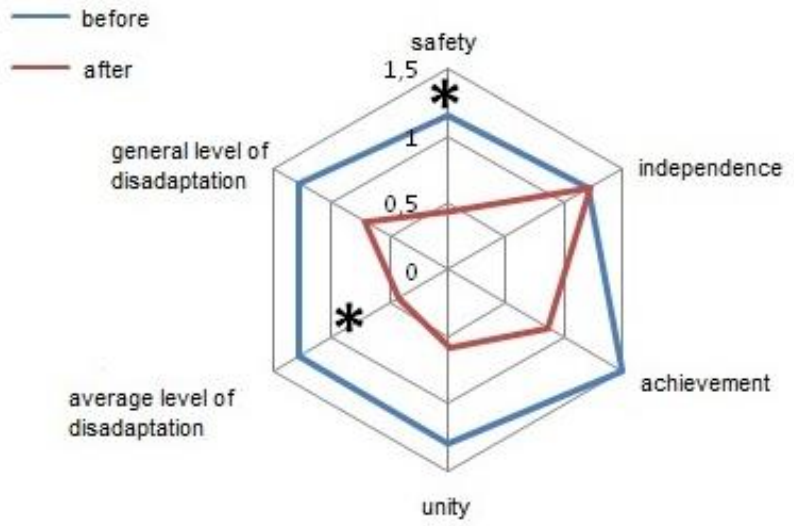

Fig. 3. Parameters of emotional disadaptation in patients before and after treatment

to the initial level was noted in the total power of the HRV spectrum and in the coefficient of autonomic balance. As a result of therapeutic stimulation, the stress index significantly decreased.

Significant changes under the light-music neurostimulation also took place in the indicators of emotional disadaptation (Fig. 3).

It can be seen that after the procedure of cognitive rehabilitation in stroke patients there is a significant decrease in almost all components of emotional disadaptation. The average level of disadaptation significantly ($P < 0.001$) decreases from 5.8 ± 0.8 to 3.9 ± 0.5 points.

A survey of patients about subjective feelings during stimulation procedures showed that they positively assessed the treatment sessions and considered the light-music adaptive neurostimulation to be pleasant and calming, reducing stress and improving emotional state.

Discussion

Despite many years of research, there are still no reliable stroke biomarkers available for use in clinical practice (Montaner *et al.*, 2020). In our work, in order to determine potential markers of acute cerebrovascular accident, the indicators of digital psychophysiological mapping were compared in patients with stroke and healthy people from the control group. The patients were found to have a number of indicators that were significantly different from the norm and could claim the role of stroke biomarkers. Among them there are lowered values of the power and peak frequency of the EEG alpha rhythm, significantly lowered HRV indices, as well as a significantly higher degree of emotional disadaptation.

As for EEG indicators, fluctuations in the power/frequency of the EEG alpha rhythm form the basis of the adaptive mechanism, reflecting the level of activation of neuronal populations (Mierau *et al.*, 2017). A reduced frequency of individual alpha peaks is a potential biomarker for impairment of cognitive functions such as attention, working memory, or problem solving (Ramsay *et al.*, 2021). A reduced power of the EEG alpha rhythm suggests cortical hyperactivity and may be associated with the consequences of chronic stress as a result of the disease (Golonka *et al.*, 2019).

The analysis of HRV showed that the patients had significantly reduced relative to the norm values of the total HRV spectral power and the autonomic balance coefficient, as well as significantly higher levels of the HRV stress index. These indicators are the biomarkers of decreased adaptive potential, decreased activity

of the central circuit of autonomous regulation, and increased tension of regulatory systems (Polevaya *et al.*, 2019). It is quite natural that, at the same time, significantly higher levels of emotional disadaptation are recorded in stroke patients.

As a result of bimodal light-music stimulation, in which some EEG characteristics (EEG oscillators) control sound (musical) stimulation, and other EEG characteristics (native EEG) simultaneously control light stimulation, patients demonstrate a normalization of all the described indicators of the functional state. Thus, the values of the power and frequency of the EEG alpha rhythm significantly increase and approach the norm, indicating the formation of an «alpha state», which is characterized by general relaxation with a decrease in the level of stress, anxiety and depression (Frederick, 2012). Positive shifts under the influence of EEG-guided adaptive neurostimulation also occur in the parameters of the cardiovascular system and in the cognitive-emotional sphere of stroke patients. The observed positive effects are based on the mechanisms of multisensory integration (Roy *et al.*, 2021), mechanisms of controlled neuroplasticity (Naryshkin *et al.*, 2020), and resonance mechanisms of the central nervous system (Fedotchev, 2019).

It is important to emphasize that the method of EEG-guided adaptive neurostimulation used in our work corresponds to a progressive trend in modern neurophysiology associated with the widespread introduction into clinical practice of non-invasive methods of adaptive neurostimulation using automatic modulation of sensory stimuli by a person's own rhythmic processes. As shown in a recent review (Fedotchev *et al.*, 2021), the main advantages of this approach are high personalization of treatment procedures, the joint participation of mechanisms of multisensory integration, neuroplasticity, and resonance mechanisms of the brain, as well as automatic, without the patient's conscious efforts, control of sensory stimulation.

Conclusion

The undertaken study shows that the developed methodology of digital psychophysiological mapping is an effective tool for identifying precise quantitative signs that determine the psychophysiological status of patients with acute cerebrovascular accident. The revealed features of this category of patients can be used as the biomarkers of post-stroke disorders and contribute to an objective clarification of their causes.

The method of EEG-guided adaptive neurostimulation used in this work demonstrates the possibility of effective cognitive rehabilitation of patients with stroke even with a single application. In further studies, it seems necessary to trace the dynamics of changes in the psychophysiological parameters of stroke patients during the course of such therapeutic procedures.

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The authors declare that there is no conflict of interest.

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