



Biofeedback Training in Rehabilitation of Patients with Neurological Disorders in Post-COVID Syndrome: a Randomized Controlled Trial

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Abstract

Introduction. The high prevalence of post-COVID syndrome (PCS), which frequently manifests with emotional disturbances, cognitive impairment, and asthenia, necessitates effective rehabilitation methods. One potential approach is electroencephalography (EEG)-based biofeedback (BFB) therapy, though its use in PCS management has been explored in only a few studies to date.

The study aimed to evaluate the effects of EEG α -rhythm BFB training on emotional state and cognitive function recovery, and reduction of asthenia symptoms in PCS patients.

Materials and methods. Patients diagnosed with U09. Post-COVID-19 condition were randomly assigned to two groups of 10 participants each. The main group underwent 12–15 sessions of EEG α -rhythm BFB training using the NeuroPlay-6C headset with the Neurocorrection of COVID-19 Psychoemotional Consequences protocol, while the control group received identical training without biofeedback. Assessments performed before and after the intervention included: emotional state evaluation (State-Trait Anxiety Inventory [STAI], Short Health Anxiety Inventory [SHAI], Beck Depression Inventory [BDI], Psychological Stress Measure [PSM-25]), cognitive function assessment (Addenbrooke's Cognitive Examination III [ACE-III], Schulte tables, Stroop test, Tower of London test, N-back test, 10-word memory test), assessment of asthenia (Multidimensional Fatigue Inventory [MFI]), and sleep quality evaluation (Insomnia Severity Index [ISI]).

Results. In both groups, the training resulted in a significant reduction of personal anxiety, psychological stress, depression, and asthenia. The main group additionally demonstrated decreased health-related anxiety and improved information retention parameters. Intergroup comparison revealed more pronounced dynamics in the main group: greater reduction of general fatigue manifestations, increased immediate word recall volume, and improved retention of verbal information in working memory. The proportion of patients transitioning to milder symptom severity levels on individual scales was comparable between both groups.

Conclusion. EEG α -rhythm biofeedback training can be implemented at the outpatient rehabilitation stage for PCS patients.

Keywords: post-COVID syndrome; asthenia; emotional disorders; cognitive impairment; electroencephalographic biofeedback

Ethics approval. The study was conducted non-invasively in accordance with Helsinki Declaration ethical standards, with patients' voluntary informed written consent. The protocol was approved by the Local Ethics Committee of the Russian Center of Neurology and Neurosciences (Protocol No. 9-5/22 dated October 19, 2022).

Source of funding. The study was not supported by any external sources of funding.

Conflict of interest. The authors declare no apparent or potential conflicts of interest related to the publication of this article.

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For citation: Cherkasova A.N., Ikonnikova E.S., Lyukmanov R.Kh., Kirichenko O.A., Mokienko O.A., Konyshev V.A., Zonov A.A., Suponeva N.A., Piradov M.A. BFB training in rehabilitation of patients with neurological disorders in post-COVID syndrome: a randomized controlled trial. *Annals of Clinical and Experimental Neurology*. 2025;19(3):14–26.

DOI: <https://doi.org/10.17816/ACEN.1358>

EDN: <https://elibrary.ru/VXVXFW>

Received 07.05.2025 / Accepted 21.07.2025 / Published 30.09.2025

БОС-тренинг в реабилитации пациентов с неврологическими нарушениями при постковидном синдроме: рандомизированное контролируемое исследование

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Аннотация

Введение. Распространённость постковидного синдрома (ПКС), среди проявлений которого высока частота встречаемости нарушений эмоциональной сферы, когнитивных функций и проявлений астении, требует разработки методов их преодоления. Одним из таких методов может стать терапия с использованием биологической обратной связи (БОС) по электроэнцефалографии (ЭЭГ), изучение которой в отношении ПКС ограничено единичными работами.

Цель исследования – оценить влияние БОС-тренинга по α -ритму ЭЭГ на восстановление эмоционального состояния, когнитивных функций, снижение проявлений астении у пациентов с ПКС.

Материалы и методы. Пациентов с диагнозом «U09. Состояние после COVID-19» рандомизировали в 2 группы по 10 человек. Участники основной группы проходили 12–15 тренировок БОС-тренинга по α -ритму ЭЭГ с помощью гарнитуры «NeuroPlay-6C» по программе «Нейрокоррекция психоэмоциональных последствий COVID-19». В контрольной группе применяли те же тренировки, но без обратной связи. До и после тренинга оценивали состояние эмоциональной сферы (Опросник Спилбергера–Ханина, Краткий опросник тревоги о здоровье, Шкала депрессии Бека, Шкала психологического стресса), когнитивных функций (Адденбрукская шкала оценки когнитивных функций III, «Таблицы Шульте», тест Струпа, «Башни Лондона», N-back, «10 слов»), параметры астении (Субъективная шкала оценки астении) и качества сна (Индекс тяжести инсомнии).

Результаты. В обеих группах после тренинга произошло значимое снижение личностной тревожности, психологического стресса, депрессии и астении. В основной группе также отмечено снижение тревоги о здоровье и улучшение параметров запоминания информации. При межгрупповом сравнении в основной группе наблюдалась более выраженная динамика снижения проявлений общей астении, увеличения объёма непосредственного воспроизведения слов, удержания вербальной информации в рабочей памяти. Количество пациентов, перешедших на более лёгкий уровень проявления симптомов по отдельным шкалам, в двух группах было сопоставимым.

Заключение. БОС-тренинг по α -ритму ЭЭГ может применяться на амбулаторном этапе реабилитации пациентов с ПКС.

Ключевые слова: постковидный синдром; астения; нарушения эмоциональной сферы; когнитивные нарушения; биологическая обратная связь по электроэнцефалографии

Этическое утверждение. Исследование выполнено неинвазивным методом в соответствии с этическими нормами Хельсинкской декларации при добровольном информированном письменном согласии пациентов. Протокол исследования одобрен локальным этическим комитетом Российского центра неврологии и нейронаук (протокол № 9-5/22 от 19.10.2022).

Источник финансирования. Авторы заявляют об отсутствии внешних источников финансирования при проведении исследования.

Конфликт интересов. Авторы заявляют об отсутствии явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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Для цитирования: Черкасова А.Н., Иконникова Е.С., Люкманов Р.Х., Кириченко О.А., Мокиенко О.А., Конышев В.А., Зонов А.А., Супонева Н.А., Пирадов М.А. БОС-тренинг в реабилитации пациентов с неврологическими нарушениями при постковидном синдроме: рандомизированное контролируемое исследование. *Анналы клинической и экспериментальной неврологии*. 2025;19(3):14–26

DOI: <https://doi.org/10.17816/ACEN.1358>

EDN: <https://elibrary.ru/VXVXFW>

Поступила 07.05.2025 / Принята в печать 21.07.2025 / Опубликовано 30.09.2025

Introduction

COVID-19, which has been spreading worldwide since late 2019, has led to significant medical and social challenges, one of these being the so-called post-COVID-19 condition or post-COVID syndrome (PCS). This condition was first defined by the World Health Organization using the Delphi methodology in October 2021 [1]. According to a large meta-analysis, the prevalence of PCS among patients who recovered from COVID-19 was 41.79% [2].

Neurological and mental disorders are widely represented among PCS symptoms. Meta-analyses indicate that the most frequently reported symptoms include fatigue, sleep disturbances, anxiety, depression, and cognitive impairment. The reported prevalence rates of these symptoms vary but remain consistently high [3–5]. Research is ongoing into the causes of these and other PCS symptoms, with proposed mechanisms including prolonged inflammation, direct neurotoxic and neurotropic effects of the SARS-CoV-2 virus on the central nervous system, pandemic-related stress factors, and others [6, 7].

Given the widespread prevalence of PCS, treatment and rehabilitation methods should be developed, with their effectiveness evaluated. Studies are being conducted on both pharmacological therapies and non-pharmacological interventions [8–10]. One promising approach is electroencephalography (EEG)-based biofeedback (BFB) therapy – neurotraining or neurofeedback. This modality involves regulating various parameters of brain electrical activity through real-time feedback. Numerous studies demonstrate the application of BFB therapy in rehabilitating neurological patients with cognitive and emotional impairments [11]. As many of these impairments are present in PCS, this method may prove effective for managing its symptoms.

In 2022, Russian authors published results from the first controlled study evaluating the efficacy of EEG α -rhythm BFB training in post-COVID patients with emotional disturbances. Participants in the intervention group ($n=24$) completed 18 sessions using the Neuro V system (Neurobotics) with customized α -rhythm stimulation exercises. The control group ($n=16$) did not receive BFB therapy. Psychological assessments were performed in both groups before and after the intervention (or without it). At baseline, the groups showed no differences in state anxiety, trait anxiety, depression, or psychological stress levels. Post-intervention comparisons revealed statistically significant improvements across all measured parameters in the intervention group [12].

Czech researchers conducted a pilot study demonstrating reduced anxiety and depression severity lasting at least 1 month after 5 neurofeedback sessions using the Othmer method in a group of 10 PCS patients [13]. A study by Korean researchers showed the effectiveness of EEG α -rhythm and sensorimotor rhythm neurofeedback as part of a comprehensive rehabilitation program for post-COVID cognitive and emotional impairments in older adolescents [14]. Additionally, case reports have been published describing the use of EEG-based biofeedback therapy for COVID-19 sequelae [15, 16].

The study aims to evaluate the effects of EEG α -rhythm biofeedback training on emotional state recovery, cognitive function improvement, and asthenia reduction in PCS patients within a blinded randomized controlled trial with active control.

Materials and methods

Study design

This blind randomized controlled trial was conducted at the Institute of Neurorehabilitation and Recovery Technologies of the Russian Center of Neurology and Neurosciences from June 2022 to June 2024 in an outpatient setting. The study design is shown in Fig. 1. A total of 20 patients were enrolled and randomized into two groups using the sealed envelope method. Prior to the BFB-training, all participants underwent neurological examination and qualitative neuropsychological assessment using A.R. Luria's syndromic analysis [17] to identify the structure of higher mental function impairments in PCS (these data will be presented separately). Quantitative assessments of emotional state, cognitive functions, and sleep quality were performed before the first and after the last training session. Participants in the main group underwent EEG α -rhythm BFB-training, while the control group received identical training without BFB. The following measures were implemented to ensure blinding: all patients underwent identical diagnostic and training procedures, including EEG headset placement and use of the same software. Participants were not informed about the principles of the BFB system or their group assignment. All participants received identical instructions and were trained under the same conditions, except for the provision of BFB.

The study duration for participants was 21–27 days according to the following schedule: neurological examination and neuropsychological assessment (1 day), quantitative evaluation of emotional status, cognitive functions, and sleep quality before training sessions (1 day), 12–15 training days on week-

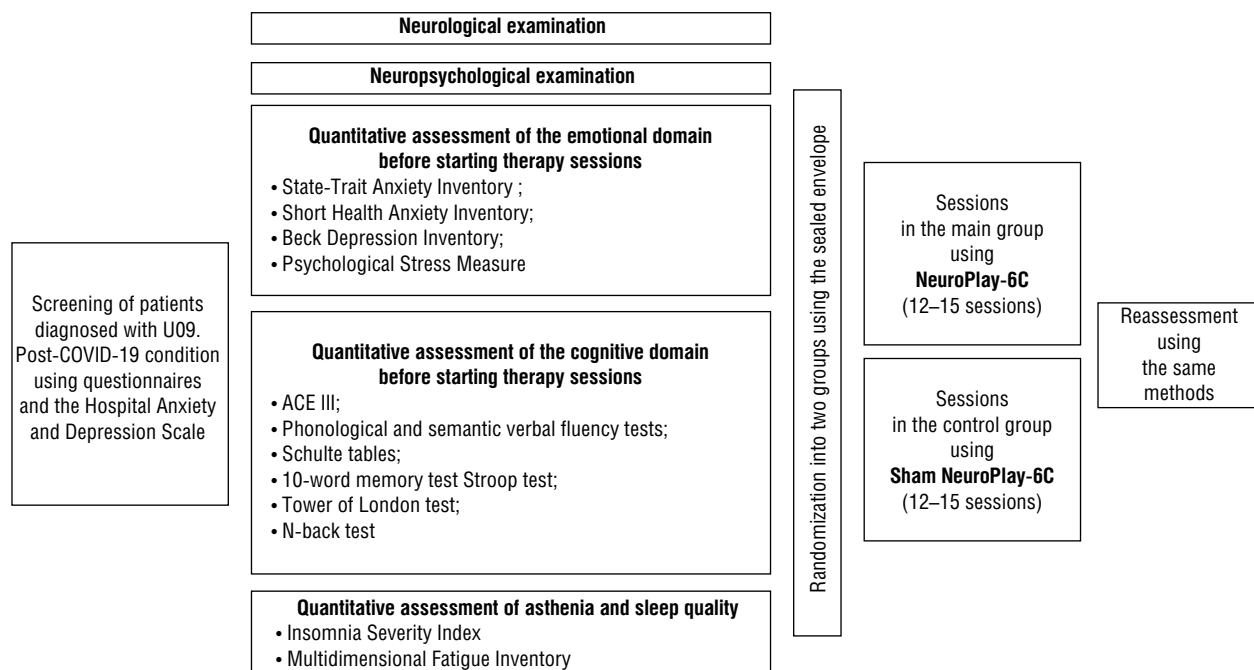


Fig. 1. Study design.

days with weekend breaks (participants were allowed up to 3 non-consecutive missed training sessions during the course, which had to be made up), and quantitative evaluation of emotional status, cognitive functions, and sleep quality after training sessions (1 day). Eighteen patients completed all 15 training sessions, while two patients ended the study at the 14th and 12th training sessions, respectively, due to external circumstances unrelated to the study.

The study protocol was approved by the Local Ethics Committee of the Russian Center of Neurology and Neurosciences (Protocol No. 9-5/22 dated October 19, 2022). Participation was entirely voluntary, with each patient providing written informed consent.

Eligibility criteria

Study participants were recruited through announcements posted on electronic information resources, bulletin boards at the Russian Center of Neurology and Neurosciences, and in special social media groups for PCS patients. A specialized questionnaire was developed for screening, containing questions about COVID-19 history (disease confirmation through medical records, time since infection, severity, current symptoms, chronic conditions, and medications). A separate section of the questionnaire focused on detailed assessment of anxiety, depression, asthenia, cognitive impairments, and sleep disorders – the key symptoms of interest in this study. The questionnaire along with the Hospital Anxiety and Depression Scale (HADS) [18] were sent upon request following telephone conversations with potential participants, during which they received detailed information about study timelines/format and could ask questions. After analyzing questionnaires and HADS results, participants preliminarily meeting inclusion criteria were invited for neurological

examination to confirm the diagnosis of U09. Post COVID-19 condition.

Inclusion criteria: Diagnosis of U09. Post COVID-19 condition; subclinical or mild clinical manifestations of anxiety and/or depression (HADS score ≤ 16); self-reported symptoms from the depression/anxiety group, cognitive impairment group, and/or sleep disturbances/asthenia group associated with COVID-19; age ≥ 18 years; informed consent.

Exclusion criteria: Presence of other conditions that could explain anxiety, depression, cognitive impairment, sleep disturbances, or asthenia; use of antidepressants, anxiolytics, or other medications affecting studied functions during dose titration or adjustment periods.

Withdrawal criteria: Patient withdrawal of consent; patient-reported escalation of anxiety/depression symptoms to severe clinical manifestations.

During the study period, 87 applications for participation received through various channels were analyzed. Forty-six patients declined participation during the detailed telephone briefing about the outpatient setting, geographical location, and study duration. Nineteen patients were excluded after questionnaire and HADS scale analysis due to meeting various exclusion criteria. Two other patients were excluded after neurological examination (one was referred for psychiatric consultation, the other due to contraindicated medication use).

Consequently, 20 PCS patients were enrolled in the main study. Five patients had confirmed COVID-19 more than once, with disease duration calculated from the episode when PCS symptoms first appeared. According

to questionnaires, 18 patients reported symptoms across all analyzed categories, while 2 reported symptoms in all categories except cognitive impairments. At the time of the study, 2 patients were taking antidepressants in stable doses; other participants were not receiving pharmacological treatment.

EEG α -rhythm biofeedback training

Patients in the main group underwent 12–15 training sessions of 30–50 minutes each using EEG α -rhythm biofeedback technology with the NeuroPlay-6C system (“Neurobotics”) via the built-in Neurocorrection of Psychoemotional Consequences of COVID-19 protocol. The headset and software were provided for free use. The headset is a wireless mobile 6-channel EEG recording system (Fp1, Fp2, T3, T4, O1, O2 channels) utilizing dry electrodes mounted on a specialized headband secured around the head. The recorded signals are transmitted to the main device via Bluetooth. The software analyzes EEG spectral characteristics to provide patients with biofeedback about their physiological state.

During training sessions, patients sat at a table in comfortable chair facing a computer monitor. Each session included a theoretical component explaining the upcoming exercises and a practical component for their implementation. During task performance, patients followed voice-guided instructions focusing on breath control, muscle relaxation, mental training, and meditation practices. All training sessions were conducted with closed eyes. Participants received auditory feedback about their physiological state during exercises. Failed task performance triggered increasing noise that masked background music perception. When patients returned to the target state with registered α -rhythm activity, the noise ceased. The main group participants learned to self-regulate their state using BFB during training.

Control group patients completed 12–15 training sessions (30–50 minutes each) using the Sham-NeuroPlay EEG program simulating BFB via the built-in Neurocorrection of COVID-19 Psychoemotional Consequences protocol. This protocol version was specially provided by Neurobotics for the study. Identical to the main group, control participants wore electrode headbands and performed state regulation exercises with the program’s voice assistant, but without actual feedback.

Instruments for assessing patients’ condition before and after training

To study the impact of training on the emotional state in both groups before and after the intervention, electronically completed questionnaires were used:

- The State-Trait Anxiety Inventory (STAI [19] adapted by Yu.L. Khanin [20]), containing two scales: state (reactive) anxiety and trait anxiety (symptom severity ranges: 0–29 points – low anxiety level, 30–45 – moderate, 46–80 – high);
- The Short Health Anxiety Inventory (SHAI [21] adapted by T.A. Zhelonkina et al. [22]), assessing total scores (maximum 54 points) and three subscales: health anxiety,

fear of negative consequences of illness, and vigilance to bodily sensations;

- The Beck Depression Inventory (BDI [23] adapted by N.V. Tarabrina [24]), evaluating total scores (symptom severity: 0–9 – no depressive symptoms, 10–15 – mild depression, 16–19 – moderate, 20–29 – severe, 30–63 – very severe), along with cognitive-affective and somatic subscales;
- The Psychological Stress Measure (PSM-25 [25] adapted by N.E. Vodopyanova [26]), assessing total scores (stress severity: 0–99 – low stress level, 100–155 – moderate, > 155 – high).

To study the effect of training on cognitive functions, both groups of participants underwent quantitative neuropsychological assessment before and after the experimental intervention. The assessment was conducted by a qualified neuropsychologist using methods targeting both general cognitive screening and evaluation of specific cognitive functions that, according to literature data [10], are most susceptible to impairment in PCS.

The following blank assessment tools were used:

- Screening Addenbrooke’s Cognitive Examination III (ACE-III) [27], validated by N.A. Varako et al. [28], which assesses total scores (maximum 100 points) across 5 domains: attention (max 18 points), memory (max 26 points), verbal fluency (max 14 points), language (max 26 points), and visuospatial function (max 16 points);
- Phonological and semantic verbal fluency test administered within the ACE-III framework but separately scored based on the total number of correct words generated per minute;
- Schulte tables [29], with calculated parameters including work efficiency (mean time per 5 tables), index of work warming-up (time for first table divided by mean time), and psychological stability index (time for fourth table divided by mean time) according to A.Yu. Kozyreva’s method;
- A.R. Luria’s 10-word memory test [17], recording parameters of immediate/delayed word recall volume and the number of trials required for complete memorization.

The Stroop test [30], which assessed interference effect parameters under word reading and color naming conditions (automatically calculated by the software), was administered using the Schuhfried hardware-software complex (<https://www.schuhfried.com/en/>).

Other computerized neuropsychological tests were conducted using Psychology Experiment Building Language Battery software [31]:

- The Tower of London test [32], which measured the total number of moves required to solve all planning subtests and the total time spent completing the entire test;
- The N-back test [33] under dual-task working memory conditions (simultaneous maintenance of letter and spatial stimulus sequences) with a comparison task between current on-screen stimuli and those presented n steps earlier ($n = 1, 2, 3$). For analysis, series with $n = 2$ and 3 were considered, recording the number of correct responses and false alarms for both letter and spatial stimuli. After test completion, the d' -prime sensitivity index (d') [34] was

calculated for each stimulus type in every series ($n = 2$ and 3) using the formula:

$$d' = Z(\text{hit rate}) - Z(\text{false alarm rate}),$$

where hit rate = number of patient's correct responses / maximum possible correct responses; false alarm rate = number of patient's false alarms / number of non-target stimuli; these rates were standardized using Z-transformation.

In addition to the techniques targeting emotional and cognitive domains, patients' subjective sleep quality was assessed using the Insomnia Severity Index (ISI [35], adapted by E.I. Rasskazova et al. [36]), which recorded total scores with the following severity categories: 0–7 points – normal, 8–14 points – mild sleep disturbances, 15–21 points – moderate, and 22–28 points – severe. Manifestations of asthenia were evaluated using the Multidimensional Fatigue Inventory (MFI-20 [37], Russian-translated version), with registration of total scores (maximum possible score: 100) and scores across 5 subscales: general fatigue, reduced activity, reduced motivation, physical fatigue, and mental fatigue.

Statistical Analysis

Due to the small sample size and non-normal distribution of data for several variables (according to the Kolmogorov–Smirnov test), non-parametric methods were used for statistical analysis. Intergroup differences in age and all baseline study variables were assessed using the Mann–Whitney U test for two independent samples. Fisher's exact test was used to compare groups based on the nominal variable of participants' sex. The training effect within each group was evaluated using the Wilcoxon signed-rank test (W) for two related samples (comparing preand post-training indicators). For statistical comparison of intervention protocols in each group, delta changes between preand post-training indicators were calculated for all specified variables. These changes were compared using the Mann–Whitney U test for two independent samples. The analysis also included patients who transitioned to milder levels of anxiety, depression, psychological stress, and sleep disturbances in each group (assessed using the State-Trait Anxiety Inventory, Beck Depression Inventory, Psychological Stress Measure, and Insomnia Severity Index). Intergroup comparison of the proportion of such

patients was performed using Fisher's exact test. The statistical significance level was set at 0.05. Calculations were performed using IBM SPSS Statistics v.23 software. Data are presented as median [25%, 75% quartile].

Results

Baseline Comparison of Patient Groups

Demographic and baseline clinical characteristics of the main and control groups are presented in Table 1. The groups showed no differences in sex, age, time since COVID-19 infection, or HADS scores used during participant screening.

Both groups underwent quantitative assessments of emotional status, cognitive functions, and sleep disturbances prior to the training. Comparative analysis of all variables revealed significant intergroup differences in Psychological Stress Measure scores. Stress levels in the control group were higher than those in the main group, with median scores in both groups corresponding to moderate stress levels. Differences were also observed in one parameter of the Stroop test (interference effect during word reading condition). All other baseline parameters showed no significant differences between groups (Table 2).

According to the scales assessing the severity of emotional and sleep disturbances, the severity levels in both groups were comparable (when comparing the median values within each scale's score ranges):

- state and trait anxiety scores indicated high levels;
- depression scores corresponded to a mild level;
- stress scores were at a moderate level;
- sleep quality scores suggested mild disturbances.

Cognitive screening using the ACE-III revealed no overt cognitive impairments suggestive of dementia (≤ 88 points, sensitivity 1.00) in either group (Table 2).

Assessment of intragroup dynamics of study participants' condition

1. Intragroup dynamics of emotional domain

When comparing preand post-training indicators in both the main and control groups, significant improvement was observed across several parameters (hereinafter figures show results for main scale scores; subscale data are described in the text):

Table 1. Demographics and baseline characteristics of two groups

Characteristic	Main group ($n = 10$)	Control group ($n = 10$)	Mann–Whitney U test value	p
Sex	4 males, 6 females	1 male, 9 females		0.303
Age	41 [32; 50]	31 [24; 40]	30	0.143
Time since COVID-19 (months)	23 [15; 26]	16 [9; 18]	26	0.075
HADS — anxiety assessment	8 [5; 11]	8 [6; 10]	32	0.190
HADS — depression assessment	9 [8; 10]	7 [5; 11]	45	0.739

Table 2. Comparison of two patient groups across all assessed parameters before intervention

Parameter	Main group (<i>n</i> = 10)	Control group (<i>n</i> = 10)	Mann-Whitney U test value	<i>p</i>
Emotional domain				
STAI, state anxiety	49.5 [37.3; 55.0]	49.5 [37.0; 54.3]	50	1.000
STAI, trait anxiety	56 [42.8; 60.8]	50.5 [43.7; 63.5]	48.5	0.912
SHAI, total score	13 [10; 17]	13 [8.8; 21.0]	48.5	0.912
SHAI, health anxiety	4.5 [3.0; 7.3]	5.5 [2.0; 9.3]	46	0.796
SHAI, fear of negative consequences of illness	5 [3.8; 6.3]	3.5 [3.0; 5.3]	35	0.280
SHAI, vigilance to bodily sensations	3.5 [1.8; 6.0]	4.5 [2.8; 6.5]	39	0.436
BDI, total score	11.5 [8.0; 14.7]	15.5 [9.8; 17.8]	35.5	0.280
BDI, cognitive-affective subscale	6 [5.0; 8.3]	8 [6.0; 11.3]	32.5	0.190
BDI, somatic subscale	5 [3; 7]	5.5 [3.8; 7.5]	44	0.684
PSM-25	102 [87; 115]	115 [99; 120]	18	0.015
Cognitive domain parameters				
ACE-III, total score	98 [95.5; 99.3]	98 [95.5; 98.3]	41	0.529
ACE-III, attention	18 [18; 18]	18 [17; 18]	39.5	0.436
ACE-III, memory	25.5 [25; 26]	25 [25; 25]	31.5	0.165
ACE-III, verbal fluency	13 [11.8; 14.0]	13 [12.8; 13.3]	45.5	0.739
ACE-III, language	26 [25; 26]	26 [25.8; 26.0]	46.5	0.796
ACE-III, visuospatial function	16 [15; 16]	16 [15.5; 16.0]	47	0.853
Phonological verbal fluency	17.5 [14; 19]	18 [17; 21.5]	40	0.481
Semantic verbal fluency	22.5 [18.5; 25.3]	22.5 [16.5; 26.0]	50	1.000
Schulte tables, efficiency	32.3 [26.1; 41.4]	28.7 [27.1; 39.4]	44	0.684
Schulte tables, work warming-up	0.96 [0.92; 1.01]	0.99 [0.91; 1.05]	41.5	0.529
Schulte tables, psychological stability	0.99 [0.95; 1.08]	1.06 [0.97; 1.13]	37	0.353
10-word memory test, immediate recall volume	6 [5.8; 7.0]	8 [6; 8]	25.5	0.063
10-word memory test, delayed recall volume	9 [7.8; 10.0]	9 [7.8; 10.0]	34	0.247
10-word memory test, number of trials to complete memorization	3.5 [3.0; 5.3]	2.5 [2.0; 4.2]	49	0.971
Stroop test, interference in word reading condition	0.2 [0.17; 0.22]	0.11 [0.09; 0.15]	22	0.035
Stroop test, interference in color naming condition	0.1 [0.08; 0.17]	0.08 [0.05; 0.10]	28	0.105
Tower of London, total number of moves	150 [136; 162]	158 [151; 166]	34	0.247
Tower of London, completion time	392 [361; 533]	344 [297; 623]	34	0.247
N-back, <i>n</i> = 2, letter stimuli, <i>d'</i>	1.2 [0.60; 2.05]	1.47 [0.68; 2.13]	46.5	0.796
N-back, <i>n</i> = 2, spatial stimuli, <i>d'</i>	1.8 [0.80; 2.28]	1.63 [0.64; 2.13]	46	0.796
N-back, <i>n</i> = 3, letter stimuli, <i>d'</i>	1.07 [0.48; 1.15]	1.11 [0.72; 1.86]	40	0.481
N-back, <i>n</i> = 3, spatial stimuli, <i>d'</i>	0.84 [0.16; 1.17]	0.93 [0.64; 1.12]	47	0.853
Sleep quality and asthenia assessment indicators				
ISI	9 [2.8; 17.0]	12.5 [6.0; 17.3]	40.5	0.481
MFI-20, total score	65 [49.5; 70.5]	68.5 [55.0; 76.5]	34	0.247
MFI-20, general fatigue	16 [14.8; 16.3]	14.5 [13.8; 17.0]	41.5	0.529
MFI-20, reduced activity	13.5 [9.8; 16.3]	13.5 [8.7; 17.3]	49	0.971
MFI-20, reduced motivation	9 [6; 12]	11.5 [9; 15]	26	0.075
MFI-20, physical fatigue	11.5 [9.0; 14.3]	13 [11.8; 14.5]	40.5	0.481
MFI-20, mental fatigue	12 [7.5; 17.3]	13 [11.8; 14.5]	44.5	0.684

- reduction in trait anxiety (Fig. 2, A);
- reduction in psychological stress (Fig. 2, B);
- reduction in overall Beck Depression Inventory scores (Fig. 2, C), including scores on the cognitive-affective subscale (main group: $W = -2.814$; $p = 0.005$; control group: $W = -2.537$; $p = 0.012$) and somatic subscale (main group: $W = -1.998$; $p = 0.046$; control group: $W = -2.537$; $p = 0.012$);
- reduction in scores on the SHAI vigilance to bodily sensations subscale (main group: $W = -2.558$; $p = 0.011$; control group: $W = -2.701$; $p = 0.007$).

Additionally, the main group demonstrated reduced overall SHAI health anxiety scores, which was not observed in the control group (Fig. 2, D). No changes were observed in other assessed variables.

2. Intragroup dynamics of cognitive domain

When comparing preand post-training indicators in the main group, improvements were observed in the performance of A.R. Luria's 10-words memory test: increased volume of immediate word recall ($W = -2.356$; $p = 0.018$) and reduced number of attempts required to memorize all 10 words ($W = -2.565$; $p = 0.010$). To illustrate these changes, we present the dynamics of the 10-word learning curve in Patient No. 7 from the main group (Fig. 3). No other significant changes in cognitive domain parameters were identified.

In the control group, cognitive changes showed bidirectional effects: post-training improvements in total completion time for the Tower of London test ($W = -2.497$; $p = 0.013$), but reduced efficiency in maintaining letter stimuli in working memory (N-back test, $n = 3$, letter stimuli, $d' - W = -2.293$; $p = 0.022$). No other significant changes were observed.

3. Intragroup dynamics of sleep quality and asthenia manifestations

When comparing preand post-training indicators in both the main and control groups, a significant reduction in asthenia manifestations was observed, both in the total score of the MFI (Fig. 4) and in individual subscales:

- general fatigue (main group: $W = -2.670$; $p = 0.008$; control group: $W = -2.025$; $p = 0.043$);
- reduced activity (main group: $W = -2.677$; $p = 0.007$; control group: $W = -2.388$; $p = 0.017$);
- physical fatigue (main group: $W = -2.113$; $p = 0.035$; control group: $W = -2.120$; $p = 0.034$);
- mental fatigue (main group: $W = -2.257$; $p = 0.024$; control group: $W = -2.094$; $p = 0.036$).

The control group also showed improvement in the reduced motivation subscale ($W = -2.002$; $p = 0.045$).

No significant improvements in sleep quality were demonstrated in either group.

Intergroup comparison of intervention efficacy

When comparing delta changes (degree of improvement across all specified variables), statistically significant intergroup differences were observed for two cognitive measures.

The experimental group showed greater improvement compared to the control group in immediate recall scores on A.R. Luria's 10-word memory test ($U = 25.5$; $p = 0.036$), as well as higher efficiency in maintaining letter stimuli in working memory (N-back test; $n = 3$; letter stimuli, $d' - U = 23.5$; $p = 0.034$). Intergroup differences were also observed on the general fatigue subscale of the MFI, with more substantial changes in the experimental group compared to controls ($U = 19.5$; $p = 0.019$). Changes across all other measured parameters were comparable between groups.

For statistical comparison of the two interventions, we analyzed the number of patients transitioning to milder severity levels of anxiety, depression, psychological stress, and sleep disturbances in both groups. The proportion of such patients on each scale was comparable between experimental and control groups (Table 3).

Discussion

In this blinded randomized controlled trial, both EEG α -rhythm BFB training and various psychological practices without feedback demonstrated positive outcomes, including reductions in trait anxiety, psychological stress, depressive symptoms, and fatigue. The BFB therapy group additionally showed decreased health-related anxiety and improved performance on the 10-word recall memory test. Psychological interventions without feedback exhibited mixed effects on specific cognitive domains.

When comparing intervention protocols, BFB therapy demonstrated superior efficacy in reducing general fatigue, enhancing immediate word recall during learning, and maintaining verbal information in working memory. However, both protocols showed comparable results in the proportion of patients achieving milder symptom severity levels based on emotional state and sleep quality questionnaires.

The obtained results regarding EEG α -rhythm BFB training align with published data on the effective use of biofeedback therapy for anxiety disorders [38], depression [39], stress [40], and asthenia [41] outside the context of PCS. Furthermore, existing evidence demonstrates the influence of EEG α -rhythm BFB training on working and episodic memory in healthy individuals [42]. The cognitive improvements observed in our study may result both from the direct effects of biofeedback therapy on the examined functions and from the more pronounced reduction of asthenia in the main study group, which could enhance neurodynamic aspects of cognitive processing and consequently lead to increased immediate recall capacity and reduced number of trials required for memorization in the 10-word memory test.

The results obtained from various psychological practices indicate that breathing control exercises, muscle relaxation techniques, mental training, and meditation practices exert an independent positive effect on several emotional parameters and manifestations of asthenia, regardless of the feedback. Consequently, the data obtained through BFB therapy may be partially explained by non-specific effects of the applied exercises rather than the feedback mechanism itself.

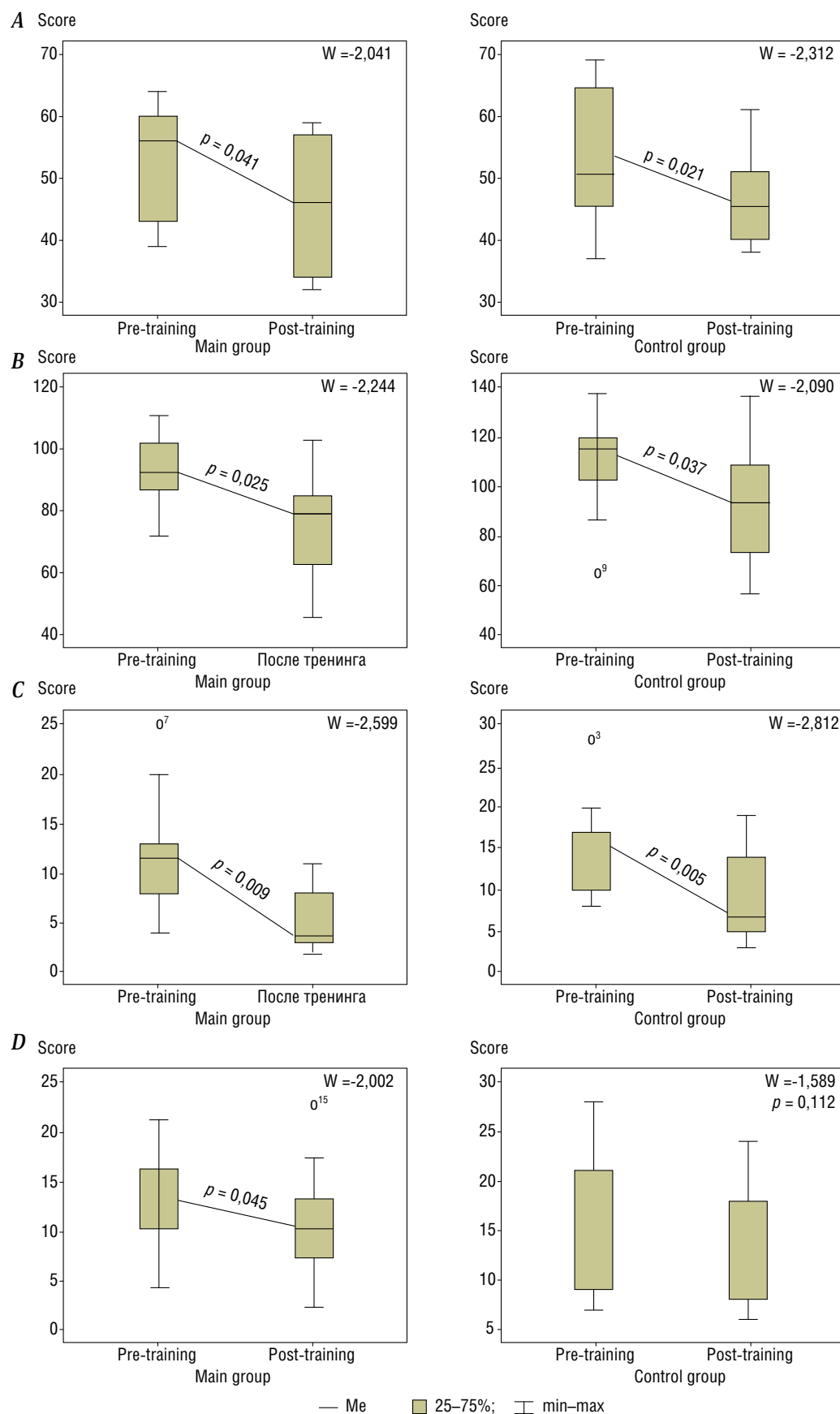


Fig. 2. Intra-group dynamics of trait anxiety scores on the State-Trait Anxiety Inventory (A), Psychological Stress Measure (B), Beck Depression Inventory (C), and Short Health Anxiety Inventory (D).

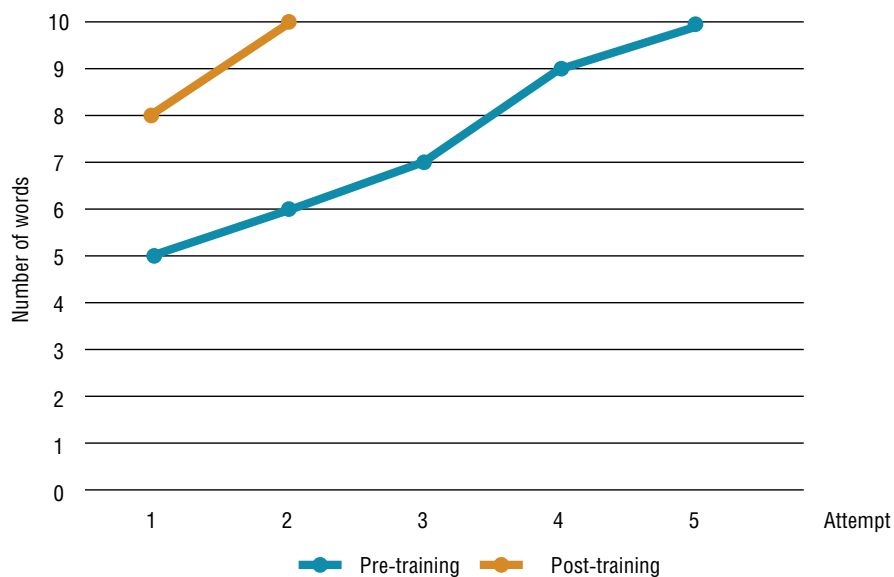


Fig. 3. Learning curves of the 10-word memory test before and after training for patient No. 7 in the main group.

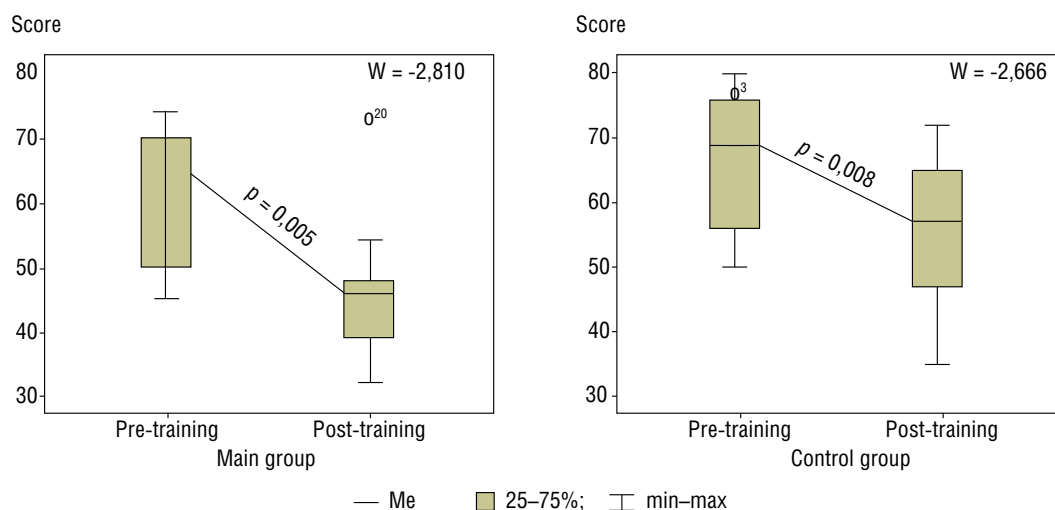


Fig. 4. Intra-group dynamics of Multidimensional Fatigue Inventory total scores in both groups.

Table 3. Comparison of the proportion of patients achieving transition of symptoms to milder severity levels

Proportion	Main group (n = 10)	Control group (n = 10)	p
Achieved improvement on STAI, state anxiety, n (%)	5 (50%)	6 (60%)	1.000
Achieved improvement on STAI, trait anxiety, n (%)	2 (20%)	1 (10%)	1.000
Achieved improvement on BDI, n (%)	6 (60%)	5 (50%)	1.000
Achieved improvement on PSM-25, n (%)	2 (20%)	4 (40%)	0.628
Achieved improvement on ISI, n (%)	4 (40%)	3 (30%)	1.000

Limitations of this study include small sample sizes (which may account for baseline differences in psychological parameters between groups), lack of preliminary statistical power calculations and sample size estimation, and absence of neurophysiological analysis of EEG parameter changes pre and post-training. In this study, the control group received no feedback, potentially raising participants' suspicions about the intervention given that both groups wore headsets and received identical instructions during each session.

In future studies, the use of sham feedback in the control group may help elucidate the specific contribution of feedback mechanisms. Additionally, introducing a no-intervention group could help control for placebo effects associated with study participation. To comprehensively assess the efficacy of BFB therapy, patient evaluations should be conducted at specific intervals (1 month, 6 months, 1 year) post-intervention.

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