

# Therapeutic Possibilities for the Correction of Cognitive and Psychoemotional Impairments in Patients with Post-Covid Syndrome

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**Abstract:** This article discusses the therapeutic possibilities for the correction of cognitive and psychoemotional impairments in patients with post-covid syndrome. The search for a method of rehabilitation of cognitive impairment, non-invasive, painless and having a long-term effect after the end of the course of treatment remains relevant. These developments include the method of bioacoustic correction (BAC) - an innovative technique based on the activation of neuroplasticity processes by synchronizing endogenous neural activity with afferent neurodynamics provoked by sensory input.

**Keywords:** Post-covid syndrome, psychoemotional disorders, cognitive impairment, bioacoustic correction method.

## 1. Introduction

### Relevance

The neurological complications of SARS-CoV-2 coronavirus infection COVID-19 are extremely diverse (5,7). For example, COVID-19 increases the risk of stroke, encephalopathy, cerebral microbleeds, and autoimmune diseases, such as Guillain-Barré syndrome [6]. Given that at the present stage, all health reserves have been directed to fighting the pandemic and developing a vaccine, the condition of patients who have had COVID-19 has not been studied so actively.

Nevertheless, recently there have been more and more publications about such a formidable complication of COVID-19 as cognitive impairment (CI). Risk factors for severe COVID-19 and CI overlap to a large extent and include older age, obesity, and the presence of comorbid conditions such as hypertension and type 2 diabetes. Such patients are potentially at high risk of developing CI during and after various inflammatory processes [4,8], as well as in connection with their anesthesia [8].

Thus, people who are most susceptible to complications from COVID-19 are also potentially the most susceptible to developing CI in an inflammatory process. Many studies have shown that CI in some patients with acute respiratory distress syndrome (ARDS) persisted for 5 years after the disease (9,10). That is why in this study we decided to consider such a complication of COVID-19 as CI.

The search for a method of rehabilitation of cognitive impairment, non-invasive, painless and having a long-term effect after the end of the course of treatment remains relevant. These developments include the method of bioacoustic correction (BAC) - an innovative technique based on the activation of neuroplasticity processes by synchronizing endogenous neural activity with afferent neurodynamics provoked by sensory input. Activation of neuroplasticity contributes to the restoration of the processes of maturation of brain structures, as well as the inclusion of morphofunctional compensatory mechanisms (1,2). The basis of the method is the computer transformation of the patient's electroencephalogram into an acoustic signal and the presentation of this signal to the patient in real time, thereby performing sensory EEG-dependent stimulation. BAC-therapy contributes to the normalization of the psychophysiological state, there is an improvement in mood, a decrease in increased anxiety, emotional tension, fatigue, sleep and mood normalize, aggressiveness decreases (3).

Thus, at present, a non-drug method for the treatment of diseases of the central nervous system based on bioacoustic correction is a generally available method for treating a wide range of diseases of the nervous system. At the same time, it is impossible not to note the harmlessness of the method, its high efficiency, the possibility of using it in childhood, the possibility of reducing the drug load on the body.

**Purpose of the study.** To analyze the structure of cognitive impairments and evaluate the effectiveness of the method of bioacoustic correction of cognitive impairments in patients with post-COVID syndrome.

## 2. Material and research methods

Patients were examined on the basis of the Bukhara Regional Multidisciplinary Medical Center. The study included 100 young and middle-aged people from 30 to 55 years old (main group), with a verified diagnosis of the consequences of COVID-19 coronavirus infection, confirmed by laboratory methods of research and after negative results (PCR, ELISA) for SARS-CoV-2, 15-35 weeks after the onset of the disease, which made up the main group (Table 1). The control group consisted of 20 healthy subjects of the appropriate sex and age composition who had not had a coronavirus infection or other viral infection over the past 6 months and had no acute and decompensated chronic pathology at the time of observation.

**Table 1. Distribution of patients by age and sex categories**

Group	Sign	Men	Women	Total
Main (MG)	Abc.	42	58	100
	%	42	58	100
	Average age, years	59±7,2	63±7,5	62±6,7
Control (CG)	Abc.	8	12	20
	%	40	60	100
	Average age, years	55,6±6,79	59,4±6,8	58±7,03

Patients in the MG and CG of observation were comparable in age and gender (Table 1).

The diagnosis of post-covid syndrome (PCS) was made according to the classification of post-covid conditions proposed by the National Institute for Health and Excellence (NICE) of Great Britain and approved by WHO (post-covid syndrome - symptoms lasting more than 12 weeks, not explained by an alternative diagnosis, capable of changing over time, disappearing and reappearing, affecting many body systems).

All patients received standard therapy: vitamin and mineral complex, relaxing massage of the back muscles, inhalations with mineral water according to indications.

The patients were divided into two subgroups, the A-subgroup included 36 people who received BAC-therapy, 10-15 sessions, lasting 20 minutes. BAC therapy was not combined with medication. The B-subgroup consisted of 64 patients who received standard therapy (Table 2).

**Table 2. Distribution of patients with MG by subgroups.**

Group	Sign	A subgroup	B subgroup	Total
Main	Abc.	36	64	100

(MG)	%	36,0	64,0	100,0
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In a comprehensive clinical examination of patients, the generally accepted clinical examination of the somatic status, neurological examination using the MMSE scale, Luria's "10 words" test, Schulte's technique were used. The test for the study of cognitive functions - MMSE (Mini Mental Scale Examination) provides an assessment of orientation in place, time, concentration, perception, memory, speech, execution of a three-stage command, reading and drawing according to a model. The evaluation of the data obtained, expressed in points, was carried out according to a special table.

**Method of "Bioacoustic correction" (BAC)** implemented in the Synchro-S hardware-computer complex. Registration certificate № FSR 2010/07223 dated March 01, 2016, certificate of conformity (GOST R) No. ROSS RU.ME.HO263 dated 04.22.2013, license for the production of medical equipment № FS-99-04-004808 dated 06.28.16, patent № 2410025, 24228927, 2492839. (Fig.1).

**Hardware-computer complex "Synchro-S".**



**Picture 1. Hardware-computer complex "Synchro-S".**

The Bioacoustic Correction (BAC) method was developed by neurophysiologists of the Physiological Department named after A.I. I.P. Pavlov FGBNU "IEM" (group of neurodynamic correction of the pathology of brain functions). The physiological basis of the BAC method is sensory EEG-dependent stimulation. This method uses various acoustic (musical, verbal and other) stimuli synchronized and consistent with the current bioelectrical activity of the brain and presented to the patient in real time, that is, the patient is presented with an acoustic image of his own EEG in real time. Important adjustable parameters for presenting this image are: sound volume (set separately for each EEG channel), type of sound (vocal, instrumental, formant, verbal), exposure intensity (selected from 10% to 100% - sets the level of correlation of acoustic stimuli with the original EEG), procedure duration (from 1 to 25 minutes).

The patient listens to the acoustic image of his own bioelectrical activity of the brain for a set time, with other set parameters. The patient does not receive any cognitive tasks for voluntary control of the presented acoustic stimuli and control of his own functional state. The only task of the patient is to listen to the presented sounds. However, the level of attention to the presented acoustic image is not a key condition for BAC procedures, which makes it possible to use the method regardless of the age and degree of preservation of the patient's cognitive functions. BAC has a number of advantages over other types of treatment: non-drug and non-invasive treatment of functional disorders of the central nervous system; lack of addiction, side effects and age restrictions; compatibility and acceleration of other types of treatment, reduction of drug load, with some nosologies, the possibility of replacing drug treatment. Each BAC procedure is controlled by EEG recording on

4 channels in on-line mode (review and indexometric analysis). After each procedure, it is possible to evaluate the change in various EEG parameters (indexometric, pattern, cross-correlation and other types of mathematical analyzes).

**The principle of operation of the Synchro-S complex:** Biopotentials of the brain are recorded in the monopolar mode with a combined ear electrode from 4 sensors placed on the patient's head in the position of the right forehead, left forehead, right occiput, left occiput. Biopotentials of the brain are amplified, preliminarily analog filtered and digitized. Further, the information is transmitted to the computer through the interface with galvanic isolation. The software package of the complex provides the formation of arrays of incoming signal values, their digital filtering, the conversion of incoming signals into an audio image, the display of these signals in real time on a PC screen, the saving of the entered data on a computer hard disk and their subsequent processing. The generated sound image is fed through a standard audio output to the speaker system or headphones and presented to the patient in real time (Fig. 2).



Figure 2.

**Method Mechanisms:** The technological basis of the LHC method is the feedback principle, when the recorded (in this case physiological) parameter is returned to the source after the necessary transformation. This principle is basic for almost all regulatory processes and is widely used in well-known biofeedback methods (BFB). However, in contrast to BFB methods, in the BAC method, the patient is not faced with the task of arbitrary (cognitive) regulation of the transformed physiological parameter. On the contrary, the therapeutic application of the LHC method is based on the principles of involuntary self-regulation. The content of the concept of involuntary self-regulation is not in the technical or cognitive compensation of disturbed physiological reactions, **and in the activation of the natural processes of self-regulation and regenerative functions of the body**, which are normally carried out involuntarily, but were suppressed as a result of an unfavorable combination of environmental factors, illness, or individual personality traits.

**Mathematical processing of the obtained** data was carried out by the method of analysis of variations. The average values ( $M$ ) and their average error ( $\pm m$ ) were determined, the differences between the average values ( $0$ ), the correspondence criterion ( $x_2$ ), the probability value ( $p$ ).

The relationship between the studied parameters was determined using the linear correlation coefficient ( $\pm r$ ). The results were considered statistically significant at  $p < 0.05$ . The assessment of direct correlation was considered: up to  $\pm 0.3$  - small; from  $\pm 0.3$  to  $\pm 0.7$  - medium;  $\pm 0.7$  to  $1.0$  large.

**Research results.** In the pathogenesis of the development of clinical manifestations in COVID-19, thrombus formation of vessels of various calibers of different tissues and organs, including cerebral vessels, lies. That is, diffuse ischemia occurs against the background of multiple thromboses, which causes dysfunction of various

organs and systems. In our work, we studied the psycho-emotional and cognitive sphere of patients on the background of COVID-19, which is also caused by vascular lesions of the brain. Therefore, for the treatment of these symptoms, a neuropeptide preparation was chosen by nature (safety, efficacy) and having indications for asthenia, cognitive impairment, anxiety.

In connection with the above facts, it seems relevant to study the effectiveness and tolerability of BAC therapy in the treatment of a wide range of psychoemotional and cognitive disorders in patients with cerebrovascular diseases.

The cognitive status (CS) of patients was assessed at 6 months using neuropsychological scales (MMSE, Schulte table, memorization test 10 words).

#### *MMSE Cognitive Status Assessment*

The Mini Mental Status Assessment (MMSE) is widely used around the world to assess the state of cognitive functions. In our study, the assessment of cognitive status by the MMSE test showed the presence of statistically significant differences between the groups. It should be noted that the effectiveness of this technique depends on the severity of the cognitive deficit, i.e. it is not sensitive enough to mild to moderate cognitive impairment ( ).

The data obtained were categorized as follows: 28 or more points - the norm; 25–27 points - pre-dementia disorders; 24 or less points - demential CI. The results of this operation are presented in table 3.

Comparing the dynamics of the severity of CI in subgroups (according to the MMSE scale), we can note:

-among persons with severe CI (24 points or less) of the A-subgroup, in 50% of cases (p 0.02) there was a regression to mild CI (25%) and recovery to normal (25%), in the B-subgroup 33% of cases regressed only to the level of moderate CI;

- mild CI detected in patients of the A-subgroup at the beginning of the observation period on the MMSE scale regressed after 6 months: 67% had normal test indicators, 33% had no significant dynamic changes (p 0.004), in the B-subgroup 35% of patients recovered CF indicators to normal, 47% remained moderate CI.

- patients without CI at the visit by the end of the observation period in the A-subgroup in 90% of cases remained with indicators within the normal range (28 points and above), 10% had progression of CI to the degree of moderate, among patients in the control group over the same period of time 47% had normal indicators on the MMSE scale, and 53% had moderate CI (intergroup differences according to the nonparametric Mann-Whitney test p 0.012, regression of normal indicators in the control group had a statistical significance of p 0.003 in an intragroup comparison according to the nonparametric paired Wilcoxon test).

Statistical significance (p<0.05) in intergroup comparison (chi-square test) of categorized data on the MMSE test showed significant differences in the A-subgroup (Table 3). Despite the fact that the initial data on all cognitive tests in the A-subgroup were slightly worse than those in the B-subgroup, after treatment in the A-subgroup we see a higher result than in the compared subgroup.

**Table 3 Dynamics of the cognitive status of patients on scales (M +  $\delta$ )**

Scales, tests	A subgroup		B subgroup		CG
	Before treatment	After treatment	Before treatment	After treatment	
<b>MMSE (balls)</b>	20,3±0,7	25,9±2,7*	22,1±1,6	24,8±2,6	26,2±0,2
<b>Schulte (points)</b>	55,8±1,9	62,1±3,8*	53,9±2,5	58,4±4,1*	65,6±3,9
<b>Test score 10 words (seconds)</b>					
<b>Short playback</b>	5,0±0,2	4,5±1,9*	5,1±0,33	4,8±2,2	3,4±1,6

	5,3±0,8	4,8±1,5*	6,9±0,35	5,6±2,2*	4,1±1,7
<b>Delayed playback</b>					

Note: \* - significant difference between the results before and after treatment ( $p < 0.05$ ).

When comparing using the Wilcoxon test for conjugated samples, as well as intergroup comparison (Mann-Whitney test), the dynamics of p-significance had the following indicators: statistical significance was determined only in the A-subgroup during comparison, it was at this point in time that the most significant increase in test scores occurred. The earlier the BAC therapy is carried out, the faster the positive dynamics in the acute period is noted, the longer the drug intake contributed to a more stable positive dynamics in the future (consolidation of the achieved result).

Comparison of quantitative data using the Mann-Whitney test showed an approximate to statistically significant difference between subgroups at visit 1 ( $p = 0.068$ ), and at subsequent visits - a significant statistical significance of differences (visit 2  $p = 0.02$ , visit 3  $p = 0.007$ , visit 4  $p = 0.01$ ). The statistical significance of the differences between subgroups at visit 1 was 0.04 (Freeman-Holton). It should be noted that at visits 3 and 4 there were no patients with dementia in the main group, while in the control group the percentage of patients with severe CI increased to 18% (3 people). At the same time, among patients of the A-subgroup, over a given period of time, the performance of the neuropsychological test MMSE improved significantly (by 67%).

#### *Assessment of cognitive status with a 10-word test*

Interesting results were obtained when processing the 10-word memorization test (this test reflects the state of memory, the process of memorizing words and storing memorized information). The indicator of short-term memory showed intergroup statistically significant differences in delayed reproduction of information (Table 3). The indicator of delayed recall after treatment in the B-subgroup had a positive trend, and in the A-subgroup it had a more pronounced statistically significant positive trend, which confirms the effective effect of BAC therapy on mnemonic functions. There was an increase in the number of reproduced words, the quality of delayed memory improved (by 25%) ( $p = 0.02$ ).

The statistical significance of intergroup differences is determined at visit 1 and all subsequent visits by the chi-square test and at visits 1 ( $p = 0.047$ ), 4 ( $p = 0.015$ ) by the Mann-Whitney test.

Intergroup differences were assessed, the criterion of the total cognitive score was applied (comparison base - CG and visit 0), significant statistically significant dynamics was observed when comparing group indicators.

#### *Schulte's level of attention*

The results of data processing according to the Schulte test are quite interesting. The technique is used to study the rate of sensorimotor reactions and characteristics of attention, the level of mental performance. The average time to complete a task according to one table is normally 30–40 seconds [].

As can be seen from Table 3, the descriptive statistics (mean  $\pm$  standard deviation) are quite different between the study groups. The Schulte test does not involve a variable assessment of cognitive status. It seems to the researcher that precisely because of this, and also because of the small sample sizes, the processing results do not have p-significance. In a visit comparison of the two studied populations (Mann-Whitney test), close to the critical value of the quantitative indicator of the degree of distrust in the conclusion about the presence of a connection ( $p = 0.05$ ) was observed at visits 1 and 2, at visits 3 and 4, statistical significance increased to 0.023 and 0.016, respectively.

However, the most interesting are intra-group comparisons (Wilcoxon's T-test). In the control group, no statistically significant differences were observed, both in stepwise comparison (visit 0 1  $p = 0.49$ , visit 0 2  $p = 0.834$ , visit 0 3  $p = 0.366$ , visit 0 4  $p = 0.257$ ), and in pairwise comparison of the primary data of visit 0 with each subsequent one (visit 0 1  $p = 0.49$ , visit 0 2  $p = 0.743$ , visit 0 3  $p = 0.675$ , visit 0 4  $p = 0.224$ ). In the main group, when comparing visit 0 in pairs with subsequent ones, the statistical significance has a pronounced tendency to stabilization (visit 0 1  $p = 0.026$ , visit 0 2  $p = 0.237$ , visit 0 3  $p = 0.773$ , visit 0 4  $p = 0.576$ ), and in stepwise comparison it acquires a significant statistical value of the p indicator (visit 0 1  $p = 0.026$ , visit 0 2  $p = 0.008$ , visit 0 3  $p = 0.01$ , visit 0 4  $p = 0.009$ ).



### 3. Conclusion

1. Analysis of the above confirms that half of the patients have CI, which during the entire period of rehabilitation have instability, at best fixed at the level of mild CI and moderate CI. The most pronounced effect of BAC-therapy affected the stabilization of neuropsychological testing parameters in the cognitive sphere during the rehabilitation period, compared with the parameters in patients receiving standard therapy ( $p = 0.017$ ).
2. The level of attention according to the Schulte test, despite the absence of statistically significant differences when comparing categorized data (test performance for 40 seconds and more than 40 seconds), in the group of patients who received BAC therapy, had a significantly more pronounced positive dynamics than in the group of patients who were on standard treatment. This is confirmed by the result of comparing quantitative data. It follows that a decrease in attention, exhaustion during the test was noted in both groups in most patients. The identified neuropsychological signs of the disease, which were expressed in a decrease in attention, inertia, and a decrease in memorization observed at the beginning of the study, tend to fluctuate, which indicates a disruption in the functioning of brain neurons in conditions of ischemia against the background of lung tissue damage. However, in the main group, a slight improvement in concentration, reaction speed, and a decrease in fatigue during the test were recorded compared to the control group. The results achieved in the cognitive sphere were more stable and persisted throughout the course of BAC therapy. Restoration of impaired functions, reduction of the consequences of ischemic damage indicate the effectiveness of the ongoing BAC therapy.

### 3. References

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