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Clinical aspects of nonlinear dynamics of cognitive processes: features of sensorimotor activity in patients at the clinical phase of COVID-19

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Abstract. The mechanisms of retrograde or anterograde neuronal transport ensure the migration of SARS-CoV-2 viruses to motor and sensory terminals, which can provoke significant distortions in the processes of information pattern recognition and the formation of action programs. The *purpose* of this study is to experimentally determine the dynamic modes of the cognitive system in patients with COVID-19. Cognitive processes are displayed in the space of parameters of sensorimotor activity when solving problems of different levels of complexity on the COGNITOM WEB platform. Patients and healthy individuals are presented with the same sets of stimuli in the same functional contexts. Covid-specific modes of information processing were manifested in a sharp decrease in the speed of cognitive processes and an increase in the number of missed target events.

Keywords: cognitive processes, information technology, digitalization, COVID-19.

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Introduction

The properties of information systems are manifested in the distortions that they introduce into the information signal. Digitalization of distortions in various functional states opens up new opportunities for constructing biologically plausible models of cognitive systems, taking into account the age, clinical and individual characteristics of the cognitive agent.

The COVID-19 pandemic has actualized a complex of pathological conditions associated with the risks of cognitive impairment: severe acute respiratory syndrome (SARS), chronic stress, multisystem inflammatory syndrome, disseminated intravascular coagulation syndrome [1]. A significant proportion of patients with COVID-19 have extremely low blood oxygen saturation, but, remarkably, there are disproportionately few symptoms of cerebral, or "happy"hypoxia. Oxygen starvation of the brain can provoke neurological disorders, especially in areas of the brain that are

very sensitive to hypoxia. Cognitive dysfunction is promoted by ischemic or hypoxic lesions of the hippocampus, basal ganglia, cerebellum, functional disorders typical of SARS. Specific changes in cognitive processes may be associated with specific neurotropic manifestations of coronavirus activity [2]. The properties of SARS-CoV-2 as a catalyst and accelerator of aggregation of brain proteins contribute to serious damage to the structure and function of the central nervous system (CNS), including infections of immune macrophages, microglia or astrocytes, severe encephalitis, toxic encephalopathy and severe acute demyelinating lesions. FMRI data indicate that the foci of destruction extend to the complex of subcortical structures, capture the thalamus, basal ganglia and neocortex zones included in the limbic system. The neuroanatomic scheme of brain lesions is in good agreement with the neuroarchitecture of dopaminergic pathways. It is no coincidence that one of the manifestations of the action of SARS-CoV-2 is a decrease in dopamine activity in the nigrostriate complex [3]. Mechanisms of retrograde or anterograde neuronal transport ensure the migration of viruses into motor and sensory terminals, which can provoke significant distortions of sensorimotor reactions of any complexity level. Thus, SARS-CoV-2 affects the main components of the neural platform supporting key cognitive processes:

1) damage to the exteroceptive and interoceptive sensory channels provokes a violation of the perceptual processes of displaying objective signals into signs of subjective information images and signals of reverse afferentation;
2) the destruction of the thalamus provokes a violation of the process of concentration of information resources on the most significant objects and events, that is, selective attention;
3) hypoxic lesions of the hippocampus provoke disturbances in the dynamic memory system and provoke distortions in the processes of preserving and reproducing information images;
4) degradation of the dopaminergic system distorts evaluative functions, disrupts locomotor processes, provokes a reduction of emotions, including vital ones, such as "pain".

A repertoire of cognitive problems associated with COVID-19 is known from the reports of patients: confused consciousness, difficulty concentrating, reduction of motor activity, impaired coordination of movements, loss of smell and taste, decreased visceral sensitivity, a sharp reduction in evaluative functions and motivations [4]. About 70% of patients after discharge from the hospital had a cognitive deficit, which manifested itself in a decrease in the speed and accuracy of cognitive processes against the background of depression and anxiety disorders. Data on the speed and accuracy of cognitive processes in patients in the clinical dangerous phase of COVID-19 are extremely scarce. Unique opportunities for objectification are opened thanks to the use of remote monitoring methods based on WEB platforms with a set of interactive sensorimotor tests. Our work presents the results of measuring cognitive functions based on the COGNITOM [5] WEB platform and identifies the features of working with information images in patients in the clinical phase of the disease.e.

1. Methods

30 volunteers took part in the study: 15 patients with a positive result of the analysis for SARS-CoV-2 RNA by PCR, pneumonia of varying severity, saturation no higher than 95 and temperature no higher than 37°C aged 40 to 63 years (COVID group); 15 healthy aged 40 to 54 years. Exclusion criterion: the presence of neurological and psychiatric diseases.

To measure cognitive functions on the WEB platform COGNITOM (cogni-nn.ru) [5] 3 interactive contexts (tests) were formed, including a universal motor component (pressing a key) and various cognitive components: a simple sensorimotor reaction test, a "7 words"memory test and a modification of the Stroop test. The cognitive components of the tests were distinguished by the complexity of the decision-making rules and, accordingly, by the cognitive processes that

ensure successful reactions. The cognitive component of each test includes storing in working memory the target features and the way of action, perception, selective attention, decision-making and launching an action program. The "simple sensorimotor reaction"test provided a minimum level of cognitive load: for success, it is enough to single out one sign — the presence/absence of a sensory event. The "7 words"memory test is more difficult: it is necessary to store 7 well-known words (verbal images) in memory and monitor the presence/absence of the target image on the monitor screen. The modified Stroop test differed in the number of target features and the complexity of operations with information images: it is necessary to detect a sensory event (the appearance of a word denoting color on the screen), determine the correspondence of the verbal (meaning of the word) and sensory image (the color of letters in the image of the word), control the identity of these images.

In each of the three tests, four indicators of the speed and accuracy of the cognitive process were measured:

1) the time interval between the appearance of the image on the monitor screen and the moment of pressing the button (CogR, milliseconds);
2) the number of skips of the target stimulus (ERR1);
3) number of double taps (ERR2);
4) the number of clicks on a non-targeted stimulus (ERR3).

Thus, according to the totality of all measurements, the mode of cognitive processes was displayed in the space of 12 parameters.

In the test "Simple sensorimotor Activity"(SSMA), 70 identical stimuli were presented sequentially (a red circle with a diameter of 5 cm), an interstimulus interval of 1000 ms, an exposure of 100 ms. Task: press the button as soon as the image of the circle appears on the screen. The duration of the test is no more than 2 minutes.

In the "7 words"(MEMORY) test, it was suggested to memorize 7 words: face, red, church, velvet, violet, cat, time. 58 words were consistently presented, of which 19 were targeted. The interstimulus interval is 2000 ms, the exposure is 500 ms. Task: press the button as soon as the memorized word appears on the screen. The duration of the test is no more than 3 minutes.

In the modified Stroop test (Stroop_smr), the stimuli are color images of words denoting color: red, green, blue, yellow, black. The color of the letters is assigned from the same set of options. The interstimulus interval is 1000 ms, the exposure is 500 ms. Task: press the button as soon as the color of the letters corresponds to the meaning of the word. In total, 99 incentives are consistently presented, of which 20 were targeted. The duration of the test is no more than 2 minutes. The total duration of the test was no more than 10 minutes.

Statistical analysis was carried out using the Statistica 10 program. The Mann-Whitney U-test and the Wilcoxon criterion were applied to assess the differences between the two groups, multivariate ANOVA, Spearman correlation criterion and k-means cluster analysis. Statistical significance for all analyses was established at the level of $p < 0.05$.

2. Results and discussion

The analysis of digital displays of cognitive processes revealed a complex pattern of distortions provoked by infection with the SARS-CoV-2 virus (Table. **??**).

Параметры	Группа «COVID»	Группа «КОНТРОЛЬ»	Mann–Whitney U Test, p-value
CogR_ПСМР	393.83±40.93	225.06±27.38	**0.002**
Err#1_ПСМР	4.33±1.65	1.94±0.42	0.504
Err#2_ПСМР	0.58 ±0.23	2.61± .63	**0.035**
Err#3_ПСМР	0.42±0.15	0.61±0.12	0.315
CogR_ПАМЯТЬ	786.42±22.81	563.56±31.15	**0.000**
Err#1_память	2.25±0.52	0.56±0.17	**0.007**
Err#2_память	0.08±0.08	0.00±0.00	0.247
Err#3_память	1.08±0.23	3.28±0.50	**0.002**
CogR_Stroop	735.83±21.78	691.89±9.97	**0.000**
Err#1_Stroop	6.83±1.53	2.39±0.45	**0.013**
Err#2_Stroop	0.17±0.11	0.11±0.08	0.693
Err#3_Stroop	2.75±0.52	4.22±0.39	**0.036**

To assess the effect of hypoxia on cognitive processes, an analysis of the relationship between the parameters of sensorimotor activity and the level of saturation was carried out. Of the twelve digital display parameters, two are most sensitive to hypoxia: the lower the oxygen saturation of the blood, the longer the button hold (MR) in the test "Simple sensorimotor activity"(Spearman's criterion, $r = -0.71$) and the duration of the cognitive process (CogR_MEMORY) in the test "7 words"(Spearman's criterion, $r = -0.78$). The relationship of saturation with these parameters is approximated by linear functions that allow calculating the risks of hypoxic disorders of the central nervous system based on the results of computer testing (Fig. 1).

In both simple and complex contexts, the duration of the cognitive component of sensorimotor activity in patients is longer than in healthy ones (Fig. 2). There were no significant effects associated with the complexity of the decision-making rules in different tests.

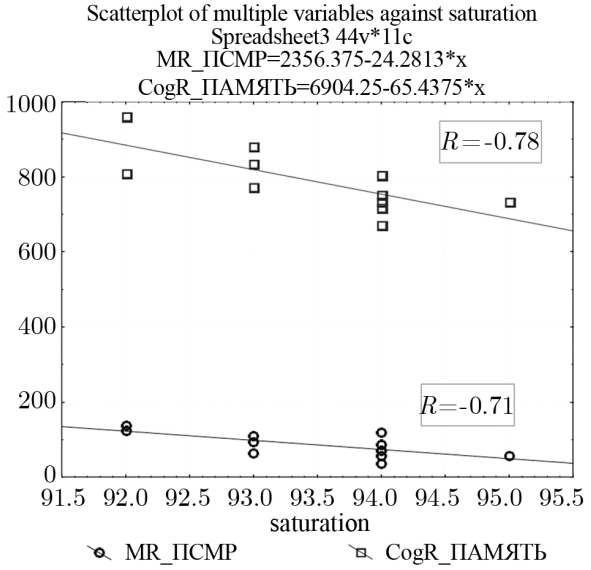

Fig. 1. Влияние насыщения крови кислородом на когнитивные процессы

Fig. 1. Effect of blood oxygen saturation on cognitive processes

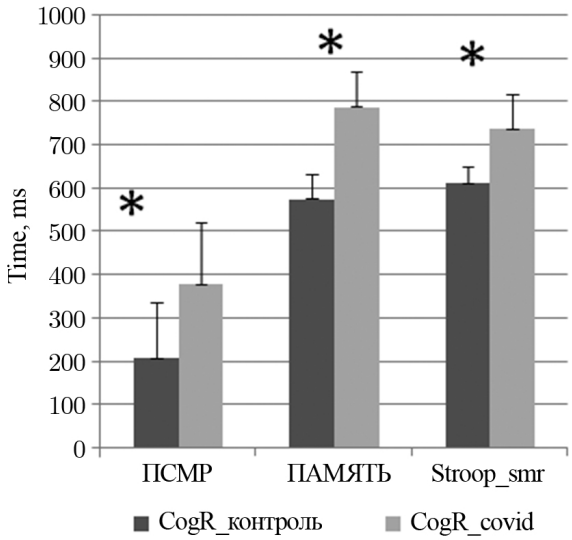

Fig. 2. Продолжительность когнитивного компонента сенсомоторной активности в группах «COVID» и «КОНТРОЛЬ». Звездочкой обозначены достоверные различия при $p < 0.05$

Fig. 2. The duration of the cognitive component of sensorimotor activity in the "COVID" and "CONTROL" groups. An asterisk indicates significant differences at $p < 0.05$

Changes in recognition accuracy in covid were assessed by the difference in the number of erroneous reactions between the "COVID"and "CONTROL"groups. With a minimum level of difficulty in the test for simple sensorimotor activity, the differences between the groups were manifested only in an increase in the number of repeated clicks on one stimulus (ERR2). In complex contexts (the "7 words"memory test and the modified Stroop test), there is no difference in such errors, but significant effects associated with the group factor (ANOVA, $F(4, 112) = 3.9276$, $p = 0.00506$) were revealed (Fig. 3) in the number of misses of the target event (ERR1) and the number of "false alarms"(ERR3). In the "COVID"group, there are significantly more omissions and significantly fewer "false alarms".

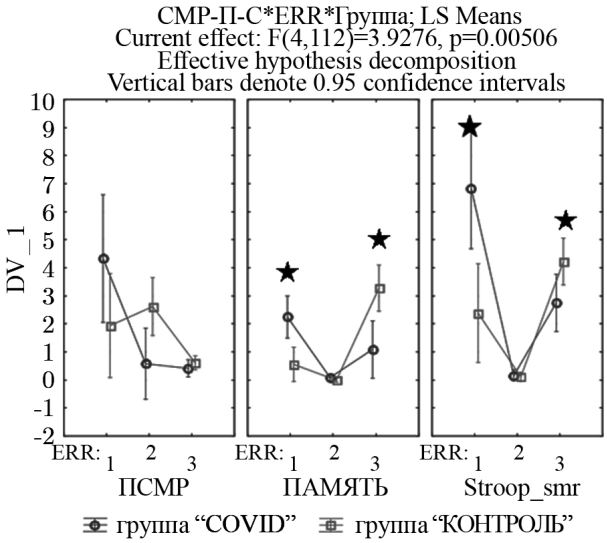

Fig. 3. Сравнительная оценка точности когнитивных процессов при заболевании COVID-19. Звездочкой обозначены достоверные различия $p < 0.05$

Fig. 3. Comparative assessment of the accuracy of cognitive processes in COVID-19 disease. An asterisk indicates significant differences $p < 0.05$

Making the right decision on the result of comparing verbal and sensory images requires significant resources of working memory and is provided by data exchange in the hippocampus cycle — basal ganglia — thalamus. In addition, the activity of the dopaminergic system is necessary for successful comparison. Thus, elements of the neural platform damaged by the SARS-CoV-2 virus are involved in the work, which inevitably leads to significant distortions of cognitive processes.

A comparative analysis of sensorimotor activity in the "COVID"and "CONTROL"groups allowed us to identify 4 most informative parameters: the duration of the cognitive component in each of the tests and the number of missed events in the Stroop test. Based on these parameters, a cluster analysis was carried out and ranges of indicators characterizing specific distortions of cognitive processes in patients in the clinical phase of COVID-19 were determined (Table. **??**).

Параметры	cluster 1 (КОНТРОЛЬ)	cluster 2 (COVID)
CogR_ПСМР (мс)	171.78–272.22	345.06–522.34
CogR_ПАМЯТЬ (мс)	520.93–655.07	713.91–850.29
CogR_Stroop (мс)	606.24–659.66	673.82–791.98
Err#1_Stroop	1.35–2.75	5.02–11.78
Чувствительность	0.94	0.75
Специфичность	0.85	0.90

Conclusions

The disruption of the structure and functions of neural networks at sight naturally manifested itself in an increase in the duration of the cognitive component of sensorimotor activity in both

simple and complex contexts. The general stage of solving problems of different levels of complexity is the process of perception. It is obvious that the transformation of the visual signal into a subjective information image is significantly slowed down due to the degradation of receptors associated with COVID-19 disease, demyelination of nerve fibers and destruction of the thalamus.

In complex functional contexts, making the right decision on the result of comparing verbal and sensory images in the Stroop test or when recognizing in the "7 words"test requires significant working memory resources and is provided by data exchange in the hippocampus — basal ganglia — thalamus cycle. In addition, the activity of the dopaminergic system is necessary for successful comparison. Thus, elements of the neural platform damaged by the SARS-CoV-2 virus are involved in the work, which inevitably leads to significant distortions of cognitive processes.

Analysis of changes in the error structure indicates an increase in the severity of the criterion chosen by the brain for screening out "false alarms". The increase in omissions of the target event and the decrease in "false alarms"indicate that the information system in covid gives preference to refusal of action. It can be assumed that the slowing down of information processing and the refusal of action are manifestations of the hypobiotic mode of the brain and are associated with a general decrease in the energy supply of physiological processes in covid [6]. The detected deficiency varies depending on the severity of respiratory symptoms, has no direct correlation with age, education, or other demographic and socio-economic variables, and is noted, including in those patients who did not have other residual symptoms.

Digital displays of cognitive processes obtained using a set of interactive tests on the COGNITOM WEB platform allowed us to determine the specifics of cognitive process distortions in patients in the clinical phase of COVID-19. The obtained data open up new possibilities for constructing a bio-plausible model of the cognitive system, taking into account the features of the neural platform in COVID-19.

References

1. Miskowiak KW, Johnsen S, Sattler SM, Nielsen S, Kunalan K, Rungby J, Lapperre T, Porsberg CM. Cognitive impairments four months after COVID-19 hospital discharge: Pattern, severity and association with illness variables. Eur. Neuropsychopharmacol. 2021;46:39–48. DOI: 10.1016/j.euroneuro.2021.03.019.
2. Beaud V, Crottaz-Herbette S, Dunet V, Vaucher J, Bernard-Valnet R, Du Pasquier R, Bart PA, Clarke S. Pattern of cognitive deficits in severe COVID-19. J. Neurol. Neurosurg. Psychiatry. 2021;92(5):567–568. DOI: 10.1136/jnnp-2020-325173.
3. Mukaetova-Ladinska EB, Kronenberg G, Raha-Chowdhury R. COVID-19 and neurocognitive disorders. Curr. Opin. Psychiatry. 2021;34(2):149–156. DOI: 10.1097/YCO.0000000000000687.
4. Devita M, Bordignon A, Sergi G, Coin A. The psychological and cognitive impact of Covid-19 on individuals with neurocognitive impairments: research topics and remote intervention proposals. Aging Clin. Exp. Res. 2021;33(3):733–736. DOI: 10.1007/s40520-020-01637-6.
5. Polevaya SA, Eremin EV, Bulanov NA, Bakhchina AV, Kovalchuk AV, Parin SB. Event-related telemetry of heart rate for personalized remote monitoring of cognitive functions and stress under conditions of everyday activity. Modern Technologies in Medicine. 2019;11(1):109–115. DOI: 10.17691/stm2019.11.1.13.
6. Drury RL, Jarczok M, Owens A, Thayer JF. Wireless heart rate variability in assessing community COVID-19. Front. Neurosci. 2021;15:564159. DOI: 10.3389/fnins.2021.564159.