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Состояние когнитивных функций при инфекции COVID-19, осложнённой вирусной пневмонией, у пациентов молодого и среднего возраста в период 2020–2022 гг.

С.С. Кабыш[1,2], С.В. Прокопенко[1,3], М.М. Абдуллаев[1], А.Д. Карпенкова[1,2], М.В. Кузнецова[2], А.В. Голикова-Черешкевич[2], О.В. Фролова[2]

[1]Красноярский государственный медицинский университет им. В.Ф. Войно-Ясенецкого, Красноярск, Россия
[2]Красноярская межрайонная клиническая больница №20 им. И.С. Берзона, Красноярск, Россия
[3]Федеральный научно-клинический центр Федерального медико-биологического агентства Российской Федерации, Красноярск, Россия

Автор, ответственный за переписку: Сергей Сергеевич Кабыш, sergioowl@yandex.ru

АННОТАЦИЯ

Обоснование. В настоящее время изучение когнитивной сферы при COVID-19 представляет собой актуальную проблему.

Цель. Определить наличие когнитивной дисфункции при помощи валидных шкал и их субшкал у пациентов в остром периоде коронавирусной инфекции, сравнить данные когнитивных нарушений в разные эпидемиологические волны.

Материал и методы. В настоящее исследование были включены две группы исследуемых. Группы №1 и №2 — пациенты, инфицированные вирусом SARS-CoV-2, в остром периоде, осложнённом пневмонией. Группа №1 госпитализирована в период с декабря 2020 г. по март 2021 г., группа №2 — с ноября 2021 г. по январь 2022 г. Для исследования нейропсихологического статуса использовали нейропсихологические шкалы MoCA, FAB, тест рисования часов и их субшкалы. Скрининг тревоги и депрессии проводили при помощи валидной шкалы HADS. Количественные данные на нормальность распределения выборки были проверены при помощи критерия Шапиро–Уилка. Для сравнения несвязанных групп использован критерий Манна–Уитни. Количественные данные представлены в виде медианы и интерквартильного размаха — Me [P_{25}; P_{75}]. Различия считали статистически значимыми при $p < 0,05$.

Результаты. Выявлены статически значимые отличия в остром периоде коронавирусной инфекции, осложнённой пневмонией, в отношении когнитивных нарушений как в группе №1, так и в группе №2. У группы №1 когнитивные нарушения были более грубыми, чем у группы №2. При сравнении по субшкалам теста MoCA данных групп №1 и №2 как при поступлении в стационар, так и ближе к выписке в группе №1 результаты были хуже, чем в группе №2, по данным субшкал «внимание», «речь», «память». Различия показателей были статистически значимыми ($p < 0,05$). По данным FAB, в группе №1 показатели при поступлении в стационар и к выписке также были хуже, чем в группе №2, высокозначимые отличия были по следующим данным: беглость речи, динамический праксис, простая и усложнённая реакция выбора, исследование хватательного рефлекса ($p < 0,001$). Тревоги и депрессии в исследуемых группах обнаружено не было.

Вывод. При помощи таких валидных шкал, как тест рисования часов, MoCA, FAB, и их субшкал доказано наличие когнитивной дисфункции у пациентов молодого и среднего возраста в разные временные интервалы наблюдения; в группе №1 нарушения были более грубыми, чем в группе №2.

Ключевые слова: *COVID-19, когнитивные нарушения, коронавирусная инфекция, пандемия*.

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The state of cognitive functions in COVID-19 complicated by viral pneumonia in young and middle-aged patients in the period 2020–2022

Sergey S. Kabysh[1,2], Semyon V. Prokopenko[1,3], Murad M. Abdullaev[1], Alena D. Karpenkova[1,2], Mary V. Kuznetsova[2], Alexandra V. Golikova-Chereshkevich[2], Olga V. Frolova[2]

[1]Krasnoyarsk State Medical University named after Professor V.F. Voyno-Yasenetsky, Krasnoyarsk, Russia
[2]Krasnoyarsk Interdistrict Clinical Hospital No. 20 named after I.S. Berzon, Krasnoyarsk, Russia
[3]Federal Scientific and Clinical Center of the Federal Medical and Biological Agency of the Russian Federation, Krasnoyarsk, Russia

Corresponding author: Sergey S. Kabysh, sergioowl@yandex.ru

ABSTRACT

BACKGROWND. Currently, the study of the cognitive sphere in COVID-19 is an urgent problem.

AIM. To determine the presence of cognitive dysfunction using valid scales MoCA, FAB, clock drawing test and their subscales in patients in the acute period of coronavirus infection, to compare the data of cognitive impairment in different epidemiological waves.

MATERIAL AND METHODS. Two groups of subjects were included in the present study. Groups No. 1 and No. 2 are patients infected with COVID-19 in the acute period, complicated by pneumonia. Group No. 1 was hospitalized in the period December 2020 — March 2021. Group No. 2 was hospitalized in the period November 2021 — January 2022. To study the neuropsychological status, the neuropsychological scales MoCA, FAB, the clock drawing test and their subscales were used. Screening for anxiety and depression and depression was performed using the valid HADS scale. Quantitative data on the normality of the distribution of the sample was tested using the Shapiro–Wilk test. The Mann–Whitney test was used to compare unrelated groups. Quantitative data are presented as median and interquartile range — Me [P_{25}; P_{75}]. Differences were considered statistically significant at $p < 0.05$.

RESULTS. Statistically significant differences were found in the acute period of coronavirus infection complicated by pneumonia and cognitive impairment in both group No. 1 and group No. 2, respectively. In group No. 1 (observation period from December 2020 to March 2021), cognitive impairments were more severe than in group No. 2 (observation period from November 2021 to January 2022). When comparing the subscales of the MoCA test of groups No. 1 and No. 2 upon admission to the hospital, and at discharge in group No. 1, the results of MoCA testing were worse than in group No. 2 according to subscales: attention, speech, memory, indicators were statistically significant ($p < 0.05$). According to the FAB data, in group No. 1, the indicators on admission to the hospital and at discharge were also worse than in group No. 2, highly significant differences were according to the data: fluency of speech, dynamic praxis, simple and complicated choice reaction, grasping reflex study ($p < 0.001$). Anxiety and depression were not found in the study groups.

CONCLUSION. With the help of such valid scales as: the clock drawing test, MoCA, FAB and their subscales, the presence of cognitive dysfunction in young and middle-aged patients at different time intervals of observation was proved; in the first group, the violations were more severe than in the group No. 2.

Keywords: *COVID-19, cognitive impairment, coronavirus infection, pandemic*.

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BACKGROUND

To date, the COVID-19 pandemic has affected more than 600 million people. Cognitive impairment is one of the neurological complications following recovery from COVID-19. However, whether cognitive impairment in COVID-19 has any unique specificity remains unknown [1, 2].

At the moment, the authors have put forward several theories for the onset of cognitive impairment in COVID-19, namely, direct neuroinvasion or the hematogenous pathway, blood–brain barrier disruption caused by cytokine storm and hypoxemia, thrombotic vascular events against hypercoagulability, an autoimmune mechanism, or a combination thereof [3]. COVID-19 survivors have a cognitive deficiency and significant impairments in executive functions, memory, and attention [4]. The degree of cognitive deficiency is compared in severity with moderate craniocerebral injury or mild Alzheimer's disease [5].

The results of many studies are dependent on questionnaires, telephone interviews, or Internet questionnaires without an objective comprehensive assessment of neuropsychological testing data by a specialist. In most studies, an adequately selected control group was not included for comparison [6, 7]. Evidence on the comparison of cognitive performance between hospitalized patients and those treated as outpatients (this group makes up the majority of those with a history of COVID-19) is insufficient. Most studies have used brief cognitive screening scales or small sample sizes.

Many authors have noted the feasibility of continuing research and emphasize the need to assess cognitive symptoms following an illness to develop strategies for rehabilitation and treatment. Early identification of patients with subtle neurological and neurocognitive symptoms can be critical for further patient management and appropriate resource allocation [8–12]. Despite extensive research on the topic, the structure of cognitive disorders, persistence in follow-up, and degree of cognitive dysfunction in patients in different outbreaks of infection remain unclear.

Thus, this study **aimed to** determine the presence of cognitive dysfunction using valid scales and their subscales in patients in the acute period of COVID-19 and compare data on cognitive impairment in different epidemiological outbreaks.

MATERIALS AND METHODS

The study was performed based on the pulmonology departments of the I.S. Berzon Krasnoyarsk Interdistrict Clinical Hospital No. 20. All participants voluntarily signed the informed consent form.

The participants (patients treated in pulmonology departments between 2020 and 2022) were distributed into two groups: group 1 included 32 patients who were hospitalized for COVID-19 complicated by pneumonia (follow-up period from December 2020 to March 2021), and group 2 included 33 patients (follow-up period from November 2021 to January 2022). The median ages of patients in groups 1 and 2 were 45 and 44 years, respectively. The study did not take into account the sex of the patients.

The inclusion criteria were as follows:

– Laboratory-confirmed COVID-19 complicated by pneumonia (or diagnosed according to the epidemiological history)

– Secondary/higher educational level

– Clear consciousness

– Body temperature up to 37.0 °C after the relief of intoxication syndrome

– Absence of respiratory failure (SpO_2[1] > 95%)

Age 18–65 years.

The exclusion criteria were as follows:

– Respiratory failure (SpO_2 < 95%; body temperature of ≥37.0 °C during examination

– Organic lesions of the central nervous system before infection with cognitive impairment or dementia before the present disease

– Comorbidity (types 1 and 2 diabetes mellitus, sub- and decompensated, use of narcotic drugs before the study, alcoholism, and decompensated cardiovascular pathologies)

– Impaired consciousness

Neuropsychological testing of cognitive functions in groups was performed after relief of intoxication syndrome (SpO_2 ≥95% and body temperature <37.0 °C) on the first days upon hospital admission and 1–2 days before discharge. The Montreal cognitive assessment (MoCA), frontal assessment battery (FAB) and their subscales, and the clock drawing test were conducted. The emotional–volitional sphere was assessed using the valid hospital anxiety and depression scale (HADS).

[1]SpO_2 — saturation of blood with oxygen.

Table 1. Results of comparing the state of cognitive functions and the emotional–volitional sphere in groups 1 and 2 upon hospital admission and discharge

Scale	Group 1	Group 2	Group 1	Group 2	*p*
	Admission[1], December 2020 to March 2021	**Admission[2],** November 2021 to January 2022	**Discharge[3],** December 2020 to March 2021	**Discharge[4],** November 2021 to January 2022	
MoCa	26 [21; 28]	25 [23; 27]	21 [18; 23]	25 [23; 29]	p_{1-2} <0.001* p_{3-4} <0.001*
FAB	13 [10; 18]	17 [15; 18]	10 [8; 12]	17 [15; 18]	p_{1-2} <0.001* p_{3-4} <0.001*
Clock drawing test	10 [9,5; 10]	9 [9; 10]	10 [9; 10]	9 [8; 10]	p_{1-2}=0.07 p_{3-4}=0.02
HADS (anxiety)	4 [2; 6]	4 [2; 6]	4 [1; 5]	4 [1; 5]	p_{1-2} <0.001* p_{3-4} <0.001*
HADS (depression)	5 [2; 7]	5 [2; 7]	5 [4; 7]	5 [4; 7]	p_{1-2} <0.001* p_{3-4} <0.001*

Note: Mann–Whitney test, *statistically significant values ($p < 0.05$).

Statistical data processing was performed in IBM SPSS Statistics version19 program (IBM Corp., Armonk, NY, USA).

The normality of the sample distribution of quantitative data was tested using the Shapiro–Wilk test. The Mann–Whitney test was used to compare unrelated groups. Quantitative data are presented as median and interquartile range, Me [P_{25}; P_{75}]. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Table 1 presents the results of comparing the state of cognitive functions and the emotional–volitional sphere of patients upon hospital admission and before discharge at different time intervals of COVID-19.

In the proposed fragment of the study, we were primarily interested in the differences in the results of assessing the cognitive status at admission and discharge between groups.

Despite the identified cognitive disorders in both groups, a more pronounced cognitive dysfunction in group 1 (admitted from December 2020 to March 2021) can be noted. Table 1 presents that at hospital discharge, group 1 had more pronounced cognitive impairment. This suggests that the virus is less active when cognitive dysfunction developed during the outbreak of COVID-19 from November 2021 to January 2022.

According to the HADS, the evaluation of the emotional–volitional sphere did not find deviations from the normal values for the entire monitoring period in groups 1 and 2. Table 2 presents data on the cognitive status using the subscales of the MoCA test at different time intervals of monitoring.

As presented in Table 2, cognitive impairments, presented in the subscales of the MoCA test, were more pronounced in group 1 at admission and discharge, and statistically significant differences were found in the time of hospital admission according to the subscales of attention ($p = 0.008$), speech ($p < 0.001$), and memory ($p = 0.017$). By discharge, the same cognitive domains were significantly different as upon admission ($p = 0.01$, $p = 0.002$, and $p = 0.008$, respectively).

Table 3 presents the results of comparing the subscales in groups 1 and 2 according to the FAB test.

Table 3 reveals regularity on the FAB scale and analysis of the MoCA scale. Cognitive disorders were more severe in group 1 than in group 2. Upon hospital admission and discharge, statistically highly significant differences were revealed in verbal fluency ($p < 0.001$), dynamic praxis ($p < 0.001$), simple choice reaction ($p < 0.001$), and study of grasping reflexes ($p < 0.001$).

DISCUSSION

The most severe disorders were noted in the first outbreak of COVID-19, where the indicators were

Таблица 2. Результаты сравнения субшкал теста MoCA при поступлении и выписке из стационара

MoCA	Group 1	Group 2	Group 1	Group 2	*p*
	Admission[1], December 2020 to March 2021	**Admission[2],** November 2021 to January 2022	**Discharge[3],** December 2020 to March 2021	**Discharge[4],** November 2021 to January 2022	
Visual–spatial skills	4.0 [3.0; 5.0]	4.0 [4.0; 5.0]	4.0 [3.0; 4.0]	4.0 [4.0; 5.0]	p_{1-2} <0.587; p_{3-4} <0.256
Naming	3.0 [3.0; 3.0]	3.0 [3.0; 3.0]	3.0 [3.0; 3.0]	3.0 [3.0; 3.0]	p_{1-2}=0.969; p_{3-4}=0.69
Attention	4.0 [2.0; 5.0]	5.0 [4.0; 6.0]	3.5 [2.0; 5.0]	5.0 [4.0; 6.0]	p_{1-2}=0.008* p_{3-4}=0.01*
Speech	1.0 [0.5; 1.0]	2.0 [1.0; 2.0]	1.0 [0.0; 1.0]	1.0 [1.0; 3.0]	p_{1-2} <0.001* p_{3-4}=0.002*
Abstraction	1.0 [0.5; 2.0]	2.0 [1.0; 2.0]	1.5 [0.5; 2.0]	2.0 [2.0; 2.0]	p_{1-2}=0.482 p_{3-4}=0.129
Memory (delayed recall)	3.0 [2.0; 4.0]	4.0 [3.0; 5.0]	2.0 [1.5; 3.0]	4.0 [3.0; 5.0]	p_{1-2}=0.017* p_{3-4}=0.008*
Orientation	6.0 [5.5; 6.0]	6.0 [6.0; 6.0]	6.0 [6.0; 6.0]	6.0 [6.0; 6.0]	p_{1-2}=0.384 p_{3-4}=0.459

Note: Mann–Whitney test, *statistically significant values ($p < 0.05$).

Table 3. Comparison of the results of the FAB subscales at hospital admission and discharge

FAB	Group 1	Group 2	Group 1	Group 2	*p*
	Admission[1], December 2020 to March 2021	**Admission[2],** November 2021 to January 2022	**Discharge[3],** December 2020 to March 2021	**Discharge[4],** November 2021 to January 2022	
Conceptualization	3.0 [3.0; 3.0]	3.0 [3.0; 3.0]	3.0 [3.0; 3.0]	3.0 [2.0; 3.0]	p_{1-2}=0.459; p_{3-4}=0.057
Verbal fluency	1.0 [0.5; 1.0]	3.0 [2.0; 3.0]	1.0 [1.0; 1.0]	3.0 [2.0; 3.0]	p_{1-2} <0.001*; p_{3-4} <0.001*
Dynamic praxis	1.0 [0.5; 2.0]	3.0 [2.0; 3.0]	2.0 [1.0; 2.0]	3.0 [2.5; 3.0]	p_{1-2} <0.001*; p_{3-4} <0.001*
Simple choice reaction	2.0 [1.0; 2.0]	3.0 [3.0; 3.0]	1.0 [1.0; 2.0]	3.0 [3.0; 3.0]	p_{1-2} <0.001*; p_{3-4} <0.001*
Complicated choice reaction	1.0 [1.0; 2.0]	3.0 [3.0; 3.0]	1.0 [1.0; 2.0]	3.0 [3.0; 3.0]	p_{1-2} <0.001*; p_{3-4} <0.001*
Study of grasping reflexes	2.0 [2.0; 2.0]	3.0 [3.0; 3.0]	2,0 [1.0; 2.0]	3.0 [3.0; 3.0]	p_{1-2} <0.001*; p_{3-4} <0.001*

Note: Mann–Whitney test, *statistically significant values ($p < 0.05$).

even worse upon discharge despite the complete somatic recovery of the patients. Mild cognitive impairments were registered in group 2, but still different from the norm. Thus, COVID-19 complicated by pneumonia causes cognitive impairment in patients without comorbid pathology. Such changes are probably associated with the possible mutation of the virus over time.

This study compared the degree and type of cognitive impairment in different outbreaks of COVID-19

with an interval of 1–1.5 years. Undoubtedly, many researchers have assessed the cognitive status in patients with COVID-19.

Crivelli et al. [13] published a meta-analysis on cognitive dysfunction in COVID-19. In 27 studies involving 2049 patients with a mean age of 56.05 years, cognitive impairment was analyzed both in the acute disease period and post-COVID period for 7 months. Cognitive decline in COVID-19 already occurs in the acute disease period and persists for a long time. Functions such as attention, executive functions, and memory were impaired.

Moreover, in 2021, Alemanno et al. examined 87 COVID-19 survivors in a rehabilitation center. According to the mini-mental state examination and MoCA tests, mild and moderate cognitive impairment was detected in 80% of the patients. In most cases, impaired concentration was registered [14].

CONCLUSIONS

1. In the case of COVID-19 complicated by pneumonia, cognitive dysfunction occurs in young and middle-aged patients without comorbid pathology.

2. From 2020 to 2022, the dynamics of cognitive disorders had changed over time. More severe disorders were registered in 2020 than in 2022, which may indicate different activities of viral infection in the development of cognitive dysfunction.

3. Further research on this topic and screening for disorders in hospitalized patients and outpatients are necessary.

ДОПОЛНИТЕЛЬНО

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ОБ АВТОРАХ

Кабыш Сергей Сергеевич, аспирант, каф. нервных болезней с курсом ПО;
ORCID: http://orcid.org/0000-0002-9029-4553;
eLibrary SPIN: 5926-3024;
e-mail: sergioowl@yandex.ru

Прокопенко Семён Владимирович, докт. мед. наук, проф., зав. каф., каф. нервных болезней с курсом ПО;
ORCID: http://orcid.org/ 0000-0002-4778-2586;
eLibrary SPIN: 1279-7072;
e-mail: s.v.proc.58@mail.ru

Абдуллаев Мурад Маголан оглы, ординатор, каф. нервных болезней с курсом ПО;
ORCID: http://orcid.org/0000-0002-2673-4999;
e-mail: murad25abdullaev@gmail.com

AUTHOR'S INFO

Sergey S. Kabysh, postgraduate student, Depart. of Nervous Diseases with a postgraduate education course;
ORCID: http://orcid.org/0000-0002-9029-4553;
eLibrary SPIN: 5926-3024;
e-mail: sergioowl@yandex.ru

Semyon V. Prokopenko, M.D., D. Sci. (Med.), Prof., Head of Depart., Depart. of the Nervous Diseases with a postgraduate education course;
ORCID: http://orcid.org/ 0000-0002-4778-2586;
eLibrary SPIN: 1279-7072;
e-mail: s.v.proc.58@mail.ru

Murad M. Abdullaev, Resident, Depart. of Nervous Diseases with a postgraduate education course;
ORCID: http://orcid.org/0000-0002-2673-4999;
e-mail: murad25abdullaev@gmail.com

Карпенкова Алёна Дмитриевна, аспирант, каф. нервных болезней с курсом ПО;
ORCID: http://orcid.org/0000-0002-9058-8818;
eLibrary SPIN: 7764-3409;
e-mail: pobejdaujay@mail.ru

Кузнецова Мэри Викторовна, врач-невролог;
ORCID: http://orcid.org/0000-0002-9909-5796;
e-mail: irem35106@gmail.com

Голикова-Черешкевич Александра Валерьевна, клинический психолог;
ORCID: http://orcid.org/0000-0002-4748-7907;
e-mail: 89658908573@mail.ru

Фролова Ольга Васильевна, врач-невролог;
ORCID: http://orcid.org/0000-0001-8807-2540;
eLibrary SPIN: 5525-7464; e-mail: Frolova_olga86@mail.ru

Alena D. Karpenkova, post-graduate student, Depart. of Nervous Diseases with a postgraduate education course;
ORCID: http://orcid.org/0000-0002-9058-8818;
eLibrary SPIN: 7764-3409;
e-mail: pobejdaujay@mail.ru

Mary V. Kuznetsova, M.D., neurologist;
ORCID: http://orcid.org/0000-0002-9909-5796;
e-mail: irem35106@gmail.com

Alexandra V. Golikova-Chereshkevich, clinical psychologist;
ORCID: http://orcid.org/0000-0002-4748-7907;
e-mail: 89658908573@mail.ru

Olga V. Frolova, M.D., neurologist;
ORCID: http://orcid.org/0000-0001-8807-2540;
eLibrary SPIN: 5525-7464; e-mail: Frolova_olga86@mail.ru