REPORT

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Cognitive, emotional-affective, anxiety and autonomic disorders in patients with a new coronavirus infection (covid-19) in the acute period

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Abstract

The purpose of this work is to identify neuropsychiatric functions in patients at Department No. 1 responsible for medical care of patients with a new coronavirus infection at the Samara City Hospital No. 7. Appropriate scales and questionnaires were used for this purpose. Cognitive impairments were found in 86% of the cases, emotional-affective impairments of varying severity in half of the subjects, an increase in reactive and personal anxiety was revealed, and vegetative disorders were observed in 78% of the subjects. Based on these data, it can be assumed that the new coronavirus infection affects the functioning of the nervous system of patients.

Keywords

New coronavirus infection, COVID-19, Cognitive skills, Emotional-affective functions, Anxiety, Autonomic nervous system

Imprint

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Introduction

The outbreak of the COVID-19 pandemic caused by SARS-CoV-2 has shown to the medical community that the possible clinical manifestations of diseases caused by viruses of the Coronaviridae family are not well understood. The damage to the nervous system and its higher functions has been particularly poorly studied, while the incidence of such damage is quite high.

According to recent studies, COVID-19 causes damage to the central nervous system, including headache, confusion, and disorientation in 25% of the cases [1]. According to another study, neurological disorders in the new coronavirus infection are observed in 36.5% of the cases, including disordering of taste and olfactory functions, myalgia, headaches and acute disorders of cerebral circulation, dizziness, mental dysfunctions, encephalitis, ataxia, the Guillain–Barré syndrome and Miller Fisher syndrome [2].

The study of magnetic resonance imaging (MRI) data in patients with anosmia (loss of smell) and ageusia (loss of gustatory sensitivity) did not reveal changes in the olfactory bulbs on both sides [16]. According to the results of 18 autopsies of COVID-19, those patients who died in April 2020, based on autopsy data, showed cerebral ischemia. During the same study, no evidence of direct viral infection was found, but only minimal inflammatory changes were demonstrated. Thus, it can be assumed that SARS-CoV-2 does not penetrate the blood-brain barrier [3]. This is also confirmed by the study of cerebrospinal fluid (CSF), which has been carried out in patients with neurological disorders against the background of the new coronavirus infection using the method of polymerase chain reaction with reverse transcriptase; as a result of this study, SARS-CoV-2 has not been detected in the CSF [15].

To date, the mechanisms of the pathogenesis of damage to the nervous system are not fully understood. It is assumed that the mechanisms of involvement of the central nervous system in the pathological process in COVID-19 are different, and the authors hereof identify 3 most likely options: 1) The cytokine storm increases the BBB permeability, which promotes the penetration of viruses, bacteria, immune cells, toxic metabolites and pro-inflammatory agents into the structures of the central nervous system. 2) It is known that SARS-CoV-2, like SARS-CoV-1, can interact with the type 2 ACE receptors, which can lead to direct damage to neurons without development of pronounced inflammation; 3) The direct effect of the virus on the respiratory center in the brain stem can cause shortness of breath, characteristic of COVID-19, without severe lung damage [4]. Neurological disorders in the new coronavirus infection can

be both the first manifestations of the disease and its complications that occur 24 hours after the onset of the disease or later [12].

Psychiatric disorders associated with the new coronavirus infection are even less covered by the scientific literature. Most of the articles are devoted to the level of anxiety disorders in the population against the background of the pandemic and self-isolation, acute stress disorders and as the novegetative syndrome after the infection. A systematic review and meta-analysis of the articles on the relationship between mental disorders and the coronavirus infection, including MERS-CoV, SARS-CoV-1 and SARS-CoV-2, suggests that confusion and psychomotor agitation are common among mental disorders for the acute period of the coronavirus infections. There is growing evidence of how the forced self-isolation has a negative impact on mental health. 53.8% of people in isolation stated that their psychological state had greatly deteriorated [19].

It was decided not to consider in this work acute cerebrovascular accidents against the background of the new coronavirus infection in connection with the study format, which is not suitable for this purpose, as well as a sufficient number of works devoted to this topic.

Therefore, we considered it important to pay attention to the study of the effect of SARS-CoV-2 on the nervous system, more specifically on the cognitive, emotional-affective, anxiety and autonomic functions of the nervous system.

Materials and methods

For this purpose, a survey was conducted to cover 50 patients diagnosed with "the new coronavirus infection" in the acute period at the age of 22 to 59 years. The median age was 48.6 years. According to the WHO classification (2016), we analyzed our evidence data as follows: young age (18–44 years) in 28% of the subjects (n = 14), average age (45–59 years) in 72% of the test subjects (n = 36). There were 38% of men (n = 19) and 62% of women (n = 31) among them. The degree of lung damage according to the CT imaging was determined as CT-1 (up to 25% of the lungs were affected) in 63% of the patients, CT-2 (26–50% of the lungs were affected) in 27% of the patients, CT-3 (51–75% of the lungs were affected) in 10% of the patients, CT-4 (more than 75% affected) in 0% of the recorded cases. According to the results of the PCR examination of the oropharyngeal smear, SARS-CoV-2 DNA was detected in 50% of the cases (n = 25). No SARS-CoV-2 DNA was detected in 50% of the recorded cases (n = 25). At the same time, the condition of all patients corresponded to the moderate course of COVID-19 in accordance with the provisional guidelines for the prevention, diagnosis and treatment of the new coronavirus infection (COVID-19), version 10. The study was conducted during March-April 2021.

As mentioned above, it is assumed that the causes of disorders of the nervous system in the new coronavirus infection are different and include the following: the direct effect of the virus on the nervous system, the systemic inflammatory response syndrome, the multiple organ dysfunction, the cerebral vascular thrombosis, the endothelial dysfunction, etc. [13, 14]. In addition, hypoxemia against the background of respiratory failure, exacerbation of concomitant chronic diseases, and cognitive impairments of old age could lead to impaired functioning of the nervous activity. The most frequent comorbidities in our study were hypertension and type 2 diabetes mellitus. Also, the patient's unwillingness or deliberate distortion of the answers when completing the questionnaires might lead to unreliable results. In order to exclude these factors as much as possible, some eligible criteria for inclusion and those from the study were developed.

We applied the study inclusion criteria as follows:

- Men and women aged 18-59 years, hospitalized from one to three days ago, who did not receive specific treatment with antiviral drugs within the above time span;
- Patients who signed their written informed consent to participate in the study.

At the same time, we used the criteria for an exclusion from the study as given below:

- Age under 18 and over 59 years old;
- Pregnancy;
- Severe concomitant somatic and / or psychiatric pathology;
- Severe and extremely severe course of Covid-19;
- Refusal to sign written informed consent.

The following methods were used for the survey: MoCA, Montreal Cognitive Assessment - the Montreal scale of cognitive assessment (Maximum score of 30; a score of 26 and over is considered normal, a score less than 26 indicates moderate cognitive impairment); the McNair and Kahn Self-Assessment Memory Inventory (Cognitive impairment should be assumed with score> 42); Beck Depression Scale II (score 0–13 is considered a variation of the norm, 14–19 indicates mild depres-

sion, 20–28 indicates moderate depression, a score of 29 or more indicates severe depression); the Spielberger-Hanin anxiety scale (a scale up to 30, the level of anxiety is low, a scale on the range 30–45 indicates the moderate level thereof, and a scale of 46 and over shows the high level thereof); the A.M. Wein's scale for assessing vegetation changes (a scale of 15 or more indicates the presence of vegetative dystonia syndrome). Questioning took place simultaneously within 2 days after hospitalization of the patient and after taking a swab from the oropharynx, but before informing the patient about the results of the PCR study. The time of questioning took an average of 10 minutes for each patient.

Research results

In our study we have obtained some interesting results. Thus, 86% of the patients have moderate cognitive impairments according to the MoCA data (mean score 22.1, PCR "+" 22.56, PCR "–" 21.64), and only 13% of the individuals noted cognitive impairment in them according to the questionnaire of self-assessment of memory by McNair and Kahn (average score 26.12, for PCR "+" 28.26, for PCR "–" 24.08). The Beck Depression Scale (mean score 9.06, PCR "+" 7.87, PCR "–" 10.32) showed a norm in 53% of the cases, mild depression in 27% of the recorded cases, moderate depression in 13% of the studied cases and severe depression in 7 % in the cases. The Spielberger-Hanin Anxiety Scale examines both reactive and personal anxiety, and we have obtained the following data on the levels of reactive anxiety in the patients with COVID-19 (average score 46.61, PCR "+" 46.58, PCR "–" 46.65): low in 4% of the patients, moderate in 44% of the examined cases, and high in 52% of the patients. The levels of personal anxiety in patients with COVID-19 (mean score 42.97, PCR "+" 42.33, PCR "–" 43.68) are reported as follows: low in 6% of the patients, moderate in 54% of the patients, and high in 39% of the cases. The syndrome of autonomic dysfunction according to the questionnaire by A.M. Wein is observed in 78% of the patients, the norm in 22% of the individuals (mean score 24.24, for PCR "+" 23.43, for PCR "–" 25.09). Average scores and percentage of the results obtained are presented in Table 1 and Table 2 given herein.

The high incidence of mild cognitive impairment requires further careful consideration of the structure of these cognitive impairments. The Montreal Cognitive Assessment Scale (MoCA) consists of several tasks, which are divided according to the areas of cognitive functions indicated below: visual-constructive skills (the maximum score of 5), naming (the maximum score of 3), memory (no scores), attention (the maximum score of 6), speech (the maximum score of 3), abstraction (the maximum score of 2), delayed reproduction (the maximum score of 5), and orientation (the maximum score of 6).

As a result of our survey, the following results were obtained: visual-constructive skills (average score – 3.88), naming (average score – 3), memory (no scores), attention (average score – 5.24), speech (average score – 1.86), abstraction (average score – 0.96), delayed reproduction (average score - 1.46), and orientation (average score – 5.7). It can be seen that the functions such as naming and orientation remain practically unaffected. The areas of cognitive function most affected are abstract thinking and delayed reproduction. Since these functions are carried out by the frontotemporal areas of the cerebral cortex, it can be assumed that these areas are involved in the pathological process in COVID-19.

The discussion of the results

To understand and evaluate the results obtained, it is necessary to compare them with the indicators in the population. For this purpose, data from large population studies can be consulted. Thus, the average score on the MoCA scale range among French-speaking people in Quebec was reported to be 26.4 [5]. In the Moroccan population, the average score on the MoCA scale range among people from 18 to 39 years old was 28.06, and among people from 40 to 59 years old it was reported to reach 27.86. [6]. At the same time, it should be noted that the average score according to the MoCA scale among patients with the new coronavirus infection in the acute period was recorded to be 22.1. Thus, a decrease in cognitive functions can be seen in patients hospitalized with diagnosis of "the new coronavirus infection" in the acute period, in comparison with the above population studies. Even in asymptomatic patients with COVID-19, cognitive decline has been observed. [7]

The data obtained using the McNair and Kahn Self-Assessment Memory Questionnaire show the opposite to the MoCA scale. It can be assumed that the reason for this is the duration of cognitive impairment. The questions presented in the questionnaire, such as "I forget phone numbers," "I forget the names of my old acquaintances," and others, require a long-term presence of cognitive impairments in order to notice by the subjects their cognitive deficit and be able to more confidently answer these questions.

Table 1

Average scores of patients with the new coronavirus infection on the scales and questionnaires completed

Scale	Average score	PCR "+"			PCR "–"			Average overall score
		Men	Women	All	Men	Women	All	
MoCA		21,18	23,64	22,56	22,74	21,22	21,64	22,1
McNair and Kahn Memory Self-Assessment Questionnaire		31	26,15	28,26	17,71	26,71	24,08	26,12
Beck Depression Scale		7,9	7,84	7,87	11,33	9,94	10,32	9,07
Personal anxiety		39,6	44,29	42,33	36,2	45,88	43,68	42,98
Reactive anxiety		44,8	47,86	46,58	42,3	48,18	46,65	46,62
A.M.Wein's questionnaire		19,27	27,25	23,43	16	29,35	25,09	24,24

Table 2

Percentage of neuropsychiatric disorders in patients with the new coronavirus infection

Scale	Number of patients,%	PCR "+"		PCR "–"	
		Men	Women	Men	Women
MoCA	Norm	0	28,57	14,29	11,76
	Moderate cognitive impairment	100	71,43	85,71	88,24
McNair and Kahn Memory Self-Assessment Questionnaire	Norm	80	84,62	100	88,24
	Cognitive impairment	20	15,38	0	11,76
Beck Depression Scale	Norm	60	61,54	50	43,75
	Mild depression	30	15,38	33,33	31,25
	Moderate depression	0	23,08	0	18,75
	Severe depression	10	0	16,67	6,25
Personal anxiety	Low level	10	0	20	5,88
	Moderate level	80	57,14	60	35,30
	High level	10	42,86	20	58,82
Reactive anxiety	Low level	10	7,14	0	0
	Moderate level	50	28,57	83,33	41,18
	High level	40	64,29	16,67	58,82
A.M.Wein's questionnaire	Norm	27,27	16,67	40	11,76
	VDS	72,73	83,33	60	88,24

Table 3

Scoring by areas according to the MoCA scale

Area	Visual constructive skills	Naming	Attention	Speech	Abstraction	Delayed reproduction	Orientation
PCR "+"	4,12	3	5,125	1,8	1,04	1,64	5,76
PCR "–"	3,64	3	5,32	1,92	0,88	1,28	5,64

The average BDI scores in the studied populations in Europe ranged from 4.18 (Norwegian men aged 18–40 years) to 10.69 (Liverpool women aged 41-65 years) [8]. The mean BDI score in a study in Denmark was reported to be 10.6 [9]. The high level of depression in men aged 25–64 years of the Tyumen region was 4.6%, the average level of depression in the same group was recorded to be 19% [21]. Among the residents of the Samara region aged 19 to 68 years, in relation to risk factors for chronic non-infectious diseases, the depression syndrome was observed in 25.2% of the surveyed individuals, including the subclinical level of depression in 21% the cases, and the clinical level in 4.2% of the recorded cases [20].

"Moderate to severe" anxiety in a study by Susan Briman among 6189 people aged 25 to 65 was experienced

by 12.5% of the men and 19% of the women [10], while the moderate and high level of anxiety among patients with the new coronavirus infection in the acute period was observed in more than 80% of the subjects. This is not surprising as these patients have many reasons for concern and fear: facing an inexperienced disease, the danger of which everyone around is talking about, including television, the Internet, word of mouth; hospitalization in the department, where all medical personnel are dressed in anti-plague suits. All this initiates fear and anxiety in patients concerned about their lives, their future and their ability to work. This is also evidenced by data from a survey conducted among the population in the late 2020 – early 2021. An increased level of anxiety was noted therein, moreover, in the age group from 18 to 24 years old, the high level of personal and situational anxiety was recorded to be 76.7% and 72.6%, respectively [17], while in 2014 the frequency of an increased level of anxiety among the population was 46.3% on average [18]. Thus, it is impossible to draw an unambiguous conclusion about what caused anxiety among patients with the new coronavirus infection in the acute period: the influence of the SARS-CoV-2 virus or some external stressors in the form of the pandemic, self-isolation and general alertness. However an increase in the level of anxiety among this group of people is indeed observed.

The postural orthostatic tachycardia syndrome and other autonomic disorders can accompany the new coronavirus infection in previously healthy patients and 6-8 months after the acute period [22]. The study of autonomic disorders under the post-Covid syndrome demonstrated the predominance of the sympathetic activity of the autonomic tone, autonomic response and autonomic support of the activity [23]. But the autonomic disorders in patients with the new coronavirus infection are present not only in the recovery period, but also in the acute period. So, using the scale for assessing autonomic changes, developed by Professor Alexander Moiseevich Vein, the vegetative dystonia syndrome is detected in 78% of the subjects. In the population, the vegetative dystonia syndrome is observed in 56% of the cases. Also, the severity of anxiety disorders increases in proportion to the severity of autonomic disorders [11].

Conclusion

Conclusions from our study can be drawn as follows:

- 86% of the patients with new coronavirus infection COVID-19 have moderate cognitive impairment, especially in case of "abstraction" and "delayed thinking" on the MoCA scale;
- Subjective feelings of memory problems are present in 13% of the COVID-19 patients;
- Emotional-affective disorders of varying severity are observed in half of the subjects;
- An increased level of reactive anxiety is found in comparison with the personal anxiety, as well as an increased level of anxiety in general;
- Autonomic dysfunction is observed in 78% of the patients with the new coronavirus infection.

Unfortunately, it should be noted that our work has some limitations. So, it was not possible to investigate the above functions in the examined patients before their disease. There is no way to unequivocally identify the effect produced by SARS-CoV-2 on the nervous system. It is all the more difficult to talk about the pathogenesis of this influence. There is still a lot of work to be done in the future, including checking whether the impairments of the cognitive, emotional-affective, anxiety and vegetative spheres persist after the acute period of the new coronavirus infection, or whether these impairments are transient. Also, it is necessary to investigate the relationship between the post-Covid syndrome and the disorders in the acute period. The world's population, and especially the health care community, will still face the consequences of COVID-19, and our task is to contribute in order to be prepared to meet the challenge.

Statement on ethical issues

Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest

None declared.

Author contributions

The authors read the ICMJE criteria for authorship and approved the final manuscript.

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