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S.A.Galkin, A.G. Peshkovskaya, S.A. Ivanova, N.A. Bokhan

COGNITIVE IMPAIRMENT IN PATIENS WITH COVID-19

The assessment of changes in the level of cognitive functions in patients who underwent COVID-19 was carried out. An analysis of more than 30 modern scientific studies for 2019-2021 showed that patients who have suffered a new coronavirus infection in varying degrees of severity, there are significant changes in the level of cognitive functioning in the form of reduced memory, executive functions, attention, etc.

Keywords: cognitive functions, cognitive deficits, memory, attention, new coronavirus infection, COVID-19.

Introduction. Almost a year after the first COVID-19 outbreak, we still have a lot to learn about how the virus affects our health. However, it is becoming increasingly clear that many patients who have had a new coronavirus infection subsequently experience a number of neurological, psychiatric, and cognitive complications. According to various studies, these symptoms are observed in about a third of patients who have experienced COVID-19 in varying degrees of severity [4]. These symptoms also persist for a long time after recovery, which negatively affects the quality of life of patients. There is now growing evidence that COVID-19 can have a damaging effect on the brain. The main neurological symptoms of COVID-19 include ischemic stroke, encephalopathy, encephalitis, and peripheral neurological disorders. However, it is estimated that about 30% of patients with neurological symptoms also suffer from cognitive impairment, with deficits in attention, control functions, short-term memory, and psychomotor processes. The prevalence of cognitive complications remains an open question, but it is safe to conclude that they are not uncommon in patients with COVID-19. Several early studies described cognitive impairment in some patients after discharge from the hospital [5, 8]. The potential mechanisms underlying these symptoms are not fully understood, but are likely multifactorial, including the direct neurotrophic effect of SARS-CoV-2, the effects of prolonged stay in the intensive care unit, the use of artificial ventilation and sedatives, brain hypoxia, systemic inflammation, secondary effects of drugs used to treat COVID-19, and peripheral organ and system dysfunction. For example, in a study conducted in France, more than one-third (15 out of 40) of patients demonstrated cognitive impairment upon discharge from the intensive care unit in the form of a dyslexic syndrome characterized by inattention, disorientation in space and impaired executive functions [20]. In addition, in a sample of 71 patients with COVID-19, those with a history of delirium (42%) had lower cognitive performance in a screening interview after hospital discharge [10].

In general, there are very few studies of patients who have undergone COVID-19 with regard to neurocognitive data, especially in Russia. In addition to rough clinical assessments of the outcome of the disease (survival and duration of hospitalization), the medical community should take into account neurological, psychological and psychiatric outcomes.

This article attempts to summarize the currently available scientific data and clinical observations on the impact of COVID-19 on human cognitive functions.

The functioning of memory. As mentioned above, it is currently unknown whether the cognitive symptoms are caused by a virus that directly affects nerve tissue, or whether they are the result of brain damage caused by low oxygen levels or an extreme immune response known as a cytokine storm. There is some evidence that the hippocampus, a region of the brain involved in memory processes, is particularly vulnerable to damage associated with COVID-19 [2, 23]. The specific vulnerability of the hippocampus to respiratory infections was indicated in earlier studies using different strains of the influenza virus. For example, in a study by Hosseini et al. Changes were found in both the morphology and functioning of the hippocampus, which was associated with short-term learning impairment and impaired spatial (short-term) memory in mice infected with the influenza virus [18]. This may explain to some extent the presence of persistent memory disorders in patients after COVID-19. If the damage to the hippocampus is indeed a consequence of COVID-19 infection, then the question arises whether this can lead to an acceleration of hippocampal-related degeneration, as occurs, for example, in Alzheimer's disease, and accelerate the onset of the disease in individuals who have not previously had symptoms. Animal studies show that inflammation associated with viral infection significantly increases the content of tau proteins and leads to a deterioration in the functioning of spatial memory [15], which in turn is considered one of the first symptoms of Alzheimer's disease.

Despite the fact that COVID-19 infection is accompanied by damage to many organs and systems, the respiratory system is in the most serious condition. A recent small study showed that 70% of critically ill patients admitted to the intensive care unit with COVID-19 needed artificial lung ventilation (ventilator) [5], who subsequently developed acute respiratory distress syndrome (ARDS) within 3 days. According to a number of clinical observations, patients who required a ventilator for various reasons had impaired attention, memory, speech fluency, information processing speed, and executive functions in 78% of cases 1 year after discharge and in about half of patients within 2 years [25, 27]. Adhikari et al. memory problems persisted up to 5 years after ARDS, which significantly affected the daily functioning of patients, especially in relation to medication intake and compliance with medical prescriptions [24]. At the same time, anxiety, depression, and post-traumatic stress syndrome, which are also common in ARDS patients, may contribute to cognitive impairment [24] in COVID-19 patients. There is some evidence that cognitive impairment occurs independently of psychological problems

GALKIN STANISLAV A., PhD Student, Mental Health Research Institute, Tomsk NRMC. e-mail: s01091994@, yandex.ruORCID iD 0000-0002-7709-3917; **PESHKOVSKAYA ANASTASIA G.,** Researcher, Mental Health Research Institute, Tomsk NRMC. ORCID iD 0000-0002-3951-395X; **IVANOVA SVETLANA A.,** DM, Professor, Head of the Laboratory of Molecular Genetics and Biochemistry, Deputy Director for Science, Mental Health Research Institute, Tomsk NRMC, Tomsk, Russian Federation. ORCID iD 0000- 0001-7078-323X; **BOKHAN NIKOLAY A.,** DM, Professor, Academician of the Russian Academy of Sciences academician, RAS, Director of the Mental Health Research Institute, head of the Department of psychiatry, psychotherapy, narcology with the course med. the psychology of the Siberian State Medical University of Russia, Tomsk, Russian Federation. ORCID iD 0000-0002-1052-855X.

and is associated with the severity of an infectious disease [25].

Executive functions. Violations of executive functions are usually associated with pathology of the frontal lobes of the brain [16]. Violations of executive functions are based on defects in attention control, difficulties in planning, abstraction, behavioral control and orientation [1]. Thus, defects can be detected, both in cognition and in behavior. A detailed review of the literature on COVID-19 shows that, in at least 26-40% of cases, there is a violation of executive functioning [3, 20]. Also, many articles talk about confusion and difficulties with attention in patients [7, 22], which indicates a violation of executive functions. It is known that encephalopathy, which is often mentioned in patients with COVID-19 [21, 29], is usually accompanied by generalized cognitive disorders, including disorders of executive functions [6].

It is also important to note that cognitive impairment may be associated with the length of hospitalization. Although the long-term effects of COVID-19 on cognitive function are not yet fully understood, early studies have shown that many patients report increased fatigue long after recovery [4, 13, 14]. Preliminary data show that recovered COVID-19 patients who experienced fatigue syndrome 2-3 months after the onset of the disease also had deficits in control functions and visual-spatial information processing [19]. Violations of executive functioning and attention have also been reported in patients after COVID-19 and in a number of other studies [12, 23]. Long-term cognitive changes are often observed after a viral infection, as part of the post-intensive care syndrome and the "post-viral fatigue" syndrome, respectively. Both syndromes are associated with a deterioration in physical, cognitive, and mental health and persist for a long time after the disease. Up to 80% of patients with ARDS experience this syndrome after intensive care, often with impaired executive functions [12, 17].

Non-specific cognitive functions. Due to the high interest of researchers in changes in cognitive functions in patients who have undergone COVID-19, many authors have simultaneously studied various aspects of cognition in the literature. For example, in a study by Zhou H. et al. The effects of COVID-19 on the cognitive functions of recovered patients (n=29) and their relationship with the immune system parameters were evaluated [26]. Cognitive functions were assessed using online neuropsychological tests: the Pathway Test (TMT). Trial Making Test) and continuous performance test (CPT, from the English Continuous Performance Test). Patients with COVID-19 showed lower CPT scores (lower reaction time and more errors), which correlated with blood levels of C-reactive protein (CRP) (r=0.557 and 0.41). Similar results were obtained in the study of Wilcox S. [28], devoted to the study of the effect of COVID-19 on cognitive functions in patients in China who were hospitalized in the infectious diseases department, and subsequently recovered. Statistically significant differences in test results were found between the COVID-19 patients and the control group only in the Continuous Performance test (CPT). Patients with COVID-19 showed more missed responses and errors in the more complex section of this test. In another study, Baker H. A. et al. [4], we studied the level of cognitive deficits in 13 patients admitted to a hospital in Lausanne, Switzerland, during the post-critical acute stage of severe COVID-19. The neuropsychological assessment consisted of two standard sets of tests: the Montreal Cognitive Assessment Scale (MoCA) and the Frontal Dysfunction Battery (FAB). MoCA data showed that 4 (30.8%) patients had moderate cognitive deficits, and 5 (38.5%) had moderate to severe deficits. The MoCA subtests revealed a selective cognitive pattern with lower control function scores in patients with relatively normal MoCA test scores, and more extensive cognitive impairments of executive functions, memory, attention, and visual-spatial functions with relatively preserved orientation and speech, in patients with severe cognitive deficits. FAB data showed executive system dysfunction in 8 (61.5%) patients. According to the FAB subtests, speech function was most affected: pronounced fluency was found in 12 (92.3%) of the 13 patients. In a study by Marcel S. et al. [9] 18 patients were examined 20-105 days after treatment for mild to moderate COVID-19. 14 (78%) patients had sustained moderate cognitive deficits in the form of worse results in the "Modified Telephone Interview for Cognitive Status screening test" (TICS-M) for mild cognitive impairment compared to 10 healthy people from the control group of the same age. To a greater extent, the authors noted a decrease in short-term memory, attention and concentration, however, the results of screening did not correlate with the duration of hospitalization and treatment. Hampshire A. et al examined a group of patients who had suffered from COVID-19, and showed an average decrease of 8.5 points in IQ level [11].

Conclusion. Over the past few months, our understanding of the prevalence, pathogenesis, and clinical heterogeneity of the new coronavirus infection has been significantly supplemented and modified. The few publications devoted to changes in cognitive functions associated with COVID-19 indicate significant cognitive disorders. It is becoming increasingly clear that one of the most important consequences of COVID-19 is cognitive deficits, even in patients with mild symptoms. Together, there is growing evidence that the CAVID-19 infection itself, as well as the consequences of an intensive course of therapy, can independently and synergistically contribute to the development of cognitive decline (Figure).

However, these studies do not provide an exhaustive answer to whether cognitive deficits are caused by the direct neu-

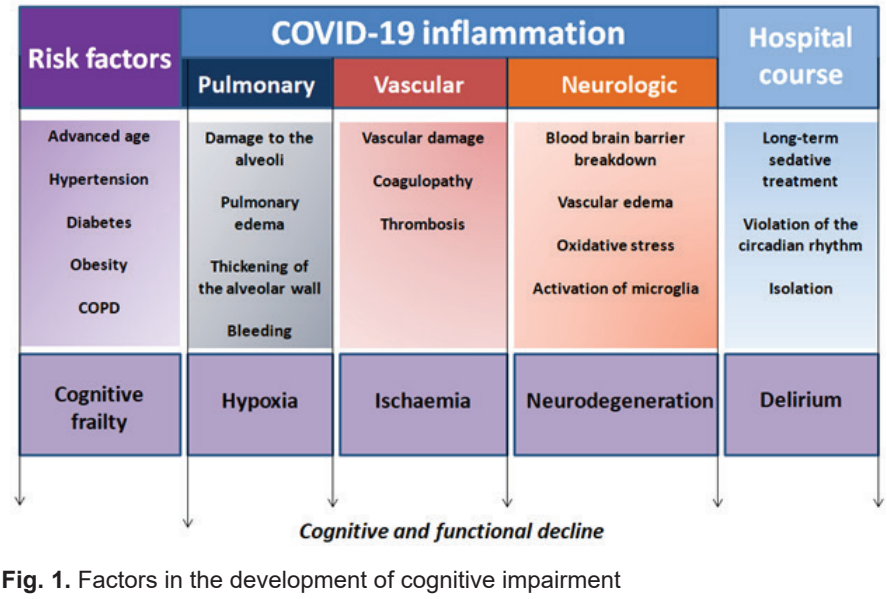

Fig. 1. Factors in the development of cognitive impairment

rotropic action of the virus or are mediated by an immune response, or other reactions.

The lack of more accurate information about functional brain disorders, including cognitive impairment, in patients with COVID-19 can be attributed to the impact that the pandemic has had on health systems, as well as the difficulty of conducting a comprehensive neuropsychological assessment. However, this information will be of great importance for identifying risk factors associated with neuropsychological symptoms, both in people with and without prior cognitive impairment, and will also shed light on the underlying mechanisms of pathogenesis. Also, to improve the quality of medical care, it is necessary to offer neuropsychological rehabilitation to those who need it. It is important and urgent to minimize the potential negative impact on cognitive and psychosocial functions and quality of life in patients who have undergone COVID-19.

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