ŁOBAZA, Paulina, KUDŁA, Martyna, ZAJĄC, Gabriela, ANTKIEWICZ, Mikołaj, ARCZYŃSKA, Aleksandra, KOCIUBA, Julia, KOŁKOWICZ, Dorota, KRUCZEK Zuzanna, KRAWCZYK, Agata, and PAWEŁCZAK, Natalia. Neurological Consequences of COVID-19: A Literature Review of Pathophysiology, Clinical Manifestations, and Therapeutic Strategies. Quality in Sport. 2025;41:60372. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.41.60372
https://apcz.umk.pl/QS/article/view/60372

The journal has had 20 points in Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 16.04.2025. Revised: 28.04.2025. Accepted: 02.05.2025. Published: 05.05.2025.

Neurological Consequences of COVID-19: A Literature Review of Pathophysiology, Clinical Manifestations, and Therapeutic Strategies

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ABSTRACT

The COVID-19 pandemic, caused by SARS-CoV-2, has become a major global health crisis with widespread effects on healthcare, society, and economies. Initially seen as a respiratory illness, it is now recognized as a multisystem disease, with growing evidence of its impact on the nervous system.

Neurological complications - such as cognitive impairment ("brain fog"), strokes, Guillain-Barré syndrome, and mood disorders - have been reported in both severe and mild COVID-19 cases, highlighting the unpredictable nature of post-COVID sequelae. These symptoms can persist long after the acute phase of infection.

The mechanisms behind these effects are complex and not yet fully understood. They include direct viral invasion of the central nervous system, immune dysregulation (e.g., cytokine storm,

autoimmunity), and blood–brain barrier disruption, all of which may lead to neuroinflammation and neurodegeneration.

The long-term neurological consequences pose significant clinical and societal challenges, requiring multidisciplinary care and tailored rehabilitation strategies. This review summarizes current knowledge on the neurological manifestations of COVID-19, underlying mechanisms, and therapeutic approaches, aiming to inform evidence-based post-COVID care.

Aim: The aim of this article is to provide a comprehensive analysis of current research exploring the relationship between SARS-CoV-2 infection and subsequent neurological disorders, the changes occurring within the central nervous system during infection, and the underlying pathophysiological mechanisms involved.

Materials and Methods: An extensive literature review was conducted using the PubMed database, with a focus on scientific publications published between 2019 and 2024. The search strategy was guided by a selection of relevant keywords, including: “SARS-CoV-2,” “COVID-19,” “neurological disorders,” “nervous system,” “neuroinflammation,” “cognitive functions,” “neuropsychological rehabilitation,” and “pathophysiology of the central nervous system.” This approach enabled the identification of peer-reviewed studies addressing the neurological consequences of COVID-19, with particular emphasis on pathophysiological mechanisms, clinical manifestations, and therapeutic strategies.

Keywords: SARS-CoV-2, COVID-19, neurological disorders, nervous system, neuroinflammation, cognitive functions, neuropsychological rehabilitation, pathophysiology of the central nervous system

Introduction to SARS-CoV-2 Infection

The first cases of infection with the novel coronavirus SARS-CoV-2 were detected at the end of 2019 in the city of Wuhan, located in Hubei Province, China. Initially, cases of pneumonia of unknown etiology were reported, but further research confirmed that they were caused by a newly identified coronavirus. The first death associated with SARS-CoV-2 infection was recorded in Wuhan at the beginning of January 2020. Over the following months, the virus

rapidly spread worldwide, leading to a global pandemic. On March 11, 2020, the World Health Organization (WHO) officially declared COVID-19 a pandemic. [1]

The disease COVID-19 is caused by the SARS-CoV-2 virus, which belongs to the genus of β-coronaviruses. It is a zoonotic pathogen capable of interspecies transmission. [2] SARS-CoV-2 shares close genetic similarities with other coronaviruses that have caused severe epidemics in the past, such as SARS-CoV and MERS-CoV. The severe acute respiratory syndrome coronavirus (SARS-CoV) emerged in Guangdong Province, China, in 2002, spreading to five continents primarily via air travel. Meanwhile, the Middle East respiratory syndrome coronavirus (MERS-CoV) was first identified in 2012 on the Arabian Peninsula, from where it spread to 27 countries. Both of these viruses, like SARS-CoV-2, originate from bats, which are considered their natural reservoir hosts. [2-4]

The COVID-19 transmission pathways play a crucial role in the rapid dissemination of SARS-CoV-2.The primary modes of transmission include respiratory droplets released during close human interaction and the potential fecal-oral route. The virus enters the body through the nasal or oral cavity, facilitating its spread. [5]

The course of COVID-19 infection varies widely, ranging from asymptomatic cases to severe cases requiring hospitalization. The severity of the disease is correlated with age and the presence of comorbidities such as hypertension, diabetes, and cardiovascular diseases. The incubation period of the virus ranges from 1 to 14 days, with a median age of infection of approximately 55 years.

The symptoms of COVID-19 are diverse, with the most common including fever, runny nose, cough, and fatigue. Some patients also experience headaches, diarrhea, and shortness of breath. In the long term, post-acute symptoms such as persistent shortness of breath (22.9%-53% of patients after two months), chest pain (21% of patients after 60 days), and palpitations (9%) have been observed. Other symptoms include muscle weakness, sleep disturbances, loss of taste and smell (11%-13.1%), as well as psychological issues such as anxiety, depression, and PTSD.

SARS-CoV-2 can infect multiple organ systems. The respiratory system is the most commonly affected, potentially leading to pneumonia and acute respiratory distress syndrome (ARDS). In addition to the respiratory system, SARS-CoV-2 infection can impact the cardiovascular, nervous, digestive, musculoskeletal, genitourinary, and dermatological systems, as well as the kidneys and circulatory system. [6]

Long-term complications of COVID-19 affect multiple organ systems. In the respiratory system, pulmonary fibrosis and oxygen dependence are commonly observed after hospital discharge. The impact on the cardiovascular system may include myocarditis and echocardiographic abnormalities. Patients recovering from COVID-19 also face an increased risk of thrombosis and microthrombosis in the lungs. The nervous system is affected by cognitive impairments, brain fog, difficulties with speech fluency, and executive function deficits. Psychologically, PTSD, depression, anxiety disorders, and insomnia are frequently reported. Dermatological complications include rashes and hair loss. Gastrointestinal effects include chronic diarrhea and microbiome alterations, while reproductive issues may include fertility disorders. Additionally, patients may experience muscle mass loss and chronic kidney disease.

Although COVID-19 is primarily a pulmonary disease, it affects the entire body and leads to multi-organ complications across various systems. In this review, we focus on the long-term complications associated with the central nervous system. [7]

Mechanisms of COVID-19 Impact on the Nervous System

Neurotropism of SARS-CoV-2 – How the Virus Affects the Nervous System

Initially, it was believed that the acute respiratory distress syndrome (ARDS) caused by SARS-CoV-2 was limited to the immune system. However, the increasing number of infections has demonstrated that COVID-19 can affect the entire body, including the peripheral and central nervous systems. Examples of central nervous system (CNS) diseases associated with COVID-19 include encephalopathy, encephalitis, acute disseminated encephalomyelitis, meningitis, ischemic and hemorrhagic stroke, cerebral venous sinus thrombosis, and endotheliitis. In the peripheral nervous system, COVID-19 has been linked to olfactory and gustatory dysfunction, muscle injury, and Guillain-Barré syndrome [8]. Although the mechanisms by which SARS-CoV-2 affects the nervous system are not yet fully understood, attention should be paid to the virus's neurotropism as well as the role of the immune system and inflammatory responses.

The infection process begins with the binding of the SARS-CoV-2 spike protein to the ACE2 receptor (angiotensin-converting enzyme 2). This interaction enables viral entry into the host cell following proteolytic cleavage of the spike protein by the transmembrane protease TMPRSS2. ACE2 is highly expressed in alveolar epithelial cells but is also found in various organs and tissues, including the cerebral cortex, kidneys, gastrointestinal tract, gallbladder, testes, and adrenal glands [8].

SARS-CoV-2 exhibits the ability to affect the central nervous system (CNS). There is evidence for the neurotropism of coronaviruses, including SARS-CoV, whose antigen and RNA have been detected in brain tissue during post-mortem analyses [9]. The mechanism of SARS-CoV-2 neuroinvasion is not fully elucidated, but it is suggested that the virus may enter the CNS via ACE2 receptors and TMPRSS2, which facilitate its cellular entry.

In contrast to encephalopathy, where there is no direct evidence of viral invasion, encephalitis may result from neuronal damage due to SARS-CoV-2 replication in neural tissue. In isolated cases, SARS-CoV-2 RNA has been detected in cerebrospinal fluid (CSF) via RT-PCR, confirming direct infection. However, in many cases, despite CNS inflammation, the virus was not detected, suggesting immune-mediated mechanisms as potential causes of neurological damage [10].

The diagnosis of SARS-CoV-2 neuroinvasion relies on neuroimaging studies, such as MRI and EEG, which may reveal focal brain lesions. Key evidence of infection includes a positive RT-PCR result from cerebrospinal fluid, the presence of specific intrathecal antibodies, and the detection of viral antigen or RNA in brain tissue [11,12].

The Role of the Immune System and Inflammatory Response

Direct invasion of the brain by SARS-CoV-2 is rare, and neurological complications are often the result of indirect effects such as excessive activation of the immune system. While the immune response is essential for combating infection, its dysregulation can lead to damage and pathological changes within the nervous system. The underlying mechanisms of COVID-19-related neuropathology include cytokine storm, direct viral damage, the production of antibodies against self-antigens, and infiltration of immune cells across the blood-brain barrier (BBB) [13].

The cytokine storm in COVID-19 is characterized by excessive immune activation, leading to the rapid release of large quantities of pro-inflammatory cytokines. This condition can provoke a severe inflammatory response, resulting in multi-organ damage, including to the lungs, and contributes to increased mortality risk [14]. Analysis of cerebrospinal fluid (CSF) from patients with neurological symptoms of COVID-19 revealed elevated levels of brain injury markers, such as neurofilament light chain (NfL), total tau (T-tau), and glial fibrillary acidic protein (GFAP), along with increased concentrations of pro-inflammatory cytokines, including IL-6, IL-8, and TNF. Importantly, most patients showed no presence of the virus or antibodies in the CSF, suggesting that central nervous system (CNS) damage is more likely due to indirect effects

of infection—primarily through immune system overactivation [15,16]. Among the cytokines particularly involved in neuropathology are IL-6, TNF, IFN-γ, and chemokines that attract neutrophils (e.g., IL-8) and monocytes (CCL2, CCL5) [17]. Animal models have shown that molecules such as CXCL1, induced by IL-1α, contribute to BBB disruption and the migration of neutrophils into brain tissue. Neutrophilic infiltrates have been observed in the brains of COVID-19 patients, supporting the involvement of this pathway in neurological pathology [18].

An interesting aspect is the role of protective cytokines such as IL-10, IL-1RA (IL-1 receptor antagonist), and hepatocyte growth factor (HGF). Their increased levels correlate with disease severity, possibly reflecting an attempt by the body to counteract excessive inflammation. For example, anakinra (an IL-1 receptor inhibitor) has demonstrated some efficacy in reducing mortality in COVID-19 patients, suggesting that modulation of cytokine pathways may be a promising therapeutic approach [19]. Another component implicated in CNS injury is the complement system, whose excessive activation (especially of C3 and C5 components) may result in microthrombi and damage to cerebral endothelial cells. Current research is ongoing into drugs that target these proteins [20]. While broad-acting immunosuppressive agents like dexamethasone may help mitigate cytokine storms, their use requires caution—as they may do more harm than good in patients with mild COVID-19. Therefore, it is crucial to develop targeted therapies that selectively inhibit harmful cytokines without impairing antiviral defense mechanisms [21]. In summary, the cytokine storm plays a significant role in the neurological complications of COVID-19, both by directly damaging neural cells and by destabilizing the blood-brain barrier. Further research into biomarkers and targeted therapies may help develop more effective strategies to protect the CNS in patients with severe infection.

SARS-CoV-2 infection can also lead to neurological complications involving autoantibodies. Their activity is primarily based on molecular mimicry—the similarity between viral proteins and human neural structures. In rare cases, anti-NMDA receptor antibodies have been observed, while peripheral syndromes such as Guillain-Barré syndrome have occurred more frequently [22,23]. The mechanisms of damage include both the direct effects of autoantibodies and secondary inflammatory processes. Excessive immune activation disrupts the BBB, releasing additional autoantigens and intensifying the autoimmune response. For instance, antiphosphatidylserine antibodies have been detected, which may promote thrombotic processes [24]. Although many cases of Guillain-Barré syndrome have been reported following COVID-19, typical anti-ganglioside antibodies were often absent, and the overall incidence of the disease did not increase during the pandemic. Currently, it is essential to differentiate

between pathogenic autoantibodies and those that merely indicate tissue injury. Further studies are needed to clarify the precise mechanisms of these processes and to support the development of more effective therapies [25].

Another aspect in analyzing the role of the immune system in post-COVID-19 neuropsychiatric disturbances is the impact of infection on central nervous system cells, particularly microglia, neurons, and astrocytes. Microglia, the resident immune cells of the brain, play a key role in the immune response to infection. Post-mortem studies in COVID-19 patients have revealed an increased number of activated microglial cells (CD68+, IBA-1+), a finding also supported by single-nucleus RNA sequencing. This activation is associated with inflammatory signaling and cellular stress and is often accompanied by microglial nodules damaging axons. Microglia can become activated even in the absence of active brain infection by SARS-CoV-2—for example, due to the spike protein (S1), which can cross the BBB and trigger inflammatory pathways. Additionally, microglia respond to cellular stress signals (DAMPs), which may arise from BBB damage. While microglial activation is necessary for infection control, its chronic presence may lead to neuronal damage and neurological symptoms. These changes may be associated with long COVID symptoms (PASC). In rodent models, microglial activation following S1 protein injection led to cognitive and anxiety-related impairments. The role of other CNS cells, such as neurons and astrocytes, remains less well understood. However, increased levels of neurodegeneration and gliosis markers have been detected in the blood of COVID-19 patients. RNA analyses and histological studies have shown reduced synaptic activity in neurons, neural cell death, decreased hippocampal neurogenesis, and demyelination in white matter. Functional changes in astrocytes have also been observed but require further investigation [26].

An equally important issue in the neuropathology of SARS-CoV-2 is the disruption of the blood-brain barrier (BBB) by the virus. The virus targets endothelial cells of cerebral vessels, increasing BBB permeability and allowing pathogens and inflammatory molecules to enter the CNS. Additionally, the cytokine storm associated with COVID-19 amplifies the inflammatory state, leading to degradation of tight junction proteins in endothelial cells and further weakening of the barrier. Autopsy studies have revealed the presence of the virus in neurons and inflammatory infiltrates in brain tissue, confirming the direct effect of infection on the BBB. Long-term consequences of these changes may include an increased risk of neurodegenerative diseases, such as Alzheimer’s disease, due to chronic inflammation and impaired brain homeostasis [27].

Cognitive and Neurological Impairments Following COVID-19

An analysis conducted on a group of 214 patients hospitalized in three specialized COVID-19 treatment centers in Wuhan, China, revealed that 36% of them exhibited neurological symptoms. These symptoms were classified according to their association with the central nervous system (CNS), peripheral nervous system (PNS), and skeletal muscles. In total, 25% of patients presented with symptoms indicative of CNS dysfunction, including dizziness (17%), headache (13%), impaired consciousness (7.5%), acute cerebrovascular events (3%), ataxia (0.5%), and seizures (0.5%) [8].

Other studies conducted in Wuhan categorized patients based on the severity of pneumonia and pulmonary function impairment. Neurological symptoms were more frequently observed in patients with severe disease compared to those with a mild course of COVID-19. Although all CNS-related symptoms were more common in the severely affected group, only impaired consciousness and acute cerebrovascular events showed statistically significant differences between the two groups [28].

Brain imaging studies in COVID-19 patients have revealed a range of abnormalities potentially associated with the observed neurological symptoms. In studies conducted in 2020 during the acute and subacute phases of SARS-CoV-2 infection, structural changes were identified in approximately 34% of patients undergoing neuroimaging, with the most predominant abnormalities located in the white matter. Hyperintense lesions on magnetic resonance imaging (MRI) or hypodensities on computed tomography (CT) accounted for 76% of all recorded abnormalities [29]. These changes often appear as diffuse lesions, primarily affecting the white matter of the frontal, temporal, parietal, and occipital lobes, although deep brain structures such as the thalamus, cingulate gyrus, and internal capsule may also be involved. In some cases, abnormalities have been observed in the brainstem, cerebellum, and corpus callosum. These findings may be associated with leukoencephalopathy, leukoaraiosis, or, more rarely, demyelinating processes [30].

Neurological disturbances prompting neuroimaging include, among others, altered consciousness, seizures, strokes, focal symptoms (e.g., paresis), and olfactory and gustatory dysfunction. Electroencephalography (EEG) in some patients has revealed generalized slowing of brain bioelectrical activity or focal epileptiform discharges, which may reflect functional disturbances linked to the infection. Less commonly, ischemic strokes, intracerebral hemorrhages, microbleeds, and cerebral edema have been reported. These conditions may result

from the direct impact of the virus on cerebral endothelial cells, systemic inflammatory responses, coagulation disorders, or hypoxia [29, 31–33].

Importantly, in some patients, neuroimaging abnormalities are transient and resolve within a few weeks, suggesting reversible damage related to the infection. However, in others, these changes may persist, potentially leading to long-term neurological deficits. In summary, neuroimaging plays a crucial role in the diagnosis and monitoring of COVID-19-related neurological complications. The predominance of white matter abnormalities, alongside less frequent but serious vascular events (strokes, hemorrhages), highlights the complex mechanisms underlying central nervous system involvement in the course of this infection. Further research is needed to better understand the long-term neurological consequences of COVID-19.

Memory and Concentration Problems: Brain Fog After COVID-19

Brain fog (BF) is a colloquial term describing subjective cognitive disturbances, including difficulties with concentration, forgetfulness, slowed thinking, and problems with organizing or articulating thoughts. Although not a disease entity in itself, it represents a significant secondary symptom in various clinical conditions—ranging from chronic fatigue and depression to autoimmune diseases. In the context of the COVID-19 pandemic, BF has garnered particular attention as a frequent and persistent symptom of post-COVID syndrome (commonly referred to as long COVID), significantly reducing patients' quality of life regardless of the severity of the initial infection.

A study by Nordvig et al. demonstrated that approximately 31.9% of patients experienced brain fog one year after infection, regardless of the severity of the acute phase of COVID-19 [34]. Interestingly, age and pre-existing comorbidities were not found to be significant risk factors for the development of BF [34]. Women more frequently reported BF symptoms than men, possibly due to physiological differences in the nervous system or immune response [34]. BF was also associated with other symptoms of long COVID, such as sleep disturbances (63% vs. 29% in individuals without BF), dyspnea (46% vs. 18%), and fatigue (49% vs. 22%). Patients with BF more often reported limitations in daily activities, changes in employment status (e.g., medical leave), and a decline in quality of life [34].

In a study by Junco et al., the long-term effects of BF were assessed in hospitalized COVID-19 patients approximately two years after infection [35]. It was shown that the severity of COVID-19 (measured by the NEWS2 score) correlated with a greater number of BF symptoms,

including difficulty focusing, a sense of “disconnection,” and daytime drowsiness. Moreover, patients with more severe disease exhibited poorer performance in cognitive assessments, particularly in working memory and attention tasks [35].

Research by Lanz-Luces et al. found that 61% of patients experienced BF, with symptom severity correlating with more frequent reports of concentration difficulties. BF persisted for up to 240 days post-infection, impacting patients' ability to perform everyday tasks [36].

In a study by Cipolli et al., the long-term effects of BF were also evaluated. In the subacute phase (4–12 weeks after infection), language functions, episodic memory, and executive functions were most frequently impaired. After 12 weeks, attention deficits, episodic memory loss, and executive dysfunctions became predominant. Patients who experienced a severe course of illness (e.g., requiring mechanical ventilation) were at greater risk of developing cognitive impairments [37].

Several studies have emphasized the association of BF with psychological disorders such as depression, anxiety, and sleep disturbances [34–36]. In the study by Junco et al., 35% of patients reported symptoms of depression, and 75% experienced sleep disturbances [35]. Notably, BF can persist for months or even years following infection, impairing patients' ability to return to normal functioning [34,35].

In a study by Asadi-Pooya et al., the prevalence of BF was assessed among 2,696 patients with documented COVID-19 in Fars province, Iran. It was found that 7.2% of participants experienced chronic BF symptoms more than 12 weeks post-infection. Significant risk factors included female sex, respiratory symptoms during the acute phase, and intensive care unit (ICU) hospitalization [39]. These findings corroborate earlier observations regarding women’s increased susceptibility to long-term COVID-19 effects and suggest that a more severe course of illness elevates the risk of cognitive disturbances.

Interestingly, this analysis did not identify age or comorbidities as significant contributors to BF, which is consistent with the findings of Nordvig et al. [34]. The authors propose that long-lasting neurological symptoms—such as concentration difficulties or disorientation—may result from both biological mechanisms (e.g., neuroinflammatory brain injury) and psychosocial consequences of the disease [39].

In contrast, the study by Khieukhajee et al. found that 61.76% of hospitalized patients demonstrated cognitive impairments based on the Montreal Cognitive Assessment (MoCA),

most frequently involving executive functions, short-term memory, and visuospatial skills [38]. Unlike the Iranian study, this research indicated that advanced age and lower education levels were significant risk factors, while clinical variables such as hypoxia, inflammatory biomarkers, and treatment methods showed no effect on cognitive outcomes [38].

Researchers point out that a lower level of education may reflect reduced cognitive reserve, increasing vulnerability to post-infectious impairments, including those related to COVID-19. Importantly, no statistically significant difference in cognitive test scores between COVID-19 patients and healthy individuals was found in multivariate analysis, underscoring the need for further longitudinal studies to determine whether SARS-CoV-2 infection indeed results in permanent cognitive damage [38].

In conclusion, findings from the reviewed studies confirm the complexity of post-COVID brain fog. Its prevalence and associated risk factors vary across populations and assessment methods. Nonetheless, BF represents a real and lasting burden for patients, negatively affecting their quality of life and social functioning. Further research is essential to clarify the pathophysiological mechanisms, standardize diagnostic tools, and develop effective therapeutic interventions—particularly for high-risk groups such as women, individuals with severe illness, and those with lower educational attainment.

Stroke and Vascular Complications

Stroke is among the most severe vascular complications that may occur during or after SARS-CoV-2 infection. An increasing number of studies indicate an elevated risk of thromboembolic events in patients following COVID-19, even among those with a mild course of the disease. These complications are particularly concerning due to their sudden onset, potential for permanent neurological damage, and association with long-term cognitive dysfunction.

In a study by Fridman et al., the incidence of stroke in patients with COVID-19 was analyzed in comparison to non-infected individuals. It was found that individuals infected with SARS-CoV-2 had a significantly higher risk of ischemic stroke, especially within the first 30 days after infection. Moreover, this elevated risk persisted for several months, particularly among hospitalized patients and those with pre-existing cardiovascular risk factors. The authors emphasized prothrombotic mechanisms triggered by the virus, including endothelial dysfunction, cytokine storm, and direct vascular injury [40].

Similarly, an analysis conducted by Cheng et al. confirmed an increased frequency of vascular complications, such as pulmonary embolism, deep vein thrombosis, and stroke during the post-

COVID recovery period. The study involved over 150,000 individuals with prior SARS-CoV-2 infection, a significant proportion of whom experienced vascular incidents within the first year after infection. Notably, even individuals with mild COVID-19 were at increased risk of thrombosis, suggesting that the long-term consequences of the infection are not limited to severe cases [41].

Comparable findings were reported in an analysis by Long et al., published in the American Journal of Emergency Medicine. The authors described a range of vascular complications, including venous thrombosis, pulmonary embolism, and the risk of cardiac and cerebral injury resulting from a generalized inflammatory response. Systemic cytokine activation and the direct action of the virus on ACE2 receptors—present in the endothelium and myocardial tissue—lead to cardiovascular dysregulation. Cardiac injury, including myocarditis, acute heart failure, and arrhythmias, was observed even in individuals without prior cardiovascular disease, potentially increasing the risk of neurological complications such as stroke or ischemic encephalopathy [42].

Particularly alarming are thrombotic complications within the nervous system. Patients with COVID-19 have demonstrated significant coagulation abnormalities, including elevated D-dimer levels, which correlate with an increased risk of pulmonary embolism and microemboli in the cerebral circulation. These mechanisms may result in strokes, including both large territorial infarctions and numerous microemboli that cause chronic cognitive deficits [42].

Both studies, along with the analysis by Long and colleagues, emphasize the need for long-term monitoring of patients post-COVID-19, particularly regarding cardiovascular and neurological systems. The high incidence of strokes and other thromboembolic events highlights the importance of implementing preventive strategies, such as anticoagulant therapy and management of risk factors (hypertension, diabetes, obesity) in individuals recovering from the infection.

Polyneuropathies and Neurological Syndromes: Guillain–Barré Syndrome

Guillain–Barré syndrome (GBS) is a rare but potentially severe autoimmune disorder of the peripheral nervous system that may occur following viral infections, including SARS-CoV-2. A growing body of evidence suggests a link between COVID-19 and the development of GBS, with symptoms emerging during or after the acute phase of infection. GBS can lead to progressive weakness, muscle paralysis, and in severe cases, respiratory failure requiring intensive care unit (ICU) admission.

A study by Toscano et al. highlighted that Guillain–Barré syndrome may develop shortly after the onset of COVID-19 symptoms, even in patients with a moderate course of the disease. The authors observed that demyelinating and axonal variants were the predominant clinical forms, with a substantial number of patients requiring respiratory support and intensive care. Their findings suggest that SARS-CoV-2 may act as a trigger for an autoimmune attack on peripheral nerves, resulting in rapid neurological deterioration [43].

Similarly, an analysis by Abu-Rumeileh et al. indicated that post-COVID GBS cases are more frequent than previously assumed and may affect both older and younger individuals, regardless of the severity of infection. The classic form of GBS was most commonly reported, though atypical variants, such as Miller Fisher syndrome, were also noted. Importantly, many patients required ICU care and prolonged neurological rehabilitation. The authors emphasized that the immune response induced by SARS-CoV-2 may persist for weeks after infection, increasing the risk of delayed neurological complications. Their results also support the consideration of GBS as a possible post-COVID manifestation, with early diagnosis and treatment potentially improving clinical outcomes [44].

Zhao et al. reported that GBS in post-COVID patients may follow an atypical clinical course, including sensory disturbances, weakness in both lower and upper limbs, and rapid deterioration in respiratory function. Notably, some patients exhibited no classical symptoms of COVID-19, complicating the recognition of a causal link between the infection and the neurological syndrome [47].

The same study described a case in which neurological symptoms preceded the development of respiratory illness, suggesting the possibility of asymptomatic COVID-19 or a delayed onset of typical viral manifestations. The authors stress the importance of differential diagnosis in patients presenting with neuropathic symptoms during the COVID-19 pandemic [47].

Further robust evidence of a potential association between SARS-CoV-2 infection and GBS was provided by a multicenter observational study conducted in Northern Italy, spanning March 2020 to March 2021. The researchers reported a 59% increase in total GBS cases compared to the previous year. Notably, COVID-19-positive patients accounted for half of all GBS cases, with peaks coinciding with waves of SARS-CoV-2 infection. Among post-COVID GBS patients, the classic clinical form (88.8%) was predominant, especially the demyelinating AIDP subtype (76.2%). These patients more frequently experienced autonomic dysfunction and

required ICU admission (49.2%). COVID-associated GBS was characterized by a more severe course and higher disability scores on the Hughes scale [46].

Comparable observations were made in a Polish case study of a 50-year-old patient who developed classic GBS 18 days after a mild COVID-19 course. Electrophysiological studies and cerebrospinal fluid analysis (showing albumin-cytological dissociation) confirmed a mixed axonal and demyelinating polyneuropathy. Following plasmapheresis therapy, the patient achieved near-complete symptom resolution. This case demonstrates that GBS can occur even after a mild SARS-CoV-2 infection and that the treatment response supports a post-infectious immune mechanism as the likely cause of neurological complications [45].

Proposed pathophysiological mechanisms include molecular mimicry between viral antigens and neural structures, activation of the complement system, and increased release of proinflammatory cytokines—all of which can contribute to demyelination and axonal damage [44, 45].

All presented cases and analyses point to the need for clinical vigilance, particularly when neurological symptoms appear in patients recovering from COVID-19. Early recognition of Guillain–Barré syndrome and timely initiation of treatment (e.g., intravenous immunoglobulin or plasmapheresis) may significantly improve prognosis and shorten hospitalization duration. Given the potentially severe course of GBS and the risk of long-term disability, long-term monitoring of patients after COVID-19 for signs of polyneuropathy and neurological syndromes is essential [43–47].

Risk Factors and Vulnerable Groups for Neurological Complications Following COVID-19

Predisposing Factors for the Development of Neurological Disorders After COVID-19

Among the most frequently identified risk factors for neurological complications following COVID-19 is the severity of the acute illness. Hospitalization, the need for mechanical ventilation, or admission to the intensive care unit significantly increase the likelihood of complications such as encephalopathy, stroke, brain fog, and Guillain–Barré syndrome (GBS) [28, 30, 35, 38, 42, 43, 45]. Direct viral mechanisms have also been implicated, including the neurotropism of SARS-CoV-2 and endothelial dysfunction, which can lead to damage of cerebral vessels and impaired microcirculation [29, 30, 42].

Other severe neurological conditions have also been observed in COVID-19 patients, including acute necrotizing encephalopathy (ANE), acute disseminated encephalomyelitis (ADEM), subacute encephalopathy, and ischemic stroke [29, 30, 33, 41]. The presence of respiratory symptoms—both during the acute phase of infection and in the context of long COVID—represents an additional risk factor for the development of brain fog and other neurological complications [36, 40].

In the case of GBS, the primary pathophysiological mechanism is considered to be an autoimmune response triggered by the infection—particularly through molecular mimicry and the production of antiganglioside antibodies [43–45].

Impact of Age, Sex, and Comorbidities

Age was a significant risk factor in several analyses—older individuals were more susceptible to severe neurological complications, including cognitive deficits and encephalopathy [28, 38, 42]. However, some studies demonstrated that younger individuals may also experience complications, as evidenced by the case of a 16-year-old boy who suffered a stroke in the course of multisystem inflammatory syndrome in children (MISC) [41]. Other studies suggested that age does not necessarily correlate with the risk of brain fog; rather, other factors such as low educational attainment may play a more prominent role [34, 36, 39].

Female sex was repeatedly identified as a significant risk factor for the development of brain fog and post-COVID cognitive symptoms [34–37, 40]. In contrast, men predominated in cases of GBS, a trend supported by findings from meta-analyses [43–45].

Comorbidities such as hypertension, diabetes, obesity, and cardiovascular diseases increase the risk of neurological complications, especially in the context of GBS and stroke [28, 42–45]. Interestingly, some studies on brain fog reported no significant association with comorbidities [34, 36, 39], highlighting the complexity and heterogeneity of the mechanisms underlying this phenomenon.

Role of Lifestyle and Psychosocial Factors

Lifestyle factors were not directly assessed in most of the reviewed studies. However, psychosocial factors such as depression, anxiety, insomnia, and social isolation have shown strong associations with neurological symptoms, particularly in the context of long-term cognitive disturbances [34–38]. These impairments negatively impact patients' quality of life and their ability to return to daily functioning and employment.

In relation to brain fog, poor sleep quality and both mental and physical fatigue are particularly relevant, often persisting for several months following infection [34–36]. The broader psychosocial consequences of the pandemic—including stress and lack of social support—may further exacerbate neurological and cognitive symptoms, even in patients who did not experience severe COVID-19 [36–38].

Therapeutic Options and Neurological Rehabilitation in Post-COVID-19 Neurological Complications

Neurological complications following COVID-19 have emerged as some of the most frequently reported long-term sequelae, significantly affecting patients' quality of life [48]. Due to the lack of specific therapeutic protocols, current management relies on a symptomatic approach, integrating pharmacological treatment with psychological interventions and neuropsychological rehabilitation [51, 52].

Pharmacotherapy for Post-COVID-19 Neurological Disorders

Currently, no medications are specifically approved for the treatment of neurological symptoms related to long COVID. In clinical practice, however, drugs with known efficacy in treating depression, anxiety, and cognitive impairments are being employed.

Antidepressants and anxiolytics, such as selective serotonin reuptake inhibitors (SSRIs) like sertraline or escitalopram, are widely used to manage mood and sleep disturbances [50]. Benzodiazepines are also used to treat acute anxiety episodes, although their use is recommended only in the short term due to the potential for dependency [48]. Literature reviews indicate that up to 20% of patients experience depressive and anxiety symptoms within the first three months after infection [50, 51].

In cases of cognitive impairment, such as "brain fog," some clinical teams have introduced nootropic agents, including donepezil (an acetylcholinesterase inhibitor) or memantine—similar to their use in mild cognitive impairment. Observational studies have shown beneficial outcomes with such interventions; however, authors emphasize the need for randomized clinical trials to confirm their efficacy and safety in the post-COVID population [48, 49, 52].

In more severe cases, particularly where neuroinflammatory components are suspected, immunomodulatory therapy may be applied, such as corticosteroids or cytokine inhibitors (e.g., tocilizumab). However, these therapies are generally reserved for patients with acute

neurological inflammation and are not part of the standard treatment for mild cognitive disorders [50].

Psychological Interventions and Neurocognitive Rehabilitation

In addition to pharmacological treatment, increasing importance is given to psychological therapies and cognitive rehabilitation, which may effectively support neurological recovery in post-COVID-19 patients.

Cognitive-behavioral therapy (CBT) is one of the most extensively studied and recommended psychotherapeutic approaches in the context of long COVID. Clinical studies have demonstrated significant improvements in depressive and anxiety symptoms, as well as sleep quality, in patients undergoing CBT [48, 51].

Neuropsychological rehabilitation is based on multimodal training of cognitive functions, including memory, attention, and executive functioning, often supported by digital tools. Programs such as the one implemented by the Institut Guttmann have shown high effectiveness—up to 74% of patients exhibited improvements in verbal memory and verbal fluency after an eight-week intervention [48]. Authors emphasize the need for standardization of these rehabilitation strategies using validated diagnostic tools such as the Wechsler Adult Intelligence Scale or the California Verbal Learning Test [52].

Moreover, relaxation techniques and mindfulness-based interventions, including Acceptance and Commitment Therapy (ACT), have demonstrated positive effects in managing chronic fatigue, stress, and frustration related to prolonged symptoms. These approaches help reduce stress and regulate emotions, thereby indirectly supporting cognitive recovery [49, 52].

Across the analyzed studies, the importance of early identification of neuropsychological deficits and the implementation of multidisciplinary treatment approaches—incorporating both pharmacological therapy and comprehensive rehabilitation—is consistently emphasized [51, 52].

The Role of Neuropsychological Rehabilitation in Post-COVID-19 Neurological Recovery

Clinical studies confirm a high prevalence of cognitive and neuropsychiatric disorders following COVID-19, with estimates suggesting that up to one-third of patients experience such complications within six months of infection [50]. In response to this phenomenon, comprehensive rehabilitation programs have been implemented—such as the model developed by the Institut Guttmann—which combine cognitive training, emotional support, and

physiotherapy. The application of such multidisciplinary programs has resulted in significant improvements in memory, attention, executive functioning, and a reduction in anxiety and depressive symptoms [48, 49].

According to data from systematic reviews, between 30% and 80% of patients who have recovered from COVID-19 exhibit long-term cognitive deficits, including problems with concentration, working memory, and executive functions [51]. Rehabilitation is particularly effective among individuals with severe forms of the disease, underscoring the importance of early therapeutic intervention [51].

Studies involving hospitalized patients have shown that neurological symptoms can persist for up to 12 months after discharge, particularly in those who required intensive care. In this population, as many as 45% reported limitations in their ability to work, while more than half struggled with daily tasks—clearly indicating the need for long-term rehabilitative support [53].

Rehabilitative Methods

Neuropsychological rehabilitation programs are multifaceted and incorporate various therapeutic strategies tailored to the individual needs of patients.

Cognitive training involves exercises designed to enhance memory, attention, and executive functions, frequently supported by digital tools [48]. Available analyses indicate that programs based on standardized tests—such as the Montreal Cognitive Assessment (MoCA)—are effective in improving cognitive functioning in individuals with post-COVID-19 syndrome [52]. In some cases, Acceptance and Commitment Therapy (ACT) and neurofeedback are also introduced to support neuroplasticity and cognitive recovery [53].

Emotional therapy, primarily based on cognitive-behavioral techniques, plays an essential role in treating coexisting mood disorders. Data presented in the literature show that the presence of depression, anxiety, and PTSD symptoms may exacerbate cognitive deficits, which confirms the need for a holistic therapeutic approach [52, 53].

Compensatory strategies, including the use of task planning tools, written notes, calendars, and mobile applications to support daily organization, can help offset deficits in memory and concentration. The effectiveness of these methods increases when they are individualized, particularly in patients with persistent symptoms and functional limitations [52, 53].

Although neuropsychological rehabilitation significantly improves quality of life, many patients do not achieve full recovery. Long-term data show that even six months after

completing therapy, nearly 45% of patients are unable to return to work at full capacity, and over 80% report limitations in social and occupational functioning [49].

Cognitive impairments have also been documented in patients who experienced mild forms of COVID-19, which confirms the need for long-term monitoring and continued therapeutic support [51]. Additionally, structural changes in the brain's white matter may underlie persistent symptoms, necessitating early neuropsychological intervention [52]. Some researchers suggest that these lasting cognitive deficits may have a neurodegenerative basis, highlighting the need for further research and individualized treatment strategies [53].

Neuropsychological rehabilitation is a key component of comprehensive treatment for patients with post-COVID-19 syndrome. The effectiveness of interventions increases when they are implemented early, adapted to individual patient profiles, and delivered through an interdisciplinary approach. Although full recovery is not always possible, these interventions significantly improve cognitive, emotional, and social functioning. The available data further emphasize the necessity of ongoing research aimed at developing optimal, long-term therapeutic models [51–53].

Conclusion

The COVID-19 pandemic has underscored the complex and multifactorial consequences of SARS-CoV-2 infection, extending far beyond acute respiratory illness. Accumulating clinical and experimental data confirm that the nervous system is particularly vulnerable, with neurological and neuropsychological sequelae emerging as prevalent and often long-lasting complications of both severe and mild cases of COVID-19.

The key mechanisms contributing to post-COVID neurological disorders include direct neurotropic effects of the virus, immune system dysregulation—such as cytokine storm and autoantibody production—and disruption of the blood-brain barrier. These processes collectively contribute to neuroinflammation, cognitive decline, cerebrovascular events, and syndromes such as Guillain–Barré. Moreover, the pandemic-induced psychological stress, sleep disturbances, and social isolation have exacerbated neuropsychiatric symptoms, further impairing patients' functioning and recovery.

A substantial proportion of individuals affected by COVID-19 report persistent symptoms such as brain fog, attention and memory deficits, mood disturbances, and fatigue—indicating long-term alterations in central nervous system functioning. Importantly, these impairments have

been observed in both hospitalized and non-hospitalized patients, including those with initially asymptomatic or mild infections.

Given the broad spectrum and persistence of neurological symptoms, effective management must incorporate multidisciplinary approaches. Pharmacological interventions—such as SSRIs, nootropics, or immunomodulatory agents—should be complemented by individualized psychological therapies and structured neurocognitive rehabilitation programs. The observed efficacy of cognitive-behavioral therapy (CBT), mindfulness-based interventions, and digital cognitive training platforms emphasizes the importance of integrative therapeutic strategies.

Understanding the underlying mechanisms and long-term implications of post-COVID neurological sequelae is essential for developing effective prevention and rehabilitation protocols. Further longitudinal studies and randomized controlled trials are urgently needed to validate therapeutic approaches and optimize care for affected individuals. In this context, neuropsychological rehabilitation emerges as a cornerstone of post-COVID care, with the potential to substantially improve cognitive, emotional, and functional outcomes in this growing patient population.

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All authors have read and agreed with the published version of the manuscript.

Founding Statement: The study did not receive funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The authors confirm that the data supporting this study are available in the article's references.

Conflict of Interest Statement: The authors declare no conflicts of interest.

Acknowledgements: Not applicable.

Bibliography:

[1] WHO Director-General's opening remarks at the media briefing on COVID-19–11 March 2020. Available at: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020

[2] Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein [published correction appears in Cell. 2020 Dec 10;183(6):1735. doi: 10.1016/j.cell.2020.11.032.]. Cell. 2020;181(2):281-292.e6. https://doi.org/10.1016/j.cell.2020.02.058

[3] Ksiazek TG, Erdman D, Goldsmith CS, et al. A novel coronavirus associated with severe acute respiratory syndrome. N Engl J Med. 2003;348(20):1953-1966. https://doi.org/10.1056/NEJMOA030781

[4] Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia [published correction appears in N Engl J Med. 2013 Jul 25;369(4):394]. N Engl J Med. 2012;367(19):1814-1820. https://doi.org/10.1056/NEJMoa1211721

[5] Bala A, Sengupta A, Matsabisa MG, Chabalala HP. Covid-19: Pathophysiology; Mechanism of Transmission and Possible Molecular Drug Target for Management. Curr Pharm Biotechnol. 2020. https://doi.org/10.2174/1874467213999200831104324

[6] Huang X, Wei F, Hu L, Wen L, Chen K. Epidemiology and Clinical Characteristics of COVID-19. Arch Iran Med. 2020;23(4):268-271. Published 2020 Apr 1. https://doi.org/10.34172/aim.2020.09

[7] Desai AD, Lavelle M, Boursiquot BC, Wan EY. Long-term complications of COVID-19. Am J Physiol Cell Physiol. 2022;322(1):C1-C11. https://doi.org/10.1152/ajpcell.00375.2021

[8] Koralnik IJ, Tyler KL. COVID-19: A Global Threat to the Nervous System. Ann Neurol. 2020;88(1):1-11. https://doi.org/10.1002/ana.25807

[9] Ding Y, He L, Zhang Q, et al. Organ distribution of severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. J Pathol. 2004;203(2):622-630. https://doi.org/10.1002/path.1560

[10] Netland J, Meyerholz DK, Moore S, Cassell M, Perlman S2008.Severe Acute Respiratory Syndrome Coronavirus Infection Causes Neuronal Death in the Absence of Encephalitis in Mice Transgenic for Human ACE2. J Virol82:.https://doi.org/10.1128/jvi.00737-08

[11] Duong L, Xu P, Liu A. Meningoencephalitis without respiratory failure in a young female patient with COVID-19 infection in Downtown Los Angeles, early April 2020. Brain Behav Immun. 2020;87:33. https://doi.org/10.1016/j.bbi.2020.04.024

[12] Huang YH, Jiang D, Huang JT. SARS-CoV-2 Detected in Cerebrospinal Fluid by PCR in a Case of COVID-19 Encephalitis. Brain Behav Immun. 2020;87:149. https://doi.org/10.1016/j.bbi.2020.05.012

[13] Dunai C, Collie C, Michael BD. Immune-Mediated Mechanisms of COVID-19 Neuropathology. Front Neurol. 2022;13:882905. https://doi.org/10.3389/fneur.2022.882905

[14] Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020;395(10229):1033-1034. https://doi.org/10.1016/S0140-6736(20)30628-0

[15] Pilotto A, Masciocchi S, Volonghi I, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Encephalitis Is a Cytokine Release Syndrome: Evidences From Cerebrospinal Fluid Analyses. Clin Infect Dis. 2021;73(9):e3019-e3026. https://doi.org/10.1093/cid/ciaa1933

[16] Domingues RB, Leite FBV, Senne C. Cerebrospinal fluid analysis in patients with COVID-19-associated central nervous system manifestations: a systematic review. Arq Neuropsiquiatr. 2022;80(5):430-439. https://doi.org/10.1590/0004-282X-ANP-2021-0117

[17] Michael BD, Bricio-Moreno L, Sorensen EW, et al. Astrocyte- and neuron-derived CXCL1 drives neutrophil transmigration and blood-brain barrier permeability in viral encephalitis. Cell Rep. 2020;32(6):108150. https://doi.org/10.1016/j.celrep.2020.108150

[18] Maiese A, Manetti AC, Bosetti C, et al. SARS-CoV-2 and the brain: a review of the current knowledge on neuropathology in COVID-19. Brain Pathol. 2021;31(6):e13013. https://doi.org/10.1111/bpa.13013

[19] Huet T, Beaussier H, Voisin O, et al. Anakinra for severe forms of COVID-19: a cohort study. Lancet Rheumatol. 2020;2(7):e393–e400. https://doi.org/10.1016/S2665-9913(20)30164-8

[20] Afzali B, Noris M, Lambrecht BN, Kemper C. The state of complement in COVID-19. Nat Rev Immunol. 2022;22(2):77–84. https://doi.org/10.1038/s41577-021-00665-1

[21] The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021;384(8):693–704. https://doi.org/10.1056/NEJMoa2021436

[22] Dotan A, Muller S, Kanduc D, et al. The SARS-CoV-2 as an instrumental trigger of autoimmunity. Autoimmun Rev. 2021;20(4):102792. https://doi.org/10.1016/j.autrev.2021.102792

[23] Kreye J, Reincke SM, Prüss H. Do cross-reactive antibodies cause neuropathology in COVID-19? Nat Rev Immunol. 2020;20(11):645–646. https://doi.org/10.1038/s41577-020-00458-y

[24] Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. Transl Res. 2020;220:1–13. https://doi.org/10.1016/j.trsl.2020.04.007

[25] Gupta M, Weaver DF. COVID-19 as a trigger of brain autoimmunity. ACS Chem Neurosci. 2021;12(14):2558–2561. https://doi.org/10.1021/acschemneuro.1c00403

[26] Vanderheiden A, Klein RS. Neuroinflammation and COVID-19. Curr Opin Neurobiol. 2022;76:102608. https://doi.org/10.1016/j.conb.2022.102608

[27] Alquisiras-Burgos I, Peralta-Arrieta I, Alonso-Palomares LA, et al. Neurological complications associated with the blood-brain barrier damage induced by the inflammatory response during SARS-CoV-2 infection. Mol Neurobiol. 2021;58(9):3842–3855. https://doi.org/10.1007/s12035-020-02134-7

[28] Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol. 2020;77(6):683–690. https://doi.org/10.1001/jamaneurol.2020.1127

[29] Virhammar J, Kumlien E, Fallmar D, et al. Acute necrotizing encephalopathy with SARS-CoV-2 RNA confirmed in cerebrospinal fluid. Neurology. 2020;95(10):445–449. https://doi.org/10.1212/WNL.0000000000010250

[30] Anzalone N, Castellano A, Scotti R, et al. Multifocal laminar cortical brain lesions: a consistent MRI finding in neuro–COVID–19 patients. J Neurol. 2020;267(10):2806–2809. https://doi.org/10.1007/s00415-020-09966-2

[31] Espinosa PS, Rizvi Z, Sharma P, et al. Neurological complications of coronavirus disease (COVID-19): encephalopathy, MRI brain and cerebrospinal fluid findings: case 2. Cureus. 2020;12(5):e7930. https://doi.org/10.7759/cureus.7930

[32] Fischer D, Threlkeld ZD, Bodien YG, et al. Intact brain network function in an unresponsive patient with COVID-19. Ann Neurol. 2020;88(4):851–854. https://doi.org/10.1002/ana.25838

[33] Parsons T, Banks S, Bae C, et al. COVID–19–associated acute disseminated encephalomyelitis (ADEM). J Neurol. 2020;267(10):2799–2802. https://doi.org/10.1007/s00415-020-09951-9

[34] Nordvig AS, Mangala R, Lau JD, et al. Brain fog in long COVID limits function and health status, independently of hospital severity and preexisting conditions. Front Neurol. 2023;14:1150096. https://doi.org/10.3389/fneur.2023.1150096

[35] Junco B, Samano Martin Del Campo D, Karakeshishyan V, et al. Long-term brain fog and cognitive impairment in previously hospitalized COVID-19 patients. PLoS One. 2023;18(6):e0309102. https://doi.org/10.1371/journal.pone.0309102

[36] Lanz-Luces JR, Aceituno H, Quiroz-Bravo F, et al. Long-lasting brain fog is related with severity clusters of symptoms in COVID-19 patients. Rev Med Chil. 2022;150(11):1484. https://doi.org/10.4067/s0034-98872022001101484

[37] Cabett Cipolli G, Alonso V, Yasuda CL, et al. Cognitive impairment in post-acute COVID-19 syndrome: a scoping review. J Neurol Surg A Cent Eur Neurosurg. 2023;84(1):1–10. https://doi.org/10.1055/s-0043-1777115

[38] Khieukhajee J, Rojana-Udomsart A, Srisarakorn P, Wongsurit T, Aungsumart S. Cognitive impairment and risk factors in post-COVID-19 hospitalized patients. Eur Neurol. 2023;86(2):1–6. https://doi.org/10.1159/000531743

[39] Asadi-Pooya AA, Akbari A, Emami A, et al. Long COVID syndrome-associated brain fog. J Med Virol. 2023;95(1):e27404. https://doi.org/10.1002/jmv.27404

[40] Siow I, Lee KS, Zhang JJYZ, Saffari SE, Ng A, Young B. Stroke as a neurological complication of COVID-19: a systematic review and meta-analysis of incidence, outcomes and predictors. J Stroke Cerebrovasc Dis. 2021;30(3):105549. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105549

[41] Syzdoł B, Rzewuska AM, Sielwanowska W, et al. Ischemic stroke in the course of COVID-19 in a 16-year-old boy. J Clin Med. 2023;12(22):6963. https://doi.org/10.3390/jcm12226963

[42] Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. Am J Emerg Med. 2020;38(7):1504–1507. https://doi.org/10.1016/j.ajem.2020.04.048

[43] Pimentel V, Wallau Luchsinger V, Leal Carvalho G, et al. Guillain-Barré syndrome associated with COVID-19: a systematic review. Brain Behav Immun Health. 2022;22:100578. https://doi.org/10.1016/j.bbih.2022.100578

[44] Mahmoud H, Alhathla A, El-Fiky A, et al. Incidence of Guillain-Barré syndrome post COVID-19: a systematic review of case reports and case series. Eur Rev Med Pharmacol Sci. 2023;27(5):2102–2114. https://doi.org/10.26355/eurrev_202303_31588

[45] Chmiela T, Rzepka M, Krzystanek E, Gorzkowska A. A 50-year-old patient with Guillain-Barré syndrome after COVID-19: a case report. Medicina (Kaunas). 2021;57(8):775. https://doi.org/10.3390/medicina57080775

[46] Filosto M, Cotti Piccinelli S, Gazzina S, et al. Guillain-Barré syndrome and COVID-19: a 1-year observational multicenter study. Eur J Neurol. 2022;29(9):2506–2514. https://doi.org/10.1111/ene.15497

[47] Masuccio FG, Tipa V, Invernizzi M, Solaro C. Guillain-Barré syndrome related and unrelated to COVID-19: clinical follow-up in the COVID-19 era. Phys Ther. 2022;102(5):pzac049. https://doi.org/10.1093/ptj/pzac049

[48] García-Molina A, García-Carmona S, Espiña-Bou M, et al. Neuropsychological rehabilitation for post–COVID-19 syndrome: results of a clinical programme and six-month follow up. Neurología (Engl Ed). 2022;37(9):729–737. https://doi.org/10.1016/j.nrleng.2022.06.007

[49] García-Molina A, Espiña-Bou M, Rodríguez-Rajo P, et al. Neuropsychological rehabilitation program for patients with post-COVID-19 syndrome: a clinical experience. Neurología (Engl Ed). 2021;36(8):567–572. https://doi.org/10.1016/j.nrleng.2021.03.003

[50] Mathern R, Senthil P, Vu N, Thiyagarajan T. Neurocognitive rehabilitation in COVID-19 patients: a clinical review. South Med J. 2022;115(3):174–179. https://doi.org/10.14423/SMJ.0000000000001371

[51] Sobrino-Relaño S, Balboa-Bandeira Y, Peña J, et al. Neuropsychological deficits in patients with persistent COVID-19 symptoms: a systematic review and meta-analysis. Sci Rep. 2023;13:12633. https://doi.org/10.1038/s41598-023-37420-6

[52] Łojek E, Egbert AR, Gambin M, et al. Neuropsychological disorders after COVID-19. Urgent need for research and clinical practice. Psychiatr Pol. 2021;55(6):1231–1244. https://doi.org/10.5114/ppn.2021.108474

[53] Frontera JA, Guekht A, Allegri RF, et al. Evaluation and treatment approaches for neurological post-acute sequelae of COVID-19: a consensus statement and scoping review from the global COVID-19 neuro research coalition. J Neurol Sci. 2023;452:120827. https://doi.org/10.1016/j.jns.2023.120827