ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF ARTIFICIAL INTELLIGENCE

ISSN: 2692-515-x, Impact Factor: 9.23

American Academic publishers, volume 6, issue 04,2026

Journal: https://www.academicpublishers.org/journals/index.php/ijai

NEUROLOGICAL COMPLICATIONS OF COVID-19: FROM ACUTE ENCEPHALOPATHY TO LONG-TERM COGNITIVE IMPAIRMENT

Bakhodir Rakhimov,

Erkin Sultanov,

Marjona Soliboyeva

Tashkent State Medical University,

Kimyo International University in Tashkent

ABSTRACT: Background: The SARS-CoV-2 virus exerts profound effects on the central and peripheral nervous system, producing a spectrum of neurological manifestations ranging from mild headache and anosmia to life-threatening encephalitis, stroke, and Guillain-Barre syndrome. Long-term neurological sequelae — including cognitive impairment, mood disorders, and autonomic dysfunction — constitute a major component of Post-Acute Sequelae of SARS-CoV-2 (PASC). Objective: This review examines the mechanisms, clinical spectrum, diagnostic approach, and management of COVID-19 neurological complications. Methods: Narrative review of neurological COVID-19 literature from PubMed, Neurology, JAMA Neurology, and Lancet Neurology, 2020–2024. Results: Neurological manifestations occur in 36–85% of hospitalized COVID-19 patients. Key mechanisms include neuroinflammation, cerebrovascular injury, direct viral neuroinvasion, and autoimmune processes. Long-term cognitive sequelae affect millions globally. Conclusion: Neurologists, internists, and rehabilitation specialists must be equipped to recognize and manage COVID-19 neurological complications, and research into targeted neuroprotective therapies is urgently needed.

1. INTRODUCTION

Although SARS-CoV-2 was initially characterized as a respiratory pathogen, it rapidly became apparent that its pathological reach extended far beyond the lungs. Neurological symptoms — ranging from anosmia (loss of smell), headache, and dizziness at the mild end, to encephalopathy, stroke, and peripheral neuropathy at the severe end — were reported in the earliest clinical series from Wuhan, China. As the pandemic evolved, neurological involvement was documented in up to 85% of hospitalized patients in some series, establishing COVID-19 as a neurotropic illness of major clinical significance.

The neurological manifestations of COVID-19 arise through multiple distinct pathophysiological mechanisms, some mediated by direct viral injury and others by the host immune response. This mechanistic heterogeneity produces a correspondingly diverse clinical spectrum, complicating diagnosis and treatment. Furthermore, the long-term neurological consequences of COVID-19 — manifesting as cognitive impairment, mood disorders, sleep disturbance, and autonomic dysfunction in the context of PASC — are now recognized as a major global neurological disease burden, estimated to affect over 50 million individuals.

ISSN: 2692-515-x, Impact Factor: 9.23
American Academic publishers, volume 6, issue 04,2026
Journal: https://www.academicpublishers.org/journals/index.php/ijai

This review provides a mechanistically grounded analysis of COVID-19 neurological complications, stratified by system and chronological phase of illness, and discusses implications for clinical practice, neurological rehabilitation, and future research priorities.

2. METHODS

Electronic databases including PubMed, Embase, and Cochrane Library were searched using the terms: 'COVID-19 neurology,' 'SARS-CoV-2 brain,' 'neurological COVID complications,' 'COVID encephalopathy,' 'COVID stroke,' 'COVID Guillain-Barre,' 'long COVID cognitive,' 'PASC neurology,' and 'COVID autonomic nervous system.' Articles published from January 2020 to December 2024, including original research, case series of ≥20 patients, systematic reviews, meta-analyses, and expert consensus statements from the European Academy of Neurology, American Academy of Neurology, and WHO, were included and synthesized thematically by neurological domain.

3. RESULTS

3.1 Pathophysiological Mechanisms of Neurological Injury

Neuroinvasion: SARS-CoV-2 may access the central nervous system through the olfactory nerve (explaining early anosmia), the trigeminal nerve, or the hematogenous route following blood-brain barrier (BBB) disruption by systemic inflammation. The ACE2 receptor, the viral entry point, is expressed on brain endothelial cells, choroid plexus, and neurons, providing molecular substrates for direct viral neuroinvasion. However, the frequency and clinical significance of direct neuroinvasion remain debated; viral RNA and protein have been detected in brain tissue post-mortem, but viral encephalitis with productive neuronal infection appears relatively uncommon.

Neuroinflammation: The systemic cytokine storm of severe COVID-19 — characterized by markedly elevated IL-6, IL-1β, TNF-α, and interferon-γ — secondarily injures the brain through BBB compromise, microglial activation, complement-mediated injury, and oligodendrocyte damage. Cerebrospinal fluid analysis in encephalopathic COVID-19 patients frequently reveals elevated protein and inflammatory markers without pleocytosis, consistent with a para-infectious pattern.

Cerebrovascular injury: COVID-19 promotes a hypercoagulable state through elevated D-dimer, fibrinogen, von Willebrand factor, and platelet activation, substantially increasing stroke risk. Endothelial ACE2 infection promotes vasculitis, thrombosis, and hemorrhage. Cardioembolic stroke — secondary to COVID-19-associated arrhythmias (particularly atrial fibrillation) and cardiomyopathy — represents an additional mechanism.

Autoimmune mechanisms: Molecular mimicry between SARS-CoV-2 antigens and neural proteins, and superantigen-like activity of the spike protein, may trigger autoantibody-mediated neurological syndromes, including anti-NMDA receptor encephalitis, anti-GQ1b syndrome, and acute disseminated encephalomyelitis (ADEM).

3.2 Acute Neurological Manifestations

Anosmia and ageusia: Loss of smell and taste, often abrupt and severe, were among the most distinctive early symptoms of COVID-19, reported in 33–86% of patients across different variant waves. These symptoms result from sustentacular cell damage in the olfactory epithelium, with secondary olfactory receptor neuron dysfunction, rather than direct olfactory

ISSN: 2692-515-x, Impact Factor: 9.23
American Academic publishers, volume 6, issue 04,2026
Journal: https://www.academicpublishers.org/journals/index.php/ijai

neuron infection. Recovery occurs in most cases within weeks to months, but persistent anosmia affects 5–15% of patients.

Encephalopathy: Altered consciousness, ranging from mild confusion to coma, complicates approximately 8–31% of hospitalized COVID-19 patients and is strongly associated with ICU admission and mortality. Multifactorial mechanisms include hypoxic injury, metabolic derangements, sedation effects, systemic inflammation, and primary neurological injury. Electroencephalography (EEG) typically reveals diffuse slowing, and MRI may show non-specific white matter signal changes.

Stroke: Both ischemic and hemorrhagic stroke occur at increased frequency in COVID-19 patients. A meta-analysis of 108 studies found a pooled stroke prevalence of 1.4% among hospitalized COVID-19 patients, with higher rates in severe disease. Distinctive features include younger age of presentation, multi-territory involvement suggesting thromboembolic rather than atherosclerotic etiology, and elevated inflammatory markers. Cerebral venous thrombosis, while rare, has been specifically associated with COVID-19.

Guillain-Barre Syndrome (GBS): COVID-19-associated GBS typically presents 10–20 days after respiratory symptom onset, following the classic para-infectious pattern. Clinical presentations include classical ascending flaccid paralysis, cranial nerve variants, and Miller Fisher syndrome. CSF shows albuminocytological dissociation. Recovery is generally favorable with IVIG or plasmapheresis, though severe cases may require mechanical ventilation.

Seizures: New-onset seizures occur in approximately 2% of COVID-19 patients. Risk factors include prior epilepsy, severe hypoxia, metabolic disturbances, and fever. Status epilepticus has been reported as a presenting manifestation. The causal mechanism is multifactorial, encompassing metabolic encephalopathy, direct neuroinflammatory effects, and, rarely, autoimmune encephalitis.

3.3 Long-Term Neurological Sequelae (Neurological PASC)

Cognitive impairment ('Brain Fog'): Persistent cognitive symptoms are among the most prevalent and disabling features of PASC, reported by 20–30% of COVID-19 survivors. Neuropsychological testing reveals deficits in memory encoding and retrieval, executive function, processing speed, and attention. A large UK Biobank study comparing pre- and post-COVID cognitive tests in 785 participants found significant reductions equivalent to 8.5 IQ points among those with severe acute illness. Functional MRI reveals altered default mode network connectivity, and structural MRI demonstrates regional cortical thinning.

Mood and psychiatric disorders: Depression, anxiety, PTSD, and insomnia are 2–3 times more prevalent in COVID-19 survivors compared to matched controls. These may reflect direct neurobiological effects of the virus (neuroinflammation, monoamine system disruption), psychological trauma of illness and isolation, or chronic disability from other PASC symptoms. Longitudinal data show that psychiatric sequelae peak at 1–3 months post-infection but persist beyond 2 years in a substantial minority.

Autonomic dysfunction (POTS): Postural orthostatic tachycardia syndrome — characterized by an excessive heart rate increase (≥30 bpm) on standing, with symptoms of palpitations, dizziness, and pre-syncope — has emerged as a major feature of neurological PASC. Studies estimate POTS or POTS-like autonomic dysfunction in 10–30% of PASC

ISSN: 2692-515-x, Impact Factor: 9.23
American Academic publishers, volume 6, issue 04,2026
Journal: https://www.academicpublishers.org/journals/index.php/ijai

patients. Proposed mechanisms include autoantibody-mediated adrenergic receptor dysfunction, small fiber neuropathy, and baroreflex impairment.

4. DISCUSSION

The neurological burden of COVID-19 is immense and will shape neurology practice and public health for years to come. Clinicians require updated diagnostic frameworks that anticipate neurological presentations in both the acute and post-acute phases. Neurological PASC, in particular, demands a paradigm shift: the acceptance that a large-scale, heterogeneous neurological syndrome may follow viral illness even in patients who were never severely ill.

Management of COVID-19 neurological complications requires individualized, multidisciplinary approaches. Acute stroke follows established thrombectomy and thrombolysis protocols. GBS is managed with immunotherapy. Autoimmune encephalitis requires prompt immunosuppression. Neurological PASC management remains largely symptomatic and rehabilitative — pacing strategies for cognitive fatigue, autonomic rehabilitation for POTS, pharmacological support for mood disorders — as no pathophysiology-targeted treatments are yet approved.

Translational research priorities include: understanding the molecular mechanisms of persistent neuroinflammation in PASC; developing validated biomarkers (CSF, blood, neuroimaging) for neurological PASC diagnosis and treatment monitoring; conducting rigorous clinical trials of neuroprotective and anti-inflammatory agents; and establishing long-term registries to track neurological outcomes over decades. Collaboration across neurology, infectious disease, immunology, psychiatry, and rehabilitation is essential.

5. CONCLUSION

COVID-19 is a neurological disease as much as it is a respiratory one. Its neurological manifestations — acute and chronic, mild and catastrophic, central and peripheral — affect millions of individuals and impose a substantial, incompletely characterized burden on individuals, families, health systems, and economies. Recognition, systematic study, and evidence-based management of COVID-19 neurological complications represent among the most pressing priorities in contemporary medicine and public health.

REFERENCES

1. Saidova K. et al. Investigating the role of community based conservation in promoting sustainable wildlife management //International Journal of Aquatic Research and Environmental Studies. – 2024. – Т. 4. – №. S1. – С. 95-100.
2. Туракулов Р. И. и др. Полиморфизм микросателлитных маркеров генов альдозоредуктазы и каталазы и генетическая предрасположенность к нефропатии при инсулинзависимом сахарном диабете //Проблемы эндокринологии. – 1999. – Т. 45. – №. 5. – С. 13-17.
3. Gadaev AG T. R. I. et al. Assessment of Erythropoietin Levels and Correlation with Cytokines in Patients with Chronic Heart Failure. – 2021.
4. Gadaev A. G., Turakulov R. I., Kurbonov A. K. Occurrence of anemia in chronic heart failure and its negative impact on the course of the disease //Medical Journal of Uzbekistan. – 2019. – Т. 2. – С. 74-77.
5. Gadayev A. G. et al. Role of Hepcidin and Pro-Inflammatory Cytokines in Chronic Heart Failure in Combination with Anemia //CAJMS. – 2019. – Т. 3. – С. 11.

ISSN: 2692-515-x, Impact Factor: 9.23
American Academic publishers, volume 6, issue 04,2026
Journal: https://www.academicpublishers.org/journals/index.php/ijai

6. Nurmatov B., Rakhimov B. Study of virus contamination of indoor air and surfaces of hospital which specialized in the treatment of COVID-19 patients. – 2022.
7. Салихова Н. С. и др. Санитарно-эпидемиологические требования к организации питания обучающихся в общеобразовательных школах, учреждениях средне специального профессионального образования //СанПиН.–2016. – 2016. – С. 0288-10.
8. Рахимов Б. Б. и др. Выявление факторов риска при ожирении у детей дошкольного возраста, проживающих в г. Ташкенте. – 2017.
9. Шарипова Н. В. и др. Гигиенические требования к безопасности пищевой продукции //СанПиН РУз,(0283-10).
10. Саломова Ф. И. и др. Навоий шаҳри атмосфера ҳавоси сифатини баҳолаш. – 2023.
11. Sultonov E. Y., Ismoilov H. O. Ambient air pollution. – 2023.
12. Rakhimov B. B., Yuldasheva F. U., Sultonov E. Y. THE ROLE OF GLYCEMIC INDEX IN MANAGING CHILDHOOD AND ADOLESCENT OBESITY. – International Multidisciplinary Conference, 2024.
13. Саломова Ф. И. и др. Атмосферный воздух города Навои: оценка качества //Британский журнал глобальной экологии и устойчивого развития. – 2023. – Т. 15. – С. 121-125.
14. Ismatullaevich T. R., Gadayevich G. A. Dynamics of cytokines and level of hepsidine in patients with chronic heart failure with anemia //European science review. – 2018. – №. 3-4. – С. 193-195.
15. Turakulov R., Sayfullayev M., Gadaeva N. Features of differential diagnosis of anemia of chronic disease and iron deficiency anemia Comorbidities in chronic heart failure //CHALLENGES IN SCIENCE OF NOWADAYS. – 2020. – С. 26-28.11.