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SARS-COV-2 AND NEURODEGENERATIVE DISEASE PROGRESSION: EXPLORING THE LINK BETWEEN VIRAL INFECTION AND NEUROLOGICAL DECLINE

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ABSTRACT

Purpose: The COVID-19 pandemic caused by SARS-CoV-2, has highlighted its systemic impact including long-term neurological consequences. Beyond acute symptoms such as encephalopathy and anosmia, evidence increasingly links SARS-CoV-2 infection to accelerated or aggravated neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), and Alzheimer's disease (AD). These disorders share pathological hallmarks such as chronic neuroinflammation, misfolded protein aggregation, and progressive neuronal loss. This review aims to elucidate the molecular mechanisms, clinical evidence, and epidemiological trends underlying the intersection between SARS-CoV-2 and neurodegeneration.

Key words: SARS Co V2, Neurodegeneration, Neuroinflamation, Protein aggregation, Alzemier disease, Parkinson disease

Methods: Studies on molecular pathways, neuroimaging results, biomarker studies, and epidemiological data connecting COVID-19 to neurodegenerative diseases were all included in the inclusion criteria. The main processes of interest included mitochondrial malfunction, cytokine-mediated neuroinflammation, hypoxia-induced neuronal death, and disruption of the blood-brain barrier (BBB).

Results: Results show a consistent correlation between SARS-CoV-2 infection and increased risk for cognitive decline and the advancement of neurodegenerative diseases. There were frequent reports of elevated pro-inflammatory cytokines, mitochondrial damage, and BBB permeability. According to MRI studies, COVID-19 survivors exhibit structural changes in their brains, especially in areas related to memory and motor control. After infection, biomarker investigations show elevated levels of tau phosphorylation, α-synuclein aggregation, and neurofilament light chain.

Conclusions: SARS-CoV-2 may exacerbate neurodegenerative processes through intertwined inflammatory, metabolic, and vascular mechanisms. Recognizing these links underscores the urgent need for longitudinal studies, early screening strategies, and targeted neuroprotective interventions. Understanding these pathways will inform future therapeutic and preventive measures to mitigate the neurological burden of COVID-19.

1 INTRODUCTION

COVID-19, primarily known for its respiratory complications is increasingly recognized for its systemic nature and neurological impacts (1). Early reports of symptoms such as anosmia (loss of smell) and ageusia (loss of taste) highlighted the neurotropic potential of SARS-CoV-2 (2). Subsequent studies have linked the virus to more severe neurological outcomes including encephalitis, cerebrovascular complications, and Guillain-Barré syndrome. The virus ability to infiltrate the central nervous system (CNS) and its systemic inflammatory effects have positioned it as a potential accelerant for neurological disorders (3). More recently, attention has shifted to long-term neurological sequelae such as brain fog, memory impairments, and cognitive deficits collectively termed "long COVID". These symptoms highlight the need to look into the wider effects of SARS-CoV-2 on the neurological system and may be signs of ongoing or chronic CNS damage (4). This paradigm shift in understanding the neurological dimensions of COVID-19 is critical as it redefines the virus's systemic burden particularly in populations already sensitivity to neurological diseases (5).

Neurodegenerative diseases such as PD, AD, and ALS represent significant public health challenges due to their increasing prevalence and lack of curative treatments. These diseases are characterized by overlapping mechanisms including neuroinflammation, oxidative stress, protein aggregation, and neuronal death (6) (7). SARS-CoV-2 infection can potentially activate or exacerbate these pathways accelerating disease onset or progression. For instance, neuroinflammation, a hallmark of neurodegeneration, is amplified during the cytokine storm triggered by severe COVID-19 (8). Similarly, mitochondrial dysfunction and oxidative stress induced by the virus align closely with mechanisms implicated in PD and ALS. The recognition of these parallels raises urgent questions about whether COVID-19 could serve as a precipitating factor in individuals predisposed to neurodegenerative conditions (9). Furthermore, the demographic overlap between populations most affected by severe COVID-19 and those at risk for neurodegeneration older adults and those with comorbidities emphasizes the importance of understanding these connections. Unraveling the

relationship between SARS-CoV-2 and neurodegenerative diseases is critical for developing preventative and therapeutic strategies tailored to these vulnerable populations (10).

2. Neurological Manifestations of SARS-CoV-2

2.1 Acute Neurological Complications

Numerous acute neurological symptoms have been associated with SARS-CoV-2 because of its capacity to affect both the central and peripheral nervous systems. Headache, Diziness, and disorientation were some of the most frequently reported neurological manifestations in the early stages of the epidemic (11). These are thought to stem from systemic inflammation and hypoxia rather than direct viral effects on the brain. A more severe manifestation includes encephalopathy characterized by altered mental states ranging from mild confusion to severe delirium. Cases of encephalitis, a direct viral invasion or an immune-mediated process have also been documented, albeit less frequently (12).

Another critical complication is COVID-19 associated hypercoagulability, which predisposes individuals to thrombotic events such as ischemic strokes. Notably, large-vessel occlusions have been observed in younger patients without pre-existing conditions raising concerns about the virus's impact on the vascular system (13). Additionally, peripheral nervous system complications including Guillain-Barré syndrome (GBS), suggest immune mediated damage to peripheral nerves triggered by viral exposure. These acute manifestations highlight the virus's multifaceted impact on neurological health and provide a foundation for investigating its long-term effects on brain function and disease (14).

2.2 Long-Term Neurological Sequelae

Beyond acute complications, a growing subset of COVID-19 survivors report lingering neurological symptoms collectively termed "long COVID" or post-acute sequelae of SARS-CoV-2 infection (PASC) (15). Neurological manifestations in long COVID are diverse including persistent fatigue, cognitive impairment (commonly referred to as "brain fog"), memory loss, and chronic headaches. These symptoms are particularly concerning because they affect individuals who experienced mild or moderate initial infections, suggesting that the neurological impacts of SARS-CoV-2 extend beyond the severity of acute illness (16).

Neuroimaging studies in long COVID patients reveal significant structural and functional changes in the brain including reduced gray matter volume in regions involved in memory, attention, and executive function. Chronic neuroinflammation, persistent viral reservoirs, and immune dysregulation have been proposed as underlying mechanisms for these changes (17). Additionally, long COVID patients often report persistent neuropathic pain and dysautonomia, further complicating their recovery. The recognition of long COVID as a syndrome with potentially debilitating neurological sequelae underscores the need for long-term monitoring and targeted interventions to mitigate its impact on survivor's quality of life (18).

2.3 Emerging Concerns

Emerging evidence suggests that even asymptomatic or mild cases of COVID-19 may carry a risk of long-term neurological changes. For instance, studies have documented micro vascular changes and subtle neurocognitive impairments in individuals who were not hospitalized for COVID-19. This raises concerns about a potential silent neurological burden that may manifest over time. Additionally, epidemiological studies indicate an increased incidence of mood disorders, such as depression and anxiety, among COVID-19 survivors suggesting a broader neuropsychiatric impact of the virus (19).

Another alarming trend is the association between COVID-19 and accelerated cognitive decline in older adults particularly those with pre-existing cognitive impairments. Some researchers have likened the virus long-term effects to a "second hit" in individuals already predisposed to neurodegeneration, potentially triggering or hastening the onset of diseases like Alzheimer's or Parkinson's (20). These findings underscore the importance of proactive neurological screening in COVID-19 survivors, even those with mild disease to identify early signs of neurodegeneration and implement timely interventions (21) (22).

3. Pathophysiology Linking SARS-CoV-2 to Neurodegeneration

3.1 Neuroinflammation and Cytokine storm

A hallmark of severe COVID-19 is the "cytokine storm" a hyper inflammatory state characterized by excessive release of pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1β. This systemic inflammation extends to the central nervous system (CNS), where it activates microglia the brain's resident immune cells. Once activated, microglia release neurotoxic substances including reactive oxygen species (ROS) and pro-inflammatory cytokines leading to neuronal damage and synaptic dysfunction (23). Chronic microglial activation has long been implicated in the pathogenesis of neurodegenerative diseases including Alzheimer's and Parkinson's. In the context of COVID-19, prolonged neuroinflammation could serve as a catalyst for these processes driving the accumulation of misfolded proteins and exacerbating neuronal loss (24) (25) . Additionally, the systemic nature of the cytokine storm means that peripheral immune cells can infiltrate the CNS, further amplifying the inflammatory response. This cascade of events not only damages existing neurons but also impairs neurogenesis, the brain's ability to regenerate and repair itself, potentially accelerating the progression of neurodegenerative diseases (26) (27).

3.2 ACE2 Receptor Expression in the Brain

The ACE2 receptor, critical for SARS-CoV-2 entry into host cells is expressed in various brain regions including neurons, astrocytes, and endothelial cells of the blood-brain barrier (BBB). This expression allows the virus to directly invade the CNS, leading to localized neuronal dysfunction and inflammation (28). Once inside the brain, the virus disrupts the renin-angiotensin system which is crucial for maintaining vascular tone and cerebral blood flow. Dysregulation of this system can lead to oxidative stress, inflammation, and neurovascular damage, all of which are implicated in neurodegenerative processes (29). Moreover, ACE2 downregulation caused by viral binding reduces the brain's ability to counteract angiotensin II-mediated oxidative stress and inflammation creating a pro-inflammatory environment conducive to neuronal injury (30). This dual role of ACE2 as both the viral entry point and a critical regulator of CNS homeostasis highlights its importance in understanding the neurological impacts of COVID-19. The virus's ability to exploit this receptor underscores the need for targeted therapeutic strategies to mitigate ACE2-related neuronal damage (31).

3.3 Blood Brain Barrier (BBB) Disruption

The BBB plays a vital role in protecting the brain from harmful substances and pathogens. In severe COVID-19 cases, systemic inflammation and elevated cytokine levels weaken BBB integrity allowing peripheral immune cells, viral particles, and neurotoxic substances to enter the CNS. Disruption of the BBB has been documented in autopsy studies of COVID-19 patients, with evidence of perivascular inflammation and endothelial damage (32) (33).

The BBB's inability to regulate the brain microenvironment contributes to neuroinflammation and neuronal damage. This breach may also facilitate the entry of amyloid beta peptides and other misfolded proteins into the brain accelerating the pathology of diseases like Alzheimer's (34). Furthermore, BBB disruption exposes neurons to peripheral toxins and immune mediators, creating a toxic environment that exacerbates oxidative stress and neurodegeneration (35). Addressing BBB integrity is thus a critical component of strategies to mitigate the neurological impacts of COVID-19 and prevent long-term damage (36).

3.4 Mitochondrial Dysfunction and Oxidative Stress

Mitochondria play a pivotal role in neuronal health by supplying energy for synaptic function regulating calcium homeostasis and controlling reactive oxygen species (ROS) production (37). SARS-CoV-2 infection disrupts mitochondrial function through direct and indirect mechanisms. Viral proteins such as ORF3c, interact with mitochondrial antiviral signaling (MAVS) proteins, impairing their role in immune signaling and leading to increased oxidative stress. Excessive ROS production, in turn damages cellular structures including lipids, proteins, and DNA, contributing to neuronal death (38) (39) (Table. 1). Mitochondrial dysfunction has long been implicated in neurodegenerative diseases like Alzheimer's and Parkinson's (40). The oxidative environment created by SARS-CoV-2 may exacerbate existing susceptibility in these diseases accelerating the aggregation of misfolded proteins, such as amyloid-beta and alpha-synuclein (41). Additionally, mitochondrial dysfunction impairs the energy supply needed for neurogenesis and synaptic plasticity, further compounding neuronal damage (42). Studies in COVID-19 patients have revealed biomarkers of mitochondrial stress such as increased lactate levels and altered mitochondrial DNA levels in plasma, providing evidence of systemic mitochondrial disruption. Understanding these mechanisms is critical for developing therapies that target mitochondrial health to prevent long-term neurodegenerative outcomes in COVID-19 survivors (43).

Table 1. Overview of key mechanisms linking SARS-CoV-2 infection to neurodegenerative diseases. Mechanisms include cytokine-driven neuroinflammation, mitochondrial dysfunction, blood-brain barrier (BBB) disruption, hypoxia, and ACE2 receptor-mediated damage. These pathways exacerbate neuronal injury, oxidative stress, and protein misfolding, contributing to the onset or progression of conditions like Alzheimer's and Parkinson's disease. References indicate supporting evidence from current literature.

Mechanism	Description	Neurodegenerative Relevance	References
Neuroinflammation	Cytokine storm and chronic microglial activation leading to neuronal damage	Found in Alzheimer's, Parkinson's; drives protein aggregation	[21], [22]
Mitochondrial Dysfunction	SARS-CoV-2 disrupts mitochondrial metabolism, increasing oxidative stress	Accelerates misfolded protein aggregation (e.g., tau, amyloid-beta)	[33], [35]
Blood-Brain Barrier (BBB) Disruption	Allows entry of peripheral toxins and immune mediators into CNS, causing neuroinflammation	Accelerates neuronal injury and facilitates amyloid beta entry	[28], [30]
Hypoxia	Oxygen deprivation activates excitotoxic pathways and neuronal death	Amplifies oxidative stress, increasing Alzheimer's pathology	[39], [41]
ACE2 Receptor Activity	Virus binding dysregulates CNS homeostasis, leading to oxidative and inflammatory damage	Contributes to neurovascular dysfunction and neuronal injury	[24], [25]

3.5 Hypoxia and Neuronal Damage

Hypoxia is a common complication in severe COVID-19, driven by respiratory failure micro vascular thrombosis, and impaired oxygen delivery to tissues. The brain is particularly sensitive to hypoxic conditions, with prolonged oxygen deprivation causing neuronal injury and death. Hypoxia induced damage occurs through multiple mechanisms including excitotoxicity, oxidative stress, and mitochondrial dysfunction (44). During hypoxia, neurons release excessive amounts of glutamate an excitatory neurotransmitter that triggers calcium influx into cells. This excitotoxicity activates enzymes that damage cellular structures leading to neuronal apoptosis (45). Moreover, hypoxia stabilizes hypoxia-inducible factor 1-alpha (HIF-1α), a transcription factor that alters gene expression and contributes to inflammation and vascular dysfunction. Chronic hypoxia also disrupts the clearance of amyloid-beta by glymphatic pathways, increasing its accumulation in the brain and accelerating Alzheimer's pathology (46). The interplay between hypoxia and neurodegeneration is particularly concerning in older COVID-19 patients or those with pre-existing cerebrovascular conditions. Hypoxia driven neuronal damage may act as a second hit worsening cognitive decline or initiating neurodegenerative processes (47). Addressing hypoxia in the acute phase of COVID-19 and understanding its long-term neurological consequences are critical for protecting brain health in affected individuals (48).

4 Clinical Evidence Linking COVID-19 and Neurodegeneration

4.1 Epidemiological Trends

Epidemiological studies have highlighted an increased risk of neurodegenerative diseases in COVID-19 survivors. Cohort studies reveal a higher incidence of Alzheimer's, Parkinson's, and other cognitive disorders in individuals who experienced severe COVID-19, particularly in older adults (49) (Table. 2). For example, a large-scale study conducted in 2022 found that older adults hospitalized with COVID-19 had a 50% higher risk of developing dementia within one year compared to uninfected individuals. These findings suggest that SARS-CoV-2 may act as a catalyst for neurodegenerative processes, particularly in vulnerable populations (50). Notably, individuals with pre-existing conditions such as hypertension, diabetes, and cardiovascular disease factors that overlap with both COVID-19 severity and neurodegenerative risk may be disproportionately affected (51). Furthermore, longitudinal studies indicate that cognitive decline may occur even in those who experienced mild COVID-19, raising concerns about a potential silent epidemic of neurodegeneration in the aftermath of the pandemic (52). These trends underscore the need for routine neurological assessments in COVID-19 survivors to identify early signs of neurodegenerative diseases and implement preventive measures (53).

Table 2. Key findings on the link between COVID-19 and neurodegenerative diseases, highlighting epidemiological trends, biomarkers, therapeutic strategies, and future research directions, with corresponding references to support each section's insights and implications.

Section	Key Points	References
4.1 Epidemiological Trends	COVID-19 survivors face an increased risk of neurodegenerative diseases such as Alzheimer's and Parkinson's. Underlying health issues may exacerbate risks.	[44],[48]
4.2 Biomarkers of Neurodegeneration in COVID-19	Biomarkers like NfL, tau protein, amyloid-beta, and inflammatory markers indicate neurodegeneration linked to SARS-CoV-2.	[49],[54]
5.1 Targeting Neuroinflammation and Oxidative Stress	Anti-inflammatory agents and antioxidants may mitigate neuroinflammation and oxidative stress. Experimental therapies targeting mitochondrial function are promising.	[55],[58]
5.2 Restoring Blood-Brain Barrier Integrity	BBB integrity can be preserved using MMP inhibitors, VEGF inhibitors, and emerging nanoparticle-based drug delivery systems.	[59],[61]
5.3 Cognitive Rehabilitation and Support for Survivors	Rehabilitation programs focusing on cognitive exercises, memory training, and neurostimulation (e.g., TMS, tDCS) can help survivors recover cognitive functions.	[62],[66]
5.4 Vaccination and Preventive Strategies	Vaccination reduces severe COVID-19 cases and long-term neurological impacts. Healthy lifestyle habits enhance resilience against neurodegeneration.	[68],[71]
6.1 Understanding Molecular Mechanisms	Research needed to explore pathways linking SARS-CoV-2 to neurodegeneration, focusing on inflammation, BBB disruption, and mitochondrial dysfunction.	[72],[74]

6.2 Longitudinal Studies and Epidemiology	Long-term studies tracking neurodegenerative trajectories in COVID-19 survivors are essential. Comparative analyses with other viral infections are needed.	[75],[77]
6.3 Development of Novel Therapeutics	Drug repurposing and novel therapies targeting neuroinflammation, BBB integrity, and mitochondrial health are critical. Natural products and nanomedicine show promise.	[78],[80]

4.2 Biomarkers of Neurodegeneration in COVID-19

Emerging biomarker studies provide molecular evidence linking SARS-CoV-2 infection to neurodegenerative processes (54). Elevated levels of neurofilament light chain (NfL), a marker of neuronal damage have been detected in the cerebrospinal fluid (CSF) and plasma of COVID-19 patients, particularly those with severe neurological symptoms (55). Similarly, increased levels of tau protein and amyloid-beta have been observed, suggesting an acceleration of Alzheimer's like pathology in some patients (56). Inflammatory markers such as IL-6, TNF-α, and C-reactive protein remain elevated in many COVID-19 survivors, reflecting ongoing systemic and neuroinflammation (57). Additionally, alterations in cerebrospinal fluid composition including increased protein levels and the presence of autoantibodies indicate BBB dysfunction and potential autoimmune mechanisms contributing to neuronal injury (58). These biomarkers not only provide insights into the pathophysiological mechanisms at play but also offer potential targets for early detection and therapeutic intervention in neurodegenerative diseases associated with COVID-19 (59). (Figure.1)

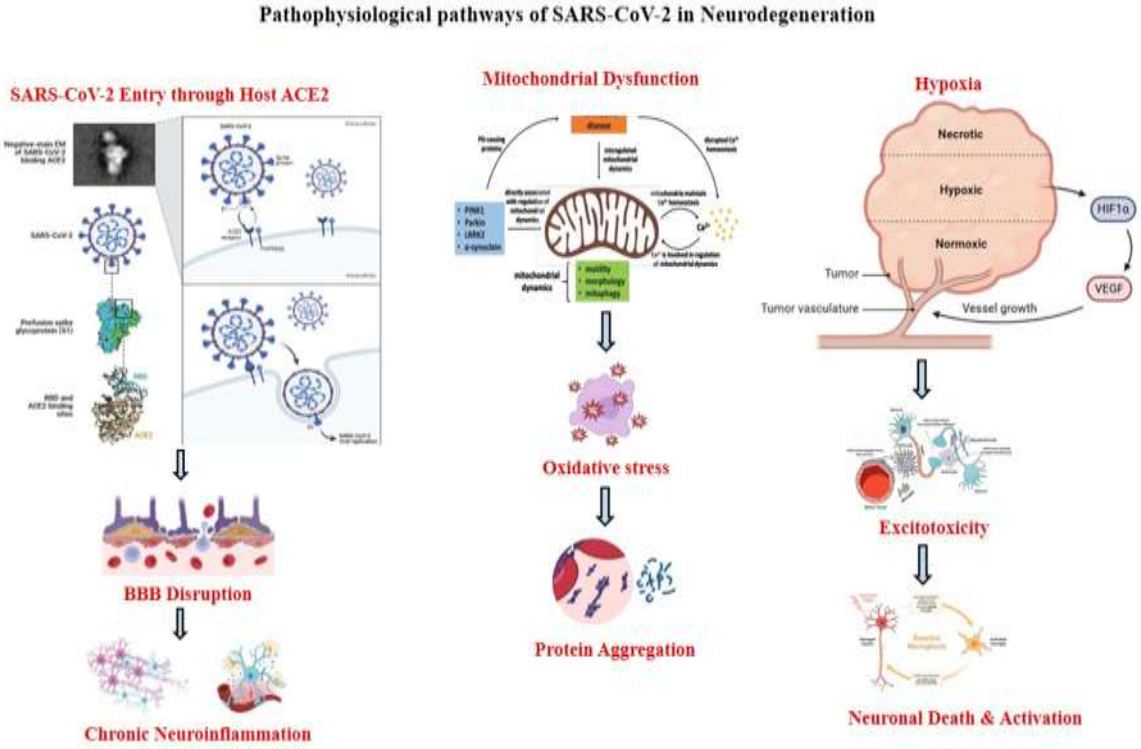

Figure. 1. Pathways illustrating the connection between SARS-CoV-2 infection and neurodegeneration. It starts with SARS-CoV-2 entering the central nervous system (CNS) via ACE2 receptors expressed on neurons, astrocytes, and the blood-brain barrier (BBB). This entry triggers neuroinflammation, marked by microglial activation and cytokine storm, leading to neuronal damage. Concurrently, mitochondrial dysfunction increases oxidative stress, which accelerates protein aggregation, including amyloid-beta and tau, key in Alzheimer's pathology. Disruption of the BBB permits neurotoxic molecules and peripheral immune cells into the CNS, amplifying inflammation and oxidative damage. Hypoxia, a common complication in severe COVID-19 cases, worsens neuronal injury through excitotoxicity and impaired glymphatic clearance of amyloid-beta. Together, these mechanisms form a cascade that links SARS-CoV-2 infection to accelerated neurodegenerative processes.

5 Therapeutic Strategies and Future Directions

5.1 Targeting Neuroinflammation and Oxidative Stress

One promising approach for mitigating the neurological impacts of COVID-19 involves targeting neuroinflammation. Anti-inflammatory agents such as corticosteroids and IL-6 inhibitors, have shown efficacy in reducing cytokine levels in severe COVID-19 cases. However, their role in long-term neuroinflammation remains under investigation. In addition, antioxidants like N-acetyl cysteine (NAC) and coenzyme Q10 could mitigate oxidative stress protecting neurons from further damage (60) (61). Experimental therapies targeting microglial activation receptors antagonists, may also prove beneficial in reducing neuroinflammation. Similarly, mitochondrial targeted treatments including mitochondrial uncouplers and antioxidants, could restore mitochondrial function and prevent neuronal apoptosis (62). These therapeutic

strategies emphasize the need for interventions that go beyond acute COVID-19 management to address the long-term neurological sequelae of the disease (63) (64).

5.2 Restoring Blood-Brain Barrier Integrity

Preserving BBB integrity is a critical goal in preventing neurodegenerative outcomes in COVID-19 survivors. Potential therapies include matrix metalloproteinase (MMP) inhibitors, which prevent BBB degradation, and vascular endothelial growth factor (VEGF) inhibitors, which reduce vascular permeability (65). Additionally, drugs like minocycline which exhibit anti-inflammatory and neuroprotective properties may help restore BBB function while mitigating neuroinflammation (66). Emerging nanomedicine approaches such as nanoparticle-based drug delivery systems, offer promising solutions for delivering neuroprotective agents directly to the brain. By targeting the BBB more effectively, these strategies could reduce systemic side effects and enhance therapeutic efficacy. Such innovations highlight the importance of a multidisciplinary approach to addressing the complex neurological challenges posed by SARS-CoV-2 (67).

5.3 Cognitive Rehabilitation and Support for Survivors

For individuals experiencing persistent cognitive and neurological impairments following COVID-19, cognitive rehabilitation programs are becoming a cornerstone of post-acute care. These programs include tailored cognitive exercises, memory training, and occupational therapy aimed at improving cognitive function and compensating for deficits in executive functioning, memory, and attention (68).

Pharmacological interventions such as acetyl cholinesterase inhibitors (used in Alzheimer's disease) are being explored as potential treatments to alleviate cognitive symptoms in long COVID patients (69). Furthermore, neurostimulation techniques, including transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) have shown promise in enhancing neural plasticity and improving cognitive outcomes in preliminary studies (70) (71). Beyond therapeutic interventions, patient support systems play an essential role in managing long-term neurological sequelae. Mental health support for anxiety, depression, and other neuropsychiatric symptoms is critical as these conditions often compound cognitive impairments (72). Integrating telemedicine into post-COVID care models can also improve access to specialized neurological and rehabilitative services for affected individuals. The development of multidisciplinary care frameworks that combine neurological, psychological, and rehabilitative expertise will be vital in addressing the broad spectrum of neurological challenges posed by SARS-CoV-2 (73).

5.4 Vaccination and Preventive Strategies

Vaccination against SARS-CoV-2 remains a critical strategy for mitigating both acute and long-term neurological effects of the virus. By reducing the severity of infection and associated systemic inflammation, vaccines indirectly protect against neuroinflammatory cascades and other factors that contribute to neurodegeneration (74). Several studies have demonstrated that vaccinated individuals are less likely to experience severe neurological complications or develop long COVID, underscoring the protective effects of immunization (75). Beyond vaccination, public health initiatives focusing on early detection and management of COVID-19 in high-risk populations including older adults and individuals with pre-existing neurological conditions are crucial. Screening for neurological symptoms during and after COVID-19 can enable early intervention reducing the risk of long-term complications (76). Additionally, promoting healthy lifestyle habits such as regular exercise, balanced nutrition, and cognitive engagement may enhance brain resilience and mitigate the risk of neurodegenerative disease progression in COVID-19 survivors (77).

6 Future Research Directions

6.1 Understanding Molecular Mechanisms

A deeper understanding of the molecular mechanisms linking SARS-CoV-2 to neurodegeneration is essential for developing targeted therapies. Future research should focus on identifying the specific pathways through which viral proteins interact with host neuronal and glial cells (78). Studies investigating the role of chronic neuroinflammation, mitochondrial dysfunction, and BBB disruption in the long-term neurological effects of COVID-19 are particularly needed (79). Furthermore, the role of genetic and epigenetic factors in modulating individual susceptibility to neurodegenerative outcomes following COVID-19 remains largely unexplored. For instance, the presence of APOE4, a genetic risk factor for Alzheimer's disease, may exacerbate neuroinflammatory responses in COVID-19 patients. Similarly, understanding the impact of SARS-CoV-2 on brain transcriptomics and proteomics could uncover biomarkers for early detection and therapeutic targeting of neurodegeneration (80).

6.2 Longitudinal Studies and Epidemiology

Longitudinal studies tracking the neurological health of COVID-19 survivors over several years are critical for understanding the long-term trajectory of SARS-CoV-2-associated neurodegeneration (81). Such studies should assess cognitive function, neuroimaging markers, and bimolecular changes in survivors across different age groups and disease severities. Large scale epidemiological research will also help determine whether COVID-19 increases the lifetime risk of developing neurodegenerative diseases and identify subgroups most at risk (82). In addition, comparative studies between COVID-19 and other viral infections such as influenza and other coronaviruses can provide insights into the unique neurological impacts of SARS-CoV-2. These efforts will contribute to a broader understanding of post-viral neurological syndromes and guide strategies for managing similar challenges in future pandemics (83).

6.3 Development of Novel Therapeutics

The urgent need for effective treatments targeting the neurological impacts of COVID-19 has spurred interest in repurposing existing drugs and developing novel therapeutics. Future research should prioritize the identification of drugs that can modulate neuroinflammation, restore mitochondrial function, and protect BBB integrity. High-throughput screening methods and advanced drug discovery platforms, including AI-driven approaches, can accelerate the development of such therapeutics (84) (85). Additionally, the exploration of neuroprotective agents derived from natural products, such as polyphenols and marine-derived bio actives, represents a promising avenue. Combining these approaches with emerging technologies, such as gene therapy and nanomedicine, could pave the way for innovative solutions to mitigate the neurological consequences of COVID-19 (86).

7 CONCLUSION

The COVID-19 pandemic has revealed the complex interplay between viral infections and neurological health highlighting SARS-CoV-2's potential to contribute to neurodegenerative processes. Through mechanisms such as neuroinflammation, mitochondrial dysfunction, and BBB disruption, the virus appears to accelerate or initiate pathways associated with diseases like Alzheimer's and Parkinson's. The long-term neurological impacts of SARS-CoV-2, particularly in the context of long COVID, underscore the need for sustained research and clinical attention. Addressing these challenges requires a multidisciplinary approach, combining advances in molecular neuroscience, epidemiology, and therapeutic development. Preventive strategies, including vaccination and early intervention, remain critical for mitigating the neurological burden of COVID-19. As we move forward, the lessons learned from this pandemic will not only enhance our understanding of post-viral neurological syndromes but also inform strategies for addressing future global health challenges. Ultimately, integrating clinical care with cutting-edge research will be key to protecting brain health in the wake of COVID-19 and beyond.

Ethical Approval and Consent to participate

Not required.

Human Ethics

Not Applicable

Availability of supporting data

The data supporting the findings of this study are available from the all authors request. All relevant data are included within the article and its supplementary materials.

Competing interests

The authors declare no competing interests.

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Declarations

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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