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PERSPECTIVE

The chronic neuropsychiatric sequelae of COVID-19: The need for a prospective study of viral impact on brain functioning

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Abstract

Introduction: The increasing evidence of SARS-CoV-2 impact on the central nervous system (CNS) raises key questions on its impact for risk of later life cognitive decline, Alzheimer's disease (AD), and other dementia.

Methods: The Alzheimer's Association and representatives from more than 30 countries—with technical guidance from the World Health Organization—have formed an international consortium to study the short-and long-term consequences of SARS-CoV-2 on the CNS—including the underlying biology that may contribute to AD and other dementias. This consortium will link teams from around the world covering more than 22 million COVID-19 cases to enroll two groups of individuals including people with disease, to be evaluated for follow-up evaluations at 6, 9, and 18 months, and people who are already enrolled in existing international research studies to add additional measures and markers of their underlying biology.

Conclusions: The increasing evidence and understanding of SARS-CoV-2's impact on the CNS raises key questions on the impact for risk of later life cognitive decline, AD, and other dementia. This program of studies aims to better understand the long-term consequences that may impact the brain, cognition, and functioning—including the underlying biology that may contribute to AD and other dementias.

KEYWORDS
cognitive decline, COVID-19, neuropsychiatry, SARS-CoV-2

1 | INTRODUCTION

The number is constantly changing, but it seems likely that by the time the pandemic spends its force about one in every 200 persons worldwide will have suffered an infection by the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Most of these individuals will survive the infection, but the public health impact of the pandemic may continue as chronic sequelae of coronavirus disease (COVID-19), resulting in disability or diminished quality of life, now attracting the term "Longcovid." Judging by what is known so far, long-term sequelae are not just likely to occur, but also likely to affect certain groups of individuals disproportionately; this only further deepens existing health disparities. Given the well-established and projected weight of neuropsychiatric disorders included in the global burden of disability, it seems particularly appropriate to take stock of what is known about the deleterious, direct effects of SARS-CoV-2 infection and COVID-19 on the central nervous system (CNS), and to project how these effects are likely to contribute to the chronic burden of disease globally in coming years. An equally important but separate issue not covered in this article is the wider societal impact of the pandemic due to its likely wider economic, social, and personal effects in the immediate and longer term.

2 | VIRAL IMPACT ON BRAIN FUNCTIONING

Neurotropic respiratory viruses have long been known to result in chronic brain pathology.[1,2] Paradigmatically, the 1918 influenza pandemic was and continues to be suspected as the underlying cause of encephalitis lethargica;[3] emerging movement disorders, profound sleep cycle abnormalities, and psychotic illness resulted in enormous burden of disease and untold suffering for affected individuals and their caregivers. Less spectacular, but perhaps more impactful at the population level, studies have suggested that common viral infections such as herpes simplex virus 1 (HSV1) may be associated with molecular processes in Alzheimer's disease (AD) dementia in human brain cells[4] and transgenic animal models.[5] Several studies have also suggested an association of HSV1 and cognitive decline.[6] Because brain inflammation accompanies the most common neurodegenerative disorders and may contribute to major psychiatric disorders, the neurological and psychiatric sequelae of COVID-19 need to be carefully tracked.[7–14]

RESEARCH IN CONTEXT

Neurotropic respiratory viruses have long been known to result in chronic brain pathology including emerging cognitive decline and dementia, movement disorders, and psychotic illness. Because brain inflammation accompanies the most common neurodegenerative disorders and may contribute to major psychiatric disorders, the neurological and psychiatric sequelae of COVID-19 need to be carefully tracked.

3 | NEUROTROPISM

Coronaviruses, especially β-coronaviruses including SARS-CoV-2, have been shown in several studies to invade the CNS.[7,12,15–17] The CoV spike glycoprotein binds angiotensin-converting enzyme 2 (ACE2) with high affinity,[18,19] and protein cleavage by specific proteases plays a key role in the brain invasion and virulence of earlier human coronavirus, and may play a role in SARS-CoV-2.[20]

SARS-CoV-2 invades respiratory and gastrointestinal epithelial cells by binding ACE2 on the cell membrane; ACE2 is also expressed in the brain, both in neurons and glia. Notably, multiple non-neuronal cell types present in the olfactory epithelium express two host receptors, ACE2 and transmembrane serine protease 2 (TMPRSS2) proteases, that facilitate SARS-CoV-2 binding, replication, and accumulation.[21] Intranasal administration of SARS-CoV-2 in mice results in rapid invasion of the brain,[22,23] and SARS-CoV-1 viral particles can be detected *post mortem* in the cerebrum, but not in the cerebellum, in humans.[24] Entry of SARS-CoV-2 into the cells through membrane fusion markedly downregulates ACE2 receptors, with loss of the catalytic effect of these receptors at the external site of the membrane.[25,26] Vascular growth factor (VEGF), which is widely distributed in the brain, may play a role in brain inflammation via the ACE2 pathway.[27] Clinical reports of patients infected with SARS-CoV-2 show that several features associated with infection and severity of the disease (ie, older age, hypertension, diabetes, cardiovascular disease) share a variable degree of ACE2 deficiency.[25,28–31] In *post mortem* brain tissue, ACE2 is expressed in the frontal cortex vasculature, and viral spike proteins cause blood-brain barrier (BBB) damage in vitro.[32]

SARS-CoV-2 neurotropism is suspected; it is based on growing evidence from clinical, pathological, and molecular studies.[7,11,12,33–47]

First, headache, hypogeusia, and anosmia appear to precede the onset of respiratory symptoms in the majority of affected patients, and ataxia and altered mental status have been documented independent of multiorgan failure.[12,21,38,48–52] There have also been documented cases of acute encephalopathy and meningoencephalitis associated with detection of SARS-CoV-2 RNA in the cerebrospinal fluid (CSF).[7,53–57] SARS-CoV-2 can also be found in the brain *post mortem*.[56] Further, pan-encephalitis and diffuse petechial hemorrhage of the entire brain have been reported,[58] particularly perivascular and interstitial encephalitis in the brain stem,[58,59] in some patients.[60]

In addition, respiratory problems due to SARS-CoV-2 are thought to be due in part to brain-stem dysregulation,[11,12,61–64] as are possibly some of the gastrointestinal symptoms.[65] Neurological symptoms may occur in their first 1 to 2 days of the clinical symptomatic phase, and cerebrovascular accidents are common within 2 weeks of the onset of the symptomatic phase.[51,65–74] While case series of para-infectious or post-infectious acute neuroinflammatory syndromes such as acute disseminated encephalomyelitis (ADEM) are reported in association with SARS-CoV-2 infection,[51,75,76] many patients with COVID-19 on intensive care units (ICUs) have corticospinal tract signs.[44] The absence of SARS-CoV-2 viral load in the CSF and the presence of oligoclonal bands in the CSF and serum of some patients suggest immune-mediated response that is not limited to intrathecal production of immunoglobulins.[8,44,56] Other common neurological manifestations include meningitis and acute demyelinating polyneuropathy.[38,49–51,68,77,78] New onset seizures, sometimes followed by anosmia, have also been reported in SARS-CoV-2–confirmed infections.[12,68,79–83] The mechanisms of causation of seizures are probably complex, and may include cortical irritation due to hemorrhages, inflammation, or metabolic changes.[12,80] Sporadic epileptiform discharges were detected in nearly half of COVID-19 patients in intensive care.[81]

Delirium can be the only presenting symptom of SARS-CoV-2 infection[84–86] even in younger patients.[56] The incidence of delirium in severely ill COVID-19 patients on ICUs is reported to be as high as 84%,[44] of which more than two thirds exhibit hyperactive delirium, despite receiving high sedation and neuroleptics.[44] The overall incidence of delirium across the clinical spectrum from mild to severely ill patients with COVID-19 is unknown. Because many patients with COVID-19 are mechanically ventilated,[87–89] a substantial proportion of patients with COVID-19 are likely to experience delirium with a currently unknown long-term outcome. In elderly patients with

dementia, delirium is a very frequent presenting symptom of SARS-CoV-2 infection[90] and carries a higher short-term mortality rate.[91]

Delirium in COVID-19 may be a feature of primary encephalopathy due to the direct intracerebral viral invasion.[92] Alternatively, secondary encephalopathy may be associated with neuroinflammatory response to SARS-Cov-2;[93,94] immune-mediated systemic response;[8,95,96] or independent complications of hypoxemia, sepsis, hypoperfusion, severe metabolic illness, and pharmacological side effects.

As evidence accumulates regarding viral neuroinvasion, there are several routes for possible transmission, including trans-synaptic transfer across infected neurons in splacnic nerves,[11,12,62,97] entry via the olfactory nerve,[21,98] infection of vascular endothelium, leukocyte migration across the BBB, and/or a conjunctival route.[11,99,100] From the olfactory bulb, SARS-CoV-2 may target the deeper parts of the brain including the thalamus and brain stem by trans-synaptic transfer described for many other viral diseases.[11,101] In some individuals, SARS-CoV-2 infection triggers a massive release of cytokines, chemokines, and other inflammation signals leading to BBB dysfunction, injury to astrocytes, activation of microglia and astrocytes promoting neuroinflammation and neuronal death.[11,62,102–104] Immune response and excessive inflammation in COVID-19 may also accelerate the progression of brain inflammatory neurodegeneration; elderly individuals are more susceptible to severe outcomes after SARS-CoV-2 infection.[105]

Because the entry points of viral invasion into the brain have direct connections to brain stem and thalamic structures, ensuing dysfunction may result in sensorimotor, mental, and behavioral disorders.[11,68,106–108] Indeed, in a case series from the UK acute alteration in personality, behavior, cognition, or consciousness was the second most common presentation of COVID-19, often occurring in younger individuals; nearly half of these individuals had new-onset psychosis, while the rest had neurocognitive (dementia-like) syndrome, or affective disorders.[51] Autoimmune encephalitides associated with antibodies against neuronal cell-surface or synaptic proteins; in those with new-onset psychosis, higher prevalence of antibodies against four other coronaviruses strains have been found,[56] and at least one confirmed case of anti-n-methyl-d-aspartate antibodies encephalitis associated with COVID-19 was reported.[109] Further, reports of individuals presenting with clinical-radiological features of limbic encephalitis and little systemic symptoms of COVID-19[56,110] suggests immune-mediated response to SARS-CoV-2.[109] Taken together, the evidence suggests a possible mechanism for SARS-CoV-2 encephalopathy and psychosis.

4 | BRAIN IMAGING

Abnormal brain imaging has emerged as a major feature of COVID-19 from all parts of the world.[111] Structural brain magnetic resonance imaging (MRI) revealed parenchymal brain abnormalities, subcortical micro- and macro-bleeds, cortico-subcortical edema, nonspecific deep white matter changes, and asymmetric olfactory bulbs *post mortem*,[112] and similar findings during hospital admission.[113–119,94,120] The abnormal imaging has been seen in an individual whose only symptom was anosmia.[121] The most common MRI findings from patients admitted to ICUs include cortical signal abnormalities on fluid-attenuated inversion recovery images, accompanied by cortical diffusion restriction or leptomeningeal enhancement, which may reflect infectious or autoimmune encephalitis, seizures, hypoglycemia, or hypoxia.[122] Acute demyelinating lesions also have been described and have been visualized on images.[76,123–125]

5 | POSSIBLE DETERMINANTS

Different host immune responses to SARS-CoV-2 infection may partially explain why males and females, young and old persons infected with this virus have markedly distinct disease severity.[126] In fact, C-reactive protein[127] and ferritin[128] levels were associated with elevated risk of COVID-19 in a dose-dependent manner, and N-terminal pro-brain natriuretic peptide (NT-proBNP) was associated with increased mortality in COVID-19 pneumonia.[129,130] Concomitant cardiac disease has an extremely poor prognosis, with higher mortality, thromboembolic events, and septic shock rates.[131]

Among hospitalized COVID-19 cases, physical inactivity, smoking, and obesity but not heavy alcohol consumption were related to increased rates of hospital admission.[127] Diabetes mellitus increases risk for dementia as well as of severe outcomes after SARS-CoV-2 infection, and is highly prevalent in certain demographics such as Black American/African Americans and Latino/Hispanic Americans,[105] and the same demographic groups appear to be at higher risk of neurological complications of COVID-19.[132] Disparities in COVID-19 hospitalizations and mortality according to ethnicity remain present, even after correcting for neighborhood, household crowding, smoking, body size, diabetes, and mental illness.[133]

6 | IMPLICATIONS FOR NEUROPSYCHIATRIC DISORDERS

Olfactory deficits have been previously reported for several viral infections,[12,134] and are characteristic of neurodegenerative disorders.[135–139] Notably, anosmia is linked to high levels of interleukin-6, an inflammatory mediator causally involved in brain disorders whose actions are blocked by tocilizumab as part of COVID-19 treatment.[140]

Systematic reviews[141,142] and meta-analysis data[143,144] have firmly established incident and prevalent stroke as independent risk factors of dementia. Likewise, typical risk factors for stroke increase the odds of dementia including coronary heart disease and carotid stenosis,[145] as well as atrial fibrillation,[146] stage 1 midlife hypertension,[147] and hyperhomocysteinemia.[148] Furthermore, MRI features of cerebral small vessel disease, ie, white matter hyperintensities, lacunes, microbleeds, perivascular spaces, and cerebral atrophy were additively associated with dementia and cognitive decline.[149–151] Therefore, it seems likely to expect that COVID-19–related cardiovascular and

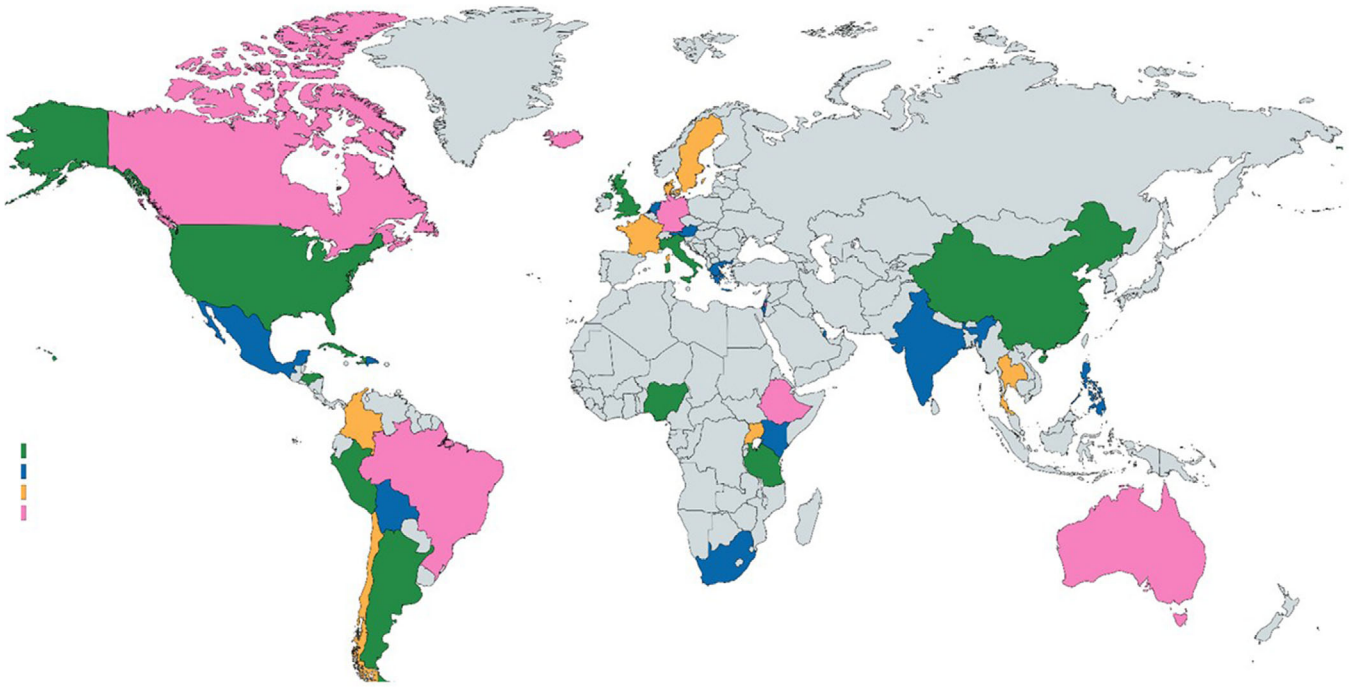

FIGURE 1 Consortium participants. Colored countries in the map represent those with at least one academic institution participating in the Consortium for Chronic Neuropsychiatric Sequelae of SARS-CoV-2

cerebrovascular disease will also contribute to a higher long-term risk of cognitive decline and dementia in recovered individuals.

Multiple lines of evidence suggest that viral infections of the brain may impact a person's risk for AD or Parkinson's disease. The present pandemic provides a unique—if unwelcome—opportunity to test the role of neurotropic viruses in a prospective fashion in individuals that have recovered from COVID-19.[152,153] The mechanisms by which neurological abnormalities result from COVID-19 remains to be fully established. Direct effects of SARS-CoV-2 itself on neuronal function and survival or glial reactivity, exaggerated cytokine responses, or anti-neuronal antibodies are all likely to contribute, as are the sequelae from cerebrovascular accidents. As pointed out above, the experience of pandemics caused by neurotropic respiratory viruses in the past—as well as the emerging data and observations of clinicians over the past several months—strongly supports an expectation of increased neuropsychiatric sequelae, including cognitive decline, motor impairment, and affective and psychotic disorders, in addition to demyelinating processes or cerebrovascular disease that occur during the acute viral infection, or may follow infection in recovered individuals.[154]

7 | PSYCHIATRIC DISORDERS

Psychiatric distress and acquired cognitive deficits after COVID-19 will likely have complex, bidirectional relationships. Impaired cognitive abilities may cause poor occupational and functional outcomes that precipitate or exacerbate mental health concerns, and poor mental health may likewise contribute to cognitive dysfunction.[155] The SARS-CoV-1 epidemic was associated with psychiatric complications. COVID-19 patients found a high level of post-traumatic stress symptoms and significantly higher level of depressive symptoms. Patients with preexisting psychiatric disorders reported worsening of psychiatric symptoms.[156] After the coronavirus pandemics in 2002 and 2012, one in five recovered individuals reported depressed mood, insomnia, anxiety, irritability, fatigue, and in one study traumatic memories and sleep disorder were frequently reported. The meta-analysis indicated that in the post-illness stage the point prevalence of post-traumatic stress disorder was 32.2%, depression was 14.9%, and anxiety disorders was 14.8%.[157]

8 | COGNITIVE DECLINE AND MOTOR IMPAIRMENT

COVID-19 results in high levels of proinflammatory cytokines, acute respiratory distress, and hypoxia, each of which may contribute to cognitive decline both in healthy and in already predisposed individuals.[14,158] After the coronavirus pandemics in 2002 and 2012, one in five recovered individuals reported memory impairment,[157] and an early report found that one in three individuals with COVID-19 had dys-executive syndrome at the time of hospital discharge.[157] Impaired cognitive abilities may cause poor occupational and functional outcomes for individuals recovered from COVID-19 that precipitate or exacerbate mental health concerns, and poor mental health may likewise contribute to cognitive dysfunction.[155]

Influenza epidemics are associated with neurological manifestations, and the H5N1 virus reportedly induces Parkinsonian pathology in mice, both findings possibly explained by the activation of

TABLE 1 COVID-19 cases per country. Numbers represent confirmed cases of COVID-19 in each country at the time of submission

Argentina	565,446
Australia	26,739
Austria	34,305
Bolivia	127,619
Brazil	4,356,690
Canada	138,555
Chile	437,983
China	85,202
Colombia	721,892
Cuba	4726
Denmark	20,571
Dominican Republic	104,110
United Kingdom	41,664
Ethiopia	64,786
Finland	8725
France	387,252
Germany	264,169
Greece	13,730
Haiti	8499
Honduras	68,620
Iceland	2174
India	5,009,290
Israel	162,273
Kenya	36,205
Mexico	671,716
Netherlands	84,778
Nigeria	56,388
Peru	733,860
Philippines	269,407
Qatar	122,214
South Africa	650,749
Spain	603,167
Sweden	87,345
Tanzania	509
Uganda	5123
United States	6,758,987
TOTAL CASES	22,735,468

inflammatory pathways.[159] However, the exact mechanisms of these effects and whether coronaviruses show a similar action remain unclear. About half of hospitalized patients are >55 years; the resulting higher age-related risk of neurodegenerative disorders is a good setting to investigate triggering and double-hit mechanisms previously hypothesized for viral infections.[160] Despite the higher mortality rate, a majority of cases are expected to recover and survive from this viral outbreak. A natural decline in ACE2 expression and the subsequent pro-inflammatory profile with aging may explain the increased severity and comorbid diabetic and hypertensive complications observed in older adults. There are potential long-term implications of SARS-CoV-2 infection in relation to accelerated brain aging, neurovascular coupling, and age-related neurodegenerative disorders.

As described above, coronaviruses can cause demyelination, neurodegeneration, and cellular senescence. SARS-CoV-2 specifically can infect endothelial cells expressing ACE2 potentially leading to further deterioration of this vascular architecture. The resulting hypoperfusion may restrict energy substrates essential for maintaining neuronal networks thereby accelerating cognitive decline in the elderly. Damage to limbic and cortical regions could cause retrograde and anterograde amnesia. As a result of ACE2 downregulation, SARS-CoV-2 infection in older adults induces aggressive secretion of pro-inflammatory cytokines.

Pro-inflammatory cytokines increase oxidative stress that damages cellular membranes and downregulates surface expression of excitatory amino acid transporters that are necessary for terminating glutamatergic signaling. The resulting elevated glutamate levels can lead to an excitotoxic environment precipitating the neuronal loss and initiating a vicious feed-forward cycle that causes further damage to the surrounding parenchyma. Viral entry into neurons may create a cytotoxic insult and initiate apoptotic pathways or create an excitatory–inhibitory imbalance. This pathway is already postulated to play a role in several neurodegenerative diseases including AD and Parkinson's disease. A slow infiltration throughout the CNS may precipitate underlying pathologies associated with age-related neurodegenerative disorders months or years after acute viral infection. The neuroinvasive potential of SARS-CoV-2 may result in senescence of several different CNS cell types including oligodendrocytes, astrocytes, and neural stem cells that can differentiate into neurons that integrate into the granule layer. Viral aggravation of underlying neuropathology has the potential to hasten the onset of or further deteriorate motor and cognitive deficits.[161]

9 | CONCLUSION AND NEXT STEPS

The increasing evidence and understanding of SARS-CoV-2's impact on the CNS raises key questions on the impact for risk of later life cognitive decline, AD, and other dementia. Scientific leaders, including the Alzheimer's Association and representatives from more than 30 countries—with technical guidance from the World Health Organization—have formed an international, multidisciplinary consortium to collect and evaluate the short- and long-term consequences of SARS-CoV-2 on the CNS. This program of studies aims to better understand the long-term consequences that may impact the brain, cognition, and functioning—including the underlying biology that may contribute to AD and other dementias.

This consortium will link study teams from around the world (Figure 1) covering more than 22 million cases at the time of submission (Table 1) to enroll two groups of individuals including people with

confirmed cases of COVID-19 sampled from hospitals that have been discharged to be evaluated for follow-up at 6, 9, and 18 months, and people who are already enrolled in existing international research studies to add additional measures and markers of their underlying biology.

CONFLICTS OF INTEREST

The authors declare no conflict of interest with the work discussed in this article.

REFERENCES

1. Itzhaki RF, Golde TE, Heneka MT, Readhead B. Do infections have a role in the pathogenesis of Alzheimer disease?. *Nat Rev Neurol*. 2020;16(4):193-197.
2. Robinson CP, Busl KM. Neurologic manifestations of severe respiratory viral contagions. *Crit Care Explor*. 2020;2(4):e0107.
3. Foley PB. Encephalitis lethargica and the influenza virus. II. The influenza pandemic of 1918/19 and encephalitis lethargica: epidemiology and symptoms. *J Neural Transm (Vienna)*. 2009;116(10):1295-1308.
4. Cairns DM, Rouleau N, Parker RN, Walsh KG, Gehrke L, Kaplan DL. A 3D human brain-like tissue model of herpes-induced Alzheimer's disease. *Sci Adv*. 2020;6(19):eaay8828.
5. Readhead B, Haure-Mirande JV, Funk CC, et al. Multiscale analysis of independent alzheimer's cohorts finds disruption of molecular, genetic, and clinical networks by human herpesvirus. *Neuron*. 2018;99(1):64-82. e7.
6. Mancuso R, Cabinio M, Agostini S, Baglio F, Clerici M. HSV-1-Specific IgG_3 titers correlate with brain cortical thinning in individuals with mild cognitive impairment and Alzheimer's disease. *Vaccines (Basel)*. 2020;8(2):255.
7. Steardo L, Jr SteardoL, Zorec R, Verkhratsky A. Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19. *Acta Physiol (Oxf)*. 2020;229(3):e13473.
8. Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun*. 2020;87:18-22.
9. Baig AM, Sanders EC. Potential neuroinvasive pathways of SARS-CoV-2: deciphering the spectrum of neurological deficit seen in coronavirus disease-2019 (COVID-19) [published online ahead of print, 2020 Jun 3]. *J Med Virol*. 2020.
10. Aamodt AH, Flinstad Harbo H, Eldøen G, Barratt-Due A, Aukrust P. How does COVID-19 affect the brain?. Hvordan påvirkes hjernen ved covid-19?. *Tidsskr Nor Laegeforen*. 2020;140(10).
11. Mao XY, Jin WL. The COVID-19 pandemic: consideration for brain infection. *Neuroscience*. 2020;437:130-131.
12. Baig AM. Neurological manifestations in COVID-19 caused by SARS-CoV-2. *CNS Neurosci Ther*. 2020;26(5):499-501.
13. Li Z, Huang Y, Guo X. The brain, another potential target organ, needs early protection from SARS-CoV-2 neuroinvasion. *Sci China Life Sci*. 2020;63(5):771-773.
14. Heneka MT, Golenbock D, Latz E, Morgan D, Brown R. Immediate and long-term consequences of COVID-19 infections for the development of neurological disease. *Alzheimers Res Ther*. 2020;12(1):69.
15. Beghi E, Feigin V, Caso V, Santalucia P, Logroscino G. COVID-19 infection and neurological complications: present findings and future predictions [published online ahead of print, 2020 Jul 1]. *Neuroepidemiology*. 2020:1-6.
16. Ng Kee Kwong KC, Mehta PR, Shukla G, Mehta AR. COVID-19, SARS and MERS: a neurological perspective. *J Clin Neurosci*. 2020;77:13-16.
17. De Santis G. SARS-CoV-2: a new virus but a familiar inflammation brain pattern. *Brain Behav Immun*. 2020;87:95-96.
18. Natoli S, Oliveira V, Calabresi P, Maia LF, Pisani A. Does SARS-Cov-2 invade the brain? Translational lessons from animal models [published online ahead of print, 2020 Apr 25]. *Eur J Neurol*. 2020.
19. Zheng M, Song L. Novel antibody epitopes dominate the antigenicity of spike glycoprotein in SARS-CoV-2 compared to SARS-CoV. *Cell Mol Immunol*. 2020;17(5):536-538.
20. Wu Y, Xu X, Yang L, Liu C, Yang C. Nervous system damage after COVID-19 infection: presence or absence?. *Brain Behav Immun*. 2020;87:55.
21. Butowt R, BilinskaK. SARS-CoV-2: olfaction, brain infection, and the urgent need for clinical samples allowing earlier virus detection. *ACS Chem Neurosci*. 2020;11(9):1200-1203.
22. Sun SH, Chen Q, Gu HJ, et al. A mouse model of SARS-CoV-2 infection and pathogenesis. *Cell Host Microbe*. 2020;28(1):124-133. e4.
23. Jiang RD, Liu MQ, Chen Y, et al. Pathogenesis of SARS-CoV-2 in transgenic mice expressing human angiotensin-converting enzyme 2. *Cell*. 2020;182(1):50-58. e8.
24. 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.
25. Verdecchia P, Cavallini C, Spanevello A, Angeli F. The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. *Eur J Intern Med*. 2020;76:14-20.
26. Hess DC, Eldahshan W, Rutkowski E. COVID-19-Related Stroke. *Transl Stroke Res*. 2020;11(3):322-325.
27. Yin XX, Zheng XR, Peng W, Wu ML, Mao XY. Vascular endothelial growth factor (VEGF) as a vital target for brain inflammation during the COVID-19 outbreak. *ACS Chem Neurosci*. 2020;11(12):1704-1705.
28. Choi JY, Lee HK, Park JH, et al. Altered COVID-19 receptor ACE2 expression in a higher risk group for cerebrovascular disease and ischemic stroke. *Biochem Biophys Res Commun*. 2020;528(3):413-419.
29. Xu D, Ma M, Xu Y, et al. Single-cell transcriptome analysis indicates new potential regulation mechanism of ace2 and nps signaling among heart failure patients infected with SARS-CoV-2. *medRxiv*. 2020;2020. https://doi.org/10.1101/2020.04.30.20081257.
30. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study [published correction appears in BMJ. 2020 Mar 31;368:m1295]. *BMJ*. 2020;368:m1091.
31. Bostancıklıoğlu M. SARS-CoV2 entry and spread in the lymphatic drainage system of the brain. *Brain Behav Immun*. 2020;87:122-123.
32. Buzhdygan TP, DeOre BJ, Baldwin-Leclair A, et al. The SARS-CoV-2 spike protein alters barrier function in 2D static and 3D microfluidic in vitro models of the human blood-brain barrier. *Neurobiol Dis*. 2020;146(Dec):105131. https://doi.org/10.1016/j.nbd.2020.105131. Epub 2020 Oct 11. https://pubmed.ncbi.nlm.nih.gov/33053430/; PMCID: PMC7547916.
33. Vavougios GD. Potentially irreversible olfactory and gustatory impairments in COVID-19: indolent vs. fulminant SARS-CoV-2 neuroinfection. *Brain Behav Immun*. 2020;87:107-108.
34. Cheng Q, Yang Y, Gao J. Infectivity of human coronavirus in the brain. *EBioMedicine*. 2020;56:102799.
35. Saleki K, Banazadeh M, Saghazadeh A, Rezaei N. The involvement of the central nervous system in patients with COVID-19. *Rev Neurosci*. 2020;31(4):453-456.
36. Zubair AS, McAlpine LS, Gardin T, Farhadian S, Kuruvilla DE, Spudich S. Neuropathogenesis and neurologic manifestations of the coronaviruses in the age of coronavirus disease 2019: a review. *JAMA Neurol*. 2020;77(8):1018-1027. https://doi.org/10.1001/jamaneurol.2020.2065. https://pubmed.ncbi.nlm.nih.gov/32469387/; PMCID: PMC7484225.
37. Tassorelli C, Mojoli F, Baldanti F, Bruno R, Benazzo M. COVID-19: what if the brain had a role in causing the deaths? *Eur J Neurol*.

2020;27(9):e41-e42. https://doi.org/10.1111/ene.14275. Epub 2020 May 14. https://pubmed.ncbi.nlm.nih.gov/32333819/; PMCID: PMC7267268.

38. Tsai ST, Lu MK, San S, Tsai CH. The neurologic manifestations of coronavirus disease 2019 pandemic: a systemic review. *Front Neurol*. 2020;11:498.
39. Das G, Mukherjee N, Ghosh S. Neurological insights of COVID-19 pandemic. *ACS Chem Neurosci*. 2020;11(9):1206-1209.
40. Wilson MP, Jack AS. Coronavirus disease 2019 (COVID-19) in neurology and neurosurgery: a scoping review of the early literature. *Clin Neurol Neurosurg*. 2020;193:105866.
41. Munhoz RP, Pedroso JL, Nascimento FA, et al. Neurological complications in patients with SARS-CoV-2 infection: a systematic review. *Arq Neuropsiquiatr*. 2020;78(5):290-300.
42. Wadman M, Couzin-Frankel J, Kaiser J, Matacic C. A rampage through the body. *Science*. 2020;368(6489):356-360.
43. Iroegbu JD, Ifenatuoha CW, Ijomone OM. Potential neurological impact of coronaviruses: implications for the novel SARS-CoV-2. *Neurol Sci*. 2020;41(6):1329-1337.
44. Helms J, Kremer S, Merdji H, et al. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med*. 2020;382(23):2268-2270.
45. Conde Cardona G, Quintana Pájaro LD, Quintero Marzola ID, Ramos Villegas Y, Moscote Salazar LR. Neurotropism of SARS-CoV 2: mechanisms and manifestations. *J Neurol Sci*. 2020;412:116824.
46. Sun T, Guan J, You C. The neuroinvasive potential of severe acute respiratory syndrome coronavirus 2. *Brain Behav Immun*. 2020;88:59.
47. Liguori C, Pierantozzi M, Spanetta M, et al. Subjective neurological symptoms frequently occur in patients with SARS-CoV2 infection. *Brain Behav Immun*. 2020;88:11-16.
48. Baig AM. Updates on what acs reported: emerging evidences of COVID-19 with nervous system involvement. *ACS Chem Neurosci*. 2020;11(9):1204-1205.
49. Ahmed MU, Hanif M, Ali MJ, et al. Neurological manifestations of COVID-19 (SARS-CoV-2): a review. *Front Neurol*. 2020;11:518.
50. Wang L, Shen Y, Li M, et al. Clinical manifestations and evidence of neurological involvement in 2019 novel coronavirus SARS-CoV-2: a systematic review and meta-analysis [published online ahead of print, 2020 Jun 11]. *J Neurol*. 2020:1-13.
51. Varatharaj A, Thomas N, Ellul MA, et al. Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. *Lancet Psychiatry*. 2020;7(10):875-882. https://doi.org/10.1016/S2215-0366(20)30287-X. Epub 2020 Jun 25. Erratum in: Lancet Psychiatry. 2020 Jul 14; https://pubmed.ncbi.nlm.nih.gov/32593341/; PMCID: PMC7316461.
52. Dinakaran D, Manjunatha N, Naveen Kumar C, Suresh BM. Neuropsychiatric aspects of COVID-19 pandemic: a selective review [published online ahead of print, 2020 May 30]. *Asian J Psychiatr*. 2020;53:102188.
53. Moriguchi T, Harii N, Goto J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *Int J Infect Dis*. 2020;94:55-58.
54. Yashavantha Rao HC, Jayabaskaran C. The emergence of a novel coronavirus (SARS-CoV-2) disease and their neuroinvasive propensity may affect in COVID-19 patients. *J Med Virol*. 2020;92(7):786-790.
55. Garg RK, Paliwal VK, Gupta A. Encephalopathy in patients with COVID-19: a review. *J Med Virol*. 2020. https://doi.org/10.1002/jmv.26207. Epub ahead of print. https://pubmed.ncbi.nlm.nih.gov/32558956/.
56. Hosseini AA, Shetty AK, Sprigg N, Auer DP, Constantinescu CS. Delirium as a presenting feature in COVID-19: neuroinvasive infection or autoimmune encephalopathy?. *Brain Behav Immun*. 2020;88:68-70.
57. 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.
58. Glatzel M. Neuropathology of COVID-19: where are the neuropathologists?. *Brain Pathol*. 2020;30(4):729.
59. von Weyhern CH, Kaufmann I, Neff F, Kremer M. Early evidence of pronounced brain involvement in fatal COVID-19 outcomes. *Lancet*. 2020;395(10241):e109.
60. Solomon IH, Normandin E, Bhattacharyya S, et al. Neuropathological features of Covid-19 [published online ahead of print, 2020 Jun 12]. *N Engl J Med*. 2020:NEJMc2019373.
61. Anoop UR, Verma K. Pulmonary edema in COVID19-A neural hypothesis. *ACS Chem Neurosci*. 2020;11(14):2048-2050.
62. Li Z, Liu T, Yang N, et al. Neurological manifestations of patients with COVID-19: potential routes of SARS-CoV-2 neuroinvasion from the periphery to the brain [published online ahead of print, 2020 May 4]. *Front Med*. 2020:1-9.
63. Montalvan V, Lee J, Bueso T, De Toledo J, Rivas K. Neurological manifestations of COVID-19 and other coronavirus infections: a systematic review. *Clin Neurol Neurosurg*. 2020;194:105921.
64. Chigr F, Merzouki M, Najimi M. Comment on "The neuroinvasive potential of SARS-CoV-2 may play a role in the respiratory failure of COVID-19 patients". *J Med Virol*. 2020;92(7):703-704.
65. Chigr F, Merzouki M, Najimi M. Autonomic brain centers and pathophysiology of COVID-19. *ACS Chem Neurosci*. 2020;11(11):1520-1522.
66. Zhou Y, Li W, Wang D, et al. Clinical time course of COVID-19, its neurological manifestation and some thoughts on its management. *Stroke Vasc Neurol*. 2020;5(2):177-179.
67. Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res*. 2020;191:9-14.
68. Nalleballe K, Reddy Onteddu S, Sharma R, et al. Spectrum of neuropsychiatric manifestations in COVID-19. *Brain Behav Immun*. 2020;88:71-74.
69. Xiong W, Mu J, Guo J, et al. New onset neurologic events in people with COVID-19 infection in three regions in China. *Neurology*. 2020;95(11):e1479-e1487. https://doi.org/10.1212/WNL.0000000000010034. Epub 2020 Jun 17. https://pubmed.ncbi.nlm.nih.gov/32554771/.
70. Mishra AK, Sahu KK, George AA, Sargent J, Lal A. Cerebrovascular events in COVID-19 patients. *Monaldi Arch Chest Dis*. 2020;90(2).
71. Merkler AE, Parikh NS, Mir S, et al. Risk of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) vs patients with influenza [published online ahead of print, 2020 Jul 2]. *JAMA Neurol*. 2020:e202730.
72. Morassi M, Bagatto D, Cobelli M, et al. Stroke in patients with SARS-CoV-2 infection: case series. *J Neurol*. 2020;267(8):2185-2192.
73. Beyrouti R, Adams ME, Benjamin L, et al. Characteristics of ischaemic stroke associated with COVID-19. *J Neurol Neurosurg Psychiatry*. 2020;91(8):889-891.
74. D'Anna L, Kwan J, Brown Z, et al. Characteristics and clinical course of Covid-19 patients admitted with acute stroke. *J Neurol*. 2020);267(11):3161-3165. https://doi.org/10.1007/s00415-020-10012-4. Epub 2020 Jun 24. https://pubmed.ncbi.nlm.nih.gov/32583054/; PMCID: PMC7313245.
75. Paterson RW, Brown RL, Benjamin L, et al. The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings [published online ahead of print, 2020 Jul 8]. *Brain*. 2020:awaa240.
76. Zanin L, Saraceno G, Panciani PP, et al. SARS-CoV-2 can induce brain and spine demyelinating lesions. *Acta Neurochir (Wien)*. 2020;162(7):1491-1494.
77. Koralnik IJ, Tyler KL. COVID-19: a global threat to the nervous system. *Ann Neurol*. 2020;88(1):1-11.
78. Gupta A, Paliwal VK, Garg RK. Is COVID-19-related Guillain-Barré syndrome different?. *Brain Behav Immun*. 2020;87:177-178.
79. Kadono Y, Nakamura Y, Ogawa Y, et al. A case of COVID-19 infection presenting with a seizure following severe brain edema. *Seizure*. 2020;80:53-55.

80. Hepburn M, Mullaguri N, George P, et al. Acute symptomatic seizures in critically ill patients with COVID-19: is there an association? [published online ahead of print, 2020 May 28]. *Neurocrit Care*. 2020:1-5.
81. Galanopoulou AS, Ferastraoaru V, Correa DJ, et al. EEG findings in acutely ill patients investigated for SARS-CoV-2/COVID-19: a small case series preliminary report. *Epilepsia Open*. 2020;5(2):314-324.
82. Gélisse P, Rossetti AO, Genton P, Crespel A, Kaplan PW. How to carry out and interpret EEG recordings in COVID-19 patients in ICU?. *Clin Neurophysiol*. 2020;131(8):2023-2031.
83. Balloy G, Leclair-Visonneau L, Péréon Y, et al. Non-lesional status epilepticus in a patient with coronavirus disease 2019. *Clin Neurophysiol*. 2020;131(8):2059-2061.
84. Alkeridy WA, Almaghlouth I, Alrashed R, et al. A unique presentation of delirium in a patient with otherwise asymptomatic COVID-19. *J Am Geriatr Soc*. 2020;68(7):1382-1384.
85. Butt I, Sawlani V, Geberhiwot T. Prolonged confusional state as first manifestation of COVID-19. *Ann Clin Transl Neurol*. 2020;(8):1450-1452.
86. Beach SR, Praschan NC, Hogan C, et al. Delirium in COVID-19: a case series and exploration of potential mechanisms for central nervous system involvement. *Gen Hosp Psychiatry*. 2020;65:47-53.
87. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study [published correction appears in Lancet. 2020 Mar 28;395(10229):1038] [published correction appears in Lancet. 2020 Mar 28;395(10229):1038]. *Lancet*. 2020;395(10229):1054-1062.
88. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ*. 2020;369:m1966.
89. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area [published online ahead of print, 2020 Apr 22]. *JAMA*. 2020;323(20):2052-2059.
90. Bianchetti A, Rozzini R, Guerini F, et al. Clinical Presentation of COVID19 in dementia patients. *J Nutr Health Aging*. 2020;24(6):560-562.
91. Poloni TE, Carlos AF, Cairati M, et al. Prevalence and prognostic value of Delirium as the initial presentation of COVID-19 in the elderly with dementia: an Italian retrospective study [published online ahead of print, 2020 Jul 30]. *EClinicalMedicine*. 2020:100490.
92. Paniz-Mondolfi A, Bryce C, Grimes Z, et al. Central nervous system involvement by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). *J Med Virol*. 2020;92(7):699-702.
93. Reichard RR, Kashani KB, Boire NA, Constantopoulos E, Guo Y, Lucchinetti CF. Neuropathology of COVID-19: a spectrum of vascular and acute disseminated encephalomyelitis (ADEM)-like pathology. *Acta Neuropathol*. 2020;140(1):1-6.
94. Kremer S, Lersy F, de Sèze J, et al. Brain MRI findings in severe COVID-19: a retrospective observational study. *Radiology*. 2020;297(2):e242-e251. https://doi.org/10.1148/radiol.2020202222. Epub 2020 Jun 16. https://pubmed.ncbi.nlm.nih.gov/32544034/; PMCID: PMC7301613.
95. Pilotto A, Odolini S, Masciocchi S, et al. Steroid-responsive encephalitis in coronavirus disease 2019 [published online ahead of print, 2020 May 17]. *Ann Neurol*. 2020.
96. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395(10229):1033-1034.
97. Bostancıklıoğlu M. Temporal correlation between neurological and gastrointestinal symptoms of SARS-CoV-2. *Inflamm Bowel Dis*. 2020;26(8):e89-e91.
98. Le Guennec L, Devianne J, Jalin L, et al. Orbitofrontal involvement in a neuroCOVID-19 patient [published online ahead of print, 2020 Jun 26]. *Epilepsia*. 2020.
99. Li J, Long X, Zhang Q, et al. Emerging evidence for neuropsychoconsequences of COVID-19 [published online ahead of print, 2020 May 6]. *Curr Neuropharmacol*. 2020.
100. Asadi-Pooya AA, Simani L. Central nervous system manifestations of COVID-19: a systematic review. *J Neurol Sci*. 2020;413:116832.
101. Gandhi S, Srivastava AK, Ray U, Tripathi PP. Is the collapse of the respiratory center in the brain responsible for respiratory breakdown in COVID-19 patients?. *ACS Chem Neurosci*. 2020;11(10):1379-1381.
102. Bhaskar S, Sinha A, Banach M, et al. Cytokine storm in COVID-19-immunopathological mechanisms, clinical considerations, and therapeutic approaches: the REPROGRAM consortium position paper. *Front Immunol*. 2020;11:1648.
103. Ray PR, Wangzhou A, Ghneim N, et al. A pharmacological interactome between COVID-19 patient samples and human sensory neurons reveals potential drivers of neurogenic pulmonary dysfunction [published online ahead of print, 2020 Jun 1]. *Brain Behav Immun*. 2020.
104. Boziki MK, Mentis AA, Shumilina M, Makshakov G, Evdoshenko E, Grigoriadis N. COVID-19 immunopathology and the central nervous system: implication for multiple sclerosis and other autoimmune diseases with associated demyelination. *Brain Sci*. 2020;10(6):345.
105. Naughton SX, Raval U, Pasinetti GM. Potential Novel Role of COVID-19 in Alzheimer's disease and preventative mitigation strategies. *J Alzheimers Dis*. 2020;76(1):21-25.
106. Ogier M, Andéol G, Sagui E, Dal Bo G. How to detect and track chronic neurologic sequelae of COVID-19? Use of auditory brainstem responses and neuroimaging for long-term patient follow-up. *Brain Behav Immun Health*. 2020;5:100081.
107. Brietzke E, Magee T, Freire RCR, Gomes FA, Milev R. Three insights on psychoneuroimmunology of mood disorders to be taken from the COVID-19 pandemic. *Brain Behav Immun Health*. 2020;5:100076.
108. Horn SR, Weston SJ, Fisher PA. Identifying causal role of COVID-19 in immunopsychiatry models. *Brain Behav Immun*. 2020;88:6-8.
109. Panariello A, Bassetti R, Radice A, et al. Anti-NMDA receptor encephalitis in a psychiatric Covid-19 patient: a case report. *Brain Behav Immun*. 2020;87:179-181.
110. Zambreanu L, Lightbody S, Bhandari M, et al. A case of limbic encephalitis associated with asymptomatic COVID-19 infection. *J Neurol Neurosurg Psychiatry*. 2020;91(11):1229-1230. https://doi.org/10.1136/jnnp-2020-323839. Epub 2020 Jul 13. https://pubmed.ncbi.nlm.nih.gov/32661082/.
111. Mankad K, Perry MD, Mirsky DM, Rossi A. COVID-19: a primer for neuroradiologists. *Neuroradiology*. 2020;62(6):647-648.
112. Coolen T, Lolli V, Sadeghi N, et al. Early postmortem brain MRI findings in COVID-19 non-survivors. *Neurology*. 2020;95(14):e2016-e2027. https://doi.org/10.1212/WNL.0000000000010116. Epub 2020 Jun 16. https://pubmed.ncbi.nlm.nih.gov/32546654/.
113. Radmanesh A, Raz E, Zan E, Derman A, Kaminetzky M. Brain imaging use and findings in COVID-19: a single academic center experience in the epicenter of disease in the United States. *AJNR Am J Neuroradiol*. 2020;41(7):1179-1183.
114. Jain R, Young M, Dogra S, et al. COVID-19 related neuroimaging findings: a signal of thromboembolic complications and a strong prognostic marker of poor patient outcome. *J Neurol Sci*. 2020;414:116923.
115. Katal S, Balakrishnan S, Gholamrezanezhad A. Neuroimaging and neurologic findings in COVID-19 and other coronavirus infections: a systematic review in 116 patients. *J Neuroradiol*. 2020;S0150-9861(20):30204. https://doi.org/10.1016/j.neurad.2020.06.007. Epub ahead of print. https://pubmed.ncbi.nlm.nih.gov/32603770/; PMCID: PMC7320684.
116. Li CW, Syue LS, Tsai YS, et al. Anosmia and olfactory tract neuropathy in a case of COVID-19 [published online ahead of print, 2020 Jun 20]. *J Microbiol Immunol Infect*. 2020.

117. Zoghi A, Ramezani M, Roozbeh M, Darazam IA, Sahraian MA. A case of possible atypical demyelinating event of the central nervous system following COVID-19 [published online ahead of print, 2020 Jun 24]. *Mult Scler Relat Disord*. 2020;44:102324.
118. Radmanesh A, Derman A, Lui YW, et al. COVID-19 -associated diffuse leukoencephalopathy and microhemorrhages. *Radiology*. 2020; 297(1):e223-e227. https://doi.org/10.1148/radiol.2020202040. Epub 2020 May 21. https://pubmed.ncbi.nlm.nih.gov/32437314/; PMCID: PMC7507998.
119. Faeez MS. Brain imaging findings in COVID-19: what do we know so far?. *J Neuroradiol*. 2020;47(5):329-330.
120. Anzalone N, Castellano A, Scotti R, et al. Multifocal laminar cortical brain lesions: a consistent MRI finding in neuro-COVID-19 patients [published online ahead of print, 2020 Jun 6]. *J Neurol*. 2020: 1-4.
121. Politi LS, Salsano E, Grimaldi M. Magnetic resonance imaging alteration of the brain in a patient with coronavirus disease 2019 (COVID-19) and Anosmia. *JAMA Neurol*. 2020;77(8):1028-1029. https://doi.org/10.1001/jamaneurol.2020.2125. https://pubmed.ncbi.nlm.nih.gov/32469400/.
122. Kandemirli SG, Dogan L, Sarikaya ZT, et al. Brain MRI findings in patients in the intensive care unit with COVID-19 infection [published online ahead of print, 2020 May 8]. *Radiology*. 2020.
123. Brun G, Hak JF, Coze S, et al. COVID-19-White matter and globus pallidum lesions: demyelination or small-vessel vasculitis?. *Neurol Neuroimmunol Neuroinflamm*. 2020;7(4):e777.
124. Novi G, Rossi T, Pedemonte E, et al. Acute disseminated encephalomyelitis after SARS-CoV-2 infection. *Neurol Neuroimmunol Neuroinflamm*. 2020;7(5):e797.
125. Abdi S, Ghorbani A, Fatehi F. The association of SARS-CoV-2 infection and acute disseminated encephalomyelitis without prominent clinical pulmonary symptoms [published online ahead of print, 2020 Jun 18]. *J Neurol Sci*. 2020;416:117001.
126. Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. *Infect Dis Poverty*. 2020;9(1):45.
127. Hamer M, Kivimäki M, Gale CR, Batty GD. Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: a community-based cohort study of 387,109 adults in UK. *Brain Behav Immun*. 2020;87:184-187.
128. Dogan L, Kaya D, Sarikaya T, et al. Plasmapheresis treatment in COVID-19-related autoimmune meningoencephalitis: case series. *Brain Behav Immun*. 2020;87:155-158.
129. Pranata R, Huang I, Lukito AA, Raharjo SB. Elevated N-terminal pro-brain natriuretic peptide is associated with increased mortality in patients with COVID-19: systematic review and meta-analysis. *Postgrad Med J*. 2020;96(1137):387-391.
130. Gao L, Jiang D, Wen XS, et al. Prognostic value of NT-proBNP in patients with severe COVID-19. *Respir Res*. 2020;21(1):83.
131. Inciardi RM, Adamo M, Lupi L, et al. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. *Eur Heart J*. 2020;41(19):1821-1829.
132. Pinna P, Grewal P, Hall JP, et al. Neurological manifestations and COVID-19: experiences from a tertiary care center at the frontline. *J Neurol Sci*. 2020;415:116969.
133. Lassale C, Gaye B, Hamer M, Gale CR, Batty GD. Ethnic disparities in hospitalisation for COVID-19 in England: the role of socioeconomic factors, mental health, and inflammatory and pro-inflammatory factors in a community-based cohort study. *Brain Behav Immun*. 2020;88:44-49.
134. Suzuki M, Saito K, Min WP, et al. Identification of viruses in patients with postviral olfactory dysfunction. *Laryngoscope*. 2007;117(2):272-277.
135. Han AY, Mukdad L, Long JL, Lopez IA. Anosmia in COVID-19: mechanisms and significance [published online ahead of print, 2020 Jun 17]. *Chem Senses*. 2020:bjaa040.
136. Dibattista M, Pifferi S, Menini A, Reisert J. Alzheimer's disease: what can we learn from the peripheral olfactory system?. *Front Neurosci*. 2020;14:440.
137. De Felice FG, Tovar-Moll F, Moll J, Munoz DP, Ferreira ST. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the central nervous system. *Trends Neurosci*. 2020;43(6):355-357.
138. Hustad E, Aasly JO. Clinical and imaging markers of prodromal Parkinson's disease. *Front Neurol*. 2020;11:395.
139. Van Regemorter V, Hummel T, Rosenzweig F, Mouraux A, Rombaux P, Huart C. Mechanisms linking olfactory impairment and risk of mortality. *Front Neurosci*. 2020;14:140.
140. Gialluisi A, de Gaetano G, Iacoviello L. New challenges from Covid-19 pandemic: an unexpected opportunity to enlighten the link between viral infections and brain disorders?. *Neurol Sci*. 2020;41(6):1349-1350.
141. Pendlebury ST, Rothwell PM. Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis. *Lancet Neurol*. 2009;8(11):1006-1018.
142. Sexton E, McLoughlin A, Williams DJ, et al. Systematic review and meta-analysis of the prevalence of cognitive impairment no dementia in the first year post-stroke. *Eur Stroke J*. 2019;4(2):160-171.
143. Kuźma E, Lourida I, Moore SF, Levine DA, Ukoumunne OC, Llewellyn DJ. Stroke and dementia risk: a systematic review and meta-analysis. *Alzheimers Dement*. 2018;14(11):1416-1426.
144. Barbay M, Diouf M, Roussel M, Godefroy O. GRECOGVASC study group. Systematic review and meta-analysis of prevalence in post-stroke neurocognitive disorders in hospital-based studies. *Dement Geriatr Cogn Disord*. 2018;46(5-6):322-334.
145. Yang Z, Wang H, Edwards D, et al. Association of blood lipids, atherosclerosis and statin use with dementia and cognitive impairment after stroke: a systematic review and meta-analysis. *Ageing Res Rev*. 2020;57:100962.
146. Islam MM, Poly TN, Walther BA, et al. Association between atrial fibrillation and dementia: a meta-analysis. *Front Aging Neurosci*. 2019;11:305.
147. Lennon MJ, Makkar SR, Crawford JD, Sachdev PS. Midlife hypertension and Alzheimer's disease: a systematic review and meta-analysis. *J Alzheimers Dis*. 2019;71(1):307-316.
148. Rochoy M, Rivas V, Chazard E, et al. Factors associated with Alzheimer's disease: an overview of reviews. *J Prev Alzheimers Dis*. 2019;6(2):121-134.
149. Rensma SP, van Sloten TT, Launer LJ, Stehouwer CDA. Cerebral small vessel disease and risk of incident stroke, dementia and depression, and all-cause mortality: a systematic review and meta-analysis. *Neurosci Biobehav Rev*. 2018;90:164-173.
150. Makin SD, Turpin S, Dennis MS, Wardlaw JM. Cognitive impairment after lacunar stroke: systematic review and meta-analysis of incidence, prevalence and comparison with other stroke subtypes. *J Neurol Neurosurg Psychiatry*. 2013;84(8):893-900.
151. Azeem F, Durrani R, Zerna C, Smith EE. Silent brain infarctions and cognition decline: systematic review and meta-analysis. *J Neurol*. 2020;267(2):502-512.
152. Saavedra JM. COVID-19, angiotensin receptor blockers, and the brain. *Cell Mol Neurobiol*. 2020;40(5):667-674.
153. Fotuhi M, Mian A, Meysami S, Raji CA. Neurobiology of COVID-19. *J Alzheimers Dis*. 2020;76(1):3-19.
154. Troyer EA, Kohn JN, Hong S. Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. *Brain Behav Immun*. 2020;87:34-39.
155. Cothran TP, Kellman S, Singh S, et al. A brewing storm: the neuropsychological sequelae of hyperinflammation due to COVID-19. *Brain Behav Immun*. 2020;88:957.
156. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. *Brain Behav Immun*. 2020;89(Oct):531-542. https://doi.org/10.1016/j.bbi.

2020.05.048. Epub 2020 May 30. https://pubmed.ncbi.nlm.nih.gov/32485289/; PMCID: PMC7260522.
157. Rogers JP, Chesney E, Oliver D, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry*. 2020;7(7):611-627.
158. Vallamkondu J, John A, Wani WY, et al. SARS-CoV-2 pathophysiology and assessment of coronaviruses in CNS diseases with a focus on therapeutic targets. *Biochim Biophys Acta Mol Basis Dis*. 2020;1866(10):165889.
159. Landreau F, Galeano P, Caltana LR, et al. Effects of two commonly found strains of influenza A virus on developing dopaminergic neurons, in relation to the pathophysiology of schizophrenia. *PLoS One*. 2012;7(12):e51068.
160. Bostanciklioglu M. Severe acute respiratory syndrome coronavirus 2 is penetrating to dementia research. *Curr Neurovasc Res*. 2020. https://doi.org/10.2174/1567202617666200522220509. Epub ahead of print. https://pubmed.ncbi.nlm.nih.gov/32442082/.
161. Hascup ER, Hascup KN. Does SARS-CoV-2 infection cause chronic neurological complications?. *Geroscience*. 2020;42(4):1083-1087.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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