REVIEW ARTICLE

Neurologia i Neurochirurgia Polska
Polish Journal of Neurology and Neurosurgery
2020, Volume 54, no. 5, pages: 378–383
DOI: 10.5603/PJNNS.a2020.0050

ISSN 0028–3843

Neurological manifestations of SARS-CoV-2 — a systematic review

Stanisław Słyk[1], Izabela Domitrz[2]

[1]Department of Neurology, Bielanski Hospital, Warsaw, Poland
[2]Department of Neurology, Faculty of Medical Sciences, Medical University of Warsaw, Warsaw, Poland

ABSTRACT

Introduction. Following two coronaviral epidemics in 2002 and 2012, December 2019 saw the emergence of a potentially fatal coronavirus — SARS-CoV-2, which originated in Wuhan, China. While most coronaviruses are responsible for mild respiratory infections, they have been demonstrated to be neuroinvasive and neurotropic for over three decades. In this review, we assess whether SARS-CoV-2 follows this trend and if the neuroinvasive potential of this novel coronavirus is worthy of further investigation.

Methods. To obtain sources for this study, we performed an online search through Pubmed, Researchgate and Google Scholar, finding 537 articles. After analysing them according to PRISMA, we included 14 in this review.

Discussion. Data regarding neurological manifestations of SARS-CoV-2 is scarce and mostly inconsistent. There are however identifiable trends which might provide a basis for future research. There is strong evidence that this novel coronavirus may be neuroinvasive and could cause a wide array of neurological symptoms and complications. Cerebrospinal fluid testing may shed more light on the occurrence of SARS-CoV-2 in the central nervous system. Clarification of the respiratory failure mechanisms requires post mortem examinations and brain tissue analysis, and further research is of the utmost importance. However, we strongly believe that the existing evidence is enough to raise awareness among clinicians and help guide them through the diagnosis and optimal therapy of COVID-19 patients.

Key words: infections, coronavirus, COVID-19, CNS, SARS-CoV-2

(*Neurol Neurochir Pol 2020; 54 (5): 378–383*)

Introduction

The first reports of human coronaviruses (HCoV) came in the 1960s from patients with the common cold [1]. Since then, six human pathogenic coronaviruses have been identified [2]. Most of them are responsible for mild respiratory infections. However, more recently we have experienced two major HCoV epidemics – severe acute respiratory syndrome (SARS) in 2002 and Middle East respiratory syndrome (MERS) in 2012. December 2019 saw the emergence of another potentially fatal coronavirus — SARS-CoV-2, which originated in Wuhan, China [3]. In contrast to the previous epidemics, the novel coronavirus quickly spread worldwide. By 12 June, 2020 it had caused 7,410,510 confirmed infections and 418,294 deaths [4] and had become of paramount global concern.

Coronaviruses have been demonstrated to be neuroinvasive and neurotropic for over three decades [5]. In this review we assess whether SARS-CoV-2 follows this trend and if the neuroinvasive potential of this novel coronavirus is worthy of further investigation.

Over the last few months, there have been numerous reports and reviews on this topic, although they have varied immensely in terms of their data presentation and conclusions. This review is an attempt to gather the available facts, suggest provisional conclusions, and encourage further research. We believe that such research is crucial in order to come closer to understanding the virus in that it makes the data more accessible and better organised.

Methods and results

To obtain sources for this study, we performed an online search through Pubmed, Researchgate and Google Scholar,

Address for correspondence: Stanisław Słyk, Cegłowska 80 Str., 01-809 Warsaw, Poland, e-mail: stslyk@gmail.com

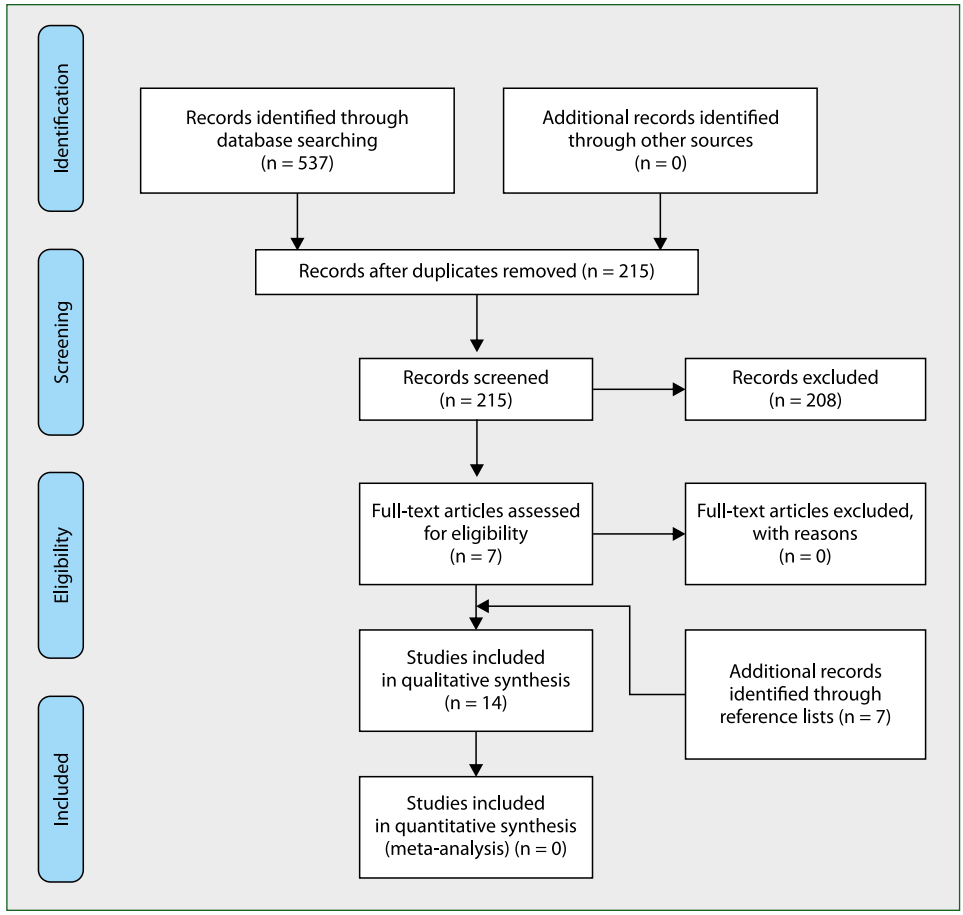

Figure 1. Flowchart of selection process according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

in which we used the key words "coronavirus" and "COVID" together with the words "neurological", "neurology", "nervous" and "CNS". We found 537 articles, which we then analysed according to PRISMA rules [6] (Fig. 1). This left us with 14 studies which we divided into two groups, set out below in Tables 1 and 2.

In Table 1 we set out those which focused specifically on neurological manifestations of COVID-19. Table 2 on the other hand includes more general research, i.e. studies which were not primarily focused on neurological disorders, however mentioned non-specific neurological symptoms or disorders.

The authors of both Chinese observational studies [7, 8] reported a high incidence of cerebrovascular diseases, including ischaemic stroke, among COVID-19 patients. Mao et. al. also stated that symptoms from the nervous system were significantly more common in severe cases than in non-severe. In addition, Helms et. al. [9] reported neurological signs in 84% of the patients who had been admitted to hospital because of acute respiratory distress syndrome (ARDS) due to COVID-19.

Single cases have also been reported suggestive of diverse symptoms [10–15]. Cerebrospinal fluid (CSF) testing has provided various results. In the first case, the CSF tested negative for SARS-CoV-2. In the second one, specific RNA was not detected in the nasopharyngeal swab, but was present in the CSF. The patient, who developed Acute Haemorrhagic Necrotising Encephalopathy visible in CT and MRI, was positive for SARS-CoV-2, but due to trauma a CSF test could not be performed.

The next two studies set out in Table 1 describe six cases of Guillain–Barré Syndrome (GBS) associated with coronaviral infection. All five patients from the first study tested positive for the novel coronavirus at the onset of neurological symptoms, while the last one had a positive test on day eight. However, CSF was either not tested or tested negative for SARS-CoV-2 RNA. The onset of the neurological symptoms also varied. For patients from the first study, onset was 5–10 days after COVID-19 manifestation, while for the patient from the latter study, it was eight days **before**. The last included study highlighted the possibility of Miller Fisher Syndrome and polyneuritis cranialis occurrence (arguably due to an aberrant immune response to the coronaviral infection) during the COVID-19 pandemic.

A more thorough CSF comparison was not possible, as the studies either did not include detailed CSF profiles or provided only selective data.

Table 1. Studies on neurological complications of COVID-19

Study	Patients	Neurological manifestation occurrence	Suggested neurological manifestation
Neurological manifestations of hospitalised patients with Coronavirus disease 2019 in Wuhan, China [7]	214	78 (36.4%)	Acute cerebrovascular diseases, impaired consciousness and skeletal muscle injury
Acute cerebrovascular disease following COVID-19: a single--centre, retrospective, observational study [8]	221	11 (5%)	Acute ischaemic stroke
		1 (0.5%)	Cerebral haemorrhage
		1 (0.5%)	Cerebral venous sinus thrombosis (CVST)
Neurological features in severe SARS-CoV-2 infection [9]	58	40 (69%)	Agitation
		39 (67%)	Corticospinal tract signs
		14 (36%)	Dysexecutive syndrome
Concomitant neurological symptoms observed in a patient diagnosed with Coronavirus disease 2019 [10]	1	1 (100%)	Altered consciousness and psychiatric symptoms, with positive signs based on neurological examination (CSF -)
A first case of meningitis/encephalitis associated with SARS--Coronavirus-2 [11]	1	1 (100%)	Headache, fatigue, generalised seizures, meningitis (CSF +)
COVID-19–associated acute haemorrhagic necrotising encephalopathy: CT and MRI features [12]	1	1 (100%)	Acute haemorrhagic necrotising encephalopathy
Guillain–Barré syndrome associated with SARS-CoV-2 [13]	5	5 (100%)	Guillain–Barré syndrome (CSF -)
Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? [14]	1	1 (100%)	Guillain–Barré syndrome
Miller Fisher syndrome and polyneuritis cranialis in COVID-19 [15]	2	1 (50%)	Miller Fisher syndrome (CSF -)
		1 (50%)	Polyneuritis cranialis (CSF -)

Table 2. Nonspecific neurological manifestations in general studies

Study	Patients	Neurological manifestation occurrence	Suggested neurological manifestation
Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [16]	41	18 (44%)	Myalgia, fatigue, headache
		3 of 38 (8%)	
Clinical course and outcomes of critically ill patients with SARS--CoV-2 pneumonia in Wuhan, China: a single-centre, retrospective, observational study [17]	52	6 (11%)	Myalgia, malaise, headache
		18 (35%)	
		3 (6%)	
Clinical characteristics of 138 hospitalised patients with 2019 novel Coronavirus-infected pneumonia in Wuhan, China [18]	138	48 (34.8%)	Myalgia, dizziness, headache
		13 (9.4%)	
		9 (6.5%)	
Epidemiological and clinical characteristics of 99 cases of 2019 novel Coronavirus pneumonia in Wuhan, China: a descriptive study [19]	99	11 (11%)	Myalgia, confusion, headache
		9 (9%)	
		8 (8%)	
Clinical features of 85 fatal cases of COVID-19 from Wuhan: a retrospective observational study [20]	85	No data	Myalgia, headache

There have been more studies on the general characteristics and symptoms of novel coronavirus patients [16–20] (Tab. 2). In all of them, headache and myalgia were reported. However, these symptoms are not specific to the nervous system and therefore it is difficult to tie them to the possible SARS-CoV-2 CNS invasion. With the disease still being relatively little understood, the reports are valuable yet remain inconsistent.

Discussion

It has been reported that neurological compromise is a part of the SARS-CoV-2 infection and might occur in up to one in three COVID-19 patients [21]. The presented studies do not provide definitive conclusions however, because the occurrence of the neurological diseases might be a coincidence

rather than a correlation. Although the data is unconvincing, there are reasons to investigate the impact of SARS-CoV-2 on the nervous system. While the novel coronavirus is a newly discovered pathogen, we have additional knowledge about other coronaviruses. They have natural neuroinvasive traits [22], although they are not very well characterised. Coronaviral RNA can be found in human brain samples [23]. It has been established that these viruses can create a persistent infection in human cells representative of the CNS [24].

As with all viral agents, there are two possible routes for the coronaviruses to enter the CNS: haematogenous or neuronal retrograde. It seems that HCoV may be able to use both ways. Infected leukocytes could provide a vector to use the haematogenous route [25], while a recent study on HCoV OC43 identifies the clear way of its neuroinvasiveness in the olfactory nerve [26]. Thus we can expect the novel coronavirus to have neuroinvasive potential. This is further reinforced by proofs we have from previous coronavirus epidemics – namely SARS and MERS. These viruses have been reported to not only appear in CSF [27] but to also cause neurological symptoms. [28–29]. Coronaviral infections have caused several acute neurological complications, including among others viral meningitis, anosmia, encephalitis, and myositis [30]. It would be logical to expect SARS-CoV-2 to be possibly neuroinvasive as well, as it in many ways resembles its predecessor SARS-CoV both genetically and clinically [31].

The knowledge we have today allows us to go further than a mere educated guess. A study by Baig et al. ties in the expression of ACE2 and neurovirulence of SARS-CoV-2 [32]. They reported that the virus disseminated in circulation may interact with its spike protein with the ACE2 receptors in the cerebral capillaries. Further interaction with neuronal ACE2 receptors could cause significant damage without much inflammation. This was previously also true for SARS-CoV [33] and might explain how the virus may use the aforementioned haematogenous entry route to the CNS. The growing number of reports indicating that SARS-CoV-2 may be responsible for anosmia and dysgeusia [34–35] suggests that the suspected olfactory route could also be confirmed.

This theory is becoming backed up by examples. We already have the first reports of a patient who tested positive for SARS-CoV-2 in CSF by gene sequencing [36]. Another patient, from the second case report in Table 1, had meningitis/encephalitis symptoms and had specific viral RNA discovered in his CSF, even though the test by nasopharyngeal swab turned out negative. Wu et al. have named viral encephalitis, infectious toxic encephalopathy, and acute cerebrovascular disease as the main nervous system diseases related to coronaviral infections [37] — the same complications as were reported in the studies set out in Table 1. Wichmann et al. from Dr Klaus Püschel's laboratory conducted post mortem examinations of PCR-confirmed COVID-19 patients. Deep venous thrombosis was revealed in seven out of 12 patients, while pulmonary embolism was a direct cause of death for four of them, thereby underlining the importance of COVID-induced coagulopathy [38]. The commonly described cerebrovascular incidents could be also caused by elevated (due to coronaviral infection) levels of anticardiolipin antibodies, as suggested by Zhang et al. [39]. Although single studies encapsulated in Tables 1 and 2 do not provide conclusive data, nonetheless in the light of other described findings we should be extremely careful and aware of the likely neuroinvasiveness of SARS-CoV-2.

There is another important aspect of the SARS-CoV-2 neurovirulence worth mentioning. The main cause of death for COVID-19 is respiratory failure [40]. Li, Bai and Hashikawa highlighted the possibility that it could be the SARS-CoV-2 CNS invasion which partially causes acute respiratory failure [41]. Previous coronaviruses (SARS-CoV, MERS-CoV) have been proven to heavily infect the thalamus and brainstem. According to Li et al., the cause of death could be suppression of the brainstem respiratory centre. This could explain why some patients are more vulnerable to death by respiratory failure. Additionally, myopathy and rhabdomyolysis were reported to occur in SARS patients [42, 43].

There is a possibility that not only could the respiratory centre in the CNS be damaged by SARS-CoV-2, but that also the muscle injuries may play a part in the process of respiratory failure [44].

All of the presented findings build towards a cohesive hypothesis. There is strong evidence supporting the theory that SARS-CoV-2 is naturally neuroinvasive and could cause a wide array of neurological symptoms and complications. CSF testing may shed more light on the occurrence of SARS-CoV-2 in the CNS. Clarification of the respiratory failure mechanisms requires post mortems and brain tissue analysis. Further research is of the utmost importance. However, we strongly believe that there is enough existing evidence to raise awareness among clinicians and help guide them through the diagnosis and optimal therapy of COVID-19 patients.

Declarations

To the best of our knowledge no conflict of interest, financial or otherwise, exists.

This publication was prepared without any external source of funding.

References

1. Su S, Wong G, Shi W, et al. Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses. Trends Microbiol. 2016; 24(6): 490–502, doi: 10.1016/j.tim.2016.03.003, indexed in Pubmed: 27012512.
2. Corman VM, Lienau J, Witzenrath M. [Coronaviruses as the cause of respiratory infections]. Internist (Berl). 2019; 60(11): 1136–1145, doi: 10.1007/s00108-019-00671-5, indexed in Pubmed: 31455974.
3. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun. 2020; 109: 102433, doi: 10.1016/j.jaut.2020.102433, indexed in Pubmed: 32113704.

4. World Health Organisation (WHO). Coronavirus disease 2019 (COVID-19) Situation Report – 144 [Internet]. WHO. 2020 . https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200612-covid-19-sitrep-144.pdf?sfvrsn=66ff9f4f_2 (2020 Jun 12).
5. Desforges M, Le Coupanec A, Brison E, et al. Neuroinvasive and neurotropic human respiratory coronaviruses: potential neurovirulent agents in humans. Adv Exp Med Biol. 2014; 807: 75–96, doi: 10.1007/978-81-322-1777-0_6, indexed in Pubmed: 24619619.
6. Moher D, Liberati A, Tetzlaff J, et al. PRISMA Group, PRISMA Group, PRISMA Group, PRISMA Group, PRISMA Group, PRISMA Group, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. Open Med. 2009; 3(3): e123–e130, indexed in Pubmed: 21603045.
7. Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol. 2020 [Epub ahead of print], doi: 10.1001/jamaneurol.2020.1127, indexed in Pubmed: 32275288.
8. Li Y, Li M, Wang M, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. Stroke Vasc Neurol. 2020 [Epub ahead of print], doi: 10.1136/svn-2020-000431, indexed in Pubmed: 32616524.
9. 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, doi: 10.1056/NEJMc2008597, indexed in Pubmed: 32294339.
10. Yin R, Feng W, Wang T, et al. Concomitant neurological symptoms observed in a patient diagnosed with coronavirus disease 2019. J Med Virol. 2020 [Epub ahead of print], doi: 10.1002/jmv.25888, indexed in Pubmed: 32293714.
11. 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, doi: 10.1016/j.ijid.2020.03.062, indexed in Pubmed: 32251791.
12. Poyiadji N, Shahin G, Noujaim D, et al. COVID-19-associated Acute Hemorrhagic Necrotizing Encephalopathy: CT and MRI Features. Radiology. 2020 [Epub ahead of print]: 201187, doi: 10.1148/radiol.2020201187, indexed in Pubmed: 32228363.
13. Toscano G, Palmerini F, Ravaglia S, et al. Guillain-Barré Syndrome Associated with SARS-CoV-2. N Engl J Med. 2020; 382(26): 2574–2576, doi: 10.1056/NEJMc2009191, indexed in Pubmed: 32302082.
14. Zhao H, Shen D, Zhou H, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? Lancet Neurol. 2020; 19(5): 383–384, doi: 10.1016/S1474-4422(20)30109-5, indexed in Pubmed: 32246917.
15. Gutiérrez-Ortiz C, Méndez A, Rodrigo-Rey S, et al. Miller Fisher Syndrome and polyneuritis cranialis in COVID-19. Neurology. 2020 [Epub ahead of print], doi: 10.1212/WNL.0000000000009619, indexed in Pubmed: 32303650.
16. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395(10223): 497–506, doi: 10.1016/S0140-6736(20)30183-5, indexed in Pubmed: 31986264.
17. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020; 8(5): 475–481, doi: 10.1016/s2213-2600(20)30079-5.
18. Wang D, Hu Bo, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020 [Epub ahead of print], doi: 10.1001/jama.2020.1585, indexed in Pubmed: 32031570.
19. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395(10223): 507–513, doi: 10.1016/S0140-6736(20)30211-7, indexed in Pubmed: 32007143.
20. Du Y, Tu L, Zhu P, et al. Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan. A Retrospective Observational Study. Am J Respir Crit Care Med. 2020; 201(11): 1372–1379, doi: 10.1164/rccm.202003-05430C, indexed in Pubmed: 32242738.
21. Finsterer J, Stollberger C. Update on the neurology of COVID-19. J Med Virol. 2020 [Epub ahead of print], doi: 10.1002/jmv.26000, indexed in Pubmed: 32401352.
22. Desforges M, Le Coupanec A, Dubeau P, et al. Human Coronaviruses and Other Respiratory Viruses: Underestimated Opportunistic Pathogens of the Central Nervous System? Viruses. 2019; 12(1), doi: 10.3390/v12010014, indexed in Pubmed: 31861926.
23. Arbour N, Day R, Newcombe J, et al. Neuroinvasion by human respiratory coronaviruses. J Virol. 2000; 74(19): 8913–8921, doi: 10.1128/jvi.74.19.8913-8921.2000, indexed in Pubmed: 10982334.
24. Arbour N, Côté G, Lachance C, et al. Acute and persistent infection of human neural cell lines by human coronavirus OC43. J Virol. 1999; 73(4): 3338–3350, indexed in Pubmed: 10074188.
25. Desforges M, Le Coupanec A, Dubeau P, et al. Human Coronaviruses and Other Respiratory Viruses: Underestimated Opportunistic Pathogens of the Central Nervous System? Viruses. 2019; 12(1), doi: 10.3390/v12010014, indexed in Pubmed: 31861926.
26. Dubé M, Le Coupanec A, Wong AHM, et al. Axonal Transport Enables Neuron-to-Neuron Propagation of Human Coronavirus OC43. J Virol. 2018; 92(17), doi: 10.1128/JVI.00404-18, indexed in Pubmed: 29925652.
27. Hung ECW, Chim SSC, Chan PKS, et al. Detection of SARS coronavirus RNA in the cerebrospinal fluid of a patient with severe acute respiratory syndrome. Clin Chem. 2003; 49(12): 2108–2109, doi: 10.1373/clinchem.2003.025437, indexed in Pubmed: 14633896.
28. Algahtani H, Subahi A, Shirah B. Neurological Complications of Middle East Respiratory Syndrome Coronavirus: A Report of Two Cases and Review of the Literature. Case Rep Neurol Med. 2016; 2016: 3502683, doi: 10.1155/2016/3502683, indexed in Pubmed: 27239356.
29. Lau KK, Yu WC, Chu CM, et al. Possible central nervous system infection by SARS coronavirus. Emerg Infect Dis. 2004; 10(2): 342–344, doi: 10.3201/eid1002.030638, indexed in Pubmed: 15030709.
30. Nath A. Neurologic complications of coronavirus infections. Neurology. 2020; 94(19): 809–810, doi: 10.1212/WNL.0000000000009455, indexed in Pubmed: 32229625.
31. Zhou L, Zhang M, Wang J, et al. Sars-Cov-2: Underestimated damage to nervous system. Travel Med Infect Dis. 2020 [Epub ahead of print]: 101642, doi: 10.1016/j.tmaid.2020.101642, indexed in Pubmed: 32220634.
32. Baig AM, Khaleeq A, Ali U, et al. Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host-Virus Interaction, and Proposed Neurotropic Mechanisms. ACS Chem Neurosci. 2020; 11(7): 995–998, doi: 10.1021/acschemneuro.0c00122, indexed in Pubmed: 32167747.
33. Netland J, Meyerholz DK, Moore S, et al. Severe acute respiratory syndrome coronavirus infection causes neuronal death in the absence of encephalitis in mice transgenic for human ACE2. J Virol. 2008; 82(15): 7264–7275, doi: 10.1128/JVI.00737-08, indexed in Pubmed: 18495771.
34. Miller RW. There's a new symptom of coronavirus, doctors say: Sudden loss of smell or taste [Internet]. USA Today . https://eu.usatoday.com/

story/news/health/2020/03/24/coronavirus-symptoms-loss-smell--taste/2897385001/ (2020 Mar 25).
35. Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. Clin Infect Dis. 2020 [Epub ahead of print], doi: 10.1093/cid/ciaa330, indexed in Pubmed: 32215618.
36. Sun T, Guan J. Novel coronavirus and the central nervous system. Eur J Neurol. 2020 [Epub ahead of print], doi: 10.1111/ene.14227, indexed in Pubmed: 32216009.
37. 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, doi: 10.1016/j.bbi.2020.03.031, indexed in Pubmed: 32240762.
38. Wichmann D, Sperhake JP, Lütgehetmann M, et al. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19. Ann Intern Med. 2020 [Epub ahead of print], doi: 10.7326/M20-2003, indexed in Pubmed: 32374815.
39. Zhang Y, Xiao M, Zhang S, et al. Coagulopathy and Antiphospholipid Antibodies in Patients with Covid-19. N Engl J Med. 2020; 382(17): e38, doi: 10.1056/NEJMc2007575, indexed in Pubmed: 32268022.
40. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020; 46(5): 846–848, doi: 10.1007/s00134-020-05991-x, indexed in Pubmed: 32125452.
41. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol. 2020; 92(6): 552–555, doi: 10.1002/jmv.25728, indexed in Pubmed: 32104915.
42. Tsai LK, Hsieh ST, Chang YC. Neurological manifestations in severe acute respiratory syndrome. Acta Neurol Taiwan. 2005; 14(3): 113–119, indexed in Pubmed: 16252612.
43. Hwang CS. Olfactory neuropathy in severe acute respiratory syndrome: report of A case. Acta Neurol Taiwan. 2006; 15(1): 26–28, indexed in Pubmed: 16599281.
44. Li YC, Bai WZ, Hashikawa T. Response to Commentary 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): 707–709, doi: 10.1002/jmv.25824, indexed in Pubmed: 32246783.