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Neuro-Covid-19: Neural Changes in SARS-COV-2 Infection

Oswaldo Jesus Rodrigues da Motta[1]*, Andréia Patrícia Gomes[2], Gabriella Luísa Costa Albuquerque[3], Leonardo Brandão Barreto[4], Tayrine Gonçalves[5], Jean Faber[6], Stefania Salvador P. Montenegro[7], Luciene Muniz Braga[8], Rodrigo Siqueira-Batista[9]

[1,2,8,9]Department of Medicine and Nursing, Universidade Federal de Viçosa, MG, Brazil.

[3,4,7,9]School of Medicine, Faculdade Dinâmica do Vale do Piranga, MG, Brazil.

[4]School of Medicine, Universidade Federal de Ouro Preto, MG, Brazil.

[5]Psychosocial Care Center (CAPS) Nise da Silveira, SP, Brazil.

[6]Paulista School of Medicine, Universidade Federal de São Paulo, SP, Brazil.

***Corresponding Author:** Oswaldo Jesus Rodrigues da Motta, PhD, Department of Medicine and Nursing, Universidade Federal de Viçosa, MG, Brazil.*

Abstract

The actual COVID-19 pandemic – disease caused by the SARS-CoV-2 virus – has already caused thousands of death in the year 2020. Among the various disorders that may occur throughout the disease's course, there are also disorders of the central nervous system. In order to investigate the potential effects of neural involvement in the novel coronavirus infection, Neuro-COVID-19, the present literature revision was carried out with a defined search strategy. Four descriptors were used: (i) "Brain", (ii) "Central Nervous System", (iii) "COVID-19", (iv) "SARS-CoV-2", which were combined to search for articles in the PubMed and ResearchGate databases. Of the 987 citations obtained, nine articles were selected. The contents extracted from these texts were organized into three categories, addressing (1) indirect, (2) direct and (3) post-infectious neurological complications. Awareness and management of neurological complications related to SARS CoV-2 infection are necessary in order to improve prognosis, especially in critically ill patients.

Keywords: *Brain, Central Nervous System, COVID-19, SARS-CoV-2.*

Introduction

The coronaviruses are a family of single-stranded positive RNA viruses that have a genome length of around 26 to 32 kb, which is considered the longest genome among the currently known RNA viruses. These microorganisms have an average diameter of 100 nm, can have a spherical or oval shape and received their name, coronavirus, due to the presence of a glycoprotein that resembles the typical shape of a crown, the S (spike) protein, in their viral envelope, responsible for binding to the host's cell membrane (WU, XU, CHEN, et al, 2020).

They are agents that target primarily the respiratory tract, provoking infections of varying intensities — usually mild to moderate — highlighting seven viruses: HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-HKU1, SARS-CoV, MERS-CoV e SARS-CoV-2. The last three pathogens have emerged in the last two decades. These viruses — that circulated among non-human animals — started to prompt disease in *Homo sapiens*, producing countless severe cases, many of which evolved to death (CUPERTINO, CUPERTINO, GOMES et al, 2010). It should be noted that SARS-CoV is the etiologic agent of SARS (Severe Acute Respiratory Syndrome); MERS-CoV is the microorganism involved in MERS (Middle East Respiratory Syndrome Coronavirus); and SARS-CoV-2 is the virus responsible for COVID-19 (Coronavirus Disease 2019).

COVID-19 appeared in 2019 in the province of Hubei's capital in China and disseminated rapidly throughout

the entire county (Matías-Guiu J, Gomez-Pinedo U, Montero-Escribano P, Gomez-Iglesias P, Porta-Etessam J, Matias-Guiu JA, 2020; WU, XU, CHEN, et al, 2020; ROTHAN, BYRAREDDY, 2020). On March 11th of 2020, the World Health Organization (WHO) declared COVID-19 a pandemic (ROTHAN, BYRAREDDY, 2020).

The clinical manifestations of COVID-19 appear after an average period of three to five days after contact with the pathogen (ASADI-POOYA, SIMANI, 2020; ROTHAN, BYRAREDDY, 2020; ASADI-POOYA, SIMANI, 2020). In this period, prior to the onset of symptoms, usually from the third day of infection, even asymptomatic or pre-symptomatic contactants can transmit the virus, which facilitates contagiousness and the rapid spread of the microorganism (KIMBALL ANNE, HATFIELD KELLY M., ARONS MELISSA, JAMES ALLISON). Initially, the symptoms are nonspecific, coursing predominantly with fatigue, fever, sore throat and coughs (ROTHAN, BYRAREDDY, 2020; ASADI-POOYA, SIMANI, 2020). Furthermore, a wide variety of signs and symptoms have been observed, such as diarrhea, nausea, myalgia, hemoptysis, rhinorrhea, headache, anosmia and dyspepsia (ROTHAN, BYRAREDDY, 2020; ASADI-POOYA, SIMANI, 2020). According to Wu e Yang (2020), in more severe cases, pneumonia can be observed, resulting in a lethality rate of around 2 to 4%. Other severe clinical conditions caused by the virus, such as Acute Respiratory Distress Syndrome (ARDS), acute cardiac injury and multiple organ failure, can lead to death (ROTHAN, BYRAREDDY, 2020; YU, XU, CHEN et al, 2020; ASADI-POOYA, SIMANI, 2020).

SARS-CoV-2, in particular, has been associated to several organic dysfunctions (CARDONA, PÁJARO, MARZOLA, VILLEGAS, SALAZAR, 2020; LI, HUANG, GUO, 2020). In this sense, some authors have been describing symptoms and signs possibly involving the central nervous system (CNS), such as headaches, dizziness, ataxia, dysgeusia, hyposmia, paraesthesia, mental confusion, seizure and acute cerebrovascular disorders (LI *et al*, 2020). It is also worth mentioning that the exact pathophysiological mechanism by which the virus promotes these changes is not yet fully understood. (WU, XU, YANG, LIU, YANG, 2020).

Based on these preliminary considerations, this article aims to describe the main neurological manifestations and possible pathophysiological mechanisms of neural disorders in SARS-CoV-2 infections.

Methods

The literature revisions was carried out by consulting the PubMed (U.S. National Library of Medicine) and ResearchGate databases. The search terms were defined based on the Health Sciences Descriptors (Decs) and involved four search strategies: (i) "Brain" AND "COVID-19"; (ii) "Brain" AND "SARS-CoV-2"; (iii) "Central Nervous System" AND "COVID-19"; (iv) "Central Nervous System" AND "SARS-CoV-2". The search resulted in 987 citations (Table 1), published from January 1st to May 31st of the year 2020, in Spanish, English and Portuguese, in OpenAcess and MEDLINE journals. Nine articles were selected from the these citations.

Table1. *Search results in the PubMed and ResearchGate databases*

Search term	PubMED	ResearchGate
"Brain" AND "COVID-19"	424	71
"Brain" AND "SARS-CoV-2"	142	65
"Central Nervous System" AND "COVID-19"	90	68
"Central Nervous System" AND "SARS-CoV-2"	69	58
TOTAL	725	262

Source: Research data (January 1st to May 31st of the year 2020).

The articles were selected based on their relevance to the topics covered in this revision, with an emphasis on the etiological, pathogenic, diagnostic, therapeutic and prophylactic aspects that relate COVID-19 to the CNS. In effect, Table 2 shows a summary of nine selected articles, relating their respective identification, study categories and issues addressed. It is also worth mentioning that, in addition to the manuscripts obtained by the bibliographic revision and described in Table 2, other useful texts were consulted to contextualize the problem.

Table2. *Summary of the 9 articles selected from the bibliographic revision*

Article and Reference	Research Method	Issues Addressed	Study Category
BUTOWT, BILINSKA (2020)	Literature revision. Ten studies were used to elaborate the article.	- The importance of collecting epidemiological data and scientific research that addresses and proves the relation between olfactory epithelium dysfunction and the appearance of changes in the nervous system. - The need for standardized tests for the early and effective detection of COVID-19 patients, addressing the importance of the olfactory epithelium as a source of biological material for testing.	Narrative revision
ASADI-POOYA, SIMANI (2020)	Systematic literature revision. Research took place in databases with a posterior analysis of each article considering defined inclusion or exclusion criteria. Eight studies were elected.	- The lack of precise and targeted documentation of signs and symptoms related to the nervous system and the scarcity of information regarding the isolation of SARS-CoV-2 in CSF and in autopsies.	Systematic revision
YE, REN, LV (2020)	Case study with a descriptive design and narrative character. One clinical case that occurred at the end of January in the city of Wuhan was used.	- The difficulty in isolating SARS-CoV-2 in CSF for the diagnosis of encephalitis, due to the transient and extremely low titles in this medium. - The lack of clarification as to the pathophysiological mechanisms of the virus that explain the occurrence of encephalitis.	Letter to the editor (Case report)
WU, XU, CHEN, et al. (2020)	Literature revision. Fifty-three studies were used to elaborate the article.	- The large number of pathophysiological mechanisms by which SARS-CoV-2 can generate clinical manifestations related to the nervous system. - The need for early identification of neurological signs and symptoms, as well as awareness on the management of neurological complications in critically ill patients.	Narrative revision
WU, XU, YANG, LIU, YANG (2020)	Perspective study supported by a narrative literature revision. Five references were used to produce the study.	- Strong association between SARS-CoV-2 and the involvement of the nervous system due to the hypothesis of the virus's potential neurotropism. - The lack of studies that prove viral infection in this tissue and the need of research that evaluates the long-term effects of COVID-19 on the nervous system.	Letter to the editor (Narrative revision)

MATÍAS-GUIU, GOMEZ-PINEDO, MONTERO-ESCRIBANO, GOMEZ-IGLESIAS, PORTA-ETESSAM, MATIAS-GUIU (2020)	Literature revision. Eighty-nine studies were used to elaborate the article.	- Description of the main manifestations caused by SARS-CoV-2 in the nervous system, as well as the probable pathophysiological mechanisms responsible for such involvement.| - The need for clinical monitoring and assessment of COVID-19 patients' prognosis and neurological symptoms.	Narrative revision
BAIG (2020)	Perspective study supported by a narrative literature revision. Eleven references were used to produce the study.	- Suggests that the similarity between SARS-CoV and SARS-CoV-2 can potentially define the mechanisms involved in the neurological conditions presented by COVID-19 patients. - The need to include loss of smell and taste as significant early signs of nervous system involvement.	Editorial commentary
ZHENGQIAN LI et al (2020)	Perspective study based on literature revision. Seventeen references were used to elaborate the letter.	- Emphasizes the possibility that the mechanism by which respiratory discomfort occurs is not only due to pulmonary inflammation, but also due to the involvement of the central respiratory center. - Analyzes some studies and mentions the main pathophysiological mechanisms by which neurological involvement occurs and how it can impact the pulmonary system.	Letter to the editor (Narrative revision)
LI, HUANG, GUO (2020)	Narrative literature revision. Eight references were used to produce the study.	- The need for early observation of neurological symptoms in patients with COVID-19 to avoid complications, in addition to pulmonary complications. - The need for scientific evidence as to the exact mechanism by which SARS-CoV-2 is capable of generating consequences in the CNS. It reinforces that the similarity between coronaviruses can be a way to understand this mechanism.	Narrative revision

Source: Bibliographic research preformed by the authors.

Results and Discussion

Among the nine articles selected to elaborate the revision, there were five narrative revisions, one systematic revision, one editorial commentary and two letters to the editor — one letter in narrative revision and the other containing a case study. The pathophysiological bases of the direct, indirect and post-infectious neurological complications were analyzed, knowing that the previous experience with patients infected with SARS-CoV, a taxonomically related virus, proved that coronaviruses affect the CNS. As described by Xu *et al*. (2020) and Li, Huang and Guo (2) the coronaviruses can cause neural injury in several ways: (1) via direct infection, through hematogenous dissemination and neural pathways; (2) secondary damage due to systemic phenomena, such as hypoxia; (3) and injury due to the post-infection immune process ((ASADI-POOYA, SIMANI, 2020; WU, XU, CHEN et al., 2020; YE, RE, LV, 2020).

Direct Neural Disorders

The direct neural complications of COVID-19 are possibly due to the SARS-CoV-2 virus's interaction with the angiotensin-converting enzyme 2 (ACE2). The enzyme is found in several structures of the human organism, such as in the respiratory tract's epithelium, in the lung parenchyma, in the gastrointestinal tract, among others, and participates as a negative regulator of the renin-angiotensin-aldosterone system, converting angiotensin II into angiotensin I-VII (CARODNA, PÁJARO, MARZOLA, VILLEGAS, SALAZAR, 2020).

SARS-CoV-2 binds to the ACE2 receptors through glycoproteins located in its viral membrane and acts by inhibiting the enzyme, which is widely expressed in the CNS, especially in the brain stem and bulb. Therefore, it is believed that there may be a direct mechanism of neurotoxicity in the brain stem, resulting from the presence of ACE2 receptors, which could contribute to the respiratory failure observed in more severe cases (GUIU, 2020). In addition, Wu et al (2020) and Cardona et al. (2020) pointed out another consequence resulting from the action of the virus on ACE2, which would be the decrease in its functionality, with a consequent increase in intracranial blood pressure and, subsequently, rupture of blood vessels, increasing the risk of CNS hemorrhage.

Liu, Hang, Guo (2020) and Cardona et al. propose that the respiratory discomfort that occurs in severe cases of COVID-19 is a result, not only of structural inflammatory damage to the lungs, but also of the injuries caused by the virus in the pneumotactic centers of the brain. Asadi and Simani (2020) pointed out that coronaviruses have the human respiratory system as their main target, in addition to having neuroinvasive capabilities. The retrograde transinaptic theory states that the virus is able to penetrate the CNS after a nasal infection, a model exemplified by Carodone et al. (2020) in his work. Neural propagation is made possible by the polarization of neurons, a property that gives them the ability to receive and transfer information, and can be retrograde or anterograde.

The central control for breathing is found within the brain stem, with participation of the solitary tract's nucleus. The CNS receives information from chemoreceptors that detect changes in oxygen and carbon dioxide concentrations. In this way, the respiratory system has a connection with the brainstem nuclei. Thus, the possible entry of the coronavirus through this structure can lead to changes in these neural groups.

Similarly, Wu et al. (2020) exemplified the possible path of the virus, beginning in the nasal epithelium and having the CNS as its destination, thanks to the anatomical organization of the olfactory nerves and the olfactory bulb within the nasal cavity and in the forebrain. When in contact with the olfactory epithelium, SARS-CoV-2 also has a direct action on its path —- causing inflammation and demyelination of the nerves that it finds — which can result in anosmia/hyposmia and dysgeusia (POONYA, SIMANI, 2020). Several studies, including those by Wu et al (2020) and Baig (2020), indicate that total anosmia or partial impairment with partial loss of smell are early markers of SARS-CoV-2 infection and indicate penetration into the CNS.

Indirect Neural Disorders

It is believed that COVID-19's indirect neurological complications are related to the cytokine storm syndrome (METHA, MCAULEY, BROWN, SANCHEZ, TATTERSAL, MANSON, et al. 2020). The entry of the virus into the human body, through the respiratory system causes an exuberant inflammatory response with the release of pro-inflammatory cytokines, such as interleukin 6 (IL-6) and granulocyte-monocyte colony stimulating factor (GM-CSF). In the first instance, the immune system's response is essential for controlling infections that normally occur; however, when there is an exacerbation of this response, there is an exuberant recruitment of cytokines, known as a cytokine storm.

Furthermore, the cytokine storm is also responsible for some neurological signs and symptoms that accompany the clinical condition, as described by Wu et al. (2020). In their studies, Wu et al. (2020), Braig (2020) and Poonya and Sarini (2020) suggest that hypoxia, respiratory and metabolic acidosis, electrolyte imbalances, as well as multiple organ failure, observed in severe cases of COVID-19, may be potential triggers for the neurological signs and symptoms manifested by these patients.

Regarding possible electrolyte and water imbalances, Olena (2020) highlights the need to investigate the hypothesis that there is competition between the SARS-CoV-2 virus's soike protein and sodium channels for the furin cleavage site. Thus, when the subunits break down, the virus has an easier entry into human cells and, consequently, the sodium channels are inactivated, causing such dysfunctions (OLENA, 2020).

Symptoms can be nonspecific — such as confusion, dizziness, ataxia and headache — or they can be more specific manifestations of the CNS, such as seizures and cerebrovascular diseases (POONYA, SARINI, 2020; MAO, 2020). Therefore, it is plausible to expect that seizures and even status epilepticus may occur. Thus, electroencephalographic monitoring is recommended, since critical patients who present changes in the level and state of consciousness, unexplained by other conditions, may have a state of non-convulsive epilepticus (POONYA, SARINI, 2020).

Infection of the respiratory tract generates a hypoxic condition in the CNS, leading to the activation of anaerobic metabolism in brain cells and the resulting accumulation of acids produced, which causes vasodilation, interstitial edema, cerebral flow obstruction and even headache due to ischemia and congestion (ABDENNOUR et al., 2012, apud WU et al, 2020). On the other hand, Li et al (2020) suggest that the potential damage to the CNS would be triggered by viral dissemination through the cerebral parenchyma, being accompanied by inflammation and endothelial dysfunction, contributing factors for cognitive alterations, which can worsen the hypoxic conditions of the respiratory distress syndrome caused by SARS-CoV-2.

Post-Infectious Neural Disorders

Post-infectious complications are later events and are related to the immune response "wrongly" directed at the host. Although there are no studies reporting SARS-CoV2 mimicry, there are studies that demonstrate the effect of SARS-CoV mimicry and, due to their genetic similarities and pathophysiological mechanisms, the new coronavirus is believed to cause similar reactions.

The immune system causes self-harm when responding to the viral infection, due to the presence of proteins in the viral membrane that resemble proteins found in the tissues of *H. sapiens.* The damage to the CNS triggered by the immune system can present itself in several ways, including encephalitis, Acute Disseminated Encephalomyelitis (ADEM), myelopathy and Guillan-Barré syndrome, among others.

Cardona et al. (2020), Ye, Ren and Lv (2020) and We et al. (2020) reported cases of viral encephalitis resulting from COVID-19 infection, with isolation of SARS-CoV-2 in cerebrospinal fluid samples from patients. Although the pathophysiological characteristic of the virus associated with encephalitis is not well described, it is believed that the immune response induced by SARS-CoV-2 causes a change in consciousness (YE, REN, LV, 2020). The same authors described other cerebrovascular conditions associated to the virus and suggest that the cytokine storm that occurs in brain tissue may be responsible for certain lesion patterns, such as necrotizing encephalopathy. Guiu et al. (2020) refer to the SARS-CoV pandemic in 2002/2003, when genetic material was found in the CNS of several patients infected by the pathogen and who presented with encephalitis, meningitis and Guillain-Barré syndrome. Recognizing that the new coronavirus has a genetic similarity greater than 80% in relation to SARS-CoV, it is expected that COVID-19 may evolve with similar injuries. Bilinski (2020) adds that SARS-CoV-2 brain infection can cause late and long-lasting neurological alterations, even in patients considered recovered and without any respiratory symptoms. In addition, the immune action on the nervous system could cause injury, inflammation and chronic brain injury (WU et al. 2020).

Wu et al. (2020) recognize the deleterious impact of SARS-CoV-2 infection on the CNS, but also signal that the mechanism involved still remains undetermined. Furthermore, further studies are needed to assess the long-term pathogenic effects of viral infection on the brain.

Final Considerations

It is believed that SARS CoV-2, together with the host's immunological mechanisms, is capable of producing distinct CNS disorders. On the other

hand, the detection of other coronaviruses in the nervous system of patients infected with these agents, suggests the microorganism's permanence, for long periods, in neural structures, without any apparent neurological disease, making the brain a reservoir for viruses. Although neurological symptoms may not be so common, their presence may justify the pathogens passage to these tissues and possible early or late neurological signs and symptoms.

When monitoring patients, findings compatible with CNS involvement should be valued, both from a diagnostic and prognostic perspective. It is extremely important that clinical examinations (mainly, pupillary and tendon reflexes), CSF and neuroradiological analyses be performed (when necessary) on patients for early identification and management of possible neurological complications. Furthermore, during autopsies it would be interesting to try to isolate SARS-CoV-2, in those patients with possible Neuro-COVID-19. Awareness of the neuro-invasive potential of the virus will have clinical importance and potential impact on the disease's treatment. Finally, awareness and management of neurological complications related to infection are essential to improve prognosis, especially in the case of critically ill patients.

References

[1] Asadi-Pooya AA, Simani L. Central nervous system manifestations of COVID-19: A systematic review [published online ahead of print, 2020 Apr 11]. **J Neurol Sci. 2020**;413:116832. doi:10.1016/j.jns.2020.116832

[2] Baig AM. Neurological manifestations in COVID-19 caused by SARS-CoV-2. **CNS Neurosci Ther**. 2020;26(5):499–501. doi:10.1111/cns.13372

[3] Butowt R, Bilinska K. SARS-CoV-2: Olfaction, Brain Infection, and the Urgent Need for Clinical Samples Allowing Earlier Virus Detection [published online ahead of print, 2020 Apr 13]. **ACS Chem Neurosci**. 2020; acschemneuro.0c00172. doi: 10.1021/acschemneuro.0c00172

[4] Conde Cardona G, Quintana Pájaro LD, Quintero Marzola ID, Ramos Villegas Y, Moscote Salazar LR. Neurotropism of SARS-CoV 2: Mechanisms and manifestations [published online ahead of print, 2020 Apr 8]. **J Neurol Sci.** 2020;412:116824. doi:10.1016/j.jns.2020.116824

[5] Cupertino MC, Cupertino GA, Gomes AP, Mayers N, Siqueira-Batista R. COVID-19 in Brazil: epidemiological update and perspectives. Asian Pac J Trop Dis. 2020; 13:193-196. doi: 10.4103/1995-7645.282215.

[6] Kimball A, Hatfield KM, Arons M, James A, Taylor J. Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020. **MMWR**. April 3, 2020. vol. 69, No. 13.

[7] Li Z, Huang Y, Guo X. The brain, another potential target organ, needs early protection from SARS-CoV-2 neuroinvasion [published online ahead of print, 2020 Mar 31]. **Sci China Life Sci**. 2020;1–3. doi:10.1007/s11427-020-1690-y

[8] Matías-Guiu J, Gomez-Pinedo U, Montero-Escribano P, Gomez-Iglesias P, Porta-Etessam J, Matias-Guiu JA. Should we expect neurological symptoms in the SARS-CoV-2 epidemic? [published online ahead of print, 2020 Apr 6]. ¿Es esperable que haya cuadros neurológicos por la pandemia por SARS-CoV-2? [published online ahead of print, 2020 Apr 6]. **Neurologia.** 2020; S0213-4853(20)30065-7. doi:10.1016/j.nrl.2020.03.001

[9] Olena, A. **SARS-CoV-2 Spike Protein Shares Sequence with a Human Protein** [published on line ahead of print, 2020 Jun 1]. The Scientist. 2020. Available in: https://www.the-scientist.com/news-opinion/sars-cov-2-spike-protein-shares-sequence-with-a-human-protein-67596

[10] PAHO/WHO. Pan American Health Organization. **Folha informativa – COVID-19** [published on line ahead of print, 2020 April 26]. Acess in 2020 April 26. Available in: https://www.paho.org/bra/index.php?option=com_content&view=article&id=6101:covid19&Itemid=875

[11] Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak [published online ahead of print, 2020 Feb 26]. **J of Autoimmunity.** 2020;109(102433). doi.org/10.1016/j.jaut.2020.102433

[12] Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses [published online ahead of print, 2020 Mar 30]. **Brain Behav Immun.** 2020; S0889-1591(20)30357-3. doi:10.1016/j.bbi.2020.03.031

[13] Wu Y, Xu X, Yang L, Liu C, Yang C. Nervous system damage after COVID-19 infection: presence or absence? [published online ahead of print, 2020 Apr 18]. **Brain Behav Immun**. 2020; doi: 10.1016/j.bbi.2020.04.043

[14] Ye M, Ren Y, Lv T. Encephalitis as a clinical manifestation of COVID-19 [published online ahead of print, 2020 Apr 10]. **Brain Behav Immun.** 2020; S0889-1591(20)30465-7. doi: 10.1016/j.bbi.2020.04.017

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