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ASPECTS OF NEUROLOGICAL CHANGES PROMOTED BY SARS-CoV-2: A MEDICAL SYSTEMATIC REVIEW RESEARCH

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ABSTRACT

The SARS-CoV-2 virus spreads around the globe and caused several symptoms, especially respiratory. However, much evidence indicates this virus causes neurological manifestations that must be investigated and understood, in order to avoid complications. In this context, this paperwork aims to compile information about the neurological changes related to the virus. Therefore, an integrative literature review study was conducted and 61 articles related to this theme were selected and analyzed. The authors searched the studies in the MEDLINE, Science Direct, and SciELO databases. The report of this review was made following the PRISMA recommendations. As a result, we found some symptoms, pathologies and syndromes related to SARS-CoV-2, including sensory loss, encephalitis, headache, meningoencephalitis, Guillain-Barré syndrome, stroke, which foment the hypothesis that Covid-19 stimulates diffuse hypercoagulation and sensory loss, mainly anosmia. Furthermore, psychiatric symptoms, such as psychosis and anxiety in patients with COVID-19, for example, but more studies are needed to explain the occurrence of certain pathologies and symptoms due to infection.

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INTRODUCTION

An outbreak of a novel coronavirus disease (Severe acute respiratory syndrome 2 – SARS-CoV-2) emerged in December 2019 in Wuhan City, China. SARS-CoV-2 is transmitted from person to person and has already caused more than 500,000 deaths and infected more than 10 million people worldwide, surpassing the number of cases of the 2003 SARS-CoV.[1] Coronavirus disease 2019 (COVID-19) pandemic has been declared by WHO as a global public threat considering its high morbidity and mortality rates.[2] Coronaviruses have some specific characteristics: they are enveloped, positive-sense, single-stranded RNA viruses and are capable of infecting a wide range of human and animal species.[1] They also have a broad tissue tropism causing acute and/or chronic damage to different body systems. Two other cross-species coronaviruses have affected global public health in the last two decades: the aforementioned SARS-CoV and the Middle East respiratory syndrome coronavirus (MERS-CoV).[3]COVID-19 is caused by a new Group 2 beta-coronavirus.[2]

COVID-19 patients' common manifestations are respiratory complications (as cough and respiratory insufficiency), fever and diarrhea in fewer cases.[1,2] Its resultant respiratory distress is thought to be not only a result of an inflammatory damage to the lugs parenchyma, but also due to damages in the respiratory centers of the brain.[4] However, although neurological symptoms were rarely described in the SARS-CoV and MERS-CoV epidemics[5], COVID-19 may cause manifestations as headache, dizziness, seizures, delirium, paresthesia and different types of encephalopathies.[6–8] The reason why the infected hosts present neurological manifestations remains elusive, but the intrinsic neurotropic properties of SARS-CoV-2 can justify the high frequency of several symptoms related to the nervous system.[2,9] Control measures as the need of strict patient isolation and of extreme contact precautions limit a detailed execution of neurological examinations and neuroimaging making it hard to identify new neurological complications and even more difficult to improve the understanding of the disease.[10] Fortunately, scientific advances of our era offer medical community higher probabilities to comprehend fundamental relationships which will

help fighting SARS-CoV-2 pandemic and its sequelae.[11]Nevertheless, by now, several virus–host interactive characteristics remain unknown.[1] There are still many hidden secrets about Covid-19 infection that are yet to be revealed and consequently, more data and scientific studies with statistical solidity are necessary.[12,13] Thus, this review aims toThe aim of the study is to highlight the relationship between neurological symptoms and Sars-Cov2 infection in humans in order to enable future research in the area.

METHODS

The report of this review was made following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (figure 1). The authors searched the studies in the MEDLINE, Science Direct, and SciELO databases from May 15, 2020, to May 22, 2020, using these descriptors: "Covid-19" AND "CNS" OR "Central Nervous System"; also "Sars-Cov-2" AND "Neurological". Only articles available in English and published in 2020 were included in this review. To ensure a broad approach to the topic, the authors searched for primary studies, which include: case reports, case studies, screening, and controlled and randomized clinical trials. All the authors participated in each phase of the review independently (screening, eligibility, and inclusion). Any disagreements between the authors were decided through recurring dialogues carried out during the production of this study. None of the were blind to the authors and the institution that published the analyzed studies. The articles' level of evidence was defined according to the American Academy of Neurology criteria for the classification of evidence in studies of causation (appendix 1). The PICO strategy was used to narrow and specify the main question this review seeks to enlighten (Table 1).

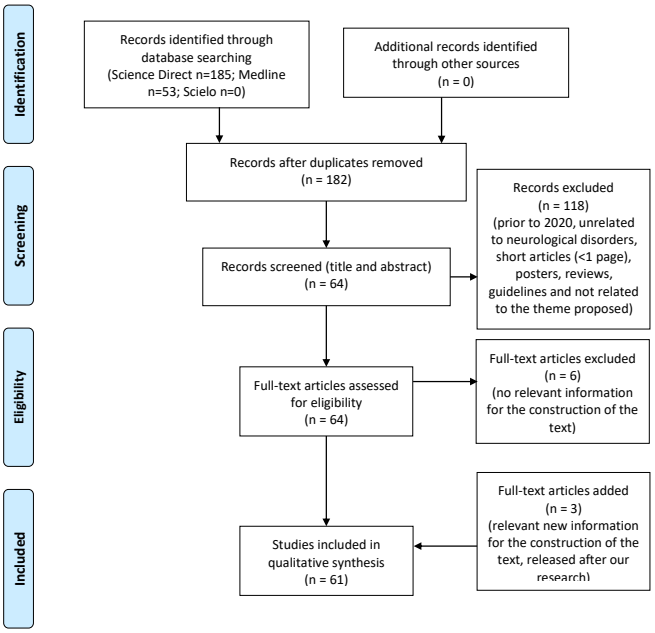

Figure 1.

RESULT AND DISCUSSION

Evidence of the relationship with neurological symptoms: Due to the current relevance of coronavirus 2019 (COVID-19) in the world, the entire neurological community is committed to assessing the consequences of this infection on the nervous system.[14]Respiratory symptoms head the clinical profile of SARS-CoV-2 and neurological manifestations are still poorly understood.[15]Severe acute respiratory syndrome 2 (SARS-CoV-2), which causes COVID-19 disease, belongs to the family of coronaviruses, which are known in the scientific community for their neurological tropism and for inducing inflammation in the brain.[15]Both SARS-CoV and SARS-CoV-2 share a similar mechanism of cell tropism, but both viruses may have differences in their ability to infect lung, intestinal and neuronal cells. [16] Since the two of them are practically identical taxonomically, it would not be surprising for the virus (COVID-19) to behave similarly.[17]states that previous experiences with taxonomically related SARS-CoV patients have overcome the uncertainty that coronaviruses affect the brain and that current cases of COVID-19 present, in addition to common respiratory complaints of the flu, neurological signs, and symptoms. Part of a blocking experiment of recombinant human ACE2 protein confirmed that similar to SARS-CoV, SARS-CoV-2 infection required binding to the angiotensin-converting enzyme 2 (ACE2) receptor. [16]ACE2 is expressed in the cells of the arterial and venous endothelium and the smooth muscle cells of the arteries of all organs of the human body. Therefore, respiratory symptoms are the most common in patients diagnosed with COVID-19, but the CNS can also be affected after damage to the blood-brain barrier.[17]With the union of the virus, negative regulation, and internalization of ACE2 across cell membranes, unregulated vasoconstriction can occur, an imbalance between the production and removal of reactive oxygen species, generating the formation of free radicals that can lead to vascular pathology.3 Baig, Khaleeq & Syeda, (2020) reported in their study the detection of ACE2 receptors in glial cells and neurons, being targets when the virus reaches the cerebral microcirculation through macrocirculation, but there is also the possibility that the virus reaches the brain through the ethmoid bone's crusty blade, close to the olfactory bulb, which may justify the finding of hyposmia.[19, 20] Among the neurological findings, headache seems to be the main primary symptom or that stands out, described as diffuse and of moderate to severe intensity, usually from sudden to gradual onset, not improving with the use of daily analgesics or being recurrent, limiting to the active phase of COVID-19.[19] Some patients reported headache in conjunction with inflammatory findings and with or without respiratory symptoms, which can be severe to the point of causing suicidal ideation. However, as the majority did not have a previous history of any type of headache and that it was restricted to the course of the disease, it is not difficult to admit the relationship of COVID-19 with this neurological symptom.[19] An important relationship evaluated by specialists was the association of SARS-COV-2 infection with encephalitis, but in an atypical way, the disease phase is self-limiting, which also indicates the involvement of the CNS in COVID-19.[21] Another important link in the report of patients who developed meningoencephalitis following the diagnosis of COVID-19 is that it suddenly evolved into a severe neuropsychological condition. In addition to the disposal of the microorganisms that usually cause this pathology, the previous knowledge that the family of this virus induces encephalitis may represent a relationship between both.[15] Neurological signs and symptoms may be caused by hypoxia and/or respiratory and metabolic acidosis occurring in an advanced course of the disease. Therefore, tests to assess the levels of serum urea, creatinine, electrolytes, and P02 and PC02 in the blood may help determine whether CNS involvement is primary or even secondary.[17]

Pathophysiology in Nervous Tissue: The SARS-CoV-2 virus enters cells via Angiotensin-Converting Enzyme 2 (ACE2) receptor, which degrades angiotensin II, similarly to SARS-CoV-1.[19, 20] This receptor is present in several organs and tissues, including in the heart, kidneys, lungs, liver vascular tissue, intestines, lymphatic tissue, and brain.[22] Thus, respiratory problems of patients with COVID may be directly related to the action of the virus in the respiratory center of the brain.[23] Sars-CoV-2 docks in the cells via spike proteins also present in Sars-CoV-1, although it is important to evince that the ACE2 receptor affinity for the Covid-19 Virus spike protein is about 20 times higher than that Sars-CoV-1 spike protein.[20] Considering the Central Nervous System (CNS), several mechanisms may contribute to an occurrence of neurological symptoms. First alternative for infection in neurological cells is that 2019n-CoV reaches the brain through the bloodstream [22], hematogenous route, which suggests a possible neurotropism. Second, SARS-CoV-2 may arrives to the brain cells through the olfactory bulb.[2, 20, 22, 24] Although it is not clear how the virus is able to reach the brain through the axons of the olfactory nerve since a recent study showed that the AC2 receptor is present in the cells of the respiratory epithelium, but it is not in the

Authors (year)	Goals	Results	Conclusion	Periodic
El Otmani et al. (2020)	It aims to report of a 70-year-old woman with rheumatoid arthritis who develops neurological symptoms	This case related a paciente with respiratory symptoms related with Sars-CoV 2 infection and motor and sensory neurophaty in all four limbs. It was compatible with GBS. In the medical investigation, Sars-CoV-2 is confirmed by RT-PCR in an oropharyngeal swab.	The authors collaborated with this case for the literature of GBS triggered by Sars-CoV 2 infection. And they suggest that new cases of GBS should be tested for COVID-19.	RevueNeurologique
Coen et al. (2020)	Report a case of a man with neurological symptoms and constipation who had an oligossymptomatic Sars-CoV 2 infection ten days before. It also reviews within the literature other cases of GBS associated with other kinds of coronavirus.	It's a case of a paciente without medical history who presents paraparesis, distal allodynia, and other symptoms, which were compatible with GBS.	The article highlights the need for clinicians should imagine that COVID-19 may induce Guillain-Barré syndrome, and remember that infectious diseases during outbreaks can cause these conditions like the recent case of the Zika vírus epidemic.	Brain, Behavior, andImmunity
Scheidl et al. (2020)	Describe a case of a 54-year-old woman with Sars-CoV-2 infection three weeks before developing neurological symptoms of AIDP.	The pacient develops symmetric paraparesis, areflexia, tingling of all extremities and numbness. She had a positive PCR COVID-19 test ten days before.	It's a case of development of GBS associated with COVID-19 without fever or respiratory symptoms which were correlated with severe neurological consequences.	Journal of peripheral nervous system
Ottaviani et al. (2020)	Report a case of a 66-year-old woman from an endemic area with fatigue and difficulty walking.	This report presentes a case of difficulty walking and acute fatigue progressing for paraplegia and weakness in upper limbs, diffuse areflexia, but with no sensory effects	This article reinforces the need for more studies in this area because it reports a case that shows no response to IV immunoglobulin. It could be also a case of para-infectious paralysis.	NeurologicalSciences
Arnaud et al. (2020)	Present a case of a 64-year-old man with Sars-CoV-2 symptoms, who developed lower limb weakness and other neurological conditions.	The patient presents lower-limb weakness, that represents a severe flaccid paraparesis. Besides that, it also found generalized areflexia and the electrophysiological exam was compatible with demyelinating neuropathy.	This case reinforces the correlation between GBS and COVID-19 through the autoimmune mechanism.	Clinicalneurophysiology
Zhao et al. (2020)	Present a case of a 61-years-old woman diagnosed with Covid-19 that presented with neurological symptoms.	The pacient had areflexia and symmetrical weakness and both lower limbs in addition she had a decrease of light touch and sensitive symptoms. The examssuggest a demyelinatingneuropathy.	This was probably the first GBS associated with Sars-CoV-2 infection. The authors highlight the limitations of this case as well as its chronology because the neurological symptoms came before the fever and the cough.	The Lancet Neurology
Camdessanch et al. (2020)	Describe a case of a 64-year-old man with Sars-CoV-2 infection. And eleven days after the symptoms he develops a neurological condition.	This case reports neurological symptoms in a paciente who had COVID-19. He had paresthesia in feet and hand that progressing for severe tetraplegia, lost of tendon reflexes and sensory symptoms, which wera compatible with GBS with demyelinating pattern.	Though neurological manifestations aren't the main complications of Sars-CoV-2 infection. It's important to know about it, mainly with this case which a clear chronology.	RevueNeurologique
Caamaño Beato (2020)	Report a case of facial diplegia in a 61-year-old male 10 days after COVID-19 infection.	The pacient presents right peripheral nerve palsy that evolve to bilateral peripheral nerve palsy with lost of blink reflexe in both eyes.	It's showed how neurological manifestations can be diverse. The authors highlight the possibility of this case being a GBS variant and the need for more cases to create a good quality about this condition.	Journalofclinicalneuroscience
Virani et al. (2020)	Presents a case of a 54-year-old male with Sars-CoV-2 infection besides other infections.	This case presents a man with Clostridium difficile and Sars-CoV 2 infection. He had numbness and weakness in loweer limbs, fever and non-productive cough in addition with absent of deep tendon reflexes. Besides that the symptoms progress for lost of strenght in four limbs.	This article highlights that the medical community should know of the neurological presentation of GBS associated with COVID-19.	IDCases
Gupta Paliwal Garg (2020)	Comment about GBS cases in COVID-19 related to literature.	This letter presents analysis about the age of pacients who were most elderly, the symptoms that these pacients had in COVID-19, like hyposmia.	It finds a poor outcome in patients with common treatment. Also, it's speculating about the pathology of COVID-19 related GBS.	Brain, Behavior, andImmunity

Figure 2. Table resumes the finds about GBS in our review

olfactory sensory neuron and indicates that the virus approach the brain via cervical lymph nodes.[22] Third, the event known as the "cytokine storm" may reaches the CNS and promote, along with other pro-inflammatory factors, inflammation of nerve cells resulting in neurovascular pathologies.[22] In addition, another study suggests that the virus access the brain through the enteric nervous system.[23]

In this review it is clear that understanding the process of interaction between the virus and ACE2 receptor, as well as the inflammatory process in nervous tissue are fundamental to understand the evolutionof Covid-19 in a patient and the symptoms that the disease can originate in the CNS.

Sensory loss, seizures and psychiatric symptoms: Coronaviruses have known mechanisms for neurological damage, which may be responsible for symptoms of sensory loss, seizures, and psychiatric symptoms in patients of COVID-19. A case report of Guillain-Barré Syndrom that led to Facial diplegia has been described as a complication directly related to a SARS-COV-2 infection after typical clinical symptoms disappeared.[11] Two cases of diplopia and ophthalmoparesis have also been identified in COVID-19 patients after respiratory affections started similar to the previous case reported.[25] This reveals that respiratory symptoms, which are the most typical clinical presentations of this disease, shouldn't be the

only concerns. Anosmia, or olfactory loss, has been identified in patients tested positive for COVID-19, and the mechanism of injury for this may be similar to previously described central and peripheral neurologic disturbances caused by coronaviruses. [26] This symptom is described as an important association during the COVID-19 pandemic and should be further researched in patients. Seizures have also been reported in COVID-19 patients with no previous known personal or familiar cases of seizuresas well on a patient with postencephalitic epilepsy.[6, 27, 28] The reports describe seizures associated with SARS-COV-2 infection, presenting or not typical COVID-19 clinical symptoms. Many other causes were investigated and discarded as possible reasons for convulsions, making COVID-19 the most possible cause for the episode. With known neurological manifestations for COVID-19, the occurrence of seizures should be considered as a probability of this viral disease in both treatment and prevention. Even though this disease endangers our Central Nervous System (CNS), the pandemic situation, in general, may have a high toll on one's mental health and the possibility to affect it negatively. Human isolation and extended time away from family and other loved ones during this period, as well as the possibility of CNS acute or long-term damage by COVID-19, must be addressed by medical teams as possible causes of delirium and other psychiatric conditions.[29] Cases of new-onset psychosis have also been reported on COVID-19 patients some with no previous psychiatric history but none with previous psychotic symptoms.[30, 31] They presented with psychotic symptoms and some of themwith acute delirium. The patients didn't have respiratory, gastrointestinal symptoms, ageusia, or anosmia and similarly presented with new and recent-onset severe anxiety, agitation, paranoia, and disorganized thinking.[31] Inflammatory responses to SARS-COV-2 infection, or "Cytokine Storm", is commonly cited as a probable mechanism that causes neuropsychiatric conditions on those patients. Most authors agree that more data is necessary to provide concrete associations on this subject as there is yet a lot to be learned about this disease, but considerations about said symptoms and their relation with COVID-19 patients need to be addressed to better understand, recognize and treat the SARS-COV-2 infection. It is important to be alert to the possible latency of SARS-COV-2 in the central nervous system, which may have repercussions in patients already cured. This is only a possibility, but an importante one to be evaluated and studied further in the years to come. [32]

Stroke: The database research has shown various studies connecting stroke and cerebrovascular disease with Covid-19. One case report described the simultaneous existence of pulmonary embolism and stroke secondary to intracranial vessel occlusion[33], which corroborates the hypothesis that Covid-19 stimulates a diffuse hypercoagulation. However, the direct correlation between stroke and SARS-COV-2 is not fully understood yet. Some risk factors are strongly associated with the severity of the disease.[34, 35] The first study that related stroke to COVID.[36] showed that they are correlated with severe forms of the disease and with neurological symptoms, including cerebrovascular effects, like stroke. Although chronic diseases, like hypertension, were found in almost all case reports, one case of a patient without these risk factors was found.[37] The facts highlight the possibility that the infection itself can cause this vascular effect. In serial case reports[38], higher levels of C-protein reactive and D-dimer levels were found in patients. Furthermore, this relation was also found in another similar study.[35] Both are coherent with the correlation between high C-protein levels and cardiovascular disease.[39] One of the strongest poor prognostic markers is neuroimaging findings.[40] A study showed that stroke is the most common finding in neuroimaging researches and has a 1.1% frequency in hospitalized infected patients. This finding establishes a reach's statistic of stroke that would be tested in other studies so it can be useful in the future to public health management.

Guillain Barré syndrome: Guillain Barré syndrome is a autoimmune disturb involving a cross-reaction in the gangliosid components of the peripheral nervous system. It is naturelly relationed with a preview some infections like *Campylobacter jejuni*, cytomegalovirus (CMV), influenza-A vírus; and recently correlated with Zika vírus and some kinds of Coronavirus. In our recente review of literature we have found nine cases of GBS associated with SARS-COV-2, within them, we have found cases of demyelinating, axonal and cases where both forms of damage coexisting.[41, 42, 43, 44] Moreover, in the cases was possible to see neuropathies with motor and sensitive pattern, what do not show a main pattern of the syndrome in Covid-19 association.[45] In review was find most cases of post-infectious, but two patients were discrebed like probably para-infectious disease, inclunding the fist case documented.[41, 46] It was also found a case report that had proposed be a rare variant of GBS [11], which the elder pacient had devoleped facial diplegia. The studies of cerebro spinal fluid (CSF) revealed in cases of this review that was tested [47], a growth in the protein level without elevated of cell count, beside that, there are no found of PCR positive for SARS-COV-2 in the CSF of all patient whom this was tested. Comparing the studies was notice that the gap between the begin of covid-19 sintoms and the begin of neurologic sintoms associeted with GBS is within a period of 5 to 25 days[42], and the time for resolution of these conditions was described in about five days with the treatment with intravenous immunoglobulin[48], except in one case. 41 Regardless of the sampling is not big enough to cloncluding a concret pattern about these cases, although it was proposed to build a model of Covid induceded syndrome [49], but it was concluded that Guillain-Barré syndrome is not a standart complication of commons cases of Covid-19.

Other findings

Several asymptomatic cases of patients diagnosed with coronavirus disease 2019 (COVID-19) presented with syncope, often preceded by dizziness, as the only symptom of the ongoing infection. With the elimination of cardiac and pulmonary causes, it is proposed that it was caused by neurally mediated mechanism or primary dysautonomia, caused directly by the virus or secondary to it, due to an autoimmune autonomic neuropathy or immunological inflammation. Ebrille et al., 2020. The reported patients suffer from some type of cardiac pathology and most were on prolonged use of angiotensin-converting enzyme (ACE) inhibitors, leading to a decrease in systemic pressure caused by the action of angiotensin II, which may have influenced the development of syncope. However, the possibility of being a symptom of the presentation of COVID-19 infection leads to the need for recognizing this finding in advance, so that the necessary precautions are taken. Ebrille et al., 2020. The treatment may not be the same for everyone. Individual genetic predisposition and susceptibility play an important role in it, and the infection may be different depending on the person affected or the SARS-CoV-2 strain (some strains from different countries have shown variations). It is also speculated, based on statistics, that Bacillus Calmette-Guérin (BCG) vaccination may have a positive effect against Covid-19. (DAS; MUKHERJEE; GHOSH, 2020). There are some challenges for treating neurological affections on Covid-19 patients. Even though recent reports indicate that harsh cases may benefit from corticosteroid therapy, it may still cause a negative outcome on the patient. Intravenous immunoglobulins (IVIg) and plasma exchange (PLEX), second-line treatments for neuroinflammatory conditions, are potentially beneficial, but brings the risk of causing micro thrombosis. Cyclophosphamide and rituximab, third-line treatments, are considered high-risk medications regarding subsequent SARS-CoV-2 infection and should only be used if other medicines have failed (NEEDHAM ET AL., 2020). Since there are many possible strategies of treatment being studied for this current pandemic, current protocols and guidelines for the treatment of SARS-CoV-2 infection may or not change soon. The potential benefits of genome-based research for the treatment and prevention of Covid-19 are yet to be confirmed and further studies should be conducted with this aim.

One case of peripheral neuropathy associated with a severe case of COVID-19 reported symmetrical polyneuropathy with weakness in lower limbs and absent of deep tendon reflexes (1). The patient was treated with glucocorticoids but unfortunately died after developing a cardiac arrest. This was an example of a report in which a Covid-19

case with neurological symptoms was not completely explained for its poor outcome. It was proposed that could be a case of Guilian-Barré syndrome induced by SARS-COV 2, which was commonly reported in previous cases(2). As said before, neuro-infectivity has been described for other coronaviruses but is still questioned for SARS-CoV-2, especially because studies have shown that COVID-19 does not cross the blood-brain barrier. The cerebrospinal fluid in research studies patients is normal, therefore, does not cause meningitis or encephalitis, but despite the lack of a clear pathophysiological mechanism, an apparent positive response to steroid treatment together with the normalization of Cerebrospinal fluid cytokines in these studies suggests that the encephalitis was mediated by a hyperinflammatory mechanism. (Filatov, et al. 2020; Pilotto, et al. 2020). It is known that the systemic inflammatory response syndrome (SIRS), which is a pathological mechanism associated with a high level of cytokines and generalized inflammation, can be precipitated by severe viral infections, thus causing encephalitis and meningoencephalitis. This is especially important in elderly patients, who are at an increased risk of altered mental status and other neurological conditions in the setting of acute infections. Nevertheless, although there was no evidence of SARS-CoV-2 in the CSF by RT-PCR, a direct CNS infection cannot be excluded. (Filatov, et al. 2020; Pilotto, et al. 2020; Dogan, et al. 2020).

CONCLUSION

Studies have been published demonstrating the deleterious effects of the Coronavirus on the CNS, and there is increasingly clear evidence in the medical literature about this relation. The coronavirus pandemic revealed various manifestations involving the CNS, which highlights the importance of research into neuropathic physiopathology to prevent the spread of the virus by asymptomatic patients who show only neurological manifestations for not knowing that they have COVID-19, and thus, not taking the care inherent in this disease. Moreover, considering the structure of CNS cells, several mechanisms may contribute to an occurrence of neurological symptoms: neurotropism, hypoxia, respiratory metabolic acidosis, through the olfactory bulb, or an event known as a cytokine storm. Even so, it is not clear how the virus can reach the brain, and it remains unknown if the CNS involvement is primary or secondary. Besides, despite their inherent limitations, the studies analyzed so far suggest that this neurological damage is been associated with symptoms and diseases as sensory loss, encephalitis, headache, meningoencephalitis, Guillain-Barré syndrome, stroke, seizures, psychiatric symptoms, such as psychosis, anxiety, and paranoia, and others neurological manifestations in patients with COVID-19 who, some of them, didn't even have respiratory or gastrointestinal symptoms, however, more studies are necessary before definitive considerations can be made. Indeed, this is based on the physiopathological explanations set out in the articles, but, in terms of the bibliographic production that is part of the scientific texts used, the study revealed that there is still little information about the relationship of COVID-19 with the SNC. This is supported by the fact that, in the set of 182 sources accessed by the MEDLINE, Science Direct, and SciELO databases, 61 are characterized as useable scientific articles, based on our exclusion criteria, to produce this bibliographical review. The report of this review was made following the PRISMA recommendations. Therefore, according to the above, it was possible to analyze and show neurological symptoms related to viral infection addressed in the study(the most diverse points inherent in COVID-19 and its possible neurological manifestations), however, as was verified, the information about the subjects addressed is, despite being well-founded in scientific research and data, in need of new studies and debates with a view to the production of future research that could deepen the knowledge about this question.

Declaration: We declare that there is no conflict of interest in this study.

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