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COGNITIVE, NEUROLOGICAL, NEUROPSYCHOLOGICAL AND NEUROPSYCHIATRIC ALTERATIONS IN POST-COVID-19 PATIENTS.

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SUMMARY

Introduction. The SARS-CoV-2 virus that causes the COVID-19 disease, reports hundreds of infections daily, the alterations and sequelae of this new pathogen have been reported globally, due to the seriousness of being an older adult and evolving seriously.

Methodology. The present work has a qualitative approach, with exploratory and descriptive intentions of the alterations at a cognitive, neuropsychological, neuropsychiatric and neurological level.

Results. In the analysis, 16 articles were included that express alterations in areas of functioning that compromise the quality of life in patients over 18 years of age, the scientific evidence is strong on the alterations caused by the new SARS-CoV-2 virus, from the deterioration of cognition, visuospatial abilities and constant headaches among other symptoms, which are of attention from a multidisciplinary perspective.

Conclusions. The transmission of the virus in the adult population poses a risk to health, this study shows alterations at the cognitive, motor and neurological level, age being a factor that predisposes the appearance of sequelae.

Keywords. COVID-19, Adults, neuropsychological disorders, cognitive impairment, neuropsychiatric sequelae, disease.

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ALTERACIONES COGNITIVAS, NEUROLÓGICAS,
NEUROPSICOLÓGICAS Y NEUROPSIQUIÁTRICAS
EN PACIENTES POST-COVID-19. UNA REVISIÓN
SISTEMÁTICA

RESUMEN

Introducción. El virus SARS CoV-2 causante de la enfermedad COVID-19, reporta cientos de contagios diariamente, las alteraciones y secuelas de este nuevo patógeno han sido reportadas a nivel global, por la gravedad que implica ser adulto mayor y evolucionar de manera grave.

Metodología. El presente trabajo tiene un enfoque cualitativo, con intenciones exploratorias y descriptivas de las alteraciones a nivel cognitivo, neuropsicológico, neuropsiquiátrico y neurológico.

Resultados. En el análisis fueron incluidos 16 artículos que expresan alteraciones en áreas de funcionamiento que comprometen la calidad de vida en pacientes mayores de 18 años, la evidencia científica es fuerte sobre las alteraciones que provoca el nuevo virus SARS Cov-2, desde el deterioro de la cognición, habilidades visuoespaciales y cefaleas constantes entre otros síntomas, que son de atención desde una perspectiva multidisciplinaria.

Conclusiones. La transmisión del virus en la población adulta supone un riesgo a la salud, este estudio evidencia las alteraciones a nivel cognitivo, motor y neurológico siendo la edad un factor que predispone la aparición de secuelas.

Palabras clave. COVID-19, Adultos, alteraciones neuropsicológicas, deterioro cognitivo, secuelas neuropsiquiátricas, enfermedad.

INTRODUCTION

At the end of 2019 in Wuhan, China, a case of atypical pneumonia with abnormal characteristics was reported that quickly began to spread, and in January 2020, health authorities recognized a new pathogen called SARS-CoV-2, which shares a strong connection with severe acute respiratory syndrome (SARS), and Middle East respiratory syndrome (MERS); This new virus is the cause of the disease COVID-19 (Wu et al., 2020), which in March 2020 was declared a global pandemic by the World Health Organization (WHO) due to its high level of contagion and mortality. (León et al., 2020; Mayo Clinic, 2021).

Among the most common symptoms are fever, cough, tiredness, loss of taste or smell, sore throat, headache, aches or pains in the body, although it can also cause diarrhea, rash or discoloration of the fingers. hands or feet, red or irritated eyes, difficulty breathing or dyspnea, loss of mobility or speech, feeling confused and chest pain (Médica Sur, 2021; WHO, 2020).

However, brain imaging of patients who have required hospitalization have revealed Central Nervous System abnormalities as an important feature of COVID-19 that compromises the patient's health; these records suggest that the virus can penetrate the blood-brain barrier and enter the central nervous system (neuroinvasion). This statement is evidenced by the following premises (Carod-Artal, 2020):

- Involvement of the central nervous system by other respiratory viruses.
- Neurological damage from coronavirus in other species.
- Animal models of infection of the central nervous system by human coronaviruses.
- Evidence of neurological complications from other coronaviruses.
- Patients with COVID-19 who have presented neurological manifestations.

This implies that the SARS-CoV-2 virus can cause neurological sequelae, with anosmia and ageusia being found more frequently, present in up to 88% of young female patients, while headaches appear in up to 34% of males. cases (Bernardo, 2021). However, other conditions

can become as serious as brain parenchymal abnormalities, subcortical microhemorrhages and macrohemorrhages, cortical subcortical swelling, and nonspecific deep changes in the white matter, triggering various pathologies: stroke, anosmia, cortical blindness, delirium, encephalitis, encephalopathy, hemiparesis, dizziness, meningitis, flaccid paralysis, psychosis, memory problems, among others (Abenza-Abildúa et al., 2020; Carod-Artal, 2020; Da Silva, 2020; García et al., 2020; Quiroz and Amarales, 2020).

For this reason, it is suggested that the COVID-19 disease causes a neurological, neuropsychological, neuropsychiatric compromise, which can be caused through a direct lesion (viral replication in the nervous system) or an indirect lesion (activation of the inflammatory cascade, toxic alterations). -metabolic, immune dysregulation and immune-mediated mechanisms), which will entail 3 types of manifestations: of the central nervous system, of the peripheral nervous system and of the muscles (Aguilar and López, 2021). For the purposes of this research, the article will focus exclusively on the clinical manifestations and alterations in perspective with the central nervous system.

In this regard, it is expected that COVID-19 will result in significant cognitive impairment (Riordan et al., 2020) that will affect a large part of the infected people, even if they were asymptomatic (Da Silva, 2020); In addition, the pandemic viral infection has reached about 362,549,889 infections around the world (Ritchie et al., 2022) and at least 70% of the survivors are expected to present some type of neurological, psychiatric or cognitive impairment after hospital discharge. (He et al., 2021; Sasannejad et al., 2020).

For this reason, the present work carried out a systematic review of the neurological, neuropsychological, neuropsychiatric and neurocognitive consequences of infection by SARS-CoV-2, with the aim of classifying the neurological sequelae of COVID-19 in the adult population.

METHOD

The present work was carried out from a qualitative approach with exploratory and descriptive purposes. Specifically, a systematic review was carried out that analyzed the neurological, neuropsychological, neuropsychiatric and neurocognitive effects of the COVID-19 disease in patients aged 18 years and older.

Sample

This was made up of articles available in the Clarivate, EBSCO Medic Latina, JStor and Scopus databases, which have been published during the years 2020 and 2022 and are in open access.

Process

The search for scientific literature was carried out in the Clarivate, EBSCO Medic Latina, JStor and Scopus databases using the terms "COVID-19", "neuropsychology", "neurocognitive" and "neuropsychiatric". With these, two search strings were created by adding the boolean operator "AND":

- 1) "COVID AND neuropsychology".
- 2) "COVID AND neuropsychiatric".
- 3) "COVID AND neurocognitive"

Filter was applied by year. The review was carried out during the months of October–November 2021, January–February and October–November 2022 with access to the databases from the BUAP Libraries electronic resources repository. For data analysis, a database was created using the Google spreadsheet.

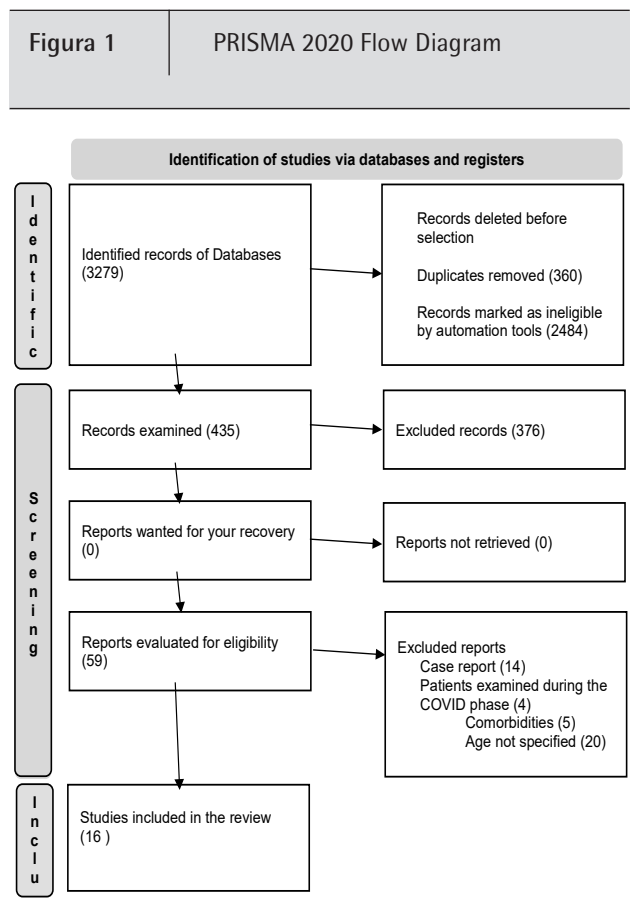
INCLUSION AND EXCLUSION CRITERIA

For the object of study, the included articles had to: 1) be scientific articles; 2) empirical; 3) open access; 4) available in Spanish or English; 5) address the neuropsychological/neuropsychiatric/neurocognitive sequelae of COVID-19 in adults older than 18 years; 6) these adults must not have had any type of medical problem prior to being infected with SARS-CoV-2; 7) all symptoms must have been reported at least 10 days after infection; 8) the data obtained should be shown by age ranges.

On the other hand, all those investigations that: 1) were of closed access were excluded; 2) were gray literature; 3) were published in any language other than Spanish or English; 4) had children or adolescents as a sample; 5) adults over 18 years of age with a medical problem prior to being infected with SARS-CoV-2; 6) had caregivers as a sample; 7) had deceased people as a sample; 8) sampled pregnant women; 9) had medical personnel as a sample; 9) the information was obtained through self-reports; 10) the information would have been obtained by telephone and 11) the information would have been obtained online.

Selection process

Clarivate yielded 483 results, EBSCO Medic Latina 36, JStor 203 results, and Scopus provided 2,197. In total, 2,506 entries were obtained, of which 349 articles were selected whose title alluded to "COVID-19," "neuro," "cognitive," "psychiatric," "psychology" and "SARS-CoV-2", and with them the systematic review began following the phases proposed by the PRISMA flowchart, whose flowchart is visible in Figure 1.



Source: Elaborated from Page et al., 2021

RESULTS

16 articles were analyzed. In this regard, the predominant language was English and the keywords found most frequently were "COVID-19" and "SARS-CoV-2". Most of the investigations used a qualitative approach with a descriptive and cross-sectional design.

The selection of the sample was non-probabilistic in all the articles, and it comprised from 4 to more than 100

participants. On the other hand, the age range was from 18 years onwards and the patients were predominantly male.

Regarding post-COVID cognitive manifestations, the literature reported cognitive impairment, memory problems, and executive dysfunction. This is detailed in Table 1.

Regarding post-COVID neurological manifestations, cerebrovascular events, seizures and neuromuscular fatigue were found. This is visible in Table 2.

Lastly, Table 3 contains the neuropsychological and neuropsychiatric manifestations, among which fatigue, depression and anxiety were found.

Table 1		Neurological sequelae in post-COVID patients	
Neurological sequelae			
Author	Year	Sample	Post-COVID manifestations
Besteher <i>et al.</i>	2022	17 women and 13 men with an average age of 47 years	Cognitive deficits
Checa <i>et al.</i>	2022	29 men and 21 women aged 51 and 65	82.35% (n=14) presented cognitive impairment
Calabria <i>et al.</i>	2022	49 men and 87 women from 20 to 88 years of age	Executive dysfunction increased steadily after infection.
García-Sánchez <i>et al.</i>	2022	22 men and 41 women from 22 to 78 years old	The most commonly affected domain was attention (61.9% of the sample).
Hellgren <i>et al.</i>	2021	28 men and 7 women from 51 to 66 years old	Sixteen of 35 patients (46%) showed cognitive impairment; 6 of these (17%) had mild/moderate cognitive impairment.
Ortelli <i>et al.</i>	2021	10 men and 1 woman from 56 to 80 years old	Cognitive fatigue and executive dysfunction.
Pinna <i>et al.</i>	2021	29 men and 21 women with an average age of 60 years	Short-term memory impairment.
Pistarini <i>et al.</i>	2021	13 men and 7 women over 50 years of age	Impairment of executive functions, short and long term memory, visuospatial abilities, abstraction and orientation.

Table 2		Neurological sequelae in post-COVID patients	
Neurological sequelae			
Author	Year	Sample	Post-COVID manifestations
Avula <i>et al.</i>	2020	Three women aged 83, 80 and 88 and a 73-year-old man	Presence of cerebrovascular event.
Besteher <i>et al.</i>	2022	17 women and 13 men with an average age of 47 years	Increased gray matter in patients with prolonged COVID.
Birberg <i>et al.</i>	2022	82 men and 54 women with an average age of 57 years	Significantly lower scores on late and immediate memory tests. Attention deficits, psychomotor speed, verbal fluency.
Dressing <i>et al.</i>	2022	17 women and 13 men with an average age of 53 years	Microembolic subacute cortical infarction in the left occipital lobe in 1 patient (65-year-old man) and mild microangiopathic changes were present in a 61-year-old patient.
Krishnan <i>et al.</i>	2022	36 women and 4 men with an average age of 44 years.	Impairment of cognitive domains.
Langavant <i>et al.</i>	2021	19 men and 7 women with a mean age of 58 years	Presence of neurological disorders, encephalitis, encephalopathy, cerebrovascular events and Guillain-Barré syndrome.
Ortelli <i>et al.</i>	2021	10 men and 1 woman from 56 to 80 years old	Neuromuscular fatigue. Flaccid tetraparesis, muscle atrophy, areflexia, anosmia, sensory disturbances.
Pinna <i>et al.</i>	2021	29 men and 21 women with an average age of 60 years	Presence of seizures, hypoxic ischemic brain injury.

Table 3 Neuropsychological and neuropsychiatric sequelae in post-COVID patients

Neuropsychological and neuropsychiatric sequelae			
Author	Year	Sample	Post-COVID Post-COVID manifestations
Ahmed <i>et al.</i>	2021	84 men and 98 women with an average age of 46 years	Poor sleep quality, probable PTSD, somatization, anxiety, anger-hostility, phobia-anxiety, obsession-compulsion
Besteher <i>et al.</i>	2022	17 women and 13 men with an average age of 47 years	Fatigue and depression.
Calabria <i>et al.</i>	2022	49 men and 87 women from 20 to 88 years of age	82.3% of people reported clinically significant levels of fatigue. Depressive and anxiety symptoms were less prevalent with 23.5% and 35.3% of patients reaching significant levels, respectively. Apathy increased steadily after infection.
Cattarinussi <i>et al.</i>	2022	33 men and 46 women with an average age of 42 years.	The most reported symptoms were fatigue (71.2%), anxiety and depression
Dressing <i>et al.</i>	2022	17 women and 13 men with an average age of 53 years	All the patients complained of difficulties with attention, memory, and multitasking skills. Additionally, 24 of 31 (77%) complained of fatigue.
Hellgren <i>et al.</i>	2021	28 men and 7 women from 51 to 66 years old	Clinically significant fatigue was reported by 25 patients (74%). Depression, anxiety.
Krishnan <i>et al.</i>	2022	36 women and 4 men with an average age of 44 years.	Anxiety, depression and recurrent fatigue.
<i>Author</i>	<i>Year</i>	<i>Sample</i>	<i>Post-COVID sequelae</i>
Lamontagne <i>et al.</i>	2021	29 women and 21 men aged 18 to 49 years	Persistent brain fog, depression, anxiety, and anhedonia.
Ortelli <i>et al.</i>	2021	10 men and 1 woman from 56 to 80 years old	Apathy.
Pinna <i>et al.</i>	2021	29 men and 21 women with an average age of 60 years	Altered mental status, headaches.

DISCUSSION

The SARS-CoV-2 virus (responsible for the current pandemic) is generating multiple effects at the neurological level, which has aroused great interest due to uncertainty about the scope and impact of this pathogen on the central nervous system. Therefore, the objective of this study was to classify the neurological sequelae of COVID-19 in the adult population:

Neurocognitive sequelae

Cognitive dysfunction is one of the most frequently reported mental health problems and can affect more than half of post-COVID patients even six months after hospital discharge (Estrada et al., 2021). In this regard, it was found that the patients presented executive dysfunction, memory problems and cognitive deficit, which is consistent with the findings made by Atuna et al (2022)

and Crivelli et al (2021). It should be noted that more and more studies are reporting a type of dysfunction at the level of processing and difficulties in recalling information, which has a functional impact on the activities of daily living of patients recovered from COVID 19. What is responsible for this effect is called "mental fog", this being one of the main neurocognitive sequelae that has been described as slow thinking, difficulty concentrating and the presence of episodes of confusion Pattnaik et al (2021).

It is worth mentioning that these alterations can arise thanks to 3 fundamental variables (Mata, 2021):

- 1) How strong was the COVID-19 disease.
- 2) Previous health conditions of each particular patient.
- 3) Areas of opportunity for care and clinical follow-up.

Therefore, it is still too early to describe the full scope that this infection can have, since almost three years after the start of the COVID 19 pandemic, the scope is evident from a neurocognitive and clinical perspective.

Neurological sequelae

According to Zambrano et al. (2022) neurological sequelae are one of the main complications present in post-COVID-19 patients and includes a wide variety of symptoms, although these could be due to the accumulation of molecular and cellular damage typical of the aging process (WHO, 2021), as well as different conditions of social vulnerability that the population faces, such as lack of personal or economic resources and lack of access to protection policies (Guerrero and Yépez, 2015).

However, in the present review, it was possible to find encephalitis, encephalopathy, sensory alterations, anosmia, Guillain-Barré syndrome, cerebrovascular events, among others. This is consistent with Da Silva (2020), Rahman et al. (2020), Sinnanovic (2021) and Yadav et al. (2020), who reported post-COVID-19 patients with headaches, dizziness, encephalopathy, delirium, seizures, hypoxia, loss of consciousness, coma, paralysis, and/or stroke.

Neuropsychological and neuropsychiatric sequelae

Manriquez et al (2021) have pointed out that there is no single and clear pattern in the neuropsychological functioning of patients, which is why it is common to find a wide variety of symptoms. In the selected samples, anxiety problems, delusions, hallucinations, depression and mental fog were observed; however, these could also be due to exposure to other factors during the pandemic, such as lockdown and economic or social problems (Ziyad et al., 2022).

Regarding the limitations of this study, it is worth noting that no comparison was made between pre and post COVID-19 patients. Similarly, although neurological and psychiatric manifestations affect both symptomatic and asymptomatic people (Da Silva, 2020). Possible differences between the two groups were not considered due to the lack of scientific evidence, in addition, other variables such as vaccination, time of confinement, severity of COVID-19, variants of SARS-CoV-2, etc. were not taken into account. Therefore, for future research, it will be necessary to present a global vision of COVID-19 in the field of neuroinfection contemplating the human being as a social and integral being in all aspects of psychological and anthropological functioning, since for Carod-Artal (2020) in specific tropical regions, co-circulation can occur of SARS-CoV-2 with the dengue, chikungunya, Zika or

Japanese encephalitis viruses, which could generate some confusion in symptoms and reach vulnerable populations or add other complementary symptoms compared to those already reported for SARS-CoV-2.

CONCLUSION

Severe cases of COVID-19 have a high risk of developing sequelae and alterations in different areas of the patient's overall functioning (cognitive, emotional, physical and motor), which frame difficulties in recovery or even the appearance of new pathologies. The sequelae reported by the patients classified as psychiatric symptoms are: depression, anxiety, and even paranoid disorder; Neurological symptoms such as recurrent headaches and loss of cognitive abilities (memory, attention and perception of the world) have also been found, and in some cases patients describe a type of mental fog that makes it impossible for them to carry out their daily lives, within their recovery with some global deficits.

In addition to this, the pandemic has greatly affected the elderly population, who are the most vulnerable due to underlying diseases, or due to the wear and tear of the organic and/or immune system; In addition, individual and socioeconomic differences mark a huge gap in medical and hospital care, where respiratory and bodily complications can be treated at different times, given that the sanitary collapse in health-providing institutions has been evident within the waves of infections.

The challenges that neuropsychology faces involve patient care and rehabilitation strategies. From a global perspective, it is essential to implement strategies that promote the mental health and quality of life of the person in recovery and of the families who directly or indirectly They have been harmed with a contagion.

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