COVID-19 ANALYSIS: IS THERE AN ASSOCIATION BETWEEN COVID-19 AND DEVELOPMENT OF COGNITIVE DEFICITS?
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Abstract

Objective: The effects of COVID-19 infection were initially thought to be limited to the respiratory system; however, recent literature suggests that the virus has systemic effects, even leading to cognitive deficits. The objective of this study is to review COVID-19 related literature to determine whether there is an association between COVID-19 infection and the development of cognitive deficits.

Method: A search for articles relevant to COVID-19, cognitive deficits, the Montreal Cognitive Assessment Tool (MoCA), and the geriatric population was performed on the MEDLINE, CINAHL, and APA PsychInfo databases.

Results: Substantial evidence exists that reports an association between COVID-19 infection and cognitive decline. The studies included in this literature review surveyed distinct populations and reported cognitive deficits in COVID-19 patients as measured by a reduction in MoCA scores. While cognitive deficits were identified as partially reversible, there were still measurable deficits in cognition post-recovery compared to healthy controls. Furthermore, the measured cognitive deficits were found to be much worse in the geriatric population.

Conclusions: Current literature shows an association between COVID-19 infection and the development of cognitive deficits. Further research should seek to characterize these cognitive deficits and determine the underlying aetiology and pathogenesis. Initiatives to develop interventions to limit or improve cognitive deficits in post COVID-19 patients is crucial, especially the elderly, given the large burden of disease within this population cohort.

Key words: geriatric psychiatry, adolescent psychiatry, covid-19, cognitive deficits, cognitive decline, montreal cognitive assessment

Introduction

COVID-19, or more formally SARS-CoV-2, is responsible for the current pandemic that initially originated in Wuhan, China and spread across the globe infecting millions of people and causing countless deaths (Ciotti et al., 2020). The first ever COVID-19 case described had pneumonia; however, since then researchers have shown that there can be a range of manifestations: from being asymptomatic to mimicking the common cold to pneumonia and potentially even Acute Respiratory Distress Syndrome (ARDS) requiring intensive care (Ciotti et al., 2020; Velavan & Meyer, 2020). When symptomatic, the infection typically presents with fever, cough, nasal congestion, fatigue, sore throat, aches and pains, hyposmia, and anosmia, which is often regarded as the characteristic sign of COVID-19 infection. Some patients have also described gastrointestinal (GI) symptoms consisting of diarrhoea and nausea (Ciotti et al., 2020). Given that SARS-CoV-2 is traditionally a respiratory virus, its mode of spread is through droplets and aerosols. This necessitated the need to wear surgical face masks, which protect against droplets, and N95/N100 respirators, which provide additional protection against aerosols. Some studies have noted the presence of SARS-CoV-2 RNA in the faeces of infected patients; thus, another potential route of transmission is faecal oral (Ciotti et al., 2020). As a result, researchers have taken to examine whether sewer systems can be used to determine the rates of infection.

SARS-CoV-2 can be divided into four subtypes: alpha (α), beta (β), gamma (γ), and delta (δ), out of which only the and subtypes infect mammals (Yuki et al., 2020). Additionally, there are four structural proteins that are important for pathogenesis – Spike
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Methods

A search for the relevant articles was conducted using the Royal College of Surgeons in Ireland’s unique research platform EBSCOhost. Specifically, MEDLINE, CINAHL, and APA PsychInfo databases were used to search for relevant articles. Refer to Table 1 for the search process.

Papers written in the English language reporting on COVID-19 and associated cognitive deficits were included. To ensure comparability amongst studies, only papers assessing cognitive deficits using MoCA were included. Additionally, articles reporting on potential therapeutic interventions to improve post-COVID-19 cognitive decline as well as those reporting on the underlying pathophysiology of cognitive decline in COVID-19 patients were included. An emphasis was also placed on the geriatric population. Articles were excluded on the basis of (1) not focused on the association between COVID-19 and cognitive deficits or (2) paper was reporting a study that is planned to take place or has yet to be completed.

Table 1. Search History

| Number | Query                                                                 | Results   |
|--------|------------------------------------------------------------------------|-----------|
| S1     | Covid-19 OR Coronavirus OR 2019-ncov OR Sars-cov-2 OR Cov-19           | 324,374   |
| S2     | Cognitive decline OR Cognitive impairment OR Cognitive function OR Cognitive dysfunction OR Cognitive deficit | 470,889   |
| S3     | Geriatrics OR Older adults OR Elderly OR Aged OR Older OR Elder OR Elderly | 8,016,526 |
| S4     | MoCA OR Montreal Cognitive Assessment OR MoCA Scale OR MoCA Cognitive Assessment Tool | 11,956    |
| S5     | S1 AND S2 AND S3 AND S4                                              | 26        |

Results

All 14 articles included report an association between COVID-19 infection and the development of cognitive deficits. In one particular study, Alemanno et al. (2021) reported that patients with more severe COVID-19 infection, as measured by the extent of respiratory assistance needed, were found to have greater cognitive deficits. 87 patients were divided into four groups based on the type of respiratory assistance required (Group 1 – Orotracheal Intubation, Group II – Non-Invasive Ventilation using Biphasic Positive Airway Pressure, Group III – Venturi Masks, Group IV – No Oxygen Therapy) and each patient’s cognitive performance was measured using the MoCA and Hamilton Rating Scale for Depression (see Table 1 for summary of outcomes in each group). MoCA scores indicated that 74.2% of Group I, 94.4% of Group II, 89.6% of Group III, and 77.8% of Group IV had cognitive deficits (Alemanno et al., 2021). Overall 80% of participants were found to exhibit cognitive deficits. Next, in a one-month follow up cognitive assessment of 56 of the original 87 patients (22 Group I, 12 Group II, 20 Group III, 2 Group IV), it was found that 12 (54.5%) group I patients, 10 (83.3%) group II patients, 17 (85%) group III patients, and all group IV patients had persistent cognitive deficits (Alemanno et al., 2021). 24 of the 56 patients (43%) also exhibited signs of Post-Traumatic Stress Disorder (PTSD). This finding of a residual decline in cognition following COVID-19 infection was also expressed by Patel et al. (2021), Zhou et al. (2020), Blazhenets et al. (2021), and Khatoonabadi et al. (2020). Zhou et al. (2020) specifically investigated 29 recovered COVID-19 patients and found that post-recovery COVID-19 patients performed worse on neuropsychological tests compared to healthy controls, indicating a persistent cognitive deficit. Similarly, Blazhenets et al. (2021) conducted a MoCA on eight COVID-19 patients at both the subacute (once patients are no longer infectious) and the chronic (approx. six months after symptom onset) stages of infection and found that there was a residual decline in cognition.

Similar results were reported by other studies. Del Brutto et al. (2021) studied a population of 93 Atahualpa residents 6-months following the onset of COVID-19 and compared cognitive function between COVID-19 positive residents (n = 52) and COVID-19 negative residents (n = 41) using the MoCA scale. It was found that 11 of the 52 COVID-19 positive residents developed cognitive decline compared to 1 of 41 COVID-19 negative residents. Thus, the odds of...
again, utilizing the MoCA scale to assess for any cognitive deficits. Similar to the aforementioned studies, MoCA scores were impaired in 21 of 38 patients (55.2%). Amalakanti et al. (2021) compared MoCA scores between asymptomatic COVID-19 patients (n = 93) and healthy controls (n = 102) and found that cognitive decline was also present in asymptomatic COVID-19 subjects.

Martillo et al. (2021) had another ground-breaking study.
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finding that linked COVID-19 to Post-Intensive Care Syndrome (PICS). Martillo et al. (2021) measured the physical domain based on patient reports, the psychiatric domain based on the Insomnia Severity Scale, Patient Health Questionnaire-9, and DSM V criteria for Post-Traumatic Stress Disorder (PTSD), as well as the cognitive domain using the MoCA in an attempt to determine the characteristics of PICS. It was found that 91% of involved patients fit the diagnostic criteria for PICS, with 48.9% having impairments in the physical domain and 20% having impairments in the cognitive domain (Martillo et al., 2021). In terms of the psychiatric domain specifically, 37.8% exhibited mild depression or extreme anxiety, 17.8% met the DSM V criteria for PTSD, and 77.2% had some form of Insomnia.

Another study conducted by Pirker-Kees et al. (2021) linked hyposmia (a tell-tale symptom of COVID-19) to reduced olfaction. Seven COVID-19 patients and seven controls in this study were subject to olfactory testing using the “Sniffin’Sticks” Screening Test as well as cognitive assessment via MoCA (Pirker-Kees et al., 2021). It was found that both olfaction and cognition were reduced in COVID-19 patients. Further, there was an association between one’s cognitive performance and the number of correctly identified odors (Pirker-Kees et al., 2021).

Discussion

There is an overwhelming amount of evidence in favour of an association between COVID-19 infection and subsequent cognitive decline. In fact, cognitive decline is not limited to the infectious period of SARS-CoV-2; rather, Alemanno et al. (2021), Patel et al. (2021), Zhou et al. (2020), Blazhenets et al. (2021), and Khatoonabadi et al. (2020) have all reported a residual decline in cognition months after recovery. This long term sequelae of infection has been termed “Long-COVID Syndrome” (Blazhenets et al., 2021). While a link between COVID-19 infection and cognitive decline has been well described, it is important to establish the exact deficits that occur. Hosp et al. (2021), Alemanno et al. (2021), Amalakanti et al. (2021), Khatoonabadi et al. (2020), and Ortelli et al. (2021) found similar deficits; these included deficits in short-term memory, attention, abstraction, long-term memory, visuoperception, and space and time orientation. It is also important to note that cognitive decline is not only limited to symptomatic COVID-19 patients, as Amalakanti et al. (2021) reported a decline in MoCA scores when comparing asymptomatic COVID-19 patients and healthy controls. Lastly, another important finding within the study conducted by Alemanno et al. (2021) worth mentioning is that the resulting cognitive deficits from COVID-19 were more severe in the elderly population. These findings were also reported by Amalakanti et al. (2021) and Heyns et al. (2021). This is of great relevance because of the world’s aging population. Further, this compounds the already heavy global burden of disease within the geriatric population.

In addition to the aforementioned deficits, Martillo et al. (2021) reported an association between COVID-19 infection and PICS. PICS is characterized by a persistent impairment in one or more of the physical, psychiatric, or cognitive domains, after leaving the Intensive Care Unit (see table 2 for common symptoms of PICS). This syndrome is an umbrella term that encompasses physical deficits, cognitive deficits, and emotional symptoms such as PTSD, Anxiety, Depression, etc. (Rawal et al., 2017). This study was ground-breaking and of great relevance, especially now, because PICS can also affect caregivers and lead to caregiver burnout. Burnout has long been an identified issue within the healthcare industry due to staff shortages, equipment shortages, long hours, and inadequate compensation (Caillet et al., 2020; El Haj et al., 2020). With COVID-19 now making clinical work more dangerous and more tiresome, burnout has been steadily increasing amongst healthcare workers. Clinical staff describe feeling “empty” or “worn out” and often suffer from detachment from both their personal and professional lives (El Haj et al., 2020). This poses a risk not only to patients, but also to our own healthcare workers. For this reason, even a small amount of burnout cannot be ignored and strategies to counter burnout should be sought (Caillet et al., 2020; El Haj et al., 2020).

Table 3. Common Symptoms of PICS (Kosinski et al., 2020)

| Domain            | Common Manifestations                  |
|-------------------|---------------------------------------|
| Physical Deficits | - Weakness                             |
|                   | - Pain                                 |
|                   | - Shortness of breath                  |
|                   | - Difficulty with movement or exercises|
| Cognitive Deficits| - Difficulty thinking                  |
|                   | - Difficulty in remembering            |
|                   | - Difficulty concentrating             |
| Emotional Deficits| - Anxiety                              |
|                   | - Irritability                         |
|                   | - Depression                           |
|                   | - PTSD                                 |
|                   | - Sleep disturbances                   |

Research into the underlying mechanism for the development of cognitive decline following COVID-19 infection is scarce (García-Grimshaw et al., 2022). Del Brutto et al. (2021), Hosp et al. (2021) and Pirker-Kees et al. (2021) propose that SARS-CoV-2 gains access to the CNS via the olfactory system. Del Brutto et al. (2021) identified the virus’ mechanism of entry using Positron Emission Tomography (PET), in which they reported that SARS-CoV-2 enters the CNS through the olfactory bulb following binding to the ACE2 receptor in the nasal epithelium. CNS involvement is further propagated by the fact that CNS cells such as astrocytes, oligodendrocytes, and neurons also express the ACE2 receptor (Pirker-Kees et al., 2021). Given this idea, it is thought that olfactory dysfunction is associated with cognitive decline and may be predictive for progression to more severe cognitive disorders such as dementia and Parkinson’s Disease (Dintica et al., 2019; Domellöf et al., 2017; Marin et al., 2018; Saini et al., 2020). Thus, olfactory dysfunction may be considered a reliable predictor of cognitive decline, and early identification of olfactory dysfunction should be sought in order to prevent rapid progression to cognitive decline (Dintica et al., 2019; Domellöf et al., 2017; Doty et al., 1997; Marin et al., 2018; Pirker-Kees et al., 2021; Shin et al., 2019).

García-Grimshaw et al. (2022) sought to elucidate the underlying pathophysiology of cognitive decline in a sample of 92 recovered COVID-19 patients (54 men, 38 women) after 6 months of discharge from the hospital. The study identified that the decline in cognition was associated with hypoxemia and the thrombo-inflammatory response secondary to COVID-19 infection. This finding is supported by other
studies, as hypoxemia has long been known to cause atrophy of neurological structures (García-Grimshaw et al., 2022; Miskowiak et al., 2021). Specific reductions in different MoCA domains can be explained by loss of specific structures. For example, atrophy of the hippocampus secondary to hypoxemia or inflammation may lead to impaired verbal memory and executive function (García-Grimshaw et al., 2022). Additionally, Del Brutto et al. (2021) identified viral activity in the CNS through an abnormal uptake of fluorine-18 fluorodeoxyglucose (\(^{18}\text{FDG}\)) in limbic structures (such as the frontal cortex, cingulate gyrus, thalamus, and hypothalamus. This abnormal uptake of \(^{18}\text{FDG}\) correlates with dysfunction of these structures and may explain other cognitive symptoms experienced by COVID-19 positive patients. Excessive inflammation and coagulability is also thought to lead to structural alterations in white matter tracts, as well as decreased cortical thickness, and decreased cerebral blood flow (García-Grimshaw et al., 2022). This in turn leads to disruptions of the Blood Brain Barrier (BBB), allowing access of cytokines into the CNS, which subsequently damage structures and impair neurotransmission. In addition to this, inflammatory processes and cytokine release in COVID-19 infection leads to increased concentrations of IL-6, which Qi et al. (2021) report to mediate the pathogenesis of cognitive dysfunction. It is important to consider that apart from SARS-CoV-2 infection itself, other factors regarding the pandemic also contribute to cognitive decline. It may be difficult to distinguish cognitive decline associated with these other factors from cognitive decline secondary to COVID-19 infection; thus, pandemic factors such as regulations surrounding lockdowns and a lack of human interaction may pose a significant confounding bias on the results reported in several studies. Khatoonabadi et al. (2020) suggest that limited interaction with family (due to lockdowns and indoor capacity limit regulations) and invasive ventilator use increase the risk for cognitive deficits. Martillo et al. (2021) similarly suggest that individuals who lack a good social support system as a result of the constraints placed on social support, in addition to ventilator use and lack of mobilization, contribute to the development of cognitive decline. In contrast, Soto-Añari et al. (2021) refute the idea that pandemic associated factors increase the prevalence of cognitive deficits. In this study, 5245 Latin Americans over the age of 60 were studied in 10 different countries using the Montreal Cognitive Assessment (MoCA), the “Alzheimer Disease 8” scale for functional and cognitive changes, and the Yesavage depression scale. Individuals who tested positive for COVID-19 were excluded from this study, meaning that the study only measured factors associated with the COVID-19 pandemic other than the infection itself (ex. days of quarantine). The results indicated that the prevalence of dementia (a form of cognitive deficit) was not associated with the pandemic; rather, it was associated with specific socio-economic and socio-health factors such as race, age, low education level, and ethnicity (Soto-Añari et al., 2021). One explanation for this finding, however, as offered by Soto-Añari et al. (2021), could be that there was low compliance with government regulations in the countries assessed within this study thereby leading to a falsely decreased measurement of prevalence of dementia. Lastly, in light of this association between COVID-19 infection and the onset of cognitive deficits, it is essential that appropriate strategies be implemented to either reduce the development or progression of such cognitive deficits, particularly in the geriatric population where the burden of disease is already high (Heyns et al., 2021). While Blazhenets et al. (2021) identified that these cognitive deficits are reversible over time, they also found that there is a residual reduction in MoCA scores (and therefore cognitive function) when comparing chronic COVID-19 patients to healthy controls. Other studies conducted by Patel et al. (2021), Zhou et al. (2020), and Khatoonabadi et al. (2020) report the same finding. Patel et al. (2021) propose inpatient rehabilitation for all COVID-19 patients to minimize the effects of infection on cognitive decline. In their study, they report significant improvements on both the MoCA as well as the Quality Indicator for Self-Care (QI-SC) following rehabilitation.

Additionally, exercise has long been known to have protective effects on cognitive decline (Ashworth et al., 2005; Bherer, 2015; Borde et al., 2015; Desjardins-Crépeau et al., 2016; Liu-Ambrose et al., 2012). Qi et al. (2021) sought to use this principle and determine whether Qigong, a type of Chinese physical exercise and breathing control, had protective effects against COVID-19 associated cognitive decline. In a 12-week randomized control trial, serum interleukin-6 (IL-6) levels were measured in both an experimental group who performed Qigong (n = 28) and a control group (n = 27), who underwent physical stretching exercise. It was found that the Qigong intervention caused significant improvement in processing speed, sustained attention, as well as increased hippocampal grey matter volume and reduced peripheral IL-6 levels, which as mentioned prior, mediates the pathogenesis of cognitive dysfunction (Qi et al., 2021). These results are highly promising because the population tested here were mainly the elderly. Because cognitive deficits are already so prevalent in the elderly and because the elderly have both physical limitations and COVID-19 restrictions, Qigong is a promising intervention to counter cognitive decline given the current situation (Qi et al., 2021). While the mentioned interventions may require greater healthcare resources allocations in an already burdened system during the pandemic, considering such interventions may be worthwhile to prevent cognitive diseases in COVID-19 patients in the future and may bring about net savings in the long run.

Limitations

One limitation of this study was that it only included studies that used MoCA to measure cognitive deficits. This was done to ensure, to as much of an extent as possible, that there was sufficient comparability amongst the studies included in this literature review. With that exclusion, there was still sufficient evidence to support an association between COVID-19 and cognitive deficits. Another limitation is that some of the studies included in this literature review had small sample sizes, increasing the probability that the findings are due to chance. Furthermore, potential confounding variables may exist in this study. For example, some of the studies included in this review did not document subject’s previous cognitive level. This is of relevance because prior cognitive deficits may artificially increase the measurement of cognitive decline secondary to COVID-19. Additionally, the development of PTSD could also serve as a confounding variable and bias the correct assessment of cognitive function secondary to COVID-19 infection. Lastly, the duration of the stay in the hospital is another confounding variable that may individually contribute to cognitive decline, again skewing the real measurement of cognitive decline secondary to COVID-19 infection.
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Conclusion

The COVID-19 pandemic that started in December 2019 has continued due to a number of mutations arising (Yuki et al., 2020). It has infected many, caused countless deaths worldwide, and has burdened healthcare systems around the world (Ciotti et al., 2020). Since the emergence of the COVID-19 pandemic, a large number of studies have been conducted on SARS-CoV-2 and literature has now taken a focus at understanding the virus’ systemic effects. A substantial amount of data in literature suggests that COVID-19 infection is associated with cognitive deficits, and while this decline in cognition may reverse over time, studies have reported cognitive function is still not up to par with healthy controls (Patel et al., 2021). Given the uncertainty of the progression of COVID-19 in the future, these results suggest a need for psychological support, cognitive rehabilitation, and other interventions for post-COVID-19 patients, especially in the geriatric population where cognitive deficits tend to be of greater severity (Alemanno et al., 2021).

References

Alemanno, F., Houdayer, E., Parma, A., Spina, A., Del Forno, A., Scatolini, A., ... & Iannaccone, S. (2021). COVID-19 cognitive deficits after respiratory assistance in the subacute phase: A COVID-rehabilitation unit experience. PLoS one, 16(2), e0246590.

Amalakanti, S., Arepalli, K. V. R., & Jillella, J. P. (2021). Cognitive assessment in asymptomatic COVID-19 subjects. VirusDisease, 32(1), 146-149.

Ashworth, N. L., Chad, K. E., Harrison, E. L., Reeder, B. A., & Marshall, S. C. (2005). Home versus center based physical activity programs in older adults. Cochrane Database of Systematic Reviews, (1).

Blazhenets, G., Schroeter, N., Bormann, T., Thurow, J., Wagner, D., Frings, L., ... & Hosp, J. A. (2021). Slow but evident recovery from neocortical dysfunction and cognitive impairment in a series of chronic COVID-19 patients. Journal of Nuclear Medicine, 62(7), 910-915.

Borde, R., Hortobágyi, T., & Granacher, U. (2015). Dose–response relationships of resistance training in healthy old adults: a systematic review and meta-analysis. Sports medicine, 45(12), 1693-1720.

Caillet, A., Coste, C., Sanchez, R., & Allaouchiche, B. (2020). Psychological impact of COVID-19 on ICU caregivers. Anaesthesia Critical Care & Pain Medicine, 39(6), 717-722.

Ciotti, M., Ciccozzi, M., Terrinoni, A., Jiang, W. C., Wang, C. B., & Bernardini, S. (2020). The COVID-19 pandemic. Critical reviews in clinical laboratory sciences, 57(6), 365-388.

Del Brutto, O. H., Wu, S., Mera, R. M., Costa, A. F., Recalde, B. Y., & Issa, N. P. (2021). Cognitive decline among individuals with history of mild symptomatic SARS-CoV-2 infection: A longitudinal prospective study nested to a population cohort. European journal of neurology, 28(10), 3245-3253.

Dejardin-Crépeau, L., Berryman, N., Fraser, S. A., Vu, T. T. M., Kergoat, M. J., Li, K. Z., ... & Bherer, L. (2016). Effects of combined physical and cognitive training on fitness and neuropsychological outcomes in healthy older adults. Clinical Interventions in Aging, 11, 1287.

Dintica, C. S., Marseglia, A., Rizzuto, D., Wang, R., Seubert, J., Arfanakis, K., ... & Xu, W. (2019). Impaired olfaction is associated with cognitive decline and neurodegeneration in the brain. Neurology, 92(7), e700-e709.

Domellöf, M. E., Lundin, K. F., Edström, M., & Forsgren, L. (2017). Olfactory dysfunction and dementia in newly diagnosed patients with Parkinson’s disease. Parkinsonism & related disorders, 38, 41-47.

Doty, R. L., Li, C., Mannon, L. J., & Yousum, D. M. (1997). Olfactory dysfunction in multiple sclerosis. N Engl J Med, 336(26), 1918-1919.

El Haj, M., Allain, P., Annweiler, C., Boutouleau-Bretonnière, C., Chapelet, G., Gallouj, K., ... & Boudoukh, A. H. (2020). Burnout of healthcare workers in acute care geriatric facilities during the COVID-19 crisis: an online-based study. Journal of Alzheimer’s Disease, 78(2), 847-852.

Garcia-Grimshaw, M., Chirino-Pérez, A., Flores-Silva, F. D., Valdés-Ferrer, S. I., Vargas-Martínez, M. D. L. A., Jiménez-Avila, A. I., ... & Chiqueté, E. (2022). Critical role of acute hypoxemia on the cognitive impairment after severe COVID-19 pneumonia: a multivariate causality model analysis. Neurological Sciences, 1-13.

Heyns, A., Dupont, J., Gielen, E., Flamaing, J., Peers, K., Gosselin, R., ... & Tournoy, J. (2021). Impact of COVID-19: urging a need for multi-domain assessment of COVID-19 inpatients. European geriatric medicine, 12(4), 741-748.

Hosp, J. A., Dressing, A., Blazhenets, G., Bormann, T., Rau, A., Schwabenland, M., ... & Meyer, P. T. (2021). Cognitive impairment and altered cerebral glucose metabolism in the subacute stage of COVID-19. Brain, 144(4), 1263-1276.

Khatoonabadi, A. R., Joanne, Y., Nitsche, M. A., Ansaldo, A. I. (2020). Considerations about cognitive communication deficits following COVID-19. Psychiatri Clin Neurosci. 74(12), 662-663. doi: 10.1111/pcn.13159. Epub 2020 Oct 12. PMID: 32981072; PMCID: PMC7537055.

Kosinski, S., Mohammad, R. A., Pitcher, M., Haebz breaches, E., Coe, A. B., Costa, D. K., ... & McSparron, J. I. (2020). What Is Post–Intensive Care Syndrome (PICS)?. American journal of respiratory and critical care medicine, 201(8), P15-P16.

Liu-Ambrose, T., Nagamatsu, L. S., Voss, M. W., Khan, K. M., & Handy, T. C. (2012). Resistance training and functional plasticity of the aging brain: a 12-month randomized controlled trial. Neurobiology of aging, 33(8), 1690-1698.

Liu, Y. H., Wang, Y. R., Wang, Q. H., Chen, Y., Chen, X., Li, Y., ... & Wang, Y. J. (2021). Post-infection cognitive impairments in a cohort of elderly patients with COVID-19. Molecular neurodegeneration, 16(1), 1-10.

Marin, C., Vilas, D., Langdon, C., Alobid, I., López-Chacón, M., Haehnert, A., ... & Mullol, J. (2018). Olfactory dysfunction in neurodegenerative diseases. Current allergy and asthma reports, 18(8), 1-19.

Martillo, M. A., Dangayach, N. S., Tabaco, L., Spielman, L. A., Dams-O’Connor, K., Chan, C. C., ... & Escalon, M. X. (2021). Postintensive care syndrome in survivors of critical illness related to coronavirus disease 2019: Cohort study from a New York City Critical Care Recovery Clinic. Critical care medicine, 49(9), 1427-1438.

Miskowiak, K. W., Johnsen, S., Sattler, S. M., Nielsen, S., Kunalan, P., Rungby, J., ... & Porsberg, C. M. (2021). Cognitive impairments four months after COVID-19 hospital discharge: pattern, severity and association with illness variables. European Neuropsychopharmacology, 46, 39-48.

Ortelli, P., Ferrazzoli, D., Sebastianelli, L., Engl, M., Romanello, R., Nardone, R., ... & Versace, V. (2021). Neuropsychological and neuropsychiological correlates of fatigue in post-acute patients with neurological manifestations of COVID-19: Insights into a challenging
symptom. *Journal of the neurological sciences*, 420, 117271.

Patel, R., Savrides, I., Cahalan, C., Doulatani, G., O’Dell, M. W., Toglia, J., & Jaywant, A. (2021). Cognitive impairment and functional change in COVID-19 patients undergoing inpatient rehabilitation. *International Journal of Rehabilitation Research*, 44(3), 285-288.

Pirker-Kees, A., Platho-Elwischger, K., Hafner, S., Redlich, K., & Baumgartner, C. (2021). Hyposmia Is Associated with Reduced Cognitive Function in COVID-19: First Preliminary Results. *Dementia and geriatric cognitive disorders*, 50(1), 68-73.

Qi, D., Wong, N. M., Shao, R., Man, I. S., Wong, C. H., Yuen, L. P., ... & Lee, T. M. (2021). Qigong exercise enhances cognitive functions in the elderly via an interleukin-6-hippocampus pathway: A randomized active-controlled trial. *Brain, Behavior, and Immunity*, 95, 381-390.

Rawal, G., Yadav, S., & Kumar, R. (2017). Post-intensive care syndrome: an overview. *Journal of translational internal medicine*, 5(2), 90-92.

Saini, D., Mukherjee, A., Roy, A., & Biswas, A. (2020). A comparative study of the behavioral profile of the behavioral variant of frontotemporal dementia and Parkinson’s disease dementia. *Dementia and geriatric cognitive disorders extra*, 10(3), 182-194.

Shin, T., Kim, J., Ahn, M., & Moon, C. (2019). Olfactory dysfunction in CNS neuroimmunological disorders: a review. *Molecular neurobiology*, 56(5), 3714-3721.

Soto-Añari, M., Camargo, L., Ramos-Henderson, M., Rivera-Fernández, C., Denegri-Solís, L., Calle, U., ... & López, N. (2021). Prevalence of Dementia and Associated Factors among Older Adults in Latin America during the COVID-19 Pandemic. *Dementia and Geriatric Cognitive Disorders Extra*, 11(3), 213-221.

Velavan, T. P., & Meyer, C. G. (2020). The COVID-19 epidemic. *Tropical medicine & international health*, 25(3), 278.

Yuki, K., Fujiogi, M., & Koutsogiannaki, S. (2020). COVID-19 pathophysiology: A review. *Clinical immunology*, 215, 108427.

Zhou, H., Lu, S., Chen, J., Wei, N., Wang, D., Lyu, H., ... & Hu, S. (2020). The landscape of cognitive function in recovered COVID-19 patients. *Journal of psychiatric research*, 129, 98-102.