



# Limited evidence for neuropsychological dysfunction in patients initially affected by severe COVID-19

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## Abstract

**Background** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), resulting in coronavirus disease 2019 (COVID-19), has caused a pandemic. There is now considerable evidence that neuropsychological functions could be affected. We further tested this hypothesis on a sample of post COVID-19 patients, who, initially, had been severely affected.

**Methods** We tested 22 post COVID-19 patients who, after the intensive care unit (all but one), were admitted to our rehabilitation unit to be treated for severe post COVID-19 sequelae. All patients were administered a comprehensive neuropsychological battery including measures assessing perceptual, attentive, mnemonic, linguistic, and executive functions, and overall cognitive status. The patients were also administered rehabilitation measures including scales for investigating aerobic capacity/endurance deficits, dyspnea, and fatigue.

**Results** Our findings revealed that evidence of neuropsychological disorders in post COVID-19 patients was very limited. Furthermore, COVID-19 severity and other relevant variables were not correlated with patients' scores on the neuropsychological tests.

**Conclusions** We suggest that the relation between COVID-19 and neuropsychological disorders is unclear. New studies and meta-analyses are highly required to shed light on this highly complex issue.

**Keywords** SARS-CoV-2 · COVID-19 · Neuropsychology · Neuropsychological assessment

## Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), resulting in coronavirus disease 2019 (COVID-19), has caused a pandemic. There is now considerable evidence that COVID-19 can affect the brain resulting in neuropsychological disorders [1, 2]. Daroische et al. [3] reviewed the effects of COVID-19 on patients who were administered standardized neuropsychological tests. The authors included

twelve studies in which patients were tested from a few days up to 6 months following the onset of COVID-19. The severity of COVID-19 signs, in these patients, was highly variable. Daroische et al. reported the presence of various neuropsychological disorders. Global cognitive functioning was impaired in all the studies in which this domain was tested (range: 15–80%). Attention and executive functions were found to be impaired in seven studies [4–10]. Long-term memory deficits were reported in three studies [5, 6, 11]. Short-term memory deficits were reported in two studies [10, 11]. Finally, visuospatial impairment was reported in two studies [5, 8]. Daroische et al. [3] concluded that patients with COVID-19 could be affected by global cognitive impairment and/or impairment of specific cognitive functions such as attention and executive functions.

García-Sánchez et al. [12] tested 63 patients who received comprehensive neuropsychological assessment including measures of general cognitive status, attention, short-/long-term memory, language, processing speed, visuo-perceptual/visuo-constructive functions, and executive functions. The

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patients were tested, on average, after 187 days post-onset and they all reported subjective cognitive complaints. The results showed that single-domain deficits (39.7%) were less frequent than multiple-domain deficits (60.3%). The most common cognitive disorders were attention deficits (61.9%), followed by executive functions deficits (43%). Nonetheless, the reported attentional and associated executive deficits were largely unrelated to clinical factors (e.g., hospitalization, disease duration, biomarkers, or affective measures). Finally, also Aiello et al. [13] have suggested that recovered COVID-19 patients might show cognitive deficits, mostly concerning the dysexecutive-inattentive and amnesic domains.

In summary, the results of the aforementioned studies have suggested that patients with COVID-19 might be affected by a variety of neuropsychological disorders with special reference to attention/executive functions disorders and memory disorders. The aim of the present study was to replicate the findings of previous studies and to seek for any relations between COVID-19 severity and neuropsychological impairment. We focused on the consequences of severely affected COVID-19 patients, in the post COVID-19 phase. All the patients were tested with a comprehensive neuropsychological battery and rehabilitation measures to quantify COVID-19 severity.

## Method

### Participants

Twenty-two patients (mean age: 58 years, range: 41–77 years; five females), who had previously been affected by severe COVID-19, participated in the study. All patients, but one, had been initially admitted to a COVID-19 intensive care unit. Sixteen patients received artificial ventilation, whereas, in 13 of them, a tracheostomy was performed. After SARS-CoV-2 negativization, the patients were admitted to our rehabilitation unit for starting intensive treatment concerning the sequelae of respiratory dysfunction and asthenia.

### Neuropsychological and rehabilitation assessment

All patients were administered a comprehensive neuropsychological test battery (Supplemental data 1: <https://osf.io/9fgnh/>). The neuropsychological tests included various measures for assessing perceptual, attentive, mnemonic, linguistic, and executive functions, and overall cognitive status. The patients were also administered rehabilitation measures, including scales for investigating aerobic capacity/endurance deficits, dyspnea, and fatigue (Supplemental data 1: <https://osf.io/9fgnh/>). The average time between COVID-19 onset and assessment was 81 days (range: 28–278 days).

## Results

The presence of neuropsychological disorders was surprisingly limited (Supplemental data 2: <https://osf.io/9fgnh/>). On average, 95% of the patients had scores above the cutoffs on the neuropsychological battery. A more detailed analysis revealed that none of the patients showed impaired performance on measures assessing overall cognitive status, visuo-spatial short-term/working memory, and language production (semantic fluency). In total, 93.2% of the patients behaved normally on measures assessing phonological short-term/working memory; 90.9% of the patients behaved normally on measures of long-term verbal learning; 95.5% of the patients behaved normally on a measure of visuospatial perception and praxis; and 82% of the patients behaved normally on a measure of visuospatial long-term learning. Finally, on average, 96% of the patients behaved normally on measures of attention and executive functions (Supplemental data 2: <https://osf.io/9fgnh/>).

To investigate the relation between demographic variables, time since onset, neuropsychological impairment, and rehabilitation measures of COVID-19 severity, we performed Bayesian Pearson's correlations. All these correlations yielded Bayes factors (i.e., BF10) that were all below 10, suggesting the absence of any relations among the measures (see Supplemental data 3: <https://osf.io/9fgnh/>).

## Discussion

Although COVID-19 has been thought to be considerably associated with neuropsychological disorders, our findings do not support this claim. Furthermore, COVID-19 severity measured through rehabilitation scales was not correlated with patients' performance on the neuropsychological tests. It might be hypothesized that the patients:

- (1) Were not severely affected by COVID-19 initially. This is not the case, given that all patients, but one, had been initially admitted to intensive care units and most of them received artificial ventilation/tracheostomy (see also the rehabilitation measures).
- (2) Were tested after their full recovery. This is not the case, because, at the moment of assessment, the patients were still admitted in our rehabilitation unit to be treated for severe sequelae of COVID-19.
- (3) Were tested after many months from COVID-19 diagnosis. This is not the case, because we tested patients, on average, after 81 days from COVID-19 diagnosis.

Furthermore, García-Sánchez et al. [12] tested patients, on average, after 187 days from COVID-19 onset and they still reported a variety of neuropsychological disorders.

- (4) Were tested with non-sensitive and easy neuropsychological measures. This is not the case, because our neuropsychological battery was composed by very sensitive tests, which were highly comparable to those employed in the other studies.

A possible explanation for the discrepancy between the results of our study and those of other studies might be that we tested severely affected patients, who usually receive immediate, comprehensive, and adequate treatment in intensive care units. This treatment might prevent patients from being affected by cognitive sequelae [11, 14]. A limit of our study is the small sample of our patients. Note, however, that in some published studies, the reported sample was even smaller. We conclude that the investigation of the effects of COVID-19 on neuropsychological functions require further studies. Most important, it is now imperative that meta-analyses be conducted to simultaneously compare the findings of the available studies. Finally, correlational studies are needed to further explore the contribution of COVID-19 severity on neuropsychological functions and the role of premorbid risk factors. Indeed, the findings of some studies have suggested that COVID-19-recovered individuals, who did not present with premorbid risk factors for brain disorders, are less likely to present with COVID-19-related cognitive deficits [13–15].

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## Declarations

**Ethical approval** None.

**Conflict of interest** The authors declare no competing interests.

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