Medical Research Archives

European Society of Medicine

OPEN ACCESS

Published: February 29, 2024

Citation: Capistrano, A., C., et al., 2024. Neuropsychological aspects and mood profiles of patients with COVID-19: results of a preliminary case-control study with Brazilian participants. Medical Research Archives, [online] 12(2). https://doi.org/10.18103/mra.v12i2.5146

DOI: https://doi.org/10.18103/mra.v12i2.5146

ISSN: 2375-1924

RESEARCH ARTICLE

Neuropsychological aspects and mood profiles of patients with COVID-19: results of a preliminary case-control study with Brazilian participants

Ana Clara Capistrano[1], Louise do Nascimento Marques[2], Anna Beatriz Gomes Barbosa[3], Renato De Marca[1], Luis Anunciação[4*]

[1]Department of Psychology, Pontifical Catholic University of Rio de Janeiro
[2]Psychologist, MSc in Clinical Psychology
[3]Psychologist, MSc in Clinical Psychology
[4]PhD in Psychometrics, MSc in Public Health, Marques de São Vicente, 225 / L201 CEP: 22451-900 Gávea – Rio de Janeiro/RJ.

*luisfca@puc-rio.br

ABSTRACT

Background: The long-term effects of COVID-19 became a target of investigation in the years following the spread of the SARS-CoV-2 virus. The current evidence is mixed and includes studies suggesting an impairment in psychological, neuropsychological, and mood conditions, while other studies have failed to find significant differences.

Aim: We compared the cognitive and mood profiles of patients who had COVID-19 with a control group using neuropsychological measures and self-reported questionnaires.

Methodology: We implemented a case-control study from September 2021 to June 2022. We conducted an in-person neuropsychological evaluations of 45 patients who had COVID-19 and a control group of 16 participants, matching them for age, sex, education, and civil status. We evaluated their perception, attention, memory, and mood profiles. We used one-sided T-tests to check the plausibility of the hypothesis of worse results in the group of patients who had COVID-19 and we implemented a chi-squared test to assess the percentage of participants at risk for depression and anxiety in both groups.

Results: We found no significant differences on either the cognitive tests or mood profile.

Conclusion: Although preliminary, the data suggest that people who had COVID-19 have similar cognitive skills and mood profiles compared to a control group. Further research is important, given the mixed results published in the scientific literature.

Keywords: Long-COVID; Case-control, Neuropsychology; Cognition, Mood.

Introduction:

Post-COVID syndrome, also known as "Long-COVID", is characterized by a group of persistent and prolonged symptoms that can occur after the infection with the SARS-CoV-2 virus. These symptoms persist beyond the initial acute phase and might impact several health aspects. Past studies have sought to identify not only main signs and symptoms, but also the complaints reported by the population that was infected[1–3].

There are two broad groups found among these symptoms. The first is mainly related to physical symptoms and conditions (e.g., loss of smell and taste, fatigue, changes in sleep, muscle pain). The second group is more related to neuropsychological symptoms, either subjective or objective. Within this broad, it is possible to find attention and memory complaints, in addition to depressive mood, instability, and changes[4,5].

However, the state-of-the-art evidence of the cognitive impairments related to COVID-19 is mixed. Some studies have found a negative, nonsignificant effect of COVID on psychological abilities and mood states[6–9], but there are also studies in which objective and persistent impairments were not found[10].

In April 2023, we conducted a search in the PubMed database using the search terms (covid 19) AND (cognitive impairment) AND (control group). Original research articles were included if they met the following criteria: (a) they performed cognitive data collection through psychological tests and (b) they conducted comparisons between case and control groups. Table 1 presents data from the main findings on cognitive impairments in COVID-19 samples, which will be further discussed in the order of their appearance below.

Table 1. Results of the Long-COVID neuropsychological symptoms.

Authors/Year	Country	Sample	Main Results
Cian et al., 2022	Italy	Hospitalized patients with no ICU (n = 29) + Paired control group (n = 29)	RAVLT test results were significantly lower in the COVID group for learning (p=0.035), recall (p=0.03) and recognition (p=0.007). The number of people with at least 1 test below average was higher in the COVID group (p<0.001). However, Mini Mental State Exam, Digit span, Phonemic and semantic fluencies, depression level, and anxiety were not different.
Delgado-Alonso et al., 2022	Spain	Former patients with cognitive complaints (n = 50) + Paired control group (n = 50)	Former patients with cognitive complaints had significantly lower mean results, generally with small effect sizes. Attention and executive function impairments were identified in processing speed, divided attention, selective attention, visual vigilance, alertness, working

Authors/Year	Country	Sample	Main Results
			memory and inhibitory control. Lower performance in episodic memory and visuospatial processing tests were also identified. Non-significant results were achieved by the Cognitrone test (visuoperceptual analysis, continuous attention, and the speed of information-processing) and Framed Gambling Task (Cognitive Flexibility).
Demir et al., 2023	Turkey	People with mild symptoms (n = 54) + Paired control group (n = 36)	Former patients performed significantly lower on most cognitive test indicators (p: <0.001 – 0.414). Statistically different results were not identified in the depression (p=0.791) or anxiety (p=0.849) indicators.
Pihlaja et al., 2023	Finland	Patients that received ICU care (n = 82), hospitalized patients (n = 53) or people treated at home (n = 49) + non-infected participants (n=53)	The results of objective cognitive dysfunctions did not differ between the COVID and control groups (p = 0.366); in addition, the percentage of people with a general result in the cognitive test above the cut-off point was higher in the control group, but without significant differences (p = 0.693). No significant correlation was identified between objective and subjective cognitive symptoms in the COVID or control group.
Akıncı et al., 2023	Istanbul	People from 18 to 50 years infected (n = 50) + Paired control group (n = 50)	Participants in the Covid group had significantly lower cognitive performance in most applied tests: MoCA (p<0.001, d = 0.867), Clock Drawing Test (p=0.004, d = 0.602), Ö-VMPT (p:<0.001 - 0.009, d: 0.629 - 0949), Phonemic Verbal Fluency (p=0.006, d = 0.556) and TMT-A (p=0.015, d = 0.558), ROCFT Copy (p=0.040, d = 0.474), ROCFT Immediate Recall (p=0.002, d = 0.336) and Delayed Recall (p<0.001, d = 0.751), and NPI (p=0.001, d = 0.727).
Zhou et al., 2020	China	People infected (n = 29) + Paired	Overall results were not significantly different between COVID and control groups on the following cognitive tests: TMT (p = 0.703), SCT

Authors/Year	Country	Sample	Main Results
		control group (n = 29)	(p = 0.432), Digits (p = 0.843). Some indexes were significantly lower in the COVID group on the CPT test, but the results were generally not significantly different between the COVID and control groups.
Woo et al., 2020	Germany	Former hospitalized patients with no ICU care with mild to moderate symptoms (n = 18) + Healthy controls that worked in the hospital (n = 10)	Participants in the COVID group had significantly lower cognitive screening results than the control group: orientation (p = 0.9643), attention (p = 0.029), language and concentration (p = 0.009) and memory (p = 0.004). Two of the patients in the COVID group had severe cognitive complaints and results and underwent a more thorough evaluation.
Ortelli et al., 2021	Italy	Hospitalized patients with fatigue complaints (n = 12) + Paired control group (n = 4)	Cognitive outcomes were significantly lower in the COVID MoCa (p<0.001) and FAB (p<0.001) group. Similarly, the reaction time on the computerized tests were higher in the COVID group: SIT (p = 0.015) and NT (p = 0.046). Results in neuropsychiatric tests (AES and BDI) they were significantly higher in patients in the COVID group (p<0.001).
Raman et al., 2021	England	Hospitalized patients with moderate to severe symptoms (n = 58) + Paired control group (n = 30)	Mean MoCA results did not differ statistically between COVID (27, IQR 25-29) and control (27, IQR 25-29) groups. The percentage of participants in the COVID group with above-average results was higher than that of the control group. Anxiety scores were on average higher in the COVID group (M = 2.0) than in the control group (M = 0.5, p = 0.066). Similarly, the COVID group scored higher on the depression ladder (M = 3.0) than the control group (M = 1.5, p = 0.009).
Invernizzi et al., 2023	Italy	COVID group (n=13) + control group (n=27)	When comparing cognitive performance between the control group and COVID group after the infection, no significant differences

Authors/Year	Country	Sample	Main Results
			were found in error rates (p=0.651) or new strategy rates (p=0.131).
Holm et al., 2023	Iceland	People who tested positive for COVID-19 before October 2020 (n= 3098) + Contemporary matched controls (n=619) + historical controls (n=13779)	The COVID group performed worse than the contemporary control group in the logic memory test immediate recall (p<0.01) and delayed recall (p<0.01). No data was available for the other cognitive assessments used in the study's method.

These studies bring information of objective cognitive symptoms found on post-COVID samples in comparison to control groups. Various methodology designs were conducted. Therefore, investigations were done with severe cases, mild cases, and young infected people.

Pihlaja et al[11] conducted general neuropsychological screening with the MoCA test on COVID and control groups. Despite the higher prevalence of subjective complaints in the COVID group (p<0.001), the results of objective cognitive dysfunctions did not differ between the COVID and control groups (p = 0.366). Moreover, they concluded that no significant correlation was identified between objective and subjective cognitive symptoms.

Other studies that compared COVID and control groups specifically sought to investigate the performance on cognitive tests of people with more severe cases, such as moderate to severe hospitalizations[12], previous cognitive complaints[13] or the presence of other symptoms characteristic of Long-COVID[14]. Both Ortelli et al[14] and Delgado-Alonso et al[13] identified statistically significant differences in the overall cognitive functioning of participants in the COVID group compared to the control group. In addition, Delgado-Alonso et al[13] were able to identify significant impairments in the case group in several cognitive domains such as attention, executive functions, and memory. Ortelli et al[14] also pointed out that patients exhibited a significant decline in overall cognitive function as revealed by the MoCA test, with scores significantly lower than those of healthy controls (p < 0.001). Patients also scored markedly lower than healthy controls on the FAB assessment (p < 0.001).

Holm et al[15] also pointed memory recall abilities as poorer in the COVID group. On the other hand, Raman et al[12] did not identify differences in overall cognitive performance between people who were hospitalized and people who were not infected. However, the researchers identified the presence of significantly higher anxiety and depression symptoms in the COVID group compared to the control group[12].

In turn, other researchers have focused on investigating the effects of COVID-19 in patients who underwent hospitalization or hospital care[16], however without hospitalization in intensive care units,[17] and with mild to moderate symptoms[18]. Woo et al[18] identified significantly greater overall cognitive impairments in the COVID group. However, Cian et al[17] and Zhou et al[16] identified occasional, but not overall differences in the cognitive performances of the COVID group in comparison to the control group. Thus, disparities were mainly mapped in the performance of attention and memory functions.

While some researchers have engaged in studying the characteristics of Long-COVID associated with the severity of cases, others have been interested in investigating samples of young patients, with an average age of 27.2 years (SD=8.5) and 29.9 years (SD=6.9)[19,20]. In the studies by Demir et al[19]and Akıncı et al[20], impairments were observed in both overall cognitive functioning and in several domains of cognitive functioning such as attention, memory, and executive functions. On the other hand, other researchers do not report cognitive functioning differences between young adults who have been infected and young adults who were not infected[21].

Overall, several published studies suggest that people who have been infected by COVID-19 may exhibit lower cognitive performance scores compared to those who have not been infected. However, the results are not quite congruent. As previously shown, this inconsistency serves to illustrate the heterogeneity of findings. In certain cases, overall cognitive deficits are observed in infected patients, while in others, only specific cognitive deficits were observed. It is also worth noting that although significant differences were identified between the cognitive performance of people who had and did not have COVID-19, only a few studies sought to identify the magnitude of this phenomenon by calculating the effect size. Furthermore, some studies did not find differences in cognitive performance between clinical and control groups.

Studies reporting cognitive and mood state impairment tend to highlight tasks in which statistically significant results were achieved, leading to non-significant results to be overlooked. On the other hand, studies that concluded statistically insignificant or negative findings tend to explain part of these results by different sources, including their sample characteristics, low power, or the psychological tools used. Moreover, due to publication bias, we expect to find fewer studies in which negative results were found[22,23].

The initial studies investigating cognitive performance of COVID-19 patients primarily featured more severe cases, characterized by the need for hospital care, health complications requiring intervention, or complaints of cognitive decline post COVID-19 infection. In addition, most of the published studies were conducted in North America, Europe, or Asia. This lack of diversity in study locations can undermine the applicability of clinical research findings to a global context.

Recognizing a potential gap in the current literature, this study aims to assess the psychological effects of COVID-19 on a Brazilian sample with varied severity of symptoms. A case-control design was conducted in which all participants were

submitted to a neuropsychological assessment investigating cognitive and mood impairments.

Methods

This study performed a case-control design. A case control study is used in this context to investigate potential associations between exposure (here, people who have been infected with COVID-19) and outcomes (here, cognitive impairments and/or mood symptoms in the long term). Participants who had COVID-19 were first recruited to the assessment and then their matched peers with no COVID-19 medical history were recruited. The first group was labeled as "COVID group" and the second group was labeled as "Control Group". Data collection was conducted after the approval of the Brazilian National Research Ethics Committee under public note (No. 48542821.50000.5259).

Participants

The total sample consisted of 61 Brazilians. From these participants, 45 (73.77%) reported being infected with COVID-19 and 16 (26.23%) were not infected. The sample consisted of 36 (59.0%) women and 18 (37.7%) men, with a mean age of 35.33 (SD=16.43) years.

The inclusion criteria for the experimental group were as follows: (1) a diagnosis of COVID-19, e.g., a positive COVID-19 PCR test, (2) age 18 or older, and (3) consent to participate in the study. The exclusion criteria included: (1) prior cognitive or other deficit pathologies associated with the sequelae of COVID-19, and (2) severe physical or psychological conditions that may interfere with assessment. Within the COVID group, 3 out of 45 participants (6.66%) reported hospitalization due to the infection, with a mean age of 63 (SD=11.53). Among hospitalized patients, 2 out of 3 (66.6%) require oxygen supplementation or mechanical ventilation.

Participants classified as healthy controls reported having no symptoms or signs of a respiratory tract infection associated with coronavirus disease prior to the assessment. Therefore, the inclusion criteria for the control group were as follows: (1) no history of prior COVID-19 infection, (2) age 18 or older, and (3) voluntary participation in the study. The exclusion criteria for the control group were the same as those for the COVID group. Participants in the control group were matched with those in the case group based on age, sex, education level, and civil status. Table 2 displays the demographic characteristics of the participants from both groups.

Table 2. Demographic characteristics of the participants from case and control groups.

	Case (N=45)	Control (N=16)	Total sample (N=61)	*P-value*
Sex				0.648
Female	26 (57.8%)	10 (62.5%)	36 (59.0%)	
Male	18 (40.0%)	5 (31.2%)	23 (37.7%)	
Others	1 (2.2%)	1 (6.2%)	2 (3.3%)	
Age (Mean/ SD)	34.05 (14.19)	38.88 (21.59)	35.33 (16.43)	0.318
Education				0.204
Non-literate	0 (0.0%)	1 (6.2%)	1 (1.6%)	
High School	9 (20.0%)	2 (12.5%)	11 (18.0%)	
Higher education	36 (80.0%)	13 (81.2%)	49 (80.3%)	
Hospitalization				
Hospitalized	3 (6.7%)	–	3 (6.7%)	
Not hospitalized	42 (93.3%)	–	42 (93.3%)	
Civil status				0.315
Single	33 (73.3%)	9 (56.2%)	42 (68.9%)	
Married	10 (22.2%)	5 (31.2%)	15 (24.6%)	
Divorced	1 (2.2%)	0 (0.0%)	1 (1.6%)	
Widowed	1 (2.2%)	1 (6.2%)	2 (3.3%)	
Others	0 (0.0%)	1 (6.2%)	1 (1.6%)	

Procedures

All data was collected only after the participants read and signed an ethical report indicating their consent to join the research. The data collection occurred from September 2021 to June 2022.

Volunteers were recruited from multiple venues. First, we used social networks to promote the research and connect with potential participants. Next, we distributed brochures in public places such as public squares and commercial buildings. Individuals who were interested could contact the research team to schedule a neuropsychological consultation. No recruitment incentives were provided that

could potentially influence the quality of the gathered sample.

All assessments were carried out by a researcher previously trained to conduct the standardized protocol. The researcher conducting the assessments was blinded to group membership. Each assessment lasted about 1 hour and consisted of an initial interview to collect sociodemographic data and information related to COVID-19, including the date of COVID-19 diagnosis, reinfection detection, and the date of COVID-19 reinfection diagnosis. The COVID group was questioned about the severity of their COVID-19 experience, such as whether they underwent hospitalization, received hospital care, or required oxygen supplementation or mechanical ventilation. They were also asked about the presence of symptoms like fever, dry cough, shortness of breath, rapid breathing, respiratory failure, muscle and joint pain, loss of smell, loss of taste, loss of appetite, sore throat, nasal congestion, headache, diarrhea, fatigue, and any other related symptoms. Next, we implemented a series of psychological tools to assess cognitive characteristics, such as perception, attention, memory, and executive functions, as well as anxiety and depression symptom scales.

The primary factors contributing to the small sample size can be attributed to limited survey adherence and the timing of data collection. It became increasingly challenging to locate individuals who had not been affected by COVID-19 in late 2021.

Tools

To accomplish the main goal of the current study, we chose a battery that was theoretically driven to assess the cognitive and affective states of patients who had COVID-19 and their counterparts.

Verbal fluency tests (Semantic version): This test aims to assess expressive language. First, the participant is asked to name fruits and then animals for one-minute. After that, the same participant is asked to name fruits and animals in an alternating way (i.e. one animal and then one fruit). Higher scores indicate better performance. A Brazilian validation of the test is available elsewhere[24].

The Rey-Osterrieth Complex Figure Test Version A (ROCFT – Figure A): This test has the goal to evaluate skills related to attention, visuospatial orientation, planning, short-term visual memory, and psychomotor skills. The participant is shown a complex figure that they must copy. Later, the same person is asked to recreate the figure from memory[25].

The Logical Memory Test: This test is used to evaluate mnemonic aspects, mainly verbal skills. The participant is presented with a brief story and then immediately asked to recall it. After a delay, the same participant is asked to recall the previous story[26].

Then, two tools were used to evaluate naming and visual perception. The first was a probe composed of a list of simple pictures, such as a book, plane, shoes, house. This task is mainly used as a screening tool for cognitive deficits.[27] We also administered the Tahlves Visual Skills Assessment Test to investigate the mental organization capacity of fragmented images[28].

The Wechsler Scale Digits Subtest III was used to assess attention and working memory skills. In this subtest, the participant is instructed to

repeat a sequence of numbers presented to them in forward and reverse order[29].

Finally, the Brazilian version of the State-Trait Anxiety Inventory scale (STAI-S-6 and STAI-T-6)[30] and the Beck Depression Scale short version (BDI-PC)[31] were applied to assess mood aspects. The STAI-S and STAI-T investigate the participant's anxiety, either the current state of anxiety or its state. BDI-PC is a seven-item version of the BDI-II. Its main goal is to be a quick-to-respond tool to assess depressive mood.

Analysis

Statistical analyses were conducted to investigate differences in the performance of the COVID and control groups in the cognitive tests and mood questionnaires. The first version of the data was transferred from paper to spreadsheets, and then we processed the data, looking for inconsistencies and coding errors.

Categorical variables were presented as counts and percentages. Continuous variables were described by means and standard deviations. The hypotheses related to the psychological effects of COVID-19 were tested without a pre-determined order. As the demographic variables were matched between the groups, one-sided t-tests were used for each psychological task. Multiple comparisons were not carried out, and the type 1 error was not inflated due to the non-significance of the results.

We defined the risk of depression and anxiety using either the criteria of each tool or computing the standard deviation of the data. For BDI-PC, results greater than 4 were defined as "at risk"[31]. For STAI-S-6 and STAI-T-6, results 1 SD above the mean were considered at risk [30]. We corrected the p-values of the Chi-squared test when the expected value of the cell was less than 5 in 20% of the cells. We also adjusted all p-values for one-sided comparisons, considering that the alternative hypothesis was that the mean results of the control group were lower than those of the COVID group.

All analyses were performed in R with tidyverse, psych, arsenal, janitor, summarytools, apaTables and tableone functions. Codes and notes are freely available at https://osf.io/325mb/

Results

No statistically significant differences were found between the case and the control group across all neuropsychological tests. The significance level was defined as $p \leq 0.05$. The results for psychological symptoms related to anxiety and depression were remarkably similar. These results are shown in Table 3 and the Figure 1 summarizes the cognitive results.

Table 3. Summary of the neuropsychological results comparing cases and control groups.

	Case (N=45)	Control (N=16)	Total (N=61)	Statistical inference
Verbal Fluency	Mean (SD)	Mean (SD)	Mean (SD)	P-value
Animals	19.69 (5.77)	16.62 (5.37)	18.89 (5.78)	0.968
Fruits	14.64 (4.05)	12.69 (3.30)	14.13 (3.94)	0.968
Alternating	8.05 (2.03)	6.73 (1.67)	7.71 (2.02)	0.991
Rey-Osterrieth Complex Figure				
Copy	32.51 (4.43)	28.72 (8.61)	31.52 (5.98)	0.945
Recall	20.88 (6.44)	15.88 (7.46)	19.54 (7.03)	0.582
List of figures	10.00 (0.00)	9.88 (0.34)	9.97 (0.18)	0.918
Tahlves Test	11.91 (2.35)	10.69 (4.01)	11.58 (2.91)	0.867
Logical Memory				
WMS-R immediate recall	11.72 (3.81)	11.00 (3.78)	11.53 (3.78)	0.734
WMS-R late recall	9.86 (3.88)	9.60 (4.27)	9.79 (3.95)	0.582
Working memory				
Digits Span Forward	9.55 (2.44)	8.50 (2.16)	9.27 (2.40)	0.940
Digits Span Backwards	6.45 (2.33)	5.44 (2.10)	6.18 (2.30)	0.941
Total Digits Span	16.00 (4.39)	13.94 (3.86)	15.45 (4.32)	0.956
Mood and Anxiety				
STAI-State-6	11.91 (3.42)	11.25 (2.72)	11.74 (3.24)	0.779
STAI-Trait-6	15.27 (1.90)	15.47 (2.64)	15.32 (2.09)	0.398
BDI-PC	4.27 (3.40)	3.81 (3.62)	4.15 (3.43)	0.669

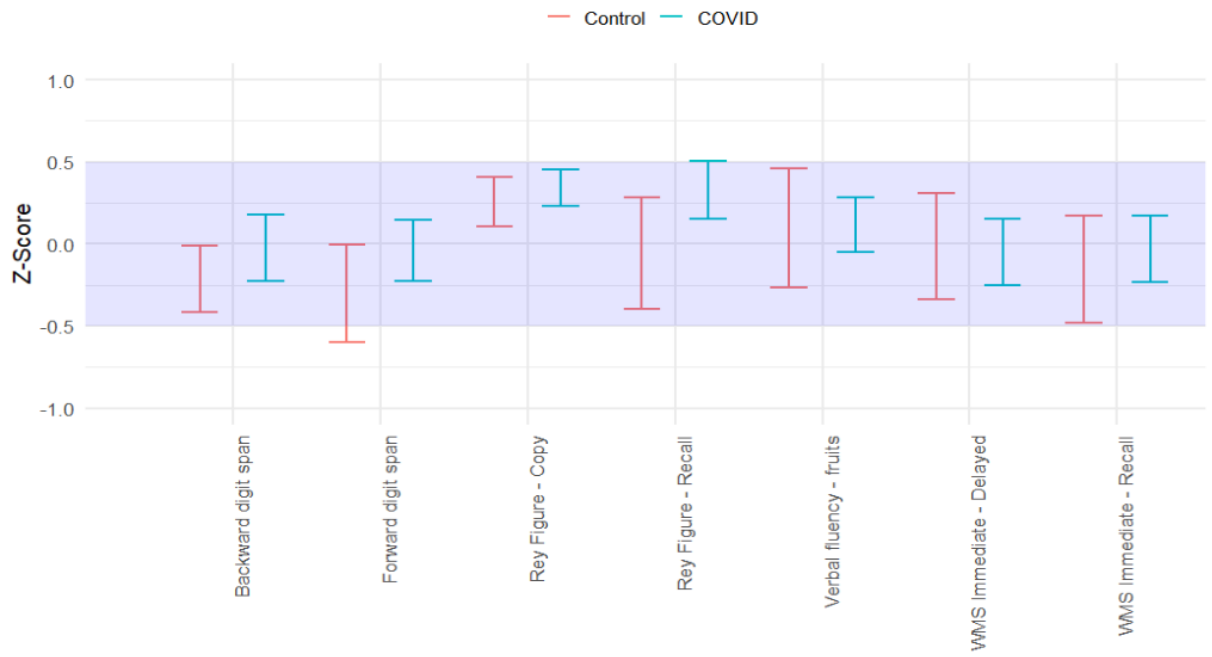

Figure 1. Z-scores for case and control groups for neuropsychological tests

These results motivated us to perform an exploratory analysis to check if the number of participants from both groups with high anxiety and depression could be different. To do so, we defined the cut-off point suggest by each tool or the standard deviation when needed. The results were also non-significant and are shown in Table 4.

Table 4. Results of the comparison of the number of participants with risk of presenting anxiety or depression.

	Case (N=45)	Control (N=16)	Total (N=61)	P-value
STAI-Trait-6				0.783
Risk	13 (29.5%)	5 (33.3%)	18 (30.5%)	
No risk	31 (70.5%)	10 (66.7%)	41 (69.5%)	
STAI-State-6				0.164
Risk	5 (11.1%)	0 (0.0%)	5 (8.2%)	
No risk	40 (88.9%)	16 (100.0%)	56 (91.8%)	
BDI-PC				0.876
Risk	21 (47.7%)	8 (50.0%)	29 (48.3%)	
No risk	23 (52.3%)	8 (50.0%)	31 (51.7%)	

Note: Risk stands for participants who had a z-score higher than 1 standard deviation or participants who had scores higher than the cut-off point suggested by the scale. No risk is determined for participants who had results lower than 1 standard deviation or lower than the cut-off point suggested by the scale.

In addition, no significant difference was found between the COVID and control groups regarding Anxiety, suggesting that both groups had similar anxiety indexes. However, it is important to state that 29.5% of the COVID group and 33.3% of the control

group had above average anxiety traits.

Similar results were found in the depression scale. No significant differences were found between both groups. Regarding the risk of presenting pathological levels of depression, 47.7% of the COVID group and 50.0% of the control group reported depression symptoms above the scale's cut-off point (4 points).

Discussion

In this study, we implemented a case-control design to check whether having "long-COVID" could impact cognitive aspects and mood traits of people. Our analyses provided us negative results, in which the following main findings are stressed: (1) we did not find significant differences in cognitive performance between both groups; and also (2) we did not find any significant differences in mood and anxiety profiles between both groups.

Negative results are often neglected by the scientific literature, which is a widely known aspect in the field.[22] In the absence of other studies with conclusions prone to the ones we found, we are limited to have a solid and deep discussion of our findings. However, other studies with a case-control method achieved similar results. Pihlaja et al[11] did not find differences in the general cognitive measurements comparing COVID cases and a control group. In their study, the Montreal Cognitive Assessment (MOCA) was used as a screening tool for neuropsychological dysfunction. Both groups performed nearly the same both 3-months after the infection (COVID group 19; 17–21 vs. Case group 19; 17-20), and 6 months after the infection.

In our study, we did not use the MOCA. However, we used a list of screening tests with similar tasks that can be found in MOCA with the goal to measure same psychological aspects. It should be noted that this study also found a higher subjective report of cognitive impairment in the COVID group compared with the control group ($p<0.001$). These results were achieved with the ABNAS questionnaire (A-B Neuropsychological Assessment Schedule), suggesting that COVID had a higher subjective cognitive complaint than the control group, but no actual objective impairment when compared to the control group[11]. In our study, many of the participants from the COVID group reported symptoms "related to memory and mental fog". However, this subjective complaint was not measured by the assessment tools of our study. Nonetheless, with the data we have, we are more favorable to believe that subjective complaint can be somehow unrelated to objective deficits.

Another study which found negative results regarding the difference of cognitive performance between the COVID group and control group was conducted by Raman et al.[12] This group conducted a multi-organ investigation including lungs, kidney, and brain evaluations, as well as psychological assessments on cognitive performance, mental health and quality of life indexes. The results found regarding cognitive performance did not show significant differences between the COVID and control group in general cognitive functioning. The tool used was also the Montreal Cognitive Assessment (MOCA) and the mean results of the COVID group were not statistically different than the control group.

Krishnan et al[32] found negative results. In their study, 20 patients were evaluated using a

comprehensive neuropsychological battery. Although mixed, their findings allow them to conclude that that the majority of patients were cognitively intact on neuropsychological testing approximately five-and-a-half-month post-onset of COVID-19 diagnosis. In their study, they found that cognitive deficits, when present, were largely seen on tests involving attention and processing speed, or aspects of executive function, which is a nonspecific pattern.

The general literature proposes cognitive decline in ex-COVID patients compared to a control group[33], even though some research groups did not find cognitive impairments[11,12]. Our study did not find statistical differences between the COVID and control group for the depression and anxiety scales. Similar results to this have been described by Demir et al[19], who investigated both cognitive and psychiatric symptoms. In the comparison between COVID and control group, no significant difference was found in depression (p=0.791) and anxiety (p=0.849) using the Hamilton Rating Scale for Depression and Anxiety.

Differences in cognitive performance following the long-term effects of COVID-19 have been a subject of study, with various factors influencing these variations. The elapsed time since diagnosis and the specific viral variant experienced by the patient emerge as critical elements in this context. Studies, such as the one conducted by Damiano et al.[34], emphasize the relevance of the post-diagnosis period, suggesting that the duration since infection may modulate the intensity and persistence of neuropsychological symptoms. Additionally, the influence of viral variants on clinical presentation was highlighted by Haidar et al[35], who observed differences in neuropsychological manifestations among different variants of the SARS-CoV-2. It is important to note that, even though the time since diagnosis was not utilized as a predictor in our study, the literature underscores its significance in understanding the long-term cognitive effects post-COVID-19.

Despite our efforts, our study has several limitations, from the more general and inner parts of several psychological studies to the ones that we can identify in our process. As already known, psychological assessment can be discussed[36]. The results of our study were obtained through measuring psychological characteristics using psychometric tools. Thus, it is possible to suggest that the employed tools may not have been sensitive to measure the characteristics under investigation, which constitutes one limitation of this study. Another potential limitation to consider is the sample size, given that the COVID group had a larger sample size than the control group.

Our findings underscore the necessity for continued investigations into the long-term symptoms of COVID-19. Many variables could influence the clinical picture of former patients over time and across different samples. Another limitation that requires acknowledgement is that we did not conduct long-term follow-up of patients. Therefore, further research in the following years can monitor the outcomes of these patients, understanding the potential effects of time and treatments on cognitive functioning.

Conclusion

Understanding the long-term effects of COVID-19 on cognitive and mood aspects has been important for the scientific community.

This study contributed to investigating these variables in a Brazilian sample collected from September 2021 to June 2022. The data analysis shows that no difference was found in objective cognitive performance when comparing the COVID and control groups. The main cognitive characteristics assessed were perception, attention, memory, and executive functions, and no difference in performance on any of these tests were observed between groups. Similar results were also found for mood characteristics, with our data indicating no difference in depression and anxiety traits.

Negative results are always a source of skepticism in the literature. One might achieve this outcome either because no difference is present or due to methodological pitfalls. At the beginning of this study, we were prone to checking how much COVID could impact psychological functions once we were convinced by the majority of the literature stating its negative effect. However, not only with the data we gathered but also after reading the extensive literature that relates COVID and psychology, we now believe that the negative effect can exist but is not a scientific law and is widespread among those who had COVID. We are aware that our study is composed of a small sample; however, we can suggest that the COVID infection might not contribute to the development of cognitive impairments or mood symptoms in the long term. Since our results can also be attributed to our study design, further research is needed to showcase more evidence of these findings.

Declaration of Interest Statement:

The authors declare no conflict of interest.

Funding:

The authors report there is no funding associated with the work featured in this article.

Acknowledgements

The authors express their gratitude to the study's participants. The authors thank the Department of Psychology at the Pontifical Catholic University of Rio de Janeiro for their resources.

ORCID ID:

1. Ana Clara Capistrano
https://orcid.org/0000-0001-5760-337X
2. Anna Beatriz Barbosa
https://orcid.org/0009-0001-0333-4239
3. Louise Marques
https://orcid.org/0000-0003-3844-6932
4. Luis Anunciação
https://orcid.org/0000-0001-5303-5782
5. Renato De Marca
https://orcid.org/0009-0002-0870-8815

Data availability statement

The data that support the findings of this study are available at https://osf.io/325mb/.

References:

1. Goldhaber NH, Kohn JN, Ogan WS, et al. Deep Dive into the Long Haul: Analysis of Symptom Clusters and Risk Factors for Post-Acute Sequelae of COVID-19 to Inform Clinical Care. *Int J Environ Res Public Health*. 2022;19(24). doi:10.3390/ijerph192416841

2. Raveendran A V., Jayadevan R, Sashidharan S. Long COVID: An overview. *Diabetes Metab Syndr*. 2021;15(3):869-875. doi:10.1016/J.DSX.2021.04.007

3. Ceban F, Ling S, Lui LMW, et al. Fatigue and cognitive impairment in Post-COVID-19 Syndrome: A systematic review and meta-analysis. *Brain Behav Immun*. 2022;101:93-135. doi:10.1016/J.BBI.2021.12.020

4. Rogers JP, Chesney E, Oliver D, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry*. 2020;7(7):611-627. doi:10.1016/S2215-0366(20)30203-0

5. Yong SJ. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. *Infect Dis (Lond)*. 2021;53(10):737-754. doi:10.1080/23744235.2021.1924397

6. Orrù G, Bertelloni D, Diolaiuti F, et al. Long-COVID Syndrome? A Study on the Persistence of Neurological, Psychological and Physiological Symptoms. *Healthcare (Basel)*.2021;9(5).doi:10.3390/HEALTHCARE9050575

7. Kubota T, Kuroda N, Sone D. Neuropsychiatric aspects of long COVID: A comprehensive review. *Psychiatry Clin Neurosci*. 2023;77(2):84-93. doi:10.1111/PCN .13508

8. Wild CJ, Norton L, Menon DK, Ripsman DA, Swartz RH, Owen AM. Disentangling the cognitive, physical, and mental health sequelae of COVID-19. *Cell Rep Med*. 2022;3(10). doi:10.1016/J.XCRM.2022.100750

9. Zawilska JB, Kuczyńska K. Psychiatric and neurological complications of long COVID. *J Psychiatr Res*. 2022;156:349-360. doi:10.1016/J.JPSYCHIRES.2022.10.045

10. Ahmad MS, Shaik RA, Ahmad RK, et al. "LONG COVID": an insight. *Eur Rev Med Pharmacol Sci*. 2021;25(17):5561-5577. doi:10.26355/EURREV_202109_26669

11. Pihlaja RE, Kauhanen LLS, Ollila HS, et al. Associations of subjective and objective cognitive functioning after COVID-19: A six-month follow-up of ICU, ward, and home-isolated patients. *Brain Behav Immun Health*. 2023;27. doi:10.1016/J.BBIH.2023.100587

12. Raman B, Cassar MP, Tunnicliffe EM, et al. Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental health, post-hospital discharge. *EClinical Medicine*. 2021;31. doi:10.1016/J.ECLINM.2020.100683

13. Delgado-Alonso C, Valles-Salgado M, Delgado-Álvarez A, et al. Cognitive dysfunction associated with COVID-19: A comprehensive neuropsychological study. *J Psychiatr Res*. 2022;150:40-46. doi:10.1016/J.JPSYCHIRES.2022.03.033

14. Ortelli P, Ferrazzoli D, Sebastianelli L, et al. Neuropsychological and neurophysiological correlates of fatigue in post-acute patients with neurological manifestations of COVID-19: Insights into a challenging symptom. *J Neurol Sci*. 2021;420. doi:10.1016/J.JNS.2020.117271

15. Holm H, Ivarsdottir E V., Olafsdottir T, et al. Physical and cognitive impact following SARS-CoV-2 infection in a large population-based case-control study. *Communications Medicine*. 2023;3(1):94-94. doi:10.1038/S43856-023-00326-5

16. Zhou H, Lu S, Chen J, et al. The landscape of cognitive function in recovered COVID-19 patients. *J Psychiatr Res*. 2020;129:98-102. doi:10.1016/J.JPSYCHIRES.2020.06.022

17. Cian V, De Laurenzis A, Siri C, Gusmeroli A, Canesi M. Cognitive and Neuropsychiatric Features of COVID-19 Patients After Hospital Dismission: An Italian Sample. *Front Psychol*. 2022;13. doi:10.3389/FPSYG.2022.908363

18. Woo MS, Malsy J, Pöttgen J, et al. Frequent neurocognitive deficits after recovery from mild COVID-19. *Brain Commun*. 2020;2(2). doi:10.1093/BRAINCOMMS/FCAA205

19. Demir B, Beyazyüz E, Beyazyüz M, Çelikkol A, Albayrak Y. Long-lasting cognitive effects of COVID-19: is there a role of BDNF? *Eur Arch Psychiatry Clin Neurosci*. 2023;273(6):1339-1347. doi:10.1007/S00406-022-01514-5

20. Akıncı B, Oğul ÖE, Hanoğlu L, et al. Evaluation of cognitive functions in adult individuals with COVID-19. *Neurol Sci*. 2023;44(3):793-802. doi:10.1007/S10072-022-06562-2

21. Invernizzi A, Renzetti S, van Thriel C, et al. Covid-19 related cognitive, structural and functional brain changes among Italian adolescents and young adults: a multimodal longitudinal case-control study. *medRxiv*. 2023;(COVID-19 SARS-CoV-2 preprints from medRxiv and bioRxiv). doi:10.1101/2023.07.19.23292909

22. MlinarićA, Horvat M, Smolčić VŠ. Dealing with the positive publication bias: Why you should really publish your negative results. *Biochem Med (Zagreb)*. 2017;27(3). doi:10.11613/BM.2017.030201

23. Nair A. Publication bias - Importance of studies with negative results! *Indian J Anaesth*. 2019;63(6):505. doi:10.4103/IJA.IJA_142_19

24. Paula JJ, Paiva GC de C, Costa D de S. Use of a modified version of the switching verbal fluency test for the assessment of cognitive flexibility. *Dementia e Neuropsychologia*. 2015; 9(3):258-264. doi: 10.1590/1980-57642015DN93000008

25. Oliveira M da S, Rigoni M dos S, Rey A. *Figuras Complexas de Rey Teste de Cópia e de Reprodução de Memória de Figuras Geométricas Complexas*. 2nd ed. Pearson Clinical; 2018.

26. Martins MR, Bolognani SAP, Pompéia S, Bueno OFA, Miranda MC. Versões Alternativas do Subteste Memória Lógica da WMS-R: Análise de Desempenho de uma Amostra Saudável da Cidade de São Paulo. *Psicologia: Reflexão e Crítica*. 2015;28(3):444-453. doi:10.1590/1678-7153.201528303

27. Nitrini R, Lefèvre BH, Mathias SC, et al. Testes neuropsicológicos de aplicação simples para o diagnóstico de demência. *Arq Neuropsiquiatr*. 1994;52(4):457-465. doi:10.1590/S0004-282X1994000400001

28. Alves L, Morávia CB, de Paula JJ, Campos AF. Teste de Organização Visual Hooper e Teste de Avaliação de Habilidade Visuoespacial (THALVES). In: *Avaliação Neuropsicológica*. Artmed; 2010:412-425.

29. Wechsler D, Trentini C, Yates D, Heck V. *WASI - Escala Wechsler Abreviada de Inteligência - Manual*. 1st ed. Pearson Clinical; 2018.

30. Fioravanti-Bastos ACM, Cheniaux E, Landeira-Fernandez J. Development and validation of a short-form version of the Brazilian state-trait anxiety inventory. *Psicologia: Reflexão e Crítica*. 2011;24(3):485-494. doi:10.1590/S0102-79722011000300009

31. Anunciação L, Caregnato M, da Silva FSC. Aspectos psicométricos do Inventário Beck de Depressão-II e do Beck Atenção Primária em usuários do Facebook. *J Bras Psiquiatr*. 2019;68(2):83-91. doi:10.1590/0047-2085000000231

32. Krishnan K, Miller AK, Reiter K, Bonner-Jackson A. Neurocognitive Profiles in Patients With Persisting Cognitive Symptoms Associated With COVID-19. *Arch Clin Neuropsychol*. 2022;37(4):729-737. doi:10.1093/ARCLIN/ACAC004

33. Daroische R, Hemminghyth MS, Eilertsen TH, Breitve MH, Chwiszczuk LJ. Cognitive Impairment After COVID-19-A Review on Objective Test Data. *Front Neurol*. 2021;12. doi:10.3389/FNEUR.2021.699582

34. Damiano RF, Rocca CC de A, Serafim A de P, et al. Cognitive impairment in long-COVID and its association with persistent dysregulation in inflammatory markers. *Front Immunol*. 2023;14:1174020-1174020. doi:10.3389/FIMMU.2023.1174020

35. Haidar MA, Jourdi H, Haj Hassan Z, et al. Neurological and Neuropsychological Changes Associated with SARS-CoV-2 Infection: New Observations, New Mechanisms. *Neuroscientist*. 2022;28(6):552-571. doi:10.1177/1073858420984106

36. Filho NH. Medida psicológica: o debate entre as perspectivas conceituais representacionista e realista. *Aval psicol*. 2014;13(3):399-408. Accessed January 24, 2024. http://pepsic.bvsalud.org/scielo.php?script=sci_abstract&pid=S1677-04712014000300012&lng=en&nrm=iso&tlng=pt