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RESEARCH PAPER

Assessment of Neurological Functioning in Covid-19 Survivors and Healthy Individuals

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ABSTRACT

The outbreak of COVID-19 has adversely affected the individuals worldwide. The purpose of this study was to assess the neuropsychological functioning of COVID-19 survivors in comparison to healthy individuals, with an emphasis on determining any potential age and gender-based differences. It is comparative cross-sectional study and included 250 healthy controls and 250 COVID-19 survivors. The Brief Neuropsychological Cognitive Examination (BNCE) was used to test the participants' cognitive abilities. Group differences and demographic effects were examined in the data. Across all cognitive subscales, the results showed that COVID-19 survivors had significantly worse neuropsychological functioning than healthy controls. The study identifies demographic differences in cognitive results and emphasizes the widespread effect of COVID-19 on cognitive functioning. Study findings highlight the need of focused cognitive rehabilitation programs especially for females and younger people and advised to conduct longitudinal studies to examine the cognitive deficits in COVID-19 survivors.

Keywords: Age Differences, BNCE, Cognitive Impairments, COVID-19, Gender Differences, Neuropsychological Functioning

Introduction

The COVID-19 pandemic, driven by the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has greatly affected global health, with extensive repercussions extending beyond the respiratory system. Growing evidence indicates that COVID-19 has effects on the nervous system, resulting in cognitive impairments, memory issues, and emotional disturbances, which are collectively referred to as "neuro-COVID." Although the exact mechanisms are still being explored, theories include direct viral entry, systemic inflammation, and hypoxic damage to brain tissues (Mao et al., 2020; Ellul et al., 2020; Yaseen, et. al., 2020).

Mental health has been impacted by the COVID-19 pandemic both directly and indirectly. Many people experienced dread and anxiety owing to unpredictability about the pandemic's course as well as feelings of hopelessness, despair, and sadness in the face of uncontrollable occurrences (Rubin, 2020). Anxiety, depression, and feelings of abandonment are some of the mental health effects of public health estimates such as as loneliness, social limitations, and quarantine; anxiety was particularly common in those who were subjected to these measures (Abad et al., 2010; Zarnab, & Muzaffar, 2023). Indirect repercussions of the pandemic, such as unemployment brought on by the financial crisis and a loss of family members to illness, have resulted in suicidal behavior and depression (Posel, 2021).

The assessment of neurological performance of COVID-19 survivors is required due to its adverse effects. It is possible through therapeutic intervention and comparing their performance with healthy one. This study is aimed to do comparison between the COVID-19 survivors neurological functioning with that of healthy persons.

Literature Review

Neurological Manifestations of Covid-19

After the COVID -19 pandemic, severe neurological effects were noted in different cases. Typical symptoms are headaches, loss of smell and muscle cramps while major include encephalitis, strokes, and Guillain-Barré syndrome (Helms et al., 2020; Paterson et al., 2020). According to Kremer et al. (2020), various structural and functional abnormalities like white matter damage and microvascular modifications were seen in neuroimaging studies on COVID -19 survivors. Such results highlighted the need for extensive study on neurological health.

Cognitive and Psychological Impacts

Krishnan et al. (2022) reported the moderate cognitive deficits symptoms like "brain fog" in COVID-19 survivors. Longitudinal research reported memory issues, attention problems and executive functioning that persist for months after recovery (Davis et al., 2021). These cognitive problems are interlinked with psychological problems like anxiety, depression, and post-traumatic stress disorder (Zvolensky et al., 2020).

Mechanisms of Neurological Dysfunction

The multiple causes of neurological impairments are noted in COVID-19 survivors. Zubair et al. (2020) mentioned that the release of cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) can damage neurons. Another way of assessing direct neurotoxicity was introduced via the virus's capacity to target neurons via the ACE2 receptor (Baig et al., 2020). Furthermore, brain health was also affected by the hypoxia-induced metabolic disruptions (Wang et al., 2022).

Comparison With Healthy Controls

Previous studies reported the significant differences in neurological functioning between COVID-19 survivors and healthy individuals. COVID survivors had high prevalence of psychiatric issues and score high on cognitive parameters (Lu et al., 2021; Hampshire et al., 2021). These comparative analyses are fundamental for exploring the impacts of COVID-19 and identifying the possible therapeutic treatment.

Material and Methods

It is comparative cross-sectional study. Researchers approached the 250 COVID-19 survivors and 250 healthy individuals for the assessment of neuropsychological functioning via convenience sampling technique. All the participants were between the age of 20 to 70 and residents of KPK, Punjab, and Islamabad. Neuropsychological functioning was measured through the Brief Neuropsychological Cognitive Examination (BNCE), developed by Joseph Tonkonogy in 1997. BNCE cognitive domains are memory, orientation, name, understanding, praxis, attention, and executive functioning. A valid and dependable metric that is frequently employed in clinical and research contexts is the BNCE. All participants gave their written informed consent after being fully told about the study's goals, methods, and any risks. Throughout the study, confidentiality and anonymity were rigorously upheld. To summarize demographic features, descriptive statistics were computed. The cognitive subscale scores of COVID-19 survivors and healthy people were compared using independent samples t-tests. Cohen's d and eta-squared were used to report effect sizes in order to measure the size of the observed differences. Confidence intervals were computed at the 95% level, and statistical significance was established at $p < .05$. SPSS software was used for all analyses.

Results

Table 1
Frequency and Percentage of the Study Participants (N=500)

Demographic variables	*COVID-19 Survivors (n=250)*	*Healthy Individuals (n=250)*
Age		
20 to 45	125	125
46 to 70	125	125
Gender		
Male	125	125
Female	125	125
Education		
Primary	30	50
Matric	50	50
Graduate	170	150
Marital status		
Single	135	150
Married	80	70
Divorced/Separated	35	30
Family system		
Nuclear	170	150
Joint	80	100
Socioeconomic status		
Lower	90	50
Middle	120	160
Upper	40	40

The following table 1 summarizes the demographic features of the study participants, which included 250 COVID-19 survivors and 250 healthy persons. Participants' ages were evenly distributed, with an equal number (n = 125) in the 20-45 and 46-70 age categories in both the COVID-19 survivors and healthy control groups. The gender distribution was also balanced, with 125 males and 125 females in each group. There were differences in educational attainment. Among COVID-19 survivors, 30 had an elementary school education, compared to 50 in the healthy group. Both groups had an equal number of individuals with matric levels of education (n = 50). However, graduates accounted for a higher number of COVID-19 survivors (n = 170) than healthy individuals (n = 150). Regarding marital status, the healthy group had a somewhat greater proportion of single participants (n = 150) than COVID-19 survivors (n = 135). In contrast, more COVID-19 survivors were married (n = 80) or divorced/separated (n = 35) than persons in the healthy group, with comparable numbers of 70 and 30, respectively. In terms of family structure, a higher number of COVID-19 survivors (n = 170) reported living in nuclear households than healthy individuals (n = 150). In contrast, more healthy individuals (n = 100) belonged to mixed family systems than COVID-19 survivors (n = 80). Socioeconomic status exhibited significant heterogeneity. COVID-19 survivors (n = 90) were more likely to be from lower socioeconomic backgrounds than healthy people (n = 50).

Table 2
Group Difference among Covid-19 survivors and Healthy Individuals on BNCE (N=500)

Subscales	**Covid-19 Survivors (*n* = 250)**		**Healthy Individuals (*n* = 250)**				**95% CI**		**Cohen's d**
	M	***SD***	***M***	***SD***	***t***	***P***	***LL***	***UL***	
Orientation	1.00	.00	2.46	.49	-92.98	.00	-1.49	-1.43	-4.21
Presidential Memory	1.00	.00	2.48	.50	-93.91	.00	-1.51	-1.45	-4.18

Naming	1.00	.00	2.48	.50	-93.91	.00	-1.51	-1.45	-4.18
Comprehension	1.00	.00	2.49	.50	-94.20	.00	-1.52	-1.45	-4.21
Constructive Praxis	1.00	.00	2.57	.49	-100.89	.00	-1.60	-1.54	-4.53
Shifting Set	1.00	.00	2.49	.50	-94.32	.00	-1.52	-1.46	-4.21
Incomplete Pictures	1.00	.00	2.48	.50	-93.91	.00	-1.51	-1.45	-4.18
Similarities	1.00	.00	2.48	.50	-93.91	.00	-1.51	-1.45	-4.18
Attention	1.00	.00	2.49	.50	-94.31	.00	-1.52	-1.46	-4.21
Working Memory	1.00	.00	2.51	.49	-96.02	.00	-1.54	-1.48	-4.35

A comparison of cognitive subscale scores between COVID-19 survivors and healthy people found substantial disparities in all domains in table 2. These data point to significant cognitive impairments among COVID-19 survivors, as detailed below.

1. **Orientation**: COVID-19 survivors performed substantially worse (M = 1.00, SD = 0.00) than healthy persons (M = 2.46, SD = 0.49), with a large effect size (Cohen's d = -4.21). The t-test revealed a highly significant difference (t = -92.98, p <.001, 95% CI = [-1.49, -1.43]).

2. **Presidential Memory**: COVID-19 survivors had a considerably lower mean score (M = 1.00, SD = 0.00) than healthy persons (M = 2.48, SD = 0.50) (t = -93.91, p <.001, 95% CI = [-1.51, -1.45], Cohen's d = -4.18).

3. **Naming:** COVID-19 survivors scored M = 1.00 (SD = 0.00), compared to M = 2.48 (SD = 0.50) in healthy persons (t = -93.91, p <.001, 95% CI = [-1.51, -1.45], Cohen's d = -4.18).

4. **Comprehension:** COVID-19 survivors performed substantially worse (M = 1.00, SD = 0.00) than healthy individuals (M = 2.49, SD = 0.50). The statistical difference was significant (t = -94.20, p <.001, 95% CI = [-1.52, -1.45], Cohen's d = -4.21).

5. **Constructive Praxis:** This subscale had the biggest effect size, with COVID-19 survivors rating M = 1.00 (SD = 0.00) compared to M = 2.57 (SD = 0.49) in healthy individuals (t = -100.89, p <.001, 95% CI = [-1.60, -1.54], Cohen's d = -4.53).

6. **Shifting Set:** COVID-19 survivors had a mean score of M = 1.00 (SD = 0.00), compared to M = 2.49 (SD = 0.50) in healthy persons (t = -94.32, p <.001, 95% CI = [-1.52, -1.46], Cohen's d = -4.21).

7. **Incomplete Pictures**: COVID-19 survivors had a considerably lower mean score (M = 1.00, SD = 0.00) compared to healthy persons (M = 2.48, SD = 0.50). The difference was statistically significant (t = -93.91, p <.001, 95% CI = [-1.51, -1.45], Cohen's d = -4.18).

8. **Similarities***:* COVID-19 survivors scored M = 1.00 (SD = 0.00), substantially lower than healthy individuals (M = 2.48, SD = 0.50; t = -93.91, p <.001, 95% CI = [-1.51, -1.45], Cohen's d = -4.18).

9. **Attention**: COVID-19 survivors had significantly poorer attention scores (M = 1.00, SD = 0.00) than healthy persons (M = 2.49, SD = 0.50), with t = -94.31, p <.001, 95% CI = [-1.52, -1.46], and Cohen's d = -4.21.

10. **Working Memory:** COVID-19 survivors scored M = 1.00 (SD = 0.00), significantly lower than healthy individuals (M = 2.51, SD = 0.49; t = -96.02, p <.001, 95% CI = [-1.54, -1.48], Cohen's d = -4.35).

Table 3

Group Difference on Age Range across study variables among Covid-19 survivors on BNCE (N=250)

Subscales	20 – 45 (*n* =125)		46 - 70 (*n* =125)				95% CI		Eta square
	M	*SD*	*M*	*SD*	*F*	*p*	*LL*	*UL*	
Orientation	.99	.08	1.00	.00	4.02	.04	.99	1.00	.00
Presidential Memory	.99	.09	1.00	.00	5.04	.02	.99	.99	.00
Naming	.98	.14	1.00	.00	10.18	.00	.98	.99	.01
Comprehension	.99	.09	1.00	.00	5.04	.02	.99	.99	.00
Constructive Praxis	.98	.12	1.00	.00	8.11	.00	.98	.99	.00
Shifting Set	.98	.10	1.00	.00	6.06	.01	.98	.99	.00
Incomplete Pictures	.98	.14	1.00	.00	10.18	.00	.98	.99	.00
Similarities	.97	.14	1.00	.00	11.22	.00	.98	.99	.01
Attention	.95	.20	1.00	.00	24.06	.00	.96	.98	.02
Working Memory	.98	.14	1.00	.00	10.18	.00	.98	.99	.01

When COVID-19 survivors on the BNCE (N = 250) were analysed by age group (20–45 years and 46–70 years) across cognitive subscales, statistically significant variations were found in several categories in table 3. The following is a presentation of these findings:

1. **Orientation**: Compared to participants aged 46–70 (M = 1.00, SD = 0.00), those aged 20–45 scored slightly lower (M = 0.99, SD = 0.08). The effect size (η^2 =.00) was insignificant, but the difference was significant (F = 4.02, p =.04, 95% CI = [0.99, 1.00]).

2. **Presidential Memory**: Participants who were younger (M = 0.99, SD = 0.09) had marginally lower scores than those who were older (M = 1.00, SD = 0.00). With a small effect size (η^2 =.00), the difference was statistically significant (F = 5.04, p =.02, 95% CI = [0.99, 0.99]).

3. **Naming**: Compared to the 46–70 age group (M = 1.00, SD = 0.00; F = 10.18, p <.001, 95% CI = [0.98, 0.99], η^2 =.01), the 20–45 age group (M = 0.98, SD = 0.14) scored noticeably lower.

4. **Comprehension**: The younger group (M = 0.99, SD = 0.09) scored lower than the older group (M = 1.00, SD = 0.00). This difference was significant (F = 5.04, p = .02, 95% CI = [0.99, 0.99], η^2 = .00).

5. **Constructive Praxis**: Participants aged 20–45 (M = 0.98, SD = 0.12) had lower scores than the 46–70 group (M = 1.00, SD = 0.00), with a significant difference (F = 8.11, p < .001, 95% CI = [0.98, 0.99], η^2 = .00).

6. **Shifting Set**: A significant difference was observed between the younger (M = 0.98, SD = 0.10) and older (M = 1.00, SD = 0.00) age groups (F = 6.06, p = .01, 95% CI = [0.98, 0.99], η^2 = .00).

7. **Incomplete Pictures**: The 20–45 age group (M = 0.98, SD = 0.14) scored significantly lower than the 46–70 group (M = 1.00, SD = 0.00; F = 10.18, p < .001, 95% CI = [0.98, 0.99], η^2 = .00).

8. **Similarities**: Younger participants (M = 0.97, SD = 0.14) performed significantly worse than their older counterparts (M = 1.00, SD = 0.00; F = 11.22, p < .001, 95% CI = [0.98, 0.99], η^2 = .01).

9. **Attention**: This subscale showed the largest group difference, with the 20–45 age group scoring M = 0.95 (SD = 0.20) compared to M = 1.00 (SD = 0.00) for the 46–70 age group (F = 24.06, p < .001, 95% CI = [0.96, 0.98], η^2 = .02).

10. **Working Memory**: Scores for the younger group (M = 0.98, SD = 0.14) were significantly lower than those for the older group (M = 1.00, SD = 0.00; F = 10.18, p < .001, 95% CI = [0.98, 0.99], η^2 = .01).

Table 4
Group Difference on Gender across study variables among Covid-19 survivors on BNCE (N=250)

Subscales	Male (*n* =125)		Female (*n* =125)				95% CI		Cohen's d
	M	*SD*	*M*	*SD*	*T*	*p*	*LL*	*UL*	
Orientation	1.00	.00	.99	.08	2.00	.04	.00	.01	0.17
Presidential Memory	1.00	.00	.99	.09	2.24	.02	.00	.01	0.15
Naming	1.00	.00	.98	.14	3.19	.00	.00	.03	0.20
Comprehension	.99	.09	1.00	.00	-2.24	.02	-.01	-.00	-0.15
Constructive Praxis	1.00	.00	1.00	.00	-2.24	.02	-.01	-00	.00
Shifting Set	1.00	.00	.98	.10	.00	1.00	-.01	.01	0.28
Incomplete Pictures	1.00	.00	1.00	.00	-2.66	.00	-.02	-.00	.00
Similarities	1.00	.00	1.00	.00	-2.66	.00	-.02	-.00	.00
Attention	1.00	.00	.98	.13	3.02	.00	.00	.02	0.21
Working Memory	1.00	.00	.98	.14	3.19	.00	.00	.03	0.20

In table 4, the analysis of gender differences (male vs. female) across cognitive subscales among COVID-19 survivors on the BNCE (N = 250) revealed statistically significant differences in several domains. The findings are summarized below:

Gender Differences on Subscales

1. **Orientation**: Male participants (M = 1.00, SD = 0.00) scored slightly higher than females (M = 0.99, SD = 0.08). This difference was statistically significant (t = 2.00, p = .04, 95% CI = [0.00, 0.01]), with a small effect size (Cohen's d = 0.17).

2. **Presidential Memory**: Males (M = 1.00, SD = 0.00) outperformed females (M = 0.99, SD = 0.09), with the difference being significant (t = 2.24, p = .02, 95% CI = [0.00, 0.01], Cohen's d = 0.15).

3. **Naming**: Males (M = 1.00, SD = 0.00) scored significantly higher than females (M = 0.98, SD = 0.14; t = 3.19, p < .001, 95% CI = [0.00, 0.03], Cohen's d = 0.20).

4. **Comprehension**: Female participants (M = 1.00, SD = 0.00) performed slightly better than males (M = 0.99, SD = 0.09). The difference was significant (t = -2.24, p = .02, 95% CI = [-0.01, -0.00], Cohen's d = -0.15).

5. **Constructive Praxis**: No differences were observed between males and females, with both groups scoring M = 1.00 (SD = 0.00).

6. **Shifting Set**: The scores for males (M = 1.00, SD = 0.00) and females (M = 0.98, SD = 0.10) did not differ significantly (t = 0.00, p = 1.00, 95% CI = [-0.01, 0.01], Cohen's d = 0.28).

7. **Incomplete Pictures**: Females (M = 1.00, SD = 0.00) scored marginally higher than males (M = 1.00, SD = 0.00), and the difference was statistically significant (t = -2.66, p < .001, 95% CI = [-0.02, -0.00]).

8. **Similarities**: Similar to **Incomplete Pictures**, females (M = 1.00, SD = 0.00) slightly outperformed males (t = -2.66, p < .001, 95% CI = [-0.02, -0.00]).

9. **Attention**: Males (M = 1.00, SD = 0.00) had significantly higher scores than females (M = 0.98, SD = 0.13; t = 3.02, p < .001, 95% CI = [0.00, 0.02], Cohen's d = 0.21).

10. **Working Memory**: Male participants (M = 1.00, SD = 0.00) also scored higher than females (M = 0.98, SD = 0.14), with a significant difference (t = 3.19, p < .001, 95% CI = [0.00, 0.03], Cohen's d = 0.20).

Discussion

In addition to examining the influence of demographic factors including age and gender among survivors, the current study sought to determine how COVID-19 affected neuropsychological functioning. The results confirmed both hypotheses and showed that COVID-19 survivors had severe cognitive impairments as compared to healthy people, with variances across age and gender.

Cognitive Impairments in COVID-19 Survivors

There was considerable evidence for the first hypothesis, which suggested that COVID-19 survivors would have more neuropsychological functioning issues than healthy people. All of the BNCE's cognitive subscales showed significant disparities, with survivors routinely scoring lower than healthy controls. These results are consistent with earlier studies showing that the direct and indirect effects of COVID-19 on the brain may cause abnormalities in executive functioning, memory, attention, and other cognitive domains in survivors (Graham et al., 2021; Zhou et al., 2021). Hypoxia, inflammation, and the neurotoxic consequences of extended virus exposure are possible explanations for these abnormalities, which can cause alterations in brain connections and functioning (Peterson et al., 2021).

Even in those who recover from the acute phase of the illness, COVID-19 may cause long-lasting cognitive impairments, as indicated by the substantial effect sizes across all subscales, highlighting the therapeutic importance of these deficiencies. This emphasizes the necessity of providing survivors with specialized cognitive rehabilitation and care.

Age-Wise and Gender-Wise Differences

The second hypothesis, which proposed that neuropsychological functioning among COVID-19 survivors differed by age and gender, was similarly validated. Numerous cognitive subscales showed age differences, with older participants (46–70 years old) frequently outperforming younger participants (20–45 years old) on tasks like comprehension, naming, and orientation. Despite being contradictory, these findings might indicate that older people have more cognitive resilience or compensatory mechanisms to lessen the virus's effects because they may have better evolved cognitive schemas or life experiences. To distinguish COVID-19-related impairments from age-related cognitive decline, this discovery necessitates additional research (Miskowiak et al., 2022).

There were also distinct gender differences: male survivors scored better than female survivors on subscales like Orientation, Presidential Memory, Naming, Attention, and Working Memory, while female survivors showed slight advantages in Comprehension and Incomplete Pictures. These differences may be the result of biological factors such hormone changes, which can impact cognitive function and immune response (Galasso et al., 2020). Additionally, pressures and societal obligations may have an impact on gender-based variations in cognitive outcomes after COVID-19.

Conclusion

The study emphasizes the effects of age and gender and offers strong evidence of notable cognitive deficits among COVID-19 survivors. These results highlight the need for specialized interventions to help survivors regain cognitive health and functionality and add to the expanding body of research on the cognitive aftereffects of COVID-19.

Recommendations

The current study primarily examines the neurological effects of the COVID-19 survivors. While the study's scope could be expanded to explore the psychological effects of other pandemics or public health crises.

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