EVALUATING MEMORY AND FLUENCY IN POST-COVID SURVIVORS COMPARED TO NON-COVID PATIENTS BASED ON ACE- III SCALE

By

Lamiya Ali Aononno
20346008

A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of
Bachelors of Pharmacy (Hons.)

School of Pharmacy
Brac University
September 2024

Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing my degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

Student's Full Name & Signature:

Lamiya Ali Aononno
20346008

Approval

The thesis titled "Evaluating Memory and Fluency in Post-COVID Survivors Compared to Non-COVID Patients Based on ACE-III Scale" submitted by Lamiya Ali Aononno (20346008), of Summer, 2020 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

Supervised By:

____

Dr. Afrina Afrose
Associate Professor
School of Pharmacy
BRAC University

Approved By:

Dean:

____

A.F.M. Yusuf Haider, PhD
Acting Dean, School of Pharmacy
Professor, Department of Mathematics and Natural Sciences
Brac University

Ethics Statement

This research was conducted with strict adherence to ethical standards, ensuring the integrity and credibility of the study. All data were collected and reported with integrity and transparency, complying with relevant ethical guidelines and regulations.

Abstract

The immediate impact of COVID-19 can be life-threatening and has devastating effects on mental health. Though changes in mental health during COVID-19 have been observed, the extent of its long-term effects is still unclear. To assess the association of COVID-19 with neurological complications, this study uses the Addenbrook Cognition Examination- III (ACE- III) to evaluate cognitive functions such as memory and fluency in post-COVID survivors and non-COVID patients. The primary objective is to study the long-term cognitive effects of COVID-19. A survey was conducted among 60 patients, using the ACE- III scale. Various statistical tests such as t-test, Cohen's d, and Fisher's exact test were used for data analysis. The findings from the memory and fluency assessments, supported by statistical tests, suggest no significant difference in cognitive abilities between individuals who have never had COVID-19 and those who have recovered. This suggests that more research is needed to gain a better understanding of the long-term cognitive effects of COVID-19. Larger sample sizes, longitudinal follow-up, and the addition of more cognitive domains could all be helpful in future research in determining any distinct effects that the virus may have on cognition over time.

Keywords: Cognitive function, Memory, Fluency, ACE- III Scale, SARS-Cov-2

Dedication

This project is dedicated to my supervisor, Dr. Afrina Afrose, whose constant support, insightful suggestions, and expertise helped me to complete this work.

Acknowledgment

I am sincerely grateful to my project supervisor, Dr. Afrina Afrose for her unwavering guidance and support during this entire project work. She has constantly given me advice and encouragement while offering helpful criticism at every stage of the work. I also want to acknowledge the National Institute of Neuro Sciences & Hospital (NINS&H) for support in data collection. Without their support, it would be difficult for us to collect all the patient's data and conduct interviews. Finally, I would like to express my gratitude to the School of Pharmacy, Brac University.

Table of Contents

List of Tables

List of Figures

List of Acronyms

COVID-19	Coronavirus Disease of 2019
IRB	Institutional Review Board
ACE- III	Addenbrooke's Cognitive Examination III
NINS&H	National Institute of Neuro Sciences & Hospital

Glossary

COVID brain fog	A range of neurocognitive symptoms such as forgetfulness, poor attention, concentration, and focusing problems that can persist for a long time usually weeks or months after COVID-19 infection.
ACE-III Scale	A cognitive screening test to assess five cognitive domains such as attention, memory, fluency, language, and visuospatial to identify cognitive impairment.
Effect Size	It is a value that indicates how meaningful the relationship between two variables is. It is used as a quantitative measure to find out the strength of a phenomenon. For example, the correlation between two variables or the mean differences in a t-test.

Chapter 1

Introduction

1.1 Background

The COVID-19 pandemic, caused by coronavirus (SARS-COV-2), has created serious health challenges around the world. It is a significant virus that affects the respiratory system but can also migrate to the central nervous system (CNS), causing neurological symptoms. Recent research has emphasized the possibility of cognitive impairment after COVID-19 infection, also known as "COVID brain fog," which can appear as memory loss, trouble concentrating, and slower cognitive processing (Li et al., 2023). Studies have also found that patients recovering from COVID-19 have aberrant neuropsychological test results, including decreased memory, fluency, and other executive abilities. These data suggest that the virus may affect several cognitive domains, including executive processes, verbal expressiveness, and working memory. In a survey of 969 adults with SARS-COV-2 infection 6-11 months ago, 26% reported minor cognitive impairment (Hartung et al., 2022). These abnormalities can last long after the initial infection, even in people who have moderate or asymptomatic instances, raising worries about the virus's long-term neurological repercussions (Sudre et al., 2021).

Although the precise process causing the cognitive dysfunctions linked with COVID-19 is still unknown, several elements are thought to be involved. COVID-19 causes direct viral infection of the central nervous system, neuroinflammation, neurotoxicity, tissue hypoxia, and microangiopathy. COVID-19 has been linked to encephalopathy, delirium, and other acute neurological disorders in extreme cases, adding to the evidence of infection with brain damage (Helms et al., 2020). Furthermore, studies have found that the pandemic's psychological consequences, including as worry, stress, and depression, may worsen or mimic cognitive impairment, particularly in vulnerable populations (Ceban et al., 2021).

Given the global prevalence of SAR-COV-2, studying how COVID-19 affects cognitive function is critical. Because reduced cognitive function can have a significant influence on daily functioning and overall quality of life, more study into prevention, treatment, and rehabilitation measures is required to mitigate the long-term effects of COVID-19.

1.2 Research Gap

Despite the growing evidence linking COVID-19 to cognitive impairments, a significant research gap remains, especially regarding the virus's long-term effects on specific cognitive domains like memory and verbal fluency. While studies have reported generalized cognitive deficits in post-COVID survivors, much of this research has focused on broad outcomes like ‘brain fog” and executive dysfunction, with less attention given to detailed neuropsychological profiles. Specifically, memory deficits, including working and long-term memory, have been inconsistently reported across studies, leaving unclear whether these issues are transient or more persistent (Becker et al., 2021). Additionally, while verbal fluency difficulties have been noted in some post-COVID patients, the mechanism driving this impairment remains poorly understood. Verbal fluency is a complex cognitive function that involves language, executive processes, and memory retrieval, but current studies have not consistently measured its specific decline with other cognitive functions (Lu et al., 2020). Another significant gap is the limited understanding of how demographic factors, age, socioeconomic status, pre-existing conditions, or the severity of infection, influence specific cognitive impairments. Some evidence suggests that older adults and those with pre-existing neurological conditions may be at greater risk for memory and fluency deficits, but there is a lack of longitudinal data to track these effects over time (Li et al., 2023).

Furthermore, the impact of mild or asymptomatic cases on memory and verbal fluency remains underexplored, as most studies have focused on individuals, who experienced severe illness (Al-Aly et al., 2022).

1.3 Objectives

The purpose of this study is to evaluate cognitive functions such as memory and fluency in post-COVID survivors and non-COVID patients. The assessment is done by using ACE- III scale which is a cognitive scale to measure various cognitive domains like memory and verbal fluency. The results will help determine whether COVID-19 affects these specific cognitive functions and whether any cognitive impairments persist after recovery.

1.4 Significance

This study holds significance as it sheds light on the cognitive impacts of COVID-19, particularly in memory and fluency. It can further help us to identify any persistent cognitive deficiencies, hence leading to a better understanding of the long-term cognitive effects of the virus. These findings can help improve patient outcomes and quality of life by guiding healthcare providers to early detection, improving diagnosis, and developing targeted interventions and rehabilitation strategies for patients experiencing cognitive impairments after recovery.

Chapter 2

Methodology

The research methodology described in this section is built upon a comparative cross-sectional design, which allows for evaluating cognitive functions such as memory and fluency between non-COVID patients and post-COVID survivors using the ACE- III scale. It is designed to outline each step, from participant selection to statistical data analysis. The systemic process undertaken in this study ensures the reliability, validity, and transparency of the data collected. The key steps undertaken in this study are-

Participants meeting specific criteria were selected from the NINS COVID-19 registry

↓

Participants were contacted and were provided with informed consent before participating

↓

Each participant opts for an in-person or video conference interview based on personal preference

↓

Data were collected using the ACE-III questionnaire

↓

Scoring was done for the ACE-III questionnaire

↓

Analyzing memory and fluency in post-COVID survivors and non-COVID individuals

2.1 Designing the Study

This study used a comparative cross-sectional approach to investigate the effects of COVID-19 on cognitive processes such as memory and fluency skills. The study population comprised 60 participants divided into post-COVID and non-COVID groups. The post-COVID group consists of 40 individuals, while the non-COVID group consists of 20 individuals. Before participation, each participant was provided informed consent. The study design allows us to evaluate memory and fluency performance between the post-COVID and non-COVID groups, resulting in a comprehensive analysis of cognitive differences related to COVID-19.

2.2 Study Population

Participants meeting pre-defined inclusion and exclusion criteria were chosen from the NINS COVID-19 registry. The eligibility requirement was that individuals must be 25 years of age or older. Participants with underlying health conditions, such as patients with cognitive deficiencies affecting speech or mobility, that might affect their cognitive performance were not included in our study sample. After careful consideration, a final sample size of 60 participants was determined, with 40 being post-COVID and 20 being non-COVID. This decision was made to ensure comparability between the groups and to reduce the number of confounding variables that might affect memory and fluency outcomes.

2.3 Data Sources

The main data source for this study was the COVID-19 registry of the National Institute of Neuro Sciences & Hospital (NINS&H). This registry allowed us to verify the participant's health status and the other relevant details for participant selection, and to ensure accurate group classification. The data source was reliable and it significantly enhanced the integrity of the research.

2.4 Data Collection Method

Data were collected using a 26-item cognitive scale called the ACE-III questionnaire. It is widely used to assess cognitive domains such as attention, memory, fluency, and others. Each participant took part in the interview either in person or via video conference based on their personal preference. Face-to-face interviews were conducted at NINS&H, and each session lasted between 30 to 45 minutes. This flexible approach allowed for thorough data collection, prioritizing participant comfort and preference.

2.5 Ethical Consideration

Strict ethical standards were followed throughout the study to ensure the confidentiality of all participants. All data were securely stored and no information was shared outside the research team. Each participant provided informed consent before participation and they were allowed to pause or withdraw at any time if they experienced discomfort during the cognitive assessments. The research was also approved by the Institutional Review Board (IRB) of the National Institute of Neurosciences & Hospital.

2.6 Data Analysis

To compare memory and fluency scores between post-COVID and non-COVID individuals, the data analysis procedure was done. Based on the ACE-III scale scores, the following statistical techniques have been applied to assess the cognitive differences between these groups.

I. **Descriptive Statistics:** The analysis started with the two groups' descriptive statistics being computed. The mean and standard deviation for the memory and fluency scores were calculated independently for post-COVID and non-COVID participants. These tests offered an initial grasp of the central tendency and variability within each group.

II. **Independent Sample T-Tests:** For both memory and fluency scores, independent sample t-tests were used to determine whether there were statistically significant differences between the two groups.

III. **Effect Size (Cohen's d):** Cohen's d has been calculated for both the memory and fluency scores to assess the size of the difference between the two groups. An estimate of the effect size is given by Cohen's d, which aids in interpreting the practical relevance of the observed differences.

IV. **Fisher's Exact Test:** Based on memory and fluency performance, individuals were categorized into two using Fisher's exact test to further investigate the association between cognitive performance and COVID-19 status. For memory, the groups were categorized as good/moderate memory (≥15) and weak memory (<15). For fluency, the groups were categorized as high/moderate fluency (8–14) and low fluency (0–7).

Chapter 3

Result

Table 1 below presents the memories scores for twenty patients who tested negative for COVID-19. Each patient's score from the ACE-III questionnaire is displayed with their identification, providing individual evaluation and comparison.

Table 1 Memory Scores of Non-COVID Patients

Patient Sl. no.	Memory Scores (non-COVID)
1	23
2	26
3	19
4	15
5	10
6	4
7	1
8	13
9	11
10	20
11	21
12	20
13	26
14	20
15	25
16	24
17	20
18	22
19	22
20	24

Mean value: 18.3

Standard Deviation: 6.94

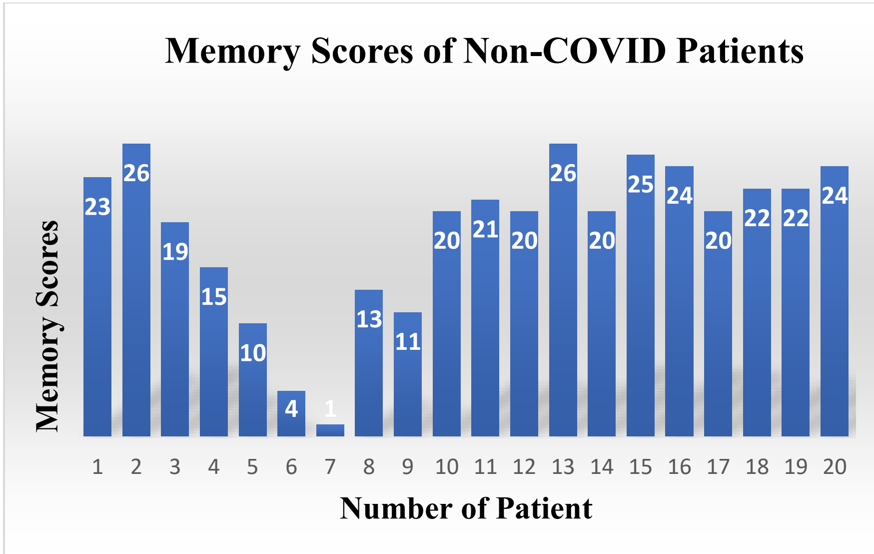

Figure 1 Graphical Representation of Memory Scores of Non-COVID Patients

The graph shows the memory scores of twenty non-COVID patients. The memory scores vary from 1 and 26. The highest recorded score is 26, and the lowest score is 1. There is significant diversity in memory performance, with the majority of individuals scoring between 10 and 26. The graph indicates clusters of higher scores, particularly in the mid-range (patients 10-20), demonstrating a trend of slightly superior memory ability among a considerable fraction of the sample. However, a few outliers with lower scores (patients 4 and 6) indicate some variation in memory capacity throughout the sample. This variance in memory performance may demand further analysis to identify the underlying causes.

Table 2 below presents the memory scores for forty patients who tested positive for COVID-19. Each patient's score from the ACE-III questionnaire is displayed with their identification, providing individual evaluation and comparison.

Table 2 Memory Scores of Post-COVID Patients

Patient Sl. no.	Memory Scores (post-COVID)
1	8
2	20
3	9
4	12
5	24
6	17
7	18
8	6
9	10
10	15
11	19
12	13
13	13
14	24
15	22
16	25
17	25
18	16
19	20
20	20
21	23
22	25
23	13
24	25
25	23
26	26
27	17
28	19
29	16
30	22
31	24
32	20
33	24
34	16
35	25
36	25
37	26
38	26
39	24
40	24

Mean value: 19.475

Standard Deviation: 5.56

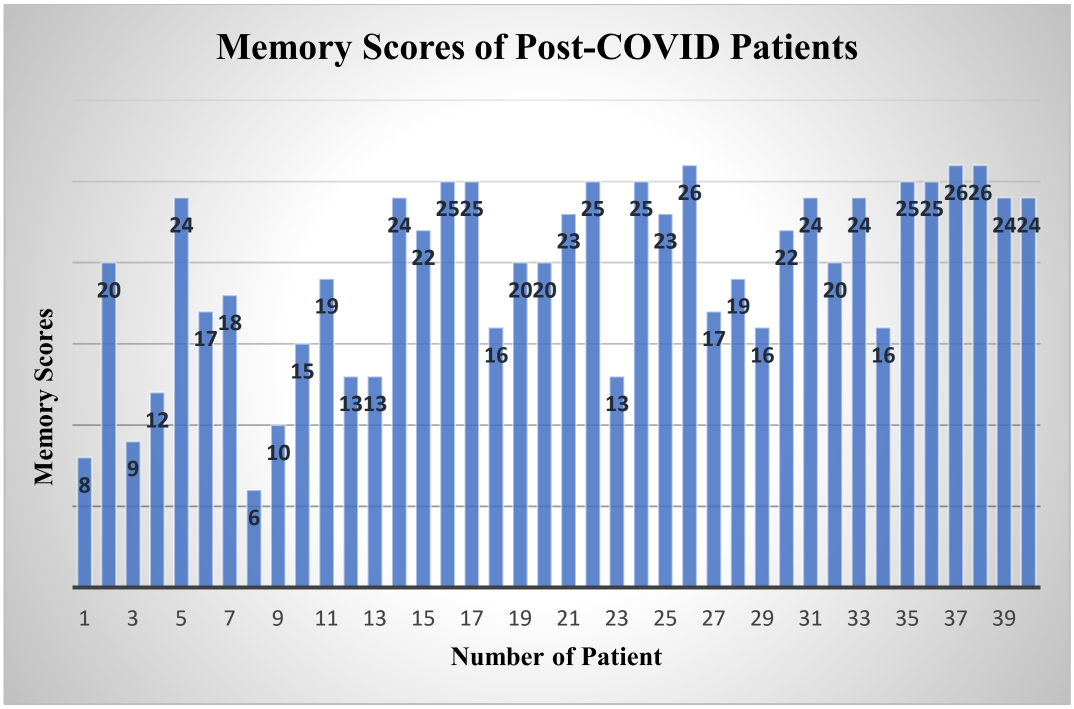

Figure 2 Graphical Representation of Memory Score of Post-COVID Patients

The graph shows the memory scores of 40 people, ranging from 6 to 26. The x-axis displays the number of patients, and the y-axis shows their memory ratings. The studies show significant diversity in memory performance among post-COVID patients. Some people, such as patient 26,37,38 earned the highest, with a score of 26, while others, such as patient 7, scored far lower, with a 6.

Statistical Tests (T-test, Cohen's d Test, Fisher Exact Test)

1. T test= $\frac{\text{MEAN OF GROUP 1}-\text{MEAN OF GROUP 2}}{\sqrt{(\frac{\text{STANDARD DEVIATION OF GROUP 1}^2}{\text{NUMBER OF SCORES IN GROUP 1}})+(\frac{\text{STANDARD DEVIATION OF GROUP 2}^2}{\text{NUMBER OF SCORES IN GROUP 2}})}}$

$$= \frac{19.475-18.5}{\left(\frac{5.56^2}{40}\right)+\left(\frac{6.94^2}{20}\right)} = \frac{0.975}{3.18} = 0.31$$

The results show that there is no statistically significant difference in mean memory scores between non-COVID and post-COVID patients, supporting the Null Hypothesis (H0).

2. Cohen's d Test:

$$s_{pooled} = \sqrt{\frac{Standard\ deviation\ of\ group\ 1^2 + Standard\ deviation\ of\ group\ 2^2}{2}}$$

$$s_{pooled} = \sqrt{\frac{5.56^2+6.94^2}{2}}$$

$$s_{pooled} = \sqrt{\frac{79.1}{2}}$$

s_{pooled} = 6.29

Now for the value of d-

$$d=\frac{Mean\ of\ group\ 1 - Mean\ of\ group\ 2}{pooled\ standard\ deviation}$$

$$d=\frac{19.475-18.5}{6.29}$$

$$d=\frac{0.975}{6.29}$$

d= 0.155

Cohen's d effect size	Interpretation
d = .0 – .19	Trivial effect
d = .20	Small effect
d = .50	Medium effect
d = .80 or higher	Large effect

After comparing post-COVID and non-COVID patients, Cohen's d-value is 0.155. This shows a relatively tiny effect size, indicating that there is minimal variance between the two groups in terms of the variable under consideration. More research may be required to explore this further and identify any potential discrete effects. So, I would do Fisher's exact test next.

3. Fisher Exact Test:

	Good/Moderate Memory (≥15)	**Bad Memory (< 15)**
Post-COVID	31 (A)	9 (B)
Non-COVID	15 (C)	5 (D)

The formula for the odd ratio is $= \frac{\frac{A}{B}}{\frac{C}{D}} = \frac{A \times D}{B \times C} = \frac{31 \times 5}{9 \times 15} = \frac{155}{135} = 1.11$

The odds ratio of 1.11 indicates that post-COVID patients are sporadically more likely to have a good/moderate memory score (≥15) than non-COVID patients. However, this is not a strong correlation.

Table 3 below presents the fluency scores for twenty patients who tested negative for COVID-19. Each patient's score from the ACE-III questionnaire is displayed with their identification, providing individual evaluation and comparison.

Table 3 Fluency Scores of Non-COVID Patients

Patient Sl. no.	Fluency Scores (non-COVID)
1	14
2	13
3	10
4	9
5	6
6	7
7	0
8	5
9	6
10	11
11	14
12	10
13	13
14	11
15	13
16	10
17	13
18	14
19	13
20	11

Mean Value: 10.15

Standard Deviation: 3.62

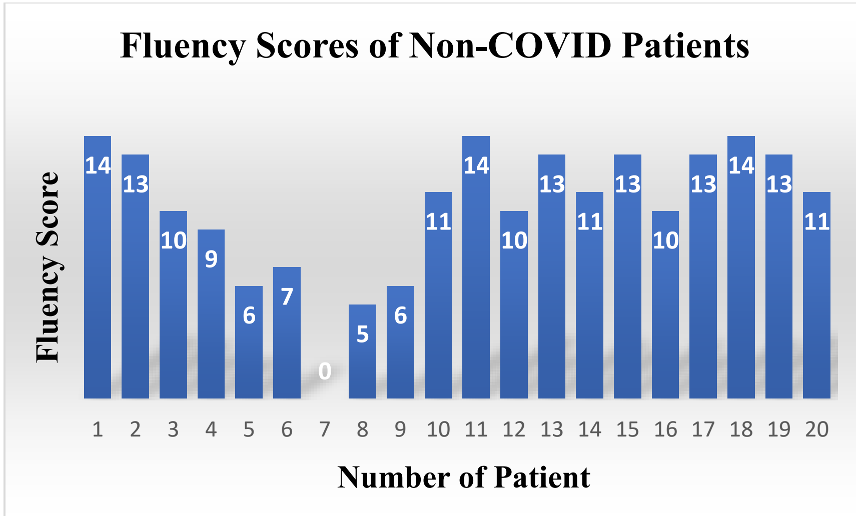

Figure 3 Graphical Representation of Fluency Scores of Non-COVID Patients

The graph shows the fluency scores of twenty non-COVID patients. The fluency scores vary from 0 and 14. The highest recorded score is 14, and the lowest score is 0. There is significant diversity in fluency performance, with the majority of individuals scoring between 10 and 14. The graph indicates clusters of higher scores, particularly in the mid-range (patients 10-20), demonstrating a trend of slightly superior fluency ability among a considerable fraction of the sample. However, a few outliers with lower scores (patients 7, 8, and 6) indicate some variation in fluency ability throughout the sample. This variance in fluency performance may demand further analysis to identify the underlying causes.

Table 4 below presents the memory scores for forty patients who tested positive for COVID-19. Each patient's score from the ACE-III questionnaire is displayed with their identification, providing individual evaluation and comparison.

Table 4 Fluency Scores of Post-COVID Patients

Patient SI. no.	Fluency Scores
1	5
2	10
3	2
4	1
5	13
6	11
7	9
8	3
9	5
10	10
11	12
12	9
13	9
14	14
15	12
16	14
17	12
18	12
19	12
20	12
21	13
22	12
23	14
24	14
25	14
26	14
27	11
28	12
29	4
30	13
31	13
32	9
33	13
34	8
35	10
36	9
37	11
38	14
39	14
40	12

Mean Value: 10.53

Standard Deviation: 3.50

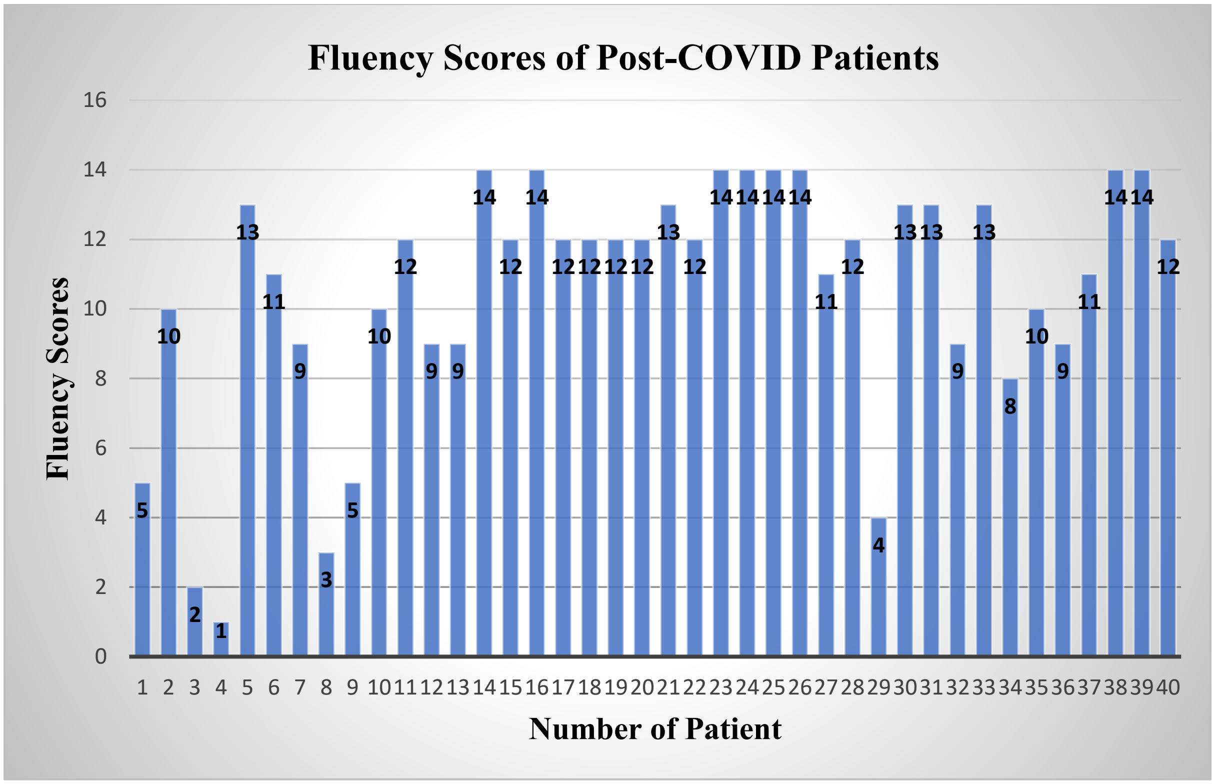

Figure 4 Graphical Representation of Fluency Scores of Post-COVID Patients

The graph shows the fluency scores of 40 people, ranging from 1 to 14. The x-axis displays the number of patients, and the y-axis shows their fluency scores. The studies show significant diversity in fluency performance among post-COVID survivors. Several individuals, including patients 14, 16, 23-26, and 38,39, achieved the highest scores, each earning 14 points. While others, such as patient 4, scored far lower, with a 1.

Statistical Tests (T-test, Cohen's d Test, Fisher Exact Test)

1. T test= $\frac{\text{MEAN OF GROUP 1} - \text{MEAN OF GROUP 2}}{\sqrt{\left(\frac{\text{STANDARD DEVIATION OF GROUP 1}^2}{\text{NUMBER OF SCORES IN GROUP 1}}\right) + \left(\frac{\text{STANDARD DEVIATION OF GROUP 2}^2}{\text{NUMBER OF SCORES IN GROUP 2}}\right)}}$

$$= \frac{10.53 - 10.15}{\left(\frac{3.50^2}{40}\right) + \left(\frac{3.62^2}{20}\right)} = \frac{0.38}{0.96} = 0.40$$

The results show that there is no statistically significant difference in mean fluency scores between non-COVID and post-COVID patients, supporting the Null Hypothesis (H0).

2. Calculation of Cohen's d:

$$s_{pooled} = \sqrt{\frac{\textit{Standard deviation of group 1}^2 + \textit{Standard deviation of group 2}^2}{2}}$$

$$s_{pooled} = \sqrt{\frac{3.50^2 + 3.62^2}{2}}$$

$$s_{pooled} = \sqrt{\frac{25.35}{2}}$$

s_{pooled} = 3.56

Now for the value of d-

$$d = \frac{\textit{Mean of group 1} - \textit{Mean of group 2}}{\textit{pooled standard deviation}}$$

$$d = \frac{10.53 - 10.15}{3.56}$$

$$d = \frac{0.38}{3.56}$$

d= 0.11

Cohen´s d effect size	Interpretation
d = .0 – .19	Trivial effect
d = .20	Small effect
d = .50	Medium effect
d = .80 or higher	Large effect

After comparing post-COVID and non-COVID patients, Cohen's d-value is 0.11. This shows a relatively tiny effect size, indicating that there is minimal variance between the two groups in terms of the variable under consideration. More research may be required to explore this further and identify any potential discrete effects. So, I would do Fisher's exact test next.

3. Fisher exact test:

	High/Moderate fluency (8-14)	Low Fluency (0-7)
Post-COVID	34 (A)	6 (B)
Non-COVID	15 (C)	5 (D)

The formula for the odd ratio is $= \frac{\frac{A}{B}}{\frac{C}{D}} = \frac{A \times D}{B \times C} = \frac{34 \times 6}{15 \times 5} = \frac{204}{135} = 1.51$

The odds ratio of 1.51 indicates that post-COVID patients are sporadically more likely to have a High/Moderate Fluency score (8-14) than non-COVID patients. However, this is not a strong correlation.

Chapter 4

Discussion

4.1 Memory Performance

Based on the memory score analysis, post-COVID patients had a slightly higher mean score of 19.475 with a standard deviation of 5.56 than non-COVID patients, who had a mean score of 18.3 with a standard deviation of 6.94. The null hypothesis (H0) was supported by the T-test result ($t = 0.31$), which demonstrated no statistically significant difference between the two groups despite the post-COVID group having a slightly higher mean. This shows that the memory scores determined by the ACE-III questionnaire were not significantly impacted by the COVID-19 recovery state.

Cohen's d value was 0.155, indicating a small impact size. This implies that the difference in memory scores between the two groups is minimal and may not reflect a significant cognitive difference. The tiny impact size supports the conclusion that there is no significant difference in memory ability between non-COVID and post-COVID negative patients.

The Fisher exact test was used to differentiate between patients with good/moderate memory (≥15) and those with poor memory (<15). The odds ratio was 1.11, indicating that post-COVID patients had just a minor advantage over non-COVID patients in terms of good or moderate memory scores. However, this link is minimal, indicating that COVID-19 recovery has little impact on memory performance, at least in the short term.

4.2 Fluency Performance

Non-COVID patients had a mean score of 10.15 (SD = 3.62), but post-COVID patients had a slightly higher mean score of 10.53 (SD = 3.50). The T-test resulted in a score of 0.40, showing no statistically significant difference in fluency performance between the two groups. This finding, like the memory test findings, supports the null hypothesis that there is no discernible difference in cognitive function between non-COVID and post-COVID negative patients.

Similar to the memory test, the fluency scores' Cohen's d value of 0.11 denotes a very tiny impact size. This shows that there is little chance that the two groups' distinct fluency results represent significant cognitive differences.

Using the Fisher exact test, patients' fluency scores were divided into two categories: low fluency (score of 0-7), and high/moderate fluency (scores of 8–14). The link is not strong enough to establish a meaningful trend, but the odds ratio of 1.51 suggests that patients who were post-COVID negative had a slightly higher likelihood of demonstrating higher fluency than non-COVID patients.

According to Graham et al. (2021), some cognitive symptoms are present in long-COVID patients but it also highlights that those with mild COVID-19 did not report any significant cognitive impairment. This suggests that the effect of COVID-19 on cognition depends on other factors like the severity of COVID-19 infection, sample size, patient’s age, socioeconomic background, and other confounding variables. Hence, to determine the cognitive outcome, it is important to consider these additional factors too.

4.3 Interpretation

The findings from the memory and fluency assessments, supported by T-tests and Cohen's d analyses, suggest that there is no significant variance in cognitive abilities between those who never had COVID-19 and those who have recovered from it. The slight variations seen in memory and fluency indicate that COVID-19 does not have a long-lasting or substantial effect on cognitive function in this group, as determined by the ACE-III questionnaire.

It is significant to highlight that although some post-COVID negative patients showed somewhat improved cognitive performance, odds ratios were extremely near to one, and effect sizes were very tiny. This provides more evidence in favor of the theory that in comparison to non-COVID persons, COVID-19 recovery does not result in appreciable changes in cognitive ability.

Although these results are helpful, they also imply that further investigation is required to examine the possible long-term cognitive impacts of COVID-19. Larger sample sizes, longitudinal follow-up, and the inclusion of more cognitive domains could all be beneficial in future research to help pinpoint any distinct effects the virus may have on cognition over time. Deeper insights into cognitive consequences after COVID-19 may also be obtained by investigating variables such as the severity of the infection, the type of treatment taken, and the amount of time after recovery.

Chapter 5

Conclusion

This study is designed to assess the cognitive effects of COVID-19 by comparing memory and fluency performance in post-COVID survivors and to those who had never had the virus. Using the ACE-III scale, the comparative cross-sectional design enabled a thorough evaluation of cognitive functioning, with a focus on memory and fluency scores.

The study's findings show that, at least in the near term, COVID-19 had no substantial impact on memory or fluency functions in those without pre-existing cognitive deficits. The small differences in scores between post-COVID and non-COVID subjects indicate that any cognitive changes caused by COVID-19 are unlikely to be significant. However, these findings highlight the need for additional study, particularly with larger sample sizes and longitudinal designs, to investigate COVID-19's possible long-term impacts on cognitive processes. Future research could look into additional cognitive domains and characteristics including infection severity and time since recovery to acquire a better understanding of COVID-19's impact on cognition throughout time.

References

Al-Aly, Z., Bowe, B., & Xie, Y. (2022). Long COVID after breakthrough SARS-CoV-2 infection. *Nature Medicine*, *28*(7), 1461–1467. https://doi.org/10.1038/s41591-022-01840-0

Becker, J. H., Lin, J. J., Doernberg, M., Stone, K., Navis, A., Festa, J. R., & Wisnivesky, J. P. (2021). Assessment of cognitive function in patients after COVID-19 infection. *JAMA Network Open*, *4*(10), e2130645. https://doi.org/10.1001/jamanetworkopen.2021.30645

Ceban, F., Nogo, D., Carvalho, I. P., Lee, Y., Nasri, F., Xiong, J., Lui, L. M. W., Subramaniapillai, M., Gill, H., Liu, R. N., Joseph, P., Teopiz, K. M., Cao, B., Mansur, R. B., Lin, K., Rosenblat, J. D., Ho, R. C., & McIntyre, R. S. (2021). Association between mood disorders and risk of COVID-19 infection, hospitalization, and death. *JAMA Psychiatry*, *78*(10), 1079. https://doi.org/10.1001/jamapsychiatry.2021.1818

Graham, E. L., Clark, J. R., Orban, Z. S., Lim, P. H., Szymanski, A. L., Taylor, C., DiBiase, R. M., Jia, D. T., Balabanov, R., Ho, S. U., Batra, A., Liotta, E. M., & Koralnik, I. J. (2021). Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized Covid-19 "long haulers." *Annals of Clinical and Translational Neurology*, *8*(5), 1073–1085. https://doi.org/10.1002/acn3.51350

Hartung, T. J., Neumann, C., Bahmer, T., Chaplinskaya-Sobol, I., Endres, M., Geritz, J., Haeusler, K. G., Heuschmann, P. U., Hildesheim, H., Hinz, A., Hopff, S., Horn, A., Krawczak, M., Krist, L., Kudelka, J., Lieb, W., Maetzler, C., Mehnert-Theuerkauf, A., Montellano, F. A., . . . Finke, C. (2022). Fatigue and cognitive impairment after COVID-19: A prospective multicentre study. *EClinicalMedicine*, *53*, 101651. https://doi.org/10.1016/j.eclinm.2022.101651

Helms, J., Kremer, S., Merdji, H., Clere-Jehl, R., Schenck, M., Kummerlen, C., Collange, O., Boulay, C., Fafi-Kremer, S., Ohana, M., Anheim, M., & Meziani, F. (2020). Neurologic features in severe SARS-COV-2 infection. *New England Journal of Medicine*, *382*(23), 2268–2270. https://doi.org/10.1056/nejmc2008597

Hugon, J., Msika, E., Queneau, M., Farid, K., & Paquet, C. (2021). Long COVID: cognitive complaints (brain fog) and dysfunction of the cingulate cortex. *Journal of Neurology*, *269*(1), 44–46. https://doi.org/10.1007/s00415-021-10655-x

Li, Z., Zhang, Z., Zhang, Z., Wang, Z., & Li, H. (2023). Cognitive impairment after long COVID-19: current evidence and perspectives. *Frontiers in Neurology*, *14*. https://doi.org/10.3389/fneur.2023.1239182

Lu, Y., Li, X., Geng, D., Mei, N., Wu, P., Huang, C., Jia, T., Zhao, Y., Wang, D., Xiao, A., & Yin, B. (2020). Cerebral Micro-Structural Changes in COVID-19 patients – an MRI-based 3-month follow-up study. *EClinicalMedicine*, *25*, 100484. https://doi.org/10.1016/j.eclinm.2020.100484

Sudre, C. H., Murray, B., Varsavsky, T., Graham, M. S., Penfold, R. S., Bowyer, R. C., Pujol, J. C., Klaser, K., Antonelli, M., Canas, L. S., Molteni, E., Modat, M., Cardoso, M. J., May, A., Ganesh, S., Davies, R., Nguyen, L. H., Drew, D. A., Astley, C. M., . . . Steves, C. J. (2021). Attributes and predictors of long COVID. *Nature Medicine*, *27*(4), 626–631. https://doi.org/10.1038/s41591-021-01292-y