Brain, Behavior, & Immunity - Health 44 (2025) 100954

Contents lists available at ScienceDirect

Brain, Behavior, & Immunity - Health

journal homepage: www.editorialmanager.com/bbih/default.aspx

The relationship between cognitive function and neuropsychiatric disorders with quantitative electroencephalogram (qEEG) on long COVID syndrome patients

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ARTICLE INFO

Keywords:
Long covid syndrome
Cognitive function
Neuropsychiatric disorders
qEEG
Brain connectivity

ABSTRACT

Background: The COVID-19 pandemic has resulted in long-term consequences for a subset of affected individuals, known as long COVID syndrome. The neurological and psychiatric effects of this condition remain incompletely understood. This study aims to evaluate heightened common mental disorders in long COVID through assessing psychiatric, cognitive, neurophysiological aspects, and emphasizing lasting mental health impacts.
Methods: This cross-sectional study compared patients with long COVID to those who had recovered from COVID-19 without residual symptoms using quantitative electroencephalogram (qEEG) analysis. We conducted qEEG analyses, and Montreal Cognitive Assessment (MoCA) and Self-Rating Questionnaire (SRQ) tests on participants. Analyses included brain spectrum examination, hemispheric asymmetry, and inter-electrode connectivity.
Results: Analyses revealed lower MoCA scores in the memory domain were lower in the long COVID group (Mann Whitney *U*test), indicating that individuals with long COVID experience more substantial cognitive deficits. There is no statistical difference for spectrum examination and hemispheric asymmetry observed in the qEEG data between the COVID and long COVID groups. Connectivity analysis showed statistically significant higher connectivity in temporal-occipital (T6-O2) in long COVID groups (Mann Whitney *U*test).
Conclusion: Our findings underscore the persistent neuropsychiatric impact of COVID-19, particularly in long COVID patients. Notably, working memory deficits in MoCA scores were identified as one of the most frequent neuropsychological symptoms in these individuals. Decreased brain connectivity indicates cognitive-sensorimotor decline and is confirmed by the frequent brain fog symptoms in long COVID.

1. Introduction

The COVID-19 pandemic had affected global world, leading to instances of both suspected and verified cases of the highly transmissible acute respiratory illness induced by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) virus (Guo et al., 2020) COVID-19 has left a profound impact on the affected individuals, with more than 30% of them, including those with asymptomatic cases, experiencing lingering symptoms even after recovering from the acute phase (Tenforde et al., 2020). Distressingly, about 80% of individuals admitted to hospitals as a result of COVID-19 might experience lingering post-COVID symptoms (Huang et al., 2021). The survivors are facing the burden of enduring prolonged symptoms and long-term consequences that persist for several weeks after their initial infection (Nalbandian

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https://doi.org/10.1016/j.bbih.2025.100954
Received 23 June 2024; Received in revised form 25 December 2024; Accepted 22 January 2025
Available online 24 January 2025

et al., 2021). These lingering effects encompass a range of issues, such as persistent fatigue, cognitive impairments, neuropsychiatric disorders like depression(Renaud-Charest et al., 2021), and physical manifestations like dyspnea, collectively referred to as long COVID (Alwan and Johnson, 2021). As the SARS-CoV-2 virus evolves, giving rise to novel variants, experts predict that the incidence of long COVID will keep rising, adding to the challenges faced by healthcare systems globally.

Long COVID has been linked to cognitive decline and neuropsychiatric disturbances, although further research is warranted to comprehend its implications fully. The cognitive impairments observed had been reported in individuals who have successfully recuperated from the effects of COVID-19 within a three-month period (Mazza et al., 2021). The study highlighted the most affected areas to be executive function and psychomotor coordination, experiencing challenges in processing information, expressing thoughts verbally, and retaining information in the short term. Furthermore, there were enduring indications of depressive symptoms, although conditions such as PTSD, anxiety, and insomnia exhibited partial amelioration in subsequent assessments. Another troublesome manifestation observed is brain fog, characterized by feelings of malaise, attention and concentration difficulties, disorientation, and struggles in finding words (Boldrini et al., 2021).

The consequences of cognitive decline and neuropsychiatric disturbances in survivors can be severe, having a notable impact on their quality of life and impeding their day-to-day pursuits. It is crucial to implement appropriate follow-up measures, such as rehabilitation or therapy, to prevent further deterioration and support those grappling with these persistent effects.

In order to enhance comprehension regarding the connection among cognitive function, neuropsychiatric disruptions, and brainwave patterns in individuals with persistent COVID-19 effects, this research constitutes an initial evaluation. The researchers employ quantitative electroencephalogram (qEEG) measurements, alongside cognitive and psychiatric tests like the Montreal Cognitive Assessment (MoCA) and Self-Rating Questionnaire (SRQ), on individuals with long COVID Syndrome. The qEEG examination aims to identify imbalances or abnormalities in brain wave activities associated with cognitive impairments. The goal would be to enhance the well-being of individuals grappling with the persistent effects of COVID-19. This prospective strategy holds promise in addressing the enduring consequences of the illness and easing the challenges those impacted.

The central aim of this research was to explore the association between cognitive function and neuropsychiatric disruptions in individuals experiencing prolonged effects of COVID-19. A novel approach using qEEG analysis was initiated, which was not previously utilized in Indonesia. Unlike previous research, which relied solely on observations and interviews of a limited sample of COVID-19 survivors over a specific period, this study aimed to employ advanced qEEG analysis to gain deeper insights into the neurological aspects of long COVID syndrome.

2. Materials and methods

2.1. Study design

This pilot cross-sectional study was conducted at Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, from October 2022 to January 2023. This national referral hospital in Indonesia handles various cases from various patients across Indonesia. This trial was registered at ClinicalTrials.gov (NCT05670418) and approved for ethical clearance from the Ethics Committee of the Faculty of Medicine, Universitas Indonesia–Cipto Mangunkusumo National General Hospital (ethical clearance number: KET-684/UN2.F1/ETIK/PPM.February 00, 2022). This study applied consecutive sampling recruiting outpatient clinic patients during the omicron wave of the COVID-19 pandemic in Indonesia.

2.2. Participants

The objective of this study was to compare two groups: those diagnosed with long-term effects of COVID-19 (long COVID) and a control group comprising individuals who have wholly recuperated from COVID-19 without manifesting any symptoms. Long COVID was defined by presenting signs and symptoms (malaise, shortness of breath, cognitive dysfunction, or others that generally impact on everyday functioning) or continuing after 12 weeks with a negative result of polymerase chain reaction (PCR) swab test (World Health Organization, 2022).

The inclusion criteria in the study were: (1) being over 18 years of age and (2) expressing a willingness to take part in the research through informed consent. Conversely, criteria led to exclusion were: (1) being pregnant, (2) having a history of chronic neurological or psychiatric diseases, (3) using neurotropic, psychotropic, or antiepileptic medications, (4) experiencing severe scalp skin conditions or burns on the head, and (5) presently confirming a positive status for COVID-19 through either an antigen or PCR swab test.

Fig. 1 illustrates the sequence of individuals adhering to the principles delineated in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (Elm et al., 2007).

2.3. Measurements

2.3.1. Electroencephalography (EEG)

The EEG recording process included a 2-min resting-state EEG with eyes closed while the participant was seated comfortably. The eyes-closed condition was specifically chosen based on recommendations from previous research, which suggests that eyes-closed resting EEG should be used as a baseline for studies that do not involve eyes-open conditions or visual stimuli in their tasks, as highlighted by this study (Barry and De Blasio, 2017). The EEG records were conducted in an electromagnetically isolated room.

The EEG data was collected using a 32-channel Mitsar-EEG-202 system (Mitsar Co. LTD., St. Petersburg, Russia). The reference electrode and ground electrode were both positioned on the mastoid. Electrodes were placed according to the extended 10–20 system, with data collected from the following channels: FP1, FP2, F3, F4, F7, F8, C3, C4, T3, T4, T5, T6, P3, P4, O1, O2, Fz and Pz. The signals were digitized at a sampling rate of 500 Hz. The electrode impedance was maintained below 10 KΩ throughout the session.

2.3.2. Psychometric

We conducted two tests to assess the participant's cognitive and psychological condition: MoCA(Panentu and Irfan, 2013) and SRQ (Prasetio et al., 2022).

The MoCA questionnaire is a widely utilized cognitive screening tool, crafted to evaluate diverse cognitive functions in individuals. The assessment usually spans approximately 10–15 min and incorporates tasks like drawing, memory recall, language comprehension, and problem-solving. A perfect score on the MoCA is 30, with a higher score indicating more proficient cognitive functioning.

The SRQ questionnaire was utilized as a psychological evaluation tool to screen for indications of psychological distress and mental health issues among individuals. With its set of yes-or-no queries, the SRQ covers a spectrum of emotional, behavioral, and physical symptoms commonly associated with conditions such as depression, anxiety, and somatic complaints.

2.4. Data analysis and statistics

2.4.1. Pre-processing

The EEG data (2 min per subject) underwent pre-processing using MATLAB (version R2023a, Mathworks Inc., Aachen, Germany), involving the utilization of both the FieldTrip toolbox(Oostenveld et al.,

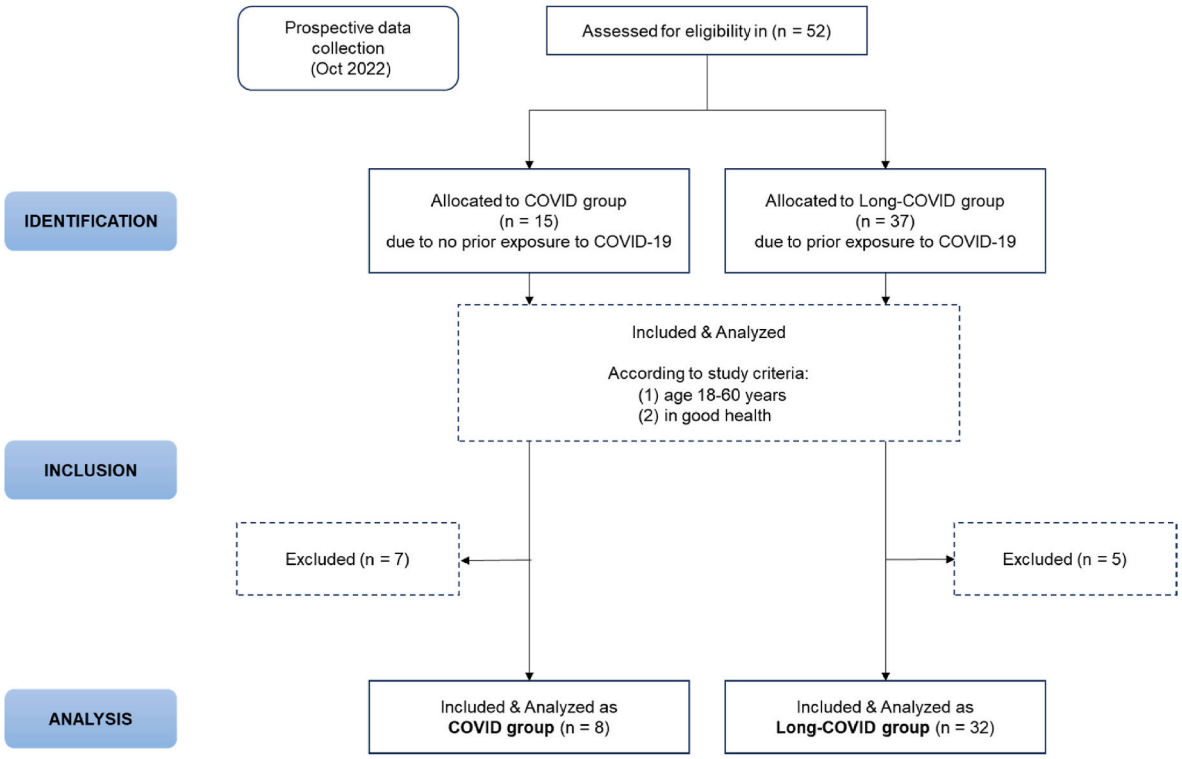

Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) flowchart of participants.

2011) and custom scripts. Initially, a Butterworth filter of sixth order was employed, featuring a high-pass configuration set at 1 Hz to remove the direct current component. Simultaneously, another 6th-order Butterworth filter was applied in a band-stop arrangement, targeting a frequency range of 49–51 Hz to eliminate power-line noise (50 Hz). Following the filtering, the data were divided into 2-s segments, known as epochs. Subsequently, a thorough visual inspection was conducted to identify and exclude epochs containing artifacts, with an average of 13.5% removed per subject (standard deviation = 7.1%). The remaining epochs were concatenated for the connectivity analysis using a simple triangular windowing technique, which retained the data's phasic component.

2.4.2. Spectral analysis

The power spectral densities (PSD) were computed per epoch using MATLAB's pwelch function. Each epoch lasted 2 s, with no overlap, and the window width was set to one-third of the sampling frequency. The frequency resolution was set at .5 Hz. Subsequently, we computed the average PSD for each participant and electrode by calculating the mean across epochs. Our analytical emphasis was on the frequency span from 1 to 40 Hz. To account for inter-subject variability and facilitate comparability between subjects, we calculated the relative PSD. This involved dividing the PSD for each frequency point by the sum of the PSD value in all data points within the same subject's dataset (Nishiyori et al., 2021). Subsequently, the PSD was divided into distinct ranges: delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), and gamma (30–40 Hz). These ranges were also used in the connectivity analysis. The representation of each frequency band is derived from the average PSD within its respective frequency range.

2.4.3. Hemispheric-asymmetry analysis

For each frequency band, we computed the asymmetries of relative PSD using specific electrode pairings, which were: FP1-FP2, F3-F4, F7-F8, T3-T4, T5-T6, C3-C4, P3-P4, and O1-O2. To calculate the laterality coefficient, we employed Equation (1).

$$\textit{Laterality Coefficient } (LC) = \frac{R - L}{R + L} \qquad \text{(Equation 1)}$$

Positive laterality values indicate asymmetry to the right hemisphere, whereas negative laterality values indicate laterality to the left hemisphere.

2.4.4. Connectivity analysis

Prior to the connectivity analysis, we applied a multitaper analysis using Discrete Prolate Spheroidal Sequences (DPSS), also known as Slepian windows. This method provides a robust spectral estimate by reducing the variance of the PSD. Zero padding was used to improve the frequency resolution by rounding the maximum trial length up to the next power of two. Subsequently, we employed the Debiased Weighted Phase Lag Index (dwPLI) as described by Vinck et al. as a statistical quantification of functional connectivity (Vinck et al., 2011). The dwPLI was utilized to measure the phase synchronization between different EEG channels. This index is particularly advantageous as it minimizes the influence of volume conduction and familiar sources, providing a more accurate representation of proper functional connectivity. The value ranges from 0 (no connectivity) to 1 (high connectivity). The frequency range of interest was set between 1 and 50 Hz to encompass the primary EEG frequency bands, including delta, theta, alpha, beta, and low gamma, which are critical for neurophysiological interpretations.

2.4.5. Statistical analysis

For each frequency band and channel/channel pair, we conducted the Shapiro–Wilk test to check for normality and subsequently, a Mann–Whitney *U*test was utilized to compare band power medians between the COVID and long COVID groups in PSD, hemispheric asymmetry, and connectivity between the two groups. In this exploratory study, we opted not to use multiple comparison problem corrections such as false discovery rate (FDR) correction or the Bonferroni test, considering the exploratory purpose of our study. The selected significance for statistical purposes was defined at alpha less than .05.

3. Results

In this study, 40 patients were analyzed, consisting of 8 COVID patients and 32 long COVID patients. The baseline demographic information for each group is presented in Table 1.

In comparing the COVID and long COVID groups, the average age in the COVID group was 27.63 years (SD: 4.37), while the long COVID group had an average age of 39.29 years (SD: 11.72) (see Table 1). All patients underwent behavioral analysis, including MoCA analysis, as well as neural analysis, encompassing spectrum analysis, asymmetry analysis, and connectivity analysis.

3.1. Psychometric analysis

The comparison of SRQ and MoCA scores between COVID group and long COVID group are shown subsequently in Figs. 2 and 3 (see Table 3).

3.2. Spectrum analysis

Spectrum analysis was carried out on all patients whose results can be seen in Fig. 4. An overview of the *p-values* of each comparison can be seen in Table 4. PSD analysis revealed reduction of alpha power but stronger delta power of the long COVID group compared to the COVID group (Fig. 4A), confirmed in the topoplot (Fig. 4B). Further analysis was carried out to find out the hemispheric lateralization of the two groups.

3.3. Asymmetry analysis

Asymmetry analysis was carried out to assess the hemispheric lateralization of COVID and long COVID patients (Fig. 5). There were no significant lateralization in all frequency bands for each electrode.

3.4. Connectivity analysis

Connectivity analysis was carried out to assess the relationship between each electrode between COVID and long COVID patients (Fig. 6). We assessed the connectivity using frequency domain connectivity analysis debiased weighted phase lag index (dwPLI) for each pair of EEG electrodes. We assessed the alpha band (10 Hz) connectivity that dominated in both groups shown in the PSD analysis (Fig. 4A).

Using dwPLI, the analysis of the difference between COVID and long COVID brain activity patterns revealed several notable findings for each group (Fig. 6A–B) and specific differences of connectivity values (Fig. 6C). There was one statistically significant result in the temporal-occipital region T6-O2 with higher connectivity in long COVID groups compared to COVID groups (*p-value* = 0.0267, *Z-value* =–2.2148, Mann Whitney *U*test) (Fig. 6D). Further, temporal lobe connectivity (T3-T6) shows predominantly red coloration indicating higher activity in COVID compared to long COVID. Central-frontal region (C3-F3) connectivity also showed predominantly red/orange coloration suggests increased activity in COVID relative to long COVID. Parietal-occipital regions (P3-O1) show predominantly blue coloration indicating lower activity in COVID compared to long COVID. Parietal-occipital regions (P4-O2) showing predominantly blue coloration similarly suggests lower activity in COVID compared to long COVID.

Table 1
Baseline demographic data of patients.

Variable	COVID		Long COVID		*p-values*
	Mean (SD)	N (%)	Mean (SD)	N (%)	
Age (years)	27.63 (4.37)		39.29 (11.72)		.0028[da]
Gender					
Male		3 (37.5%)		8 (25%)	0.6603[b]
Female		5 (62.5%)		24 (75%)	
Education					
Junior High School Degree		0 (0%)		1 (3.13%)	
High School Degree		0 (0%)		5 (15.63%)	
Associate Degree		3 (37.5%)		8 (25%)	0.6481[c]
Bachelor's Degree		5 (62.5%)		14 (43.75%)	
Master's Degree		0 (0%)		3 (9.38%)	
Doctorate Degree		0 (0%)		1 (3.13%)	

N: number; SD: standard deviation.
[a] Mann-Whitney U.
[b] Fisher Exact Test.
[c] Chi-Square Test.
[d] *p-values* less than .05 are considered statistically significant.

Table 2
Table of *p-values* for differences in SRQ score between COVID and Long COVID patients.

MoCA	SRQ Score				
	MMSE	Psychological	Psychotic	PTSD	Overall
.5060	.5610	.5638	.9639	.3811	.7

Note: *p-values* less than .05 are considered statistically significant, analyzed using Mann Whitney *U* test.

4. Discussion

4.1. Psychometric analysis

Our investigation unveiled a notably elevated score in the initial 20-item SRQ questionnaire, or SRQ-20, among long COVID patients in comparison to those with COVID. This higher score on psychiatric screening tools signifies a prevalent occurrence of common mental disorders (CMD) in long COVID patients, encompassing symptoms such as depression, anxiety, decreased energy, and somatic complaints. A separate research initiative identified a potential correlation between the severity of COVID-19 infection and the onset of psychiatric symptoms. long COVID patients exhibited significantly higher levels of depression, anxiety, cognitive decline, sleep disturbances, and post-traumatic stress disorder compared to the general population (Do et al., 2023). These findings suggest that the implication for mental health may last longer and be more prevalent than the pandemic itself Table 2.

Our research did not differentiate the severity levels among long COVID subjects. An alternative reason for the increased occurrence of psychological symptoms in long COVID patients might stem from the impact of enforced quarantine and related restrictions, leading to elevated levels of anxiety, fear, anger, and other negative emotions. These results may not be exclusively tied to facets of the COVID-19 infection, such as neurological or systemic inflammation.

In addition to psychiatric analysis, our examination revealed a significantly lower MoCA score in the memory domain among long COVID patients when compared to those with COVID. This observation is consistent with several investigations employing MoCA, where individuals encountering post-acute manifestations of COVID-19, commonly labeled as "brain fog," frequently express cognitive challenges such as inattention, diminished concentration, memory issues, and challenges in multitasking. A recent meta-analysis examining neuropsychological impairments in individuals with persistent symptoms of severe infection revealed that 30–80% of patients enduring long-term COVID symptoms spanning one to six months could encounter repercussions impacting various aspects of health, notably cognitive

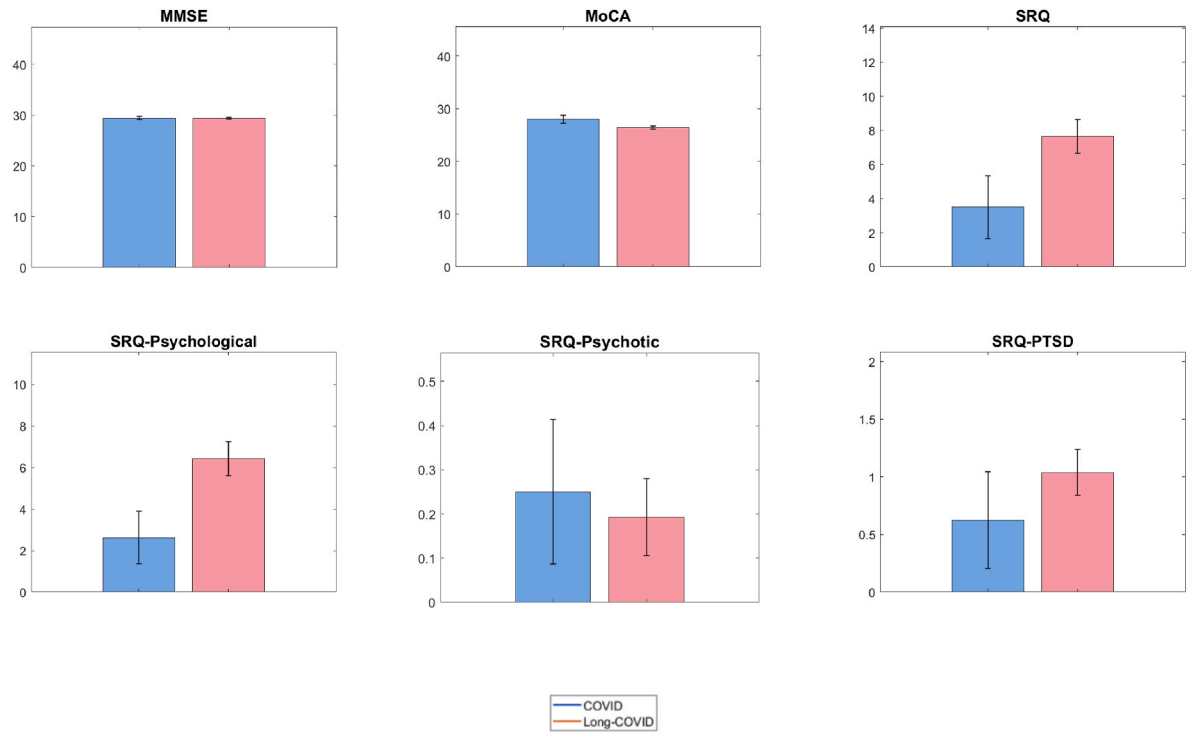

Fig. 2. Bar plot of psychometric analysis between COVID group (blue bars) and long COVID group (red bars).

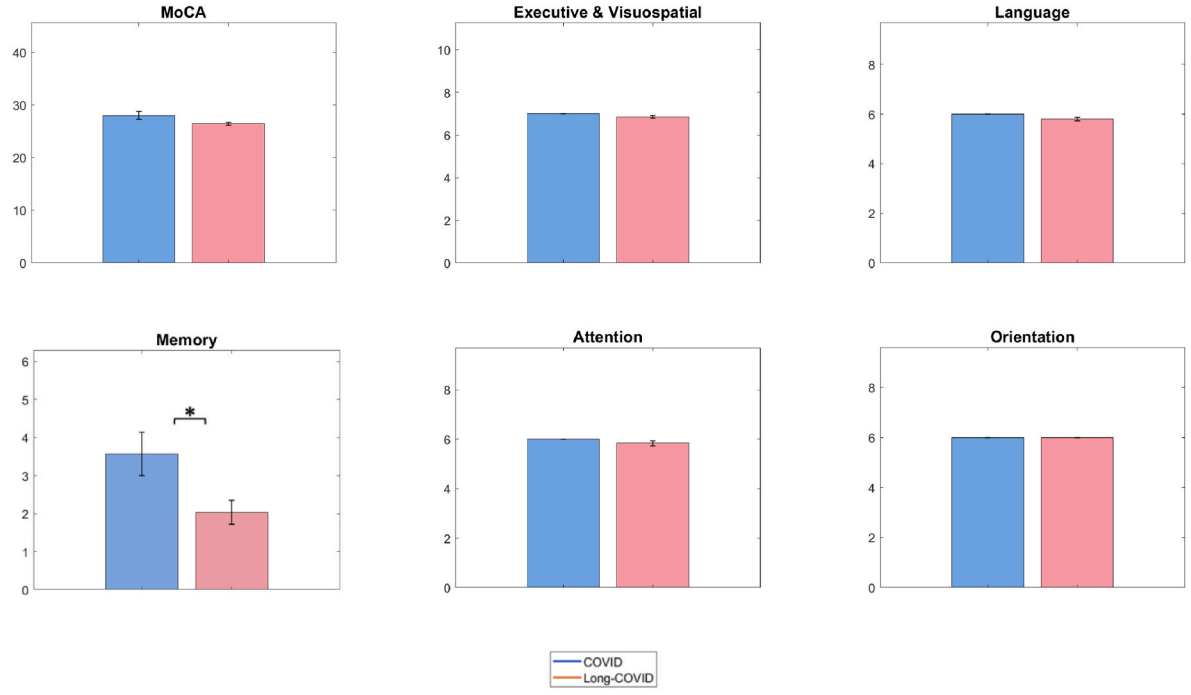

Fig. 3. Bar plot MoCA score between COVID group (blue bars) and long COVID group (red bars). The Asterisk symbols above bars denote significant results using Mann Whitney *U* test (*p-values* = .0415).

functions (Marchi et al., 2023). Notably, working memory deficits, as assessed by MoCA scores, were identified as one of the most frequent neuropsychological symptoms in these individuals (Sobrino-Relaño et al., 2023; Ferrucci et al., 2021; Graham et al., 2021).

4.2. PSD and asymmetry analysis

To enhance the focus of our study, we have narrowed our attention to frontal electrodes, aligning with our primary interest in investigating cognitive and neuropsychiatric functions related to this region. qEEG data analysis revealed several notable patterns across different frequency bands in COVID-19 and long COVID groups. Alpha activity (10

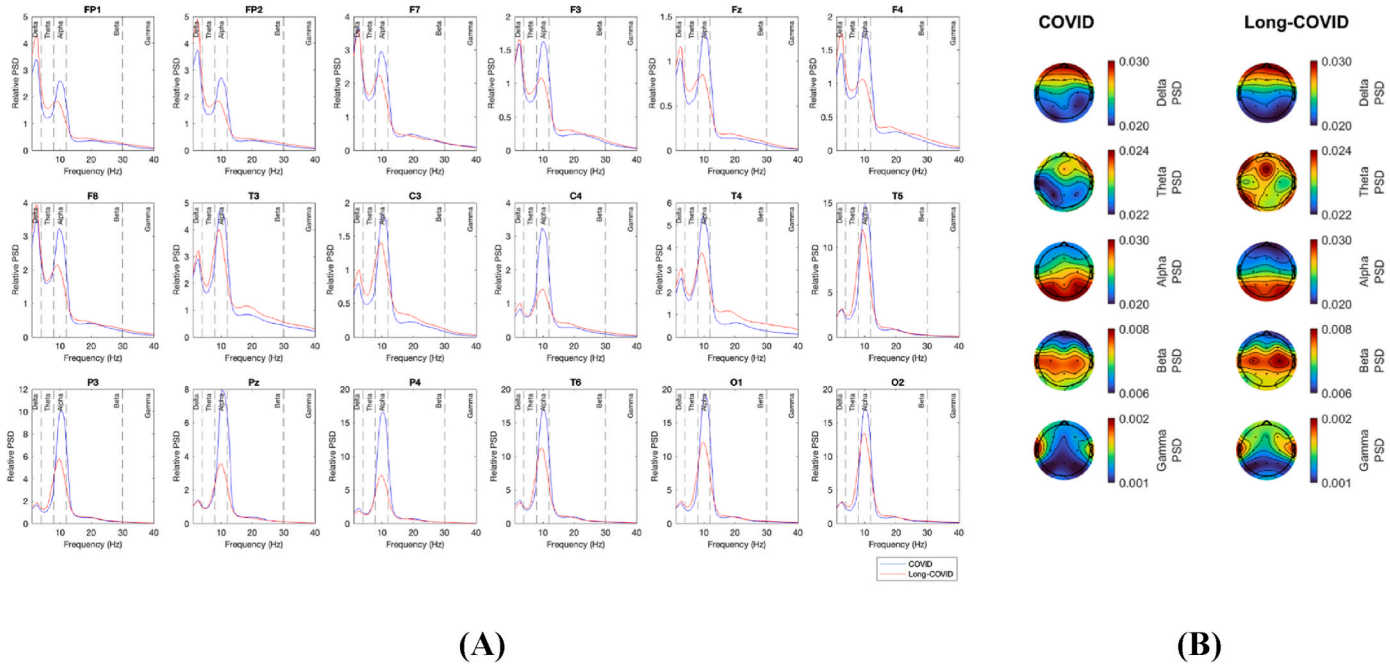

Fig. 4. Spectrum Analysis. (A) Power Spectral Density (PSD) for 18 channels EEG estimated with Slepian Window of COVID (blue) vs. long COVID (red) patients. (B) The topographic representation of averaged relative PSD of COVID (left) vs. long COVID (right) patients.

Table 3
Table of *p-values* for differences in MoCA score between COVID and Long COVID patients.

MoCA Score					
Executive & Visuospatial	Language	Memory	Attention	Orientation	Total
.3305	.2132	**.0423**[a]	.4126	–	.5060

[a] *p-values* less than .05 are considered statistically significant, analyzed using Mann Whitney *U* test.

Table 4
Table of *p-value* using Mann Whitney *U* test for evaluating differences in spectrum analysis between COVID and long COVID patients at each electrode.

	Delta	Theta	Alpha	Beta	Gamma
FP1	0.3396	0.6249	0.7704	0.5948	0.8126
FP2	0.1783	0.8579	0.5728	0.3921	0.7790
F7	0.5101	0.4777	0.8612	0.7016	0.8879
F3	0.8988	0.7826	0.5287	0.9030	0.8463
Fz	0.9125	0.5768	0.5958	0.9324	0.4726
F4	0.8100	0.9265	0.7092	0.7732	0.7064
F8	0.8736	0.8743	0.6548	0.8293	0.4496
T3	0.8364	0.2357	0.6289	0.4753	0.4592
C3	0.8347	0.4656	0.9418	0.9786	0.4146
C4	0.4768	0.4301	0.5364	0.7771	0.2227
T4	0.9688	0.2539	0.7308	0.5989	0.4106
T5	0.5817	0.3955	0.8627	0.6939	0.8288
P3	0.9045	0.3789	0.8329	0.9454	0.7947
Pz	0.7264	0.2377	0.8098	0.6006	0.7279
P4	0.9012	0.1962	0.7498	0.8861	0.7553
T6	0.6535	0.3955	0.8727	0.7405	0.8208
O1	0.9608	0.1927	0.8768	0.5142	0.9487
O2	0.9542	0.3631	0.8793	0.5604	0.6894

Hz) is consistently observed across all EEG channels, with lower amplitudes found in the long COVID group than in the COVID-19 group. Meanwhile, delta activity (2 Hz) is prominently observed in the frontal region with higher amplitude in the long COVID.

Altered alpha activity can be hypothesized to reflect changes in cortical arousal and attentional processes. This could relate to cognitive symptoms such as brain fog or difficulty concentrating, commonly reported in both acute COVID-19 and long COVID patients. Increased frontal delta activity, particularly in long COVID, may indicate persistent alterations in brain function (Triana et al., 2020). This could be associated with executive function deficits, mood disorders, or sleep disturbances, which are frequently reported in long COVID cases. The higher alpha activity in acute COVID-19 might reflect an initial compensatory mechanism or acute stress response. Conversely, the increased delta activity in long COVID could indicate more persistent brain dysfunction, potentially related to ongoing neuroinflammation or neurodegenerative processes (Livint Popa et al., 2020).

4.3. Connectivity analysis

The analysis of brain activity patterns using dwPLI revealed distinct differences between COVID-19 and long COVID groups in alpha band frequency specific, as illustrated in Fig. 6A–C. These findings contribute to the growing evidence suggesting that SARS-CoV-2 infection may have both acute and long-term effects on brain function. The observed higher connectivity in the temporal lobe region (T3-T6) for COVID-19 patients compared to long COVID patients aligns with previous research. Pastor et al. reported altered EEG band distributions in the temporal lobes of COVID-19 patients, supporting our findings. This increased activity may indicate of acute inflammatory responses or direct viral effects on temporal lobe structures during active infection aligned with the MoCA score in memory domain (Pastor et al., 2020).

The predominantly red/orange coloration in the central-frontal region (C3-F3) suggests increased activity in COVID-19 patients relative to long COVID patients. This finding may reflect alterations in executive function and cognitive processes during acute infection, potentially due to inflammatory responses or hypoxemia as reported by Wu et al. (2020). Both parietal-occipital regions (P3-O1 and P4-O2) demonstrated lower activity in COVID-19 patients compared to long COVID patients in Fig. 6. This finding is particularly interesting as it suggests potential long-term alterations in brain activity patterns in these regions for long COVID patients. This observation aligns with the study by Zanin et al., which reported changes in EEG signal characteristics over time in

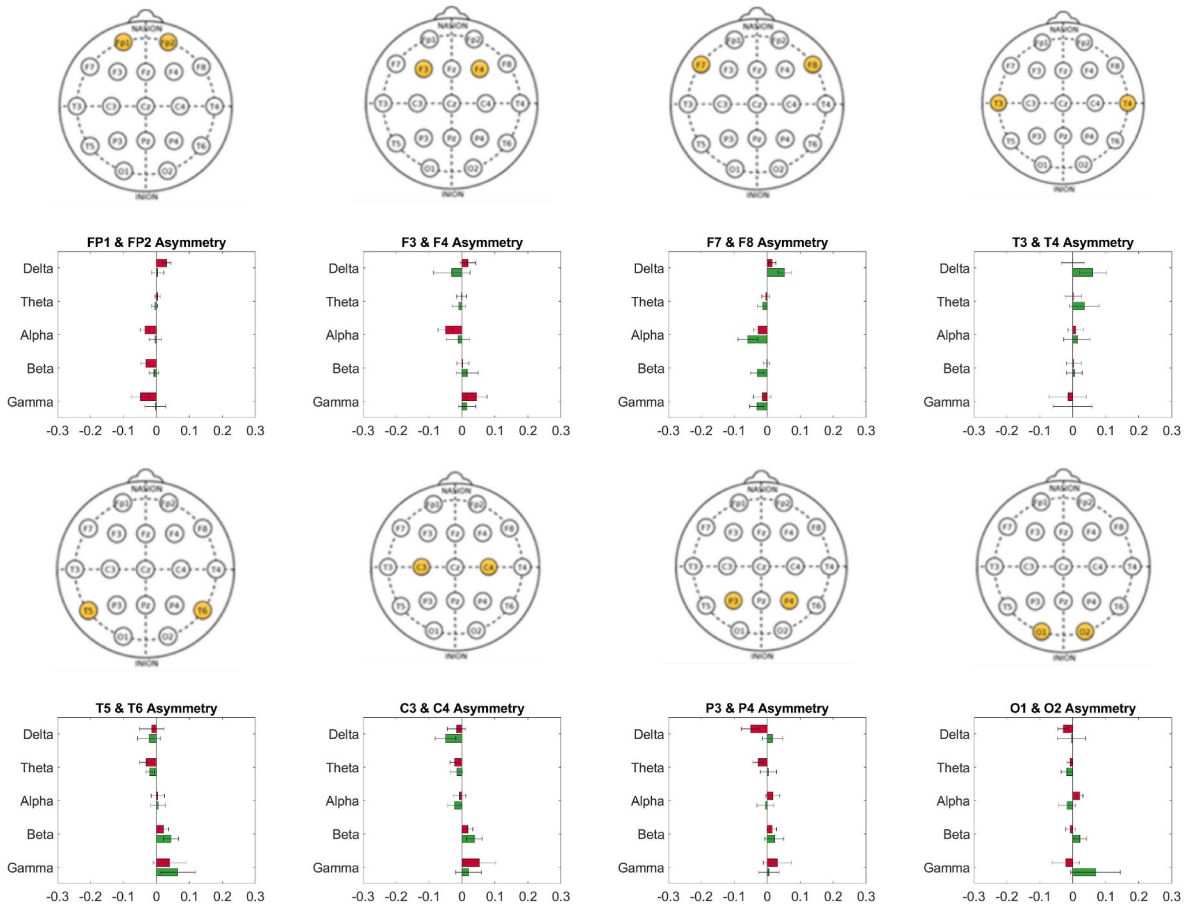

Fig. 5. Laterality value of COVID (red bars) vs Long COVID (green bars) in eight pairs channels. The error bars depict the standard error mean (SEM).

recovered COVID-19 patients (Zanin et al., 2020).

These findings collectively support the hypothesis that COVID-19 infection may lead to both acute and chronic alterations in brain activity patterns. The observed differences between COVID-19 and long COVID groups suggest that the neurological impact of SARS-CoV-2 infection may evolve over time, potentially contributing to the persistent symptoms experienced by long COVID patients. The mechanisms underlying these observed differences include inflammatory damage to neural tissues, hypoxemia-induced alterations in brain function, and direct viral damage to neurons (Pastor et al., 2020; Wu et al., 2020; Zanin et al., 2020; Pasini et al., 2020). Further research is needed to elucidate the precise mechanisms responsible for these observed differences and to determine their clinical significance.

Our findings also reveal a higher connectivity of T6-O2 electrodes in individuals with long COVID than those with COVID. The attention allocation may be involved as a bottom-up strategy which leverages the visual's ability to focus on retrieved memories (Seghier, 2013). This aligns with systematic reviews study that reported that long COVID patients predominantly occurred with episodic, long-term and visuo-spatial memories impairment (Llana et al., 2024; Shan et al., 2022). These deficits reported due to hypoxic damage interfere with the integrity of memory encoding and storage process in hippocampus and other medial temporal areas (Wang et al., 2022; Reiss et al., 2023). It is noteworthy that this result aligns with studies demonstrating memory and attention deficit in long-term COVID patients (Pilotto et al., 2021). This implies a more extensive impact beyond the initial infection phase, offering valuable insights into the complex neurological manifestations of COVID-19 and its persistent consequences.

4.4. *Limitations and future directions*

It is crucial to consider the limitations of this study when interpreting its findings. As this study applied consecutive sampling involving outpatients during COVID-19 pandemic in national hospitals, the imbalanced and limited sample data could be explained due to the reluctant patient dealing with risk of COVID-19 infection transmission from polyclinic. Potential confounding factors were not accounted for in our study (e.g., pre-existing conditions, history of medications). The need for more comprehensive neuropsychological testing beyond MoCA for functional cognitive and visual memory function evaluation. Thus, further study with multicenter, matched healthy control group, controlled confounding factors, longitudinal study for tracking cognitive and neurophysiological changes over time, and integration of neuroimaging techniques (e.g., fMRI) with qEEG for a more comprehensive assessment was needed to fully understand current gaps. The author may consider an automatic EEG IC classifier (https://github.com/sccn/ICLabel) as state-of-the-art for EEG pre-processing in future research (Pion-Tonachini et al., 2019).

5. Conclusion

In conclusion, our study underscores a higher prevalence of common mental disorders among long COVID patients, pointing to lasting mental health impacts. Our findings underscore the persistent neuropsychiatric impact of COVID-19, particularly in long COVID patients. Notably, working memory deficits in MoCA scores were identified as one of the most frequent neuropsychological symptoms in these individuals. Connectivity analysis shows a decline in visual memory functions in long COVID confirmed by the frequent brain fog symptoms in long COVID.

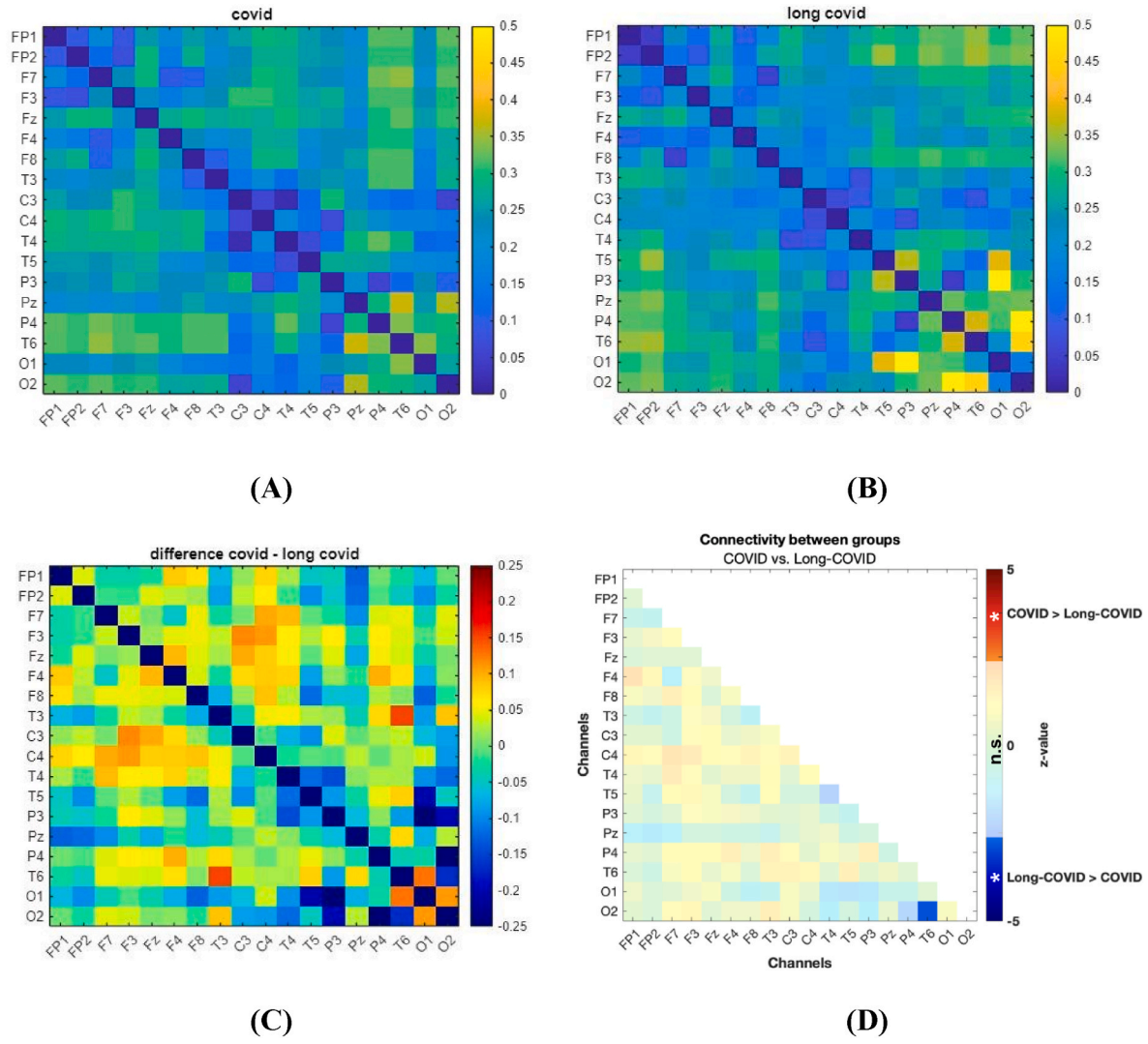

Fig. 6. Inter-electrode connectivity comparison between COVID and long COVID patients. (A). Results of debiased weighted phase lag index (dwPLI) for alpha band (10Hz) in the COVID groups, (B). Results of dwPLI analysis for alpha band (10Hz) in the long COVID groups. (C) dwPLI value differences for the alpha band (10Hz), red areas indicate COVID > long COVID; blue areas indicate COVID < long COVID. (D) *Z-value* results of dwPLI analysis. The colors represented the *Z-value* of connectivity between COVID and long COVID patients. Positive values (reddish colors) denote stronger connectivity in COVID patients; Negative values (red colors) denote stronger connectivity in long COVID patients. Vivid colors indicate significant results ($-1.96 < Z\text{-values} > +1.96$).

These findings emphasize the enduring neurological consequences of COVID-19, urging further exploration for comprehensive patient care.

Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Health Research Ethics Committee of the Faculty of Medicine at Universitas Indonesia - Cipto Mangunkusumo Hospital (ethical clearance number: KET-684/UN2.F1/ETIK/PPM. February 00, 2022 and date of approval July 11, 2022).

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

CRediT authorship contribution statement

Yetty Ramli: Writing – original draft, Validation, Methodology, Formal analysis, Conceptualization. **Pukovisa Prawiroharjo:** Writing – original draft, Validation, Methodology. **Winnugroho Wiratman:** Writing – original draft, Validation, Methodology. **Eric Tenda:** Writing – review & editing, Methodology. **Nurhadi Ibrahim:** Writing – review & editing, Formal analysis. **Damar Susilaradeya:** Formal analysis. **Abdi Reza:** Formal analysis, Data curation, Writing – original draft. **Jennifer Agatha:** Software, Formal analysis. **Rejoel Siagian:** Writing – review & editing. **Hazrina Fauhan:** Methodology. **Florencia Evelyn:** Writing – review & editing, Validation, Project administration. **Yoshikazu Ugawa:** Conceptualization. **Prasandhya Yusuf:** Writing – review & editing, Software, Formal analysis.

Funding

This research was funded by Universitas Indonesia Research Grant, International Indexed Publication program 2022 with contract number: NKB-446/UN2.RST/HKP.05.00/2022.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Yetty Ramli reports financial support was provided by Universitas

Indonesia Research Grant, International Indexed Publication program 2022. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to thank the Universitas Indonesia Research Grant, International Indexed Publication Program 2022. We extend our gratitude to the Neurology Department of the Faculty of Medicine at Universitas Indonesia and Cipto Mangunkusumo General Hospital for facilitating this research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbih.2025.100954.

Data availability

The data that has been used is confidential.

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