

Exploring the role of quantitative electroencephalography in ischaemic stroke through spectral and topographic mapping

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ABSTRACT

Introduction: Stroke is a major cause of morbidity and mortality worldwide. While electroencephalography (EEG) offers valuable data on post-stroke brain activity, qualitative EEG assessments may be misinterpreted. Therefore, we examined the potential of quantitative EEG (qEEG) to identify key band frequencies that could serve as potential electrophysiological biomarkers in stroke patients.

Materials and Methods: A single-centre case-control study was conducted in which patients admitted with stroke and healthy controls were recruited with consent. EEG was performed within 48 hours of admission for stroke patients and during outpatient assessments for controls. The EEG signals were pre-processed, analysed for spectral power using MATLAB, and plotted as topoplots.

Results: A total of 194 participants were included and equally divided into patients with ischemic stroke and controls. The mean age of our study cohort was 55.11 years (SD±13.12), with a median National Institute of Health Stroke Scale (NIHSS) score of 6 (IQR 4-6) and lacunar stroke was the most common subtype (49.5%). Spectral analysis, with subsequent topographic brain mapping, highlighted clustering of important channels within the beta, alpha, and gamma bands.

Conclusion: qEEG analysis identified significant band frequencies of interest in post-stroke patients, suggesting a role as a diagnostic and prognostic tool. Topographic brain mapping provides a precise representation that can guide interventions and rehabilitation strategies. Future research should explore the use of machine learning for stroke detection and provide individualized treatment.

KEYWORDS:

Quantitative EEG, qEEG, stroke, spectral EEG, topography

INTRODUCTION

Stroke is a heterogeneous disease that is characterized by various vascular, hemodynamic, and systemic abnormalities. It represents the second-leading cause of death and the third-leading cause of disability worldwide, according to the 2017 Global Burden of Diseases, Injuries, and Risk Factors Study

(GBD).¹ Structural brain lesions caused by stroke disrupt brain activity and reorganize functional connectivity, both locally and remotely from the affected site.² Electroencephalogram (EEG) enables non-invasive and continuous assessment of brain activity, providing qualitative or quantitative analysis of brain activity following a stroke.³ Despite the current neurodiagnostic assessment of stroke with brain and neurovascular imaging, EEG may offer the advantage of assessing neural function and electrophysiological activity in real-time. Numerous studies have been published regarding the role of EEG in early diagnosis, outcome prediction, clinical management, seizure detection, and prognosis of stroke.^{4,5}

Both qualitative and quantitative EEG (qEEG) provides valuable insights into brain activity following a stroke. In qualitative assessment, EEG patterns are divided into five main frequency bands: delta (0.5- 4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-100 Hz). However, EEG data may be fraught with misinterpretation and inter-rater variability, resulting in erroneous conclusions.⁶ Although sparsely used, EEG spectral analysis quantifies the amount of rhythmic activity of different frequencies to objectively measure the power of specific frequency bands and their spatial distribution. qEEG analysis provides well-defined features from EEG data, such as spectral power (through topological distribution on the scalp surface) and coherence (as a metric of association between channels).^{7,8} Commonly used indices to express relative power in qEEG include the relative delta power (RDP) at 1-3 Hz, delta/alpha power ratio (DAR), and delta + theta/alpha + beta power ratio (DTABR)⁹ and the brain symmetry index (BSI), which is a visual interpretation that quantifies ischemic damage over each hemisphere with good reproducibility.^{10,11} These indices have been used to investigate the associations between spectral EEGs and outcomes (such as stroke severity) following stroke.¹²

Each channel and its corresponding dominant band power may indicate variations in deficit manifestation or correlate with stroke severity. For example, band power, such as heightened beta band over the occipital region and alpha activity, are generally linked to visual performance and certain forms of attention, respectively. In this regard, the identification of the commonly affected band frequencies

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may guide supportive therapy in the future. Therefore, this study aimed to identify the potential electrophysiological biomarkers in stroke patients based on the EEG spectral content. Specifically, the observed EEG band power differences between stroke patients and those without stroke, in addition to identifying the brain regions and frequency bands that expressed the largest discrepancy between both groups.

MATERIALS AND METHODS

Study design

This single-centre case-control study was conducted in Hospital Canselor Tuanku Muhriz, the National University of Malaysia, Kuala Lumpur, Malaysia, from October 2021 to May 2023 with the approval from the local Ethics and Research Board (FF-2021-436). Patients admitted with a diagnosis of ischaemic stroke were recruited using convenience sampling. Written informed consent was obtained from all participants prior to recruitment. The inclusion criteria were those age ≥ 18 years, hospitalized with a diagnosis of ischemic stroke according to the Oxfordshire classification within 14 days of admission. Exclusion criteria were stroke mimics, such as overt infections or metabolic derangements, transient ischemic attack, neurodegenerative diseases, delirium, traumatic brain injury, previous history of neurosurgery, underlying psychiatric disorders, epilepsy, and brain tumours. The control group consisted of an equal number of participants but was not completely age- and sex-matched, in view of the difficulty in acquiring adequate participants. The participants for the control group were healthy patients receiving outpatient treatment without prior episodes of stroke or a history of epilepsy.

Clinicopathological information of each participant was collected using a data collection sheet and included sociodemographic information (e.g., age and sex), clinical history, type of stroke, risk factors, and stroke severity. To quantify the severity of stroke, we used the National Institute of Health Stroke Scale (NIHSS), a quantitative assessment tool to measure deficits following a stroke that can be completed within ten minutes. It is a fifteen-item examination with a rating of three to five per item and serves as a quantitative assessment tool to measure deficits following stroke, with a total score ranging from 0 to 42. The severity can then be clinically stratified as mild (1 - 4), moderate (5 - 15), severe (16 - 24) or very severe (≥ 25).^{13,14} It has good interrater reliability ($\kappa = 0.69$) and test-retest reliability ($\kappa = 0.66 - 0.77$).¹⁵

An EEG was recorded within 48 hours of admission for all participants in the case group and on outpatient assessment for the control group by two neurodiagnostic technologists. The EEGs were recorded using the Nicolet One Extension (V32 Amplifier) with a sampling rate of 500 Hz according to the international 10–20 system with a bipolar montage. 24 reusable gold electrodes were fixed over the scalp and earlobes and cleaned with Nuprep. The abbreviations on the EEG are as follows: Fp, frontopolar; C, central; F, frontal; T, temporal; P, parietal; and O, occipital. Each recording lasted for a minimum of 30 minutes.

EEG Analysis

The raw EEG data obtained were exported to MATLAB 2020a, a programming software for preprocessing and spectral analysis. The raw EEG data underwent data preprocessing to filter out noise and myogenic artefacts. The EEG signals were filtered from power-line interference (PLI) using a notch filter at 50 Hz and then bandpass-filtered at a low cutoff frequency (0.5 Hz) and a high cutoff frequency (70 Hz) to allow only frequencies of interest to pass for subsequent analysis. The signal of each channel was standardized to have a mean of zero and variance of 1. Average referencing was further applied by computing the average of the signals at all channels and subtracting them from the EEG signal at every channel.

Subsequently, post-processing data were used for power spectral analysis based on Fourier transform analysis. A fast Fourier transform was applied to the EEG signals of each channel. The result of the frequency analysis is expressed as the spectral power based on Fourier periodograms, that is, the squared amplitude of the fast Fourier transform of the EEG (μV^2). The band-limited power spectra or band power was computed using Matlab2020a band power function for each of the five main EEG frequency bands (i.e., delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-100 Hz)) across all channels for each subject. Topot from the EEGLAB toolbox was used to graphically visualize the frequency content of the EEG signals over the channels and pinpoint areas of interest.

Statistical Analysis

IBM SPSS Version 26 was used for the analysis of descriptive data. Categorical variables were presented as frequencies and percentages. Normality was tested using skewness and kurtosis for all continuous variables. The mean and standard deviation (SD) were for normally distributed continuous variables; however, non-parametric analysis was used when the data were not normally distributed. A paired t-test statistical analysis was performed to identify the significant difference in the EEG mean band-power differences between the stroke patient and control groups with a significant threshold set at $p\text{-value} < 0.05$ (uncorrected for multiple comparisons).

RESULTS

Clinicodemographic data

A total of 233 participants were screened. Eventually, a total of 194 participants (97 stroke patients and 97 controls) were recruited based on the study criteria and following informed consent. The mean age of the study population was 55.11 years ($\text{SD} \pm 13.12$). One hundred participants were male (56 cases, 44 controls) and 94 were female (41 cases, 53 controls). Upon analysis of the patient group, the median NIHSS score at presentation was 6 (IQR 4-6). Almost half (49.5%) of the patients with stroke had lacunar stroke, followed by partial anterior circulation stroke (29.9%). Lacunar infarcts were the most commonly observed neuroimaging finding on computed tomography (CT) of the brain, accounting for 57.7%, with middle cerebral artery territory infarcts the 2nd most commonly encountered abnormality (32%). The EEG characteristics of 40 participants in the patient group were

normal. 57 had abnormalities in EEG recording, most notably focal slowing (34 patients). The control group had normal EEG findings in all 97 participants. The clinical characteristics of the patients are summarized in Table I.

Band power comparison over each channel

Following the sociodemographic analysis, we focused on identifying band power and channels of interest between the patient and control groups. We performed univariate sample analysis using an independent sample t-test to identify significant differences between the groups, accepting a p-value <0.05 as significant. Table II elaborates the p-values of all categories of band power and corresponding channels when comparing patients with and without stroke.

Topographic brain mapping

Subsequently, we plotted a topological map to delineate the spatial representation of data across the tested channels. Colour scales were used to display the strength of specific variables or measurements at each point to aid data visualization. The dark blue and red colours indicate values closer to 1.0 and 0.1, respectively. Figure 1 shows a topographical map of the p-values obtained by comparing the patient and control groups. To assist in visualizing the areas of interest, we projected another topoplot to highlight the areas where the p-value was significant and used different hues to signify lower p-values. This is illustrated in Figure 2a. The topographical brain mapping of p-values reveals that there are statistically significant differences in the mean band power between the patient and control groups in the alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-100 Hz) frequency bands. These differences are indicated by the red regions in the corresponding maps, where the p-values are below the common threshold of 0.05, suggesting a strong likelihood that these variations are not due to chance. In contrast, the delta (0.5-4 Hz) and theta (4-8 Hz) bands show no significant differences between the two groups, as indicated by the higher p-values (represented by blue and green regions).

Overall, these findings highlight that the most substantial and statistically significant differences in brain activity between the patient and control groups are present in the higher frequency bands (alpha, beta, and gamma), which may have important implications for understanding the underlying neurological or cognitive processes.

The analysis revealed that the important channels were predominantly clustered in the band power belonging to alpha, beta and gamma bands. We calculated the difference in the mean of all significant band powers by subtracting the mean of the control from the mean of the sample data. This was performed to quantify the average disparity or variation between the groups. A positive difference indicates higher values in the sample, whereas a negative difference indicates lower values. Table III illustrates the differences in mean band power between the two groups. The non-significant band powers were slashed to avoid confusion. Figure 2b depicts the findings in Table III in the form of a topoplot to aid visualization. The regions identified in Figure 1 as having significant p-values are the same regions in Figure 2b where there are substantial differences in mean band power. When

these figures are considered together, they provide a more comprehensive view. The significant regions in Figure 1 are either positive or negative in Figure 2b, indicating whether the patient group has an increase (blue regions) or decrease (red regions) in band power. Merging these insights gives a full picture of where and how the patient group's brain activity differs from that of the control group, both in terms of significance and direction (increase or decrease). This combined analysis helps to clarify not only the presence of significant differences but also the nature of these differences in brain activity between the patient and control groups.

DISCUSSION

Demographic data

Our study population consisted mainly of patients with lacunar stroke. This could explain the lower NIHSS score in our cohort, with a mean of six (moderate severity). This is comparable to most studies in the region, with data from Asian countries suggesting a higher prevalence of small vessel disease subtypes, particularly in Southeast Asia.^{16,17} Studies from Thailand and Malaysia have suggested a high percentage of intracranial atherosclerosis (approximately 52.6% and 28%, respectively), although the current trend shows a decline.^{18,19}

Difference in EEG band power between patient and control group

Qualitative analysis of EEG in our cohort showed epileptiform changes and focal and diffuse slowing. This finding concurred with the slowing of background activity, background asymmetry, and periodic discharges frequently observed in post-stroke patients and those with poor functional outcomes.²⁰ A study by Giaquinto et al. demonstrated a higher degree of slowing over the affected hemisphere, which may improve or outlast the clinical improvement.²¹ Therefore, they suggested a possible role of EEG in monitoring neural repair and guiding rehabilitation. Focal slowing accounted for 35.1% of the EEG changes observed in our cohort with stroke. This finding is similar to that of studies showing focal and diffuse slowing as the predominant abnormality observed post-stroke. These changes are associated with a lower risk of post-stroke seizures than abnormalities such as periodic lateralized discharges.²² However, there is a link between the slowing of EEG background and cognitive impairment, as reported by Moretti et al. in their cohort with greater cerebrovascular damage.²³ Generalized slowing was also associated with poorer clinical outcomes.²⁴

We observed a significant association between alpha, beta, and gamma band powers when comparing both groups of patients. This is in line with studies demonstrating increased synchronization and lower frequency of alpha oscillations, increased high beta (21-30 Hz) compared to low beta (13-20 Hz) bands centrally, elevation of beta oscillatory power, and disruption of gamma oscillatory patterns following an acute stroke.²⁵⁻²⁷ Less efficient and more modular networks were observed, particularly in the beta and gamma bands, which explains the association in our study.²⁷ However, these changes evolve during recovery, with alpha desynchronization observed weeks after an acute stroke. A greater degree of event-related desynchrony over the affected

Table I: Clinical characteristics of patient group

Clinical characteristics	n = 97 (%)
National Institute of Health Scale Stroke	
Mild (1-4)	43 (44.3)
Moderate (5-15)	33 (34.0)
Severe (16-24)	15 (15.5)
Very severe (≥ 25).	6 (6.2)
Stroke Types:	
Total Anterior Circulation Infarct (TACI)	9 (9.3)
Partial Anterior Circulation Infarct (PACI)	29 (29.9)
Lacunar Infarct (LACI)	48 (49.5)
Posterior Circulation Infarct (POCI)	11 (11.3)
Hemispheric Involvement:	
Total Anterior Circulation Infarct (TACI)	L 4 (4.1) R 5 (5.1)
Partial Anterior Circulation Infarct (PACI)	L 16 (16.5) R 13 (13.4)
Lacunar Infarct (LACI)	L 26 (26.8) R 22 (22.7)
Posterior Circulation Infarct (POCI)	L 4 (4.1) R 3 (3.1)
Neuroimaging Characteristics:	
Middle Cerebral Artery (MCA)	31 (32.0)
Anterior Cerebral Artery (ACA)	2 (2.1)
Posterior Cerebral Artery (PCA)	5 (5.2)
Lacunar Stroke	56 (57.7)
Others	3 (3.1)
EEG Characteristics:	
Normal	40 (41.2)
Focal slowing	34 (35.1)
Diffuse slowing	18 (18.6)
Epileptiform	5 (5.2)

Note:

SD- Standard Deviation

IQR - Interquartile Range

R- Right

L- Left

side correlated with a higher degree of clinical improvement.²⁸ The increase in beta activity over time at the central region contralateral to the affected side correlated with good functional motor recovery than if the increase is seen in the affected side suggesting a role in neuroplasticity in functional recovery.²⁶

Several studies have reported a high incidence of focal or diffuse slowing in patients with acute strokes.²⁹ Our analysis did not reveal a significant difference in delta and theta band power, but this could be explained by the type of stroke in our cohort. Only one-third of the patients in our cohort had middle cerebral artery territory infarcts, whereas the majority had lacunar infarcts. Delta activity is strongly correlated with regional cerebral blood flow; therefore, it is more prominent in middle cerebral and internal carotid artery territory strokes.³

Future applications

Identifying specific band powers of interest may be essential for post-stroke rehabilitation. Different band powers are linked to different motor and non-motor functions. Beta

oscillations have been associated with movement production, whereas gamma rhythms are amplified during cognitive processes.^{30,31} These may be appreciated predominantly in different areas of the cortex. Numerous non-invasive neuromodulation techniques have been investigated, including transcranial magnetic stimulation, transcranial electrical stimulation, and transcranial focused ultrasound stimulation. Although the frequency and dosing for each indication may vary among studies, there is a need for accurate identification of the stimulation site, which could be aided by qEEG analysis.³² This would affect the overall efficacy of treatment.

The use of topographical brain mapping would further improve the identification of sites for intervention, based on the significance and area involved. This can be achieved with readily available software, as we have demonstrated that it can be integrated into the device used for neurorehabilitation. Another application is the use of qEEG in brain-computer interfaces, which could be used as a driving command for rehabilitation systems and exoskeletons or prostheses to improve overall functions. Raw

Table II: P-values of t-test of mean EEG band power differences between patient and control groups for each channel and each frequency band

Channel	Delta	Theta	Alpha	Beta	Gamma
Fp1	0.617	0.8409	0.22806	0.081487	0.25405
Fp2	0.79612	0.91956	0.14324	0.10257	0.49415
F3	0.62613	0.41135	0.059265	0.013185*	0.033681*
F4	0.41968	0.83696	0.43514	0.19042	0.37654
C3	0.14908	0.15116	0.035899*	0.032296*	0.14962
C4	0.91018	0.83967	0.058827	0.046295*	0.12752
P3	0.44359	0.23648	0.019362*	0.051704	0.1233
P4	0.69974	0.78972	0.060861	0.24813	0.57825
O1	0.33701	0.59323	0.13111	0.074822	0.17522
O2	0.18071	0.3145	0.065623	0.074138	0.38033
F7	0.20321	0.36221	0.067397	0.012234*	0.029692*
F8	0.84855	0.89918	0.13684	0.038713*	0.10717
T7	0.60718	0.86628	0.79646	0.031618*	0.034612
T8	0.053969	0.085305	0.49281	0.43906	0.24726
P7	0.59615	0.34481	0.014077*	0.047394*	0.12412
P8	0.23651	0.75712	0.56663	0.11144	0.095838
Fz	0.45013	0.22602	0.03721*	0.18748	0.77028
Cz	0.81084	0.41017	0.047992*	0.022214*	0.070232
Pz	0.14433	0.1715	0.044783*	0.006018*	0.021365*

*p-value significant at <0.05

Fp: frontopolar, C: central, F: frontal, T: temporal, P: parietal, O: occipital

Table III: Difference in mean band power between patient and control groups for each channel and each frequency band

Channel	Delta	Theta	Alpha	Beta	Gamma
Fp1	0.00011	0.000015678	-0.00012	-0.00013	-0.00007185
Fp2	0.000066032	-0.000008498	-0.00015	-0.00015	-0.00004572
F3	-0.00022	-0.00018	-0.00042	-0.00073*	-0.00063*
F4	0.001673	-0.00015	-0.00065	-0.0015	-0.00094
C3	-0.00055	-0.00028	-0.00054*	-0.00061*	-0.00044
C4	-0.00022	-0.00016	-0.00187	-0.00256*	-0.00142
P3	-0.0002	-0.00013	-0.00041*	-0.00022	-0.00009173
P4	-0.00019	-0.000064653	-0.00064	-0.00028	0.000082449
O1	-0.000151	-0.000032812	-0.00012	-0.0001	-0.00005957
O2	-0.000226	-0.0001	-0.00025	-0.00013	-0.00003550
F7	-0.00027	-0.000070885	-0.00018	-0.00022*	-0.00025*
F8	0.000074323	-0.000020166	-0.00025	-0.00031*	-0.00027
T7	-0.00009208	0.0000087818	-0.00002056	-0.00019*	-0.00026*
T8	0.000504	0.000245	0.000121	-0.00012	-0.0002
P7	0.00006443	-0.000059889	-0.00018*	-0.00013	-0.00007399
P8	0.000216	0.000032279	-0.00012	-0.00017	-0.00013
Fz	-0.00008685	-0.000061502	-0.00012*	-0.00009225	-0.00001722
Cz	0.000031926	-0.000055273	-0.00017*	-0.00017*	-0.00009517
Pz	-0.00249	-0.00131	-0.0017*	-0.0025*	-0.00126*

*difference in mean of significant band power and channels in both groups

Fp: frontopolar, C: central, F: frontal, T: temporal, P: parietal, O: occipital

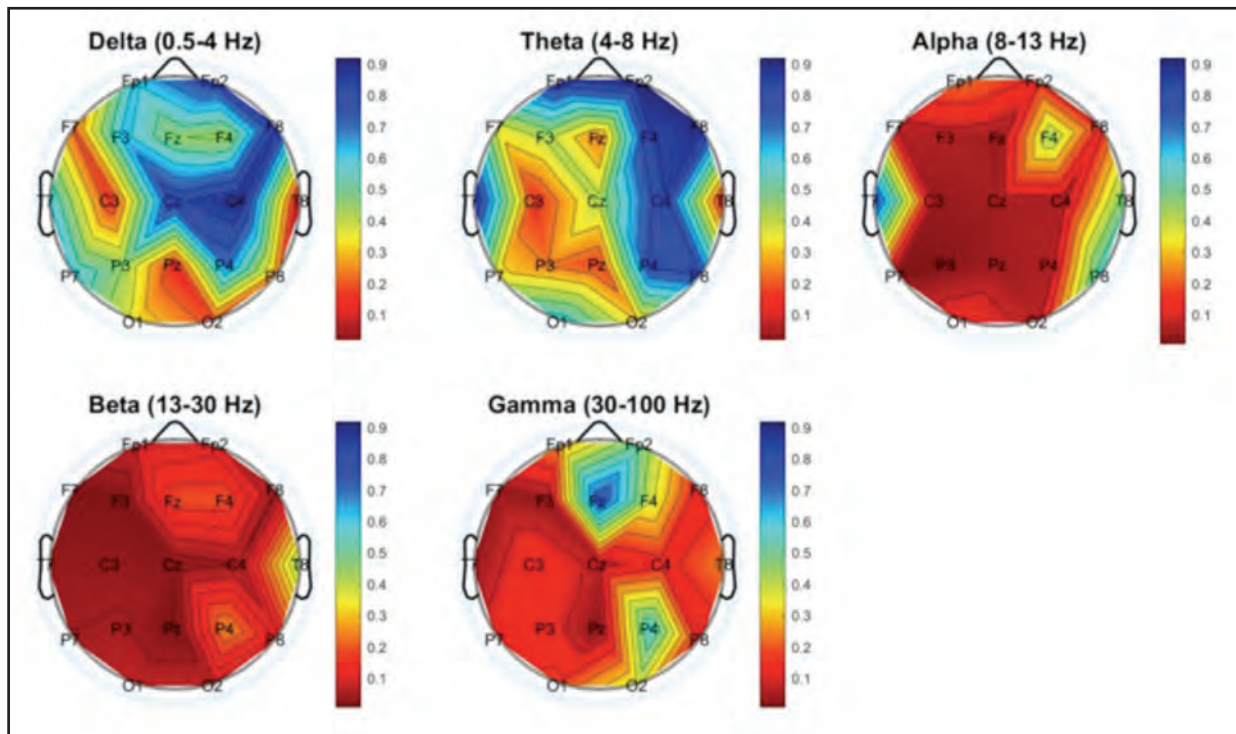


Fig. 1: Topographical brain mapping of p-values obtained from t-test of the mean band power difference between patient and control group. The coloured scale indicates the p-value; red being the lowest p-value

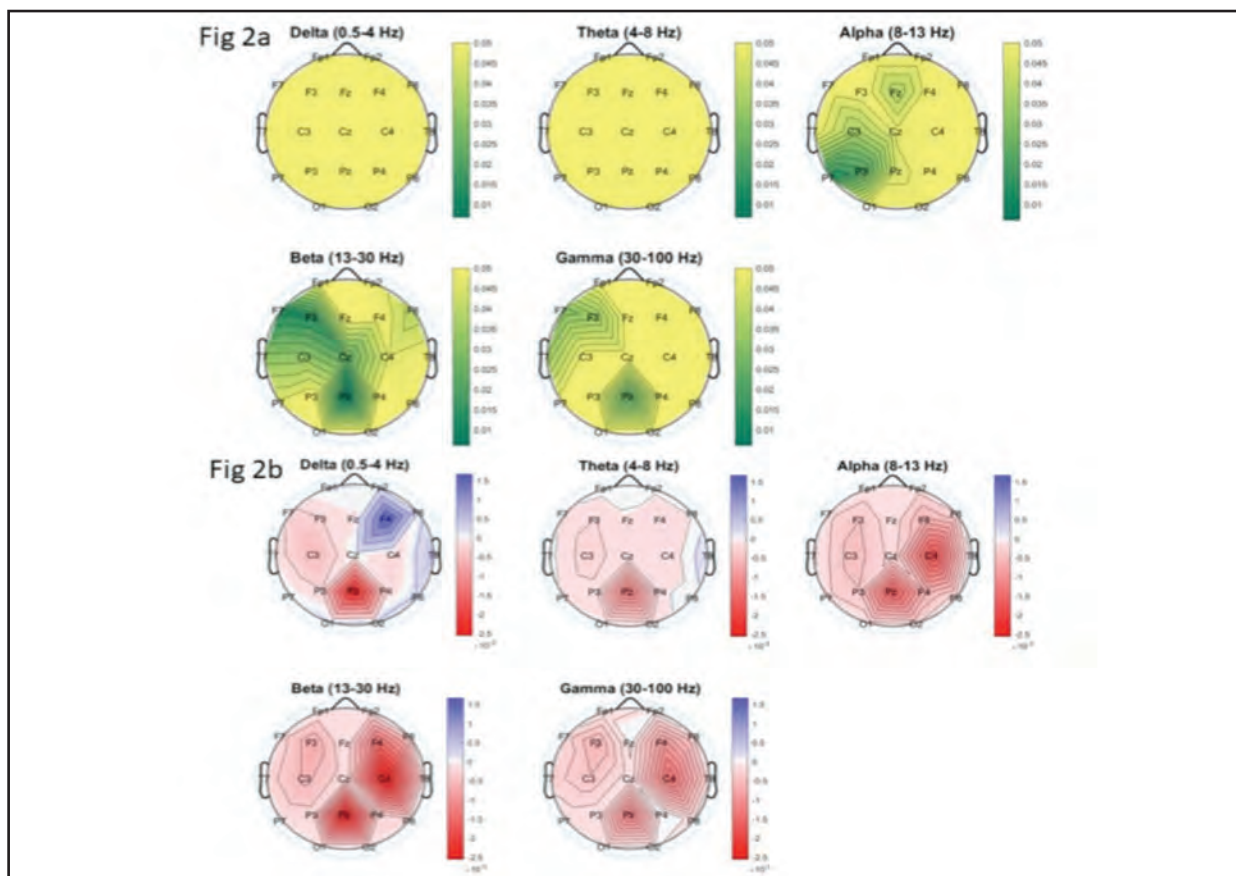


Fig. 2: a) Topographical brain mapping demonstrates only significant p-values ($p < 0.05$) when comparing band power of patient and control group. A darker hue of green indicates a lower p-value. b) Topographical brain mapping of the difference in mean band power for each channel and frequency between patient and control groups. The positive values represent an increase in mean band power (displayed in blue) in patient group relative to the control group, while the negative values signify decrease in mean band power in patient group relative to control group (displayed in red).

EEG data can be converted to produce movements in actuators to allow gross and fine motor actions, which may require electromyography as an adjunct.^{33,34}

Moving forward, we plan to improve the graphical user interface to make the program more user-friendly so that data can be extracted and utilized by neurodiagnostic technicians and rehabilitative support staff. We intend to explore the use of machine learning, such as a Support Vector Machine, to investigate whether it is possible to use band power variations to detect acute stroke, especially in the setting of stroke mimics or a history of stroke. To improve the accuracy, we aim to recruit more participants once adjustments have been made to the software algorithms.

One limitation is that our cohort included all stroke subtypes, regardless of the etiology, type of therapy administered, and area involved. This may result in EEG changes following interventions such as mechanical thrombectomy or thrombolysis. The band power significance may be altered because of the different areas of the stroke. However, we could not standardize the side or territory involved because of the limited number of participants. In addition, the median NIHSS score in our study is on the lower end and mainly lacunar type stroke which would produce localized abnormalities. Therefore, increasing the number of EEG channels studied may increase the yield of the study.

CONCLUSION

Quantitative EEG is a viable tool to identify band frequencies of interest in post-stroke patients. Accompanied by a topograph, a more precise graphical representation of the areas involved may guide further intervention and rehabilitation. We believe that the data obtained from qEEG would be important in software programming to individualize treatment in the future and to gather data objectively when searching for the validity of biomarkers in stroke research.

DECLARATION OF CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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CONTRIBUTIONS

Kok Leong Liew (KL): study concept and design, acquisition of data, analysis and interpretation, drafting the manuscript.

Juen Kiem Tan (JT), Ching Soong Khoo (CSK): acquisition of data, analysis and interpretation, and drafting the manuscript. Kai Yi Ng (KN), Wilbert Chong (WC), Yuet Teng Lew (YL), Chee-Ming Ting (CT): acquisition of data, data analysis and interpretation, revised manuscript and statistical analyses. Hernando Ombao (HO): data analysis and interpretation, revised manuscript, and statistical analyses. Nursyazwana Zolkafli (NZ): acquisition of data, analysis and interpretation, and revised manuscript. Zhen Yang Lee (ZY Lee): acquisition of data, analysis and interpretation. Hui Jan Tan (HT): Study concept and design, methodology, funding acquisition, data acquisition, drafting and revised manuscript, and study supervision. All authors read and approved the final manuscript.

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