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Quantitative EEG Correlates with NIHSS and MoCA for Assessing the Initial Stroke Severity in Acute Ischemic Stroke Patients

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Abstract

BACKGROUND: National Institutes of Health Stroke Scale (NIHSS) and Montreal Cognitive Assessment (MoCA) measure stroke severity by assessing the functional and cognitive outcome, respectively. However, they cannot be used to measure subtle evolution in clinical symptoms during the early phase. Quantitative EEG (qEEG) can detect any subtle changes in CBF and brain metabolism thus may also benefit for assessing the severity.

AIM: This study aims to identify the correlation between qEEG with NIHSS and MoCA for assessing the initial stroke severity in acute ischemic stroke patients.

METHODS: This was a cross-sectional study. We recruited 30 patients with first-ever acute ischemic stroke hospitalized in Dr. Sardjito General Hospital, Yogyakarta, Indonesia. We measured the NIHSS, MoCA score, and qEEG parameter during the acute phase of stroke. Correlation and regression analysis was completed to investigate the relationship between qEEG parameter with NIHSS and MoCA.

RESULTS: Four acute qEEG parameter demonstrated moderate-to-high correlations with NIHSS and MoCA. DTABR had positive correlation with NIHSS ($r = 0.379$, $p = 0.04$). Meanwhile, delta-absolute power, DTABR, and DAR were negatively correlated with MoCA score ($r = -0.654$, $p = 0.01$; $r = -0.397$, $p = 0.03$; and $r = -0.371$, $p = 0.04$, respectively). After adjusted with the confounding variables, delta-absolute power was independently associated with MoCA score, but not with NIHSS ($B = -2.887$, 95% CI (−4.304–−1.470), $p < 0.001$).

CONCLUSIONS: Several qEEG parameters had significant correlations with NIHSS and MoCA in acute ischemic stroke patients. The use of qEEG in acute clinical setting may provide a reliable and efficient prediction of initial stroke severity. Further cohort study with larger sample size and wide range of stroke severity is still needed.

Introduction

Assessing severity at the initial phase of a stroke is important for comprehensive stroke management [1]. The severity of a stroke at onset can affect the outcome, including mortality, duration of the treatment, stroke progression, and functional healing [2]. Stroke severity and the evolution of clinical symptoms on the 1st day of stroke are potential and significant outcome predictors. Improvements in the assessment of initial stroke severity can result in more specific management of stroke rehabilitation and can provide clearer information for patients and their families [3].

Several previous studies used initial stroke assessments with the National Institutes of Health Stroke Scale (NIHSS) as a predictor of functional outcomes [3]. NIHSS has been validated and commonly used to measure both the initial stroke severity and the response of the treatment, particularly in the acute setting [4]. Although it has many advantages, NIHSS has limited sensitivity for detecting the severity of cognitive deficits [5] and also limited utility in accurate daily monitoring of neurologic status [6]. In addition, several scale items require intact language function, thus the NIHSS overweight deficits in patients with the left versus right brain strokes. The left hemisphere strokes score 4 more points than right hemisphere stroke of similar size [7].

Initial assessment of the severity of cognitive impairment generally uses paper-based assessments, including the Montreal Cognitive Assessment (MoCA) or Mini Mental State Examination (MMSE). Assessment of cognitive function with MoCA is more recommended for cognitive disorders after stroke because the examination is more sensitive to detect mild impairment compared with the MMSE examination [8]. The test administration of MoCA was applicable in patients with mild-to-moderate stroke, either acute ischemic or hemorrhagic strokes [9], as well as in patients with TIA [10]. This test is also recommended for being used in routine clinical practice to detect cognitive impairment [10]. However, recent studies which support the clinical experience that stroke can lead to the kinds of disability (e.g., aphasia

and hemiplegia) can preclude the use of the MoCA to assess global cognitive impairment. In an aging stroke population, hearing loss and visual impairment are also problematic for administering a valid MoCA [11].

Despite its benefit for assessing initial stroke severity, NIHSS and MoCA cannot be used to detect subtle evolution in clinical symptoms. This is due to both NIHSS and MoCA are not sensitive to capture the transition from ischemia to infarct which occurs over a range of cerebral blood flow (CBF) [12]. Nonetheless, quantitative EEG (qEEG) can detect changes in CBF and brain metabolism in as little as 28–104 s [13]. EEG changes are closely tied to CBF. When normal CBF declines to approximately 25–35 ml/100 g/min, the EEG first loses its faster frequencies, then as the CBF decreases to approximately 17–18 ml/100g/min, the slower frequencies gradually increase. This represents crucial ischemic threshold at which neurons begin to lose their transmembrane gradients, leading to cell death (infarction) [14].

In addition, qEEG may benefit for predicting not only short-term prognosis, but also long-term functional outcome at 1 year after stroke [15]. Furthermore, qEEG measurement is also capable to provide objective information in a condition in which assessment of neurologic deficits is difficult or their interpretation is limited, such as in aphasic or comatose patients [16], [17]. Therefore, qEEG is a powerful tool for predicting the degree of functional disability and cognitive impairment after an acute ischemic stroke event [16], [18]. Because the present assessment tools (NIHSS and MOCA) have some limitations and are not able to detect the subtle evolution of stroke as aforementioned, we propose that qEEG may serve as a tool to assess stroke severity earlier and correlate with NIHSS and MoCA. For that reason, we aim to identify the correlation between qEEG with NIHSS and MoCA for assessing the initial stroke severity in acute ischemic stroke patients.

Methods

Study design and participants

This was a cross-sectional study. We recruited acute ischemic stroke patients who were hospitalized at neurological ward in Dr. Sardjito General Hospital Yogyakarta, a tertiary hospital in Indonesia. Data were collected during December 2018 until July 2019. The inclusion criteria were: 1) First-ever acute ischemic stroke, 2) aged >18-years-old, 3) having at least 6 years of educational experience at elementary level, 4) cooperative, can read and write, and 5) not taking memory enhancing drugs such as donepezil, galantamine, memantine, piracetam, and ginkgo biloba. The exclusion criteria were: 1) Patients who were unconscious, 2) patients with history of the previous seizure, infratentorial lesion, brain tumor, intracranial infection, traumatic brain injury, and depression, 3) patients with dementia, aphasia, or dysphasia, 4) patients with electrolyte imbalance, 5) taking antidepressant, benzodiazepine, and/or psychotropic agents, and 6) having disability before the stroke onset.

Before data collection, the participants were given the explanation regarding the study. All participants signed a written informed consent form before the investigation. A total of 30 patients were investigated in this study and included in the analysis.

Data collection and measurements

Demographic and clinical characteristics

All data were collected during acute phase of stroke patients during hospitalization. This included age, sex (male vs. female), history of hypertension (yes vs. no), history of diabetes mellitus (yes vs. no), ASPECT score, total cholesterol, low-density lipoproteins (LDL), high-density lipoproteins (HDL), triglyceride, NIHSS, MoCA-Ina, and qEEG parameter. Age was categorized as <60 and >60-years-old. ASPECT score was categorized as high risk (score <7) and low risk (score >7) [19]. Total cholesterol, LDL, HDL, and triglyceride were categorized as abnormal or not based on the guidelines from the American Association of Clinical Endocrinologists [20]. Initial stroke severity was assessed by NIHSS and MoCA-Ina (Indonesian version of MoCA). NIHSS score ranges from 0–42, with score of <5 categorized as minor stroke, while score of >6 categorized as moderate-to-severe stroke [21]. MoCA-Ina total score is 30, with score of <23 categorized as having cognitive impairment, while score of >23 categorized as normal cognitive functioning [22].

The qEEG parameters were showed in the form of absolute power. Subsequently, a manual calculation was performed to obtain delta/alpha ratio (DAR) data, by comparing the absolute power of delta divided by the absolute power of alpha. ([delta+theta]/[alpha+beta] ratio) (DTABR) was calculated by comparing the total absolute powers of delta and theta divided by the total absolute powers of alpha and beta [23].

qEEG Examination

qEEG acquisition was carried out using Fast Fourier Transform (FFT) by a technician who has been trained and experienced for more than 10 years. Examination using qEEG began with a study of reliability for three neurophysiologists who have been designated as operational operators of qEEG. Before the study, the prior perception and technique were synchronized through workshops on qEEG implementation and assessment techniques by minimizing artifacts and

reliability testing among the three neurophysiologists so as to avoid differences in each inter-rater.

qEEG examination was performed within resting conditions in a lying position and eyes closed for a duration of 12 min to get a conventional EEG recording. Examination was only done with the eyes closed and no stimulation of activation was given to trigger epileptiform waves such as photic, open eyes, or hyperventilation. The recording was performed mostly with eyes closed to minimize the artifacts from eye movements and blinking [23].

EEG data acquisition and analysis were conducted with recording electrodes using a 10–20 international system. Wave activity was recorded at 20 locations, that is, Fp1, Fpz, Fp2, F7, F3, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, Oz, and O2 [24]. The distance between inion and nasion was divided by 10%. Electrode impedance of <5 Kohms was required for all locations before recording started. The results of conventional EEG examination (raw data) of each wave were filtered between 0.5–30 Hz and viewed manually to identify artifacts from eye movement or muscle artifacts. The part of the artifact which had been identified was then marked and discarded in the next process. If there was an epoch with amplitude of more than ±100 μV, it would be removed using a filter found in the SCAN software. The raw data were then stored in the hard disk for the further analysis using qEEG brain mapping software and the visual picture was converted into several qEEG parameters. Brain mapping software converted the raw data into numerical data with a computerized FFT system using 2–5 s epoch, with a recording duration of 4 min and free of artifacts, with 10% hamming to extract absolute power with the four wave frequencies [24].

Statistical analysis

For analyzing the statistical differences between variables, we used independent t-test (for continuous variables), Mann–Whitney (for variables not normally distributed), and Chi-square test (for categorical variables). For investigating the correlation between qEEG parameters with NIHSS and MoCA-Ina, we performed bivariate analysis using Spearman correlation. All statistical analyzes were assessed by SPSS software version 25.0 (IBM Co. Ltd, NY, USA). P < 0.05 in two-tailed test indicated as statistical significance.

Ethical approval

This study received ethical approval from The Medical and Health Research Ethics Committee of the Faculty of Medicine, Universitas Gadjah Mada, Indonesia (EC No. KE/FK/0710/EC/2018). All procedures performed in this study were in accordance with the 2013 Declaration of Helsinki.

Results

Baseline characteristics

Tables 1 and 2 present the baseline characteristics of the patients. Table 1 shows demographic and clinical characteristics of the patients based on NIHSS and MoCA-Ina score. Most patients aged >60 year, male and female were in equal number. There were no differences regarding age, sex, diabetes mellitus, LDL, triglyceride, and ASPECT score based on NIHSS and MoCA-Ina score. However, patients with hypertension had lower median score of NIHSS than those without hypertension (p = 0.04). In addition, patients with abnormal total cholesterol and abnormal LDL also had lower median score of MoCA-Ina than the counterpart groups (p = 0.02 and p = 0.04, respectively).

Table 1: Demographic and clinical characteristics of patients based on NIHSS and MoCA-Ina

Characteristics	Total (n)	NIHSS		MoCA-Ina	
		Median (min–max)	p	Median (min–max)	p
Age					
>60 year	19	5 (0–9)	0.36	21 (5–26)	0.97
<60 year	11	4 (2–9)		22 (9–24)	
Sex					
Male	15	4 (2–9)	0.9	23 (5–26)	0.39
Female	15	4 (0–9)		21 (9–26)	
Hypertension					
Yes	28	4 (0–9)	0.04*	21.5 (5–26)	0.45
No	2	8 (7–9)		22.5 (19–26)	
Diabetes mellitus					
Yes	6	4 (2–8)	0.85	20.5 (9–23)	0.39
No	24	4 (0–9)		22.5 (5–26)	
Total cholesterol					
Abnormal	17	4 (0–9)	0.67	19 (5–25)	0.02*
Normal	13	5 (2–7)		23 (10–26)	
LDL					
Abnormal	10	4 (1–9)	0.77	17 (9–23)	0.06
Normal	20	4 (0–9)		23 (5–26)	
HDL					
Abnormal	11	5 (1–9)	0.39	17 (5–25)	0.04*
Normal	19	4 (0–8)		23 (9–26)	
Triglyceride					
Abnormal	10	4,5 (3–9)	0.2	19 (5–26)	0.22
Normal	20	4 (0–8)		23 (9–25)	
ASPECT score					
High risk	7	5 (2–6)	0.96	22 (13–24)	0.59
Low risk	23	4 (0–9)		21 (5–26)	

NIHSS: The National Institutes of Health Stroke Scale, MoCA-Ina: Montreal Cognitive Assessment-Indonesian version, LDL: Low-density lipoproteins, HDL: High-density lipoproteins, ASPECT: Alberta Stroke Program Early Computerized Tomography. *p < 0.05

Table 2 shows the qEEG parameters based on the categorization of NIHSS and MoCA-Ina. There were no differences in qEEG parameters based on NIHSS group. However, based on grouping of MoCA-Ina score, patients with cognitive impairment had higher delta-absolute power than those with normal cognitive functioning (p = 0.01).

Correlation between qEEG with NIHSS and MoCA

Table 3 presents the correlation between QEEG parameters with NIHSS and MoCA-Ina. DTABR had positive correlation with NIHSS although the effect was weak (r=0.379 and p=0.04). Meanwhile, delta-absolute power, DTABR, and DAR were negatively correlated with MoCA-Ina score (r = −0.654, p = 0.01; r = −0.397,

Table 2: QEEG parameters based on the categorization of NIHSS and MoCA-Ina

Parameters	NIHSS			MoCA-Ina		
	Minor (n = 13) (median)	Moderate-severe (n = 17) (median)	p	Cognitive impairment (n = 17) (median)	Normal cognitve function (n = 13) (median)	p
Delta	2152.8 (1340.9–11976.1)	1683.3 (547.5–4682.5)	0.08	2152.8 (869.3–11976.1)	1340.9 (547.5–4682.5)	0.01*
Theta	766.9 (188.8–3830.4)	373.9 (154.2–2049.7)	0.16	408.8 (188.8–3830.4)	589.1 (154.2–2049.7)	0.92
Alpha	458.6 (115.1–1811.8)	417.9 (84.8–2054.6)	0.82	372.1 (115.1–1959.1)	616.4 (84.8–2054.6)	0.66
Beta	113.3 (52.2–171.7)	142.1 (40.3–1058.5)	0.19	113.3 (52.2–473.5)	141.6 (40.3–1058.5)	0.75
DTABR	7.1 (1–76.17)	2.2 (1.01–16.89)	0.11	7.1 (1–76.2)	2.2 (1–16.9)	0.08
DAR	8.9 (0.9–104.05	2.2 (0.75–16.75)	0.19	8.9 (0.9–104.1)	2.2 (0.8–16.8)	0.09

NIHSS: The National Institutes of Health Stroke Scale, MoCA-Ina: Montreal Cognitive Assessment-Indonesian version, DTABR: (delta+theta)/(alpha+beta) ratio, DAR: delta/alpha ratio. *p<0.05

Table 3: Correlation between QEEG parameters with NIHSS and MoCA-Ina

QEEG parameters	NIHSS		MoCA-Ina	
	r	p value	R	p value
Delta	0,317	0.09	−0.654	<0.001***
Theta	0.207	0.27	−0.155	0.41
Alpha	−0.164	0.39	0.034	0.86
Beta	−0.342	0.06	0.004	0.99
DTABR	0.379	0.04*	−0.397	0.03*
DAR	0.32	0.08	−0.371	0.04*

QEEG: Quantitative electroencephalography, NIHSS: The National Institutes of Health Stroke Scale, MoCA-Ina: Montreal Cognitive Assessment-Indonesian version, DTABR: (delta+theta)/(alpha+beta) ratio, DAR: delta/alpha ratio. *p < 0.05, ***p < 0.001.

p =0.03; and r = −0.371, p = 0.04, respectively). Delta-absolute power had moderate correlation, while DTABR and DAR had weak correlation with MoCA-Ina score.

The relationships between DTABR, DAR, and delta-absolute power with NIHSS and MoCA-Ina as shown in Table 3 were further demonstrated in the scatter plots (Figures 1 and 2a-c).

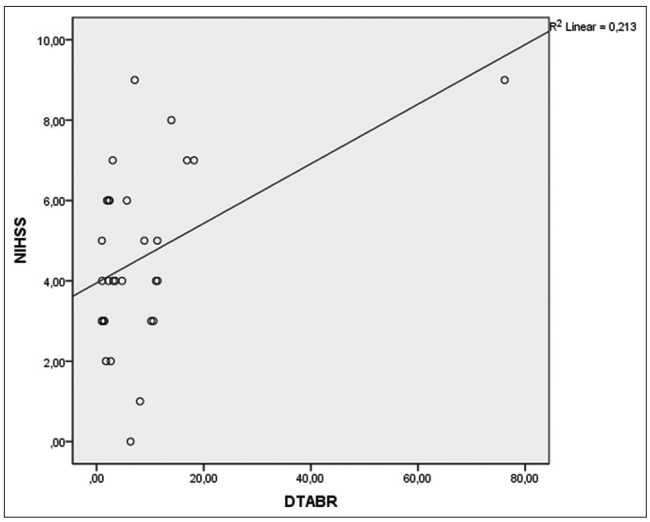

Figure 1: Scatter plot of the correlation between DTABR with NIHSS

For investigating whether qEEG parameters were independently associated with NIHSS and MoCA-Ina, we further performed multivariate regression analysis. After adjusted with the confounding variables, we found that delta-absolute power was independently associated with MoCA score, but not with NIHSS (B = −2.887, 95% CI (−4.304–−1.470), p < 0.001). However, DAR and DTABR were not associated with NIHSS or MoCA-Ina (Table 4).

Discussion

This study showed the correlation between several qEEG parameters with NIHSS and MOCA-Ina among first-ever ischemic stroke patients. There was a positive correlation between DTABR and NIHSS while negative correlations were found between delta-absolute power, DTABR, and DAR with MOCA-Ina score. It was delta-absolute power which was independently associated with MoCA-Ina, but not with NIHSS. To the best of our knowledge, this is the first study in Indonesia which showed that delta-absolute power was negatively associated with MoCA score in ischemic stroke patients.

EEG may reflect changes in CBF and metabolism within seconds as these are directly reflected in the neuronal rhythms. EEG activity correlates with CBF [25]. Prior study showed that delta activity may be related to the core ischemic region, meanwhile theta and alpha activity are possibly associated with the ischemic penumbra, flow diaschisis, and cerebral edema [26]. Theta power over the affected hemisphere correlated with plasmatic peroxide level as a marker of oxidative stress and delta power was negatively correlated with transferrin and presumed to act as a free radical scavenger in acute ischemic stroke. These findings suggest that neurophysiological signals may reflect the biological processes underlying the pathophysiology of stroke [27].

Using magneto-encephalography in patients with a first-ever ischemic stroke in the middle cerebral artery territory, it was shown that delta-absolute power over the affected hemisphere was independently associated with clinical status measured by the NIHSS score [27]. There is an observation of rapid diminution of EEG delta wave pathophysiology following the commencement of thrombolytic therapy [28]. The previous studies showed that delta power, alpha power, DAR, and DTABR were correlated with clinical and functional outcomes of stroke [29], and that alpha power as well as DTABR could serve as predictors for post-stroke outcome [30].

In this study, we found that DTABR had positive correlation with NIHSS. This corroborates the previous

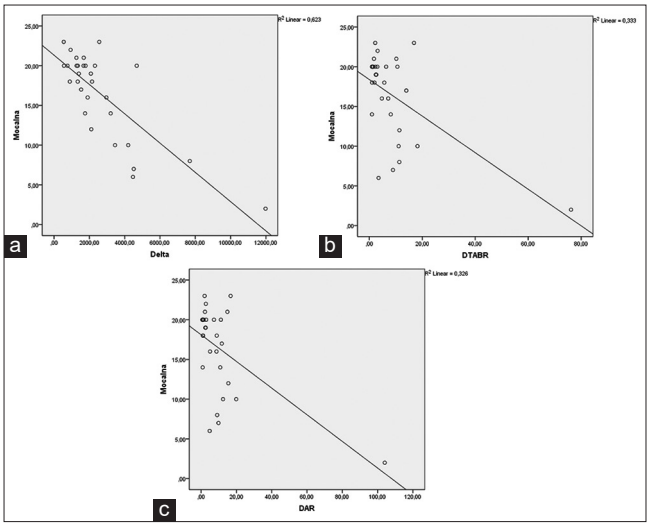

Figure 2: Scatter plot of the correlation between delta-absolute power with MoCA-Ina (a), DTABR with MoCA-Ina (b), and DAR with MoCA-Ina (c)

study which reported an increased in DAR and DTABR among moderate and severe stroke patients [14]. This increased in DAR and DTABR indicated a slowing in brain activity due to ischemia and likely impaired CBF. However, they did not find a significant increase in either DAR or DTABR in minor strokes, indicating that this measure may be useful in distinguishing stroke by severity [14]. Furthermore, our finding is also in accordance with a study which demonstrated that 7-day–12-month NIHSS outcomes were inversely related to relative alpha power and directly related to relative delta power as well as DAR and DTABR parameters [31]. Taken together, all these findings indicate that the lower the delta power and/or the higher the alpha power, the better the patient's outcome [32].

Table 4: Multivariate regression analysis of factors associated with NIHSS and MoCA-Ina

Variables	NIHSS		MoCA-Ina	
	B	95%CI	B	95%CI
Age	0.032	(−0.078–0.141)	−0.067	(−0.210–0.077)
Sex	−0.374	(−2.755–2.007)	1.833	(−1.273–4.939)
Hypertension	−2.736	(−7.471–1.998)	−6.395	(−12.57–−0.219)*
Diabetes mellitus	0.286	(−2.326–2.897)	1.637	(−1.770–5.044)
Total cholesterol	−0.62.9	(−2.965–1.708)	−2.324	(−5.372–0.724)
LDL	0.221	(−2.389–2.831)	−1.119	(−4.524–2.286)
HDL	0.173	(−2.011–2.358)	−1.510	(−4.360–1.340)
Triglyceride	0.688	(−1.646–3.022)	−1.751	(−4.796–1.295)
ASPECT score	−0.5	(−1.393–0.392)	0.017	(−1.148–1.181)
Delta	0.272	(−0.814–1.359)	−2.887	(−4.304–−1.470)***
Theta	−0.885	(−3.649–1.879)	3.258	(−0.348–6.863)
Alpha	0.966	(−1.311–3.242)	−0.482	(−3.453–2.488)
Beta	−0.883	(−7.805–6.04)	−0.504	(−9.534–8.527)
DTABR	0.598	(−0.426–1.621)	−0.485	(−1.821–0.850)
DAR	−0.397	(−1.156–0.363)	0.503	(−0.488–1.494)

NIHSS: The National Institutes of Health Stroke Scale, MoCA-Ina: Montreal Cognitive Assessment-Indonesian version, LDL: Low-density lipoproteins, HDL: High-density lipoproteins, ASPECT: Alberta Stroke Program Early Computerized Tomography. DTABR: (delta+theta)/(alpha+beta) ratio, DAR: delta/alpha ratio. *p < 0.05, ***p < 0.001.

In addition to NIHSS, prior studies demonstrated that qEEG parameters could also be used to detect cognitive impairment in acute stroke patients. In the present study, we showed that delta-absolute power, DTABR, and DAR were negatively correlated with cognitive function. The findings were in accordance with the previous study which was conducted using single-channel EEG for measuring cognitive function after stroke [33]. It was revealed that relative power theta, relative power delta, DAR, and DTABR were correlated with the MoCA score at 90 days after stroke [33]. Greater relative power of theta was associated with better cognitive outcomes; while greater values of delta, DTR, and DAR were associated with poorer cognitive outcomes [33]. Another study performed global DAR and frontal DAR assessments (four lateral frontal electrodes) in post-stroke patients. The results showed that frontal DAR, global DAR, and relative alpha power were associated with cognitive outcomes [34].

The previous studies revealed that band-power measure alone (frontal delta power) was not sensitive to predict cognitive outcomes in post-stroke patient. Instead, they found that DAR was more effective and had strong correlation for predicting cognitive impairment after stroke rather than delta power [17], [34]. This is contradictory to our finding. After controlling covariates, we found that delta power was a significant factor associated with cognitive impairment in acute stroke patients, but not DAR. Increased delta power was correlated with reductions in CBF and neuronal metabolism during focal ischemia [12], which may lead to cognitive dysfunction. Furthermore, abnormal delta power could impair attention in post-stroke patients [35], [36] and corresponds with decrease global cognitive function in many disease states [37], [38].

This study contributes to providing evidence for a negative association between delta-absolute power and cognitive function in acute ischemic stroke patients. There was also positive correlation between DTABR with NIHSS, as well as negative correlations between delta-absolute power, DTABR, and DAR with MOCA-Ina score. These findings may help to advance future research investigating qEEG parameter for predicting the functional and cognitive outcome of post-stroke patients and be useful in clinical practice. Although different from the results of the previous studies, this study showed that several qEEG parameters can be considered as predictors to assess severity in mild-to-moderate stroke patients whose subtle evolution was not seen in the previous assessment tools (NIHSS and MoCA). Another superiority is that the standardized and objective recording in qEEG could provide efficient results to prevent the risk of subjective bias as may be found from NIHSS or MoCA examination.

Nevertheless, this study has several limitations. First, due to limited funding, we could only recruit a small number of participants. Hence, the findings in the study need careful interpretation on generalization. Second, we did not investigate the relationship between qEEG parameter with the long-term outcome. Investigating the role of qEEG for predicting the long-term functional and cognitive outcome for post-stroke patient would be beneficial to help establish prevention strategies. Third, the qEEG recording was taken not in the same day after stroke onset for all the participants (varied

between day 1 until day 7). The different time after stroke onset may trigger different response of cerebral autoregulation which could lead to different findings. Finally, our findings can only be applied to those with mild or moderate stroke. For moderate-to-severe stroke patients, the results may be different. Therefore, the future longitudinal cohort study involving mild-to-severe stroke patients may provide better understanding about the role of qEEG for predicting the outcome.

Conclusions

Several qEEG parameters had significant correlation with NIHSS and MoCA in acute ischemic stroke patients. DTABR positively correlated with NIHSS, while delta-absolute power, DTABR, and DAR negatively correlated with MOCA-Ina score. The use of qEEG in acute clinical setting may provide a reliable and efficient prediction of initial stroke severity. Further cohort study with larger sample size and wide range of stroke severity is still needed.

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