

THE QUANTITATIVE ANALYSIS OF EEG DURING RESTING- AND COGNITIVE-STATES IN PATIENTS WITH SCHIZOPHRENIA FOR POTENTIAL USE AS A DISEASE MARKER

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ABSTRACT

Searching for the biological marker for schizophrenia is an interesting topic. Previous EEG study showed the greater low frequency brain waves in patients with schizophrenia, compared to healthy controls. In this study, authors planned to investigate the EEG changes in patients with schizophrenia during resting- and cognitive-states for the potential use as a disease marker. Sixteen patients with schizophrenia and sixteen healthy controls underwent EEG recording in both resting- (5 min eyes-open) and cognitive-states using the Go/Nogo task. The quantitative EEG (qEEG) by fast Fourier transform was used to reveal the absolute power in 4 brain wave frequencies including delta, theta, alpha, and beta waves. Our results showed the greater delta, theta, and alpha powers during eyes-open session in schizophrenia, compared to control groups. The similar pattern of qEEG changes in schizophrenia group were also found during Go/Nogo task, but in lesser degree compared to resting-state EEG. The main qEEG changes between 2 groups in both sessions were found in theta wave (4.5-8 Hz) over frontal electrodes. The performance in Go/Nogo task was also impaired in schizophrenia group. In conclusion, searching for EEG marker in patients with schizophrenia should be focused on theta wave over frontal electrode during resting-state.

Keywords: EEG, qEEG, schizophrenia, theta wave

1. INTRODUCTION

Schizophrenia is the common psychiatric diseases that mainly manifest with psychotic symptoms such as hallucination and delusions. Approximately 35 million people around the world suffer with schizophrenia [1]. Importantly, schizophrenia is not

only affected to a patient, but also involve with patient's family and their community. A patient with schizophrenia required a number of people for caring including psychiatrist, psychiatric nurses, other health care providers and family members. Moreover, the clinical course of schizophrenia is rather chronic and may be lifelong disease. Importantly, it is known that early diagnosis and early treatment of schizophrenia are important for better clinical outcome. However, the diagnosis of schizophrenia is solely based on clinical interview and behavioral observation according to the standard diagnostic criteria. Therefore, searching for the biological marker in schizophrenia is an interested topic and may help in early or even pre-clinical diagnosis of schizophrenia.

Electroencephalography (EEG) is the neuroscience technique for exploring the neural activities in living human. In clinical aspect, EEG is used for detecting abnormal brain activities in patients with neurological diseases. However, the utility of EEG in patients with psychiatric disorders is not much, especially for cases with schizophrenia. Although the abnormal brain activities, especially for the presence of slow brain activities are common in patients with schizophrenia, such EEG abnormalities usually reflect the disease severity rather than diagnostic marker [2]. Because of schizophrenia is diagnosed by clinical criteria and the presence of slow activities in waking state EEG recording can be found in several diseases including epilepsy [3], bipolar disorder [4] and attention deficit hyperactivity disorder (ADHD) [5]. However, most EEG data were recorded during resting-state, only few study used EEG recording during performed cognitive task [2].

Therefore, this study was planned to investigate the resting- and cognitive-states EEG recording in patients with schizophrenia for revealing the EEG characteristics of schizophrenia. The Go/Nogo task was selected, because this cognitive task aimed to

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evaluate the inhibitory control that is the important functions of frontal lobe [6]. It is generally known that frontal lobe functions in patients with schizophrenia are impaired [7]. In addition, the degree of altered brain activities between resting- and cognitive-states were also compared for the potential use of EEG as a disease or severity biomarkers of schizophrenia. The hypothesis in this study was patients with schizophrenia showed greater slow activities measured by EEG than healthy controls. The benefits of this study were to understand the pattern of altered brain activities in patients with schizophrenia and to demonstrate the possibility of EEG to use as diagnostic or disease severity markers.

2. MATERIALS AND METHODS

2.1 Participants

There were 32 participants in this study consisted of 16 patients with schizophrenia and 16 healthy controls. Patients with schizophrenia had to regularly follow-up at Somdet Chaopraya Institute of Psychiatry, Bangkok, Thailand for at least 1 year. The inclusion criteria consisted of both genders, between the ages of 25 and 50, body mass index (BMI) < 30, normal or correct-to-normal vision and hearing. The exclusion criteria were history of neurological or psychiatric disorders (except for diagnosis of schizophrenia (F20.0-F20.9 by International Classification of Diseases 10th Revision (ICD10) in schizophrenia group), history of brain surgery, metabolic diseases, and taking CNS-acting medication including first generation antihistamine. Moreover, participants in control group were not a first-degree relative of patients with schizophrenia. The participants' characteristics in both groups were shown in table 1.

Table 1. The participants' characteristics in both schizophrenia and control groups.

Participants' characteristics	Schizophrenia (n=16)	Control (n=16)	P-value
Mean age in year (age range)	40.12 (25 - 53)	41.75 (25 - 51)	0.55
Gender (men: women)	10:7	8:8	-
TMSE (score range)	25.76 (23 - 30)	27.94 (26 - 30)	<0.01
BMI	22.05	22.18	0.91

All experimental procedures in this study were performed in accordance with the 1964 Helsinki Declaration and its later amelioration or comparable ethical standard. This study was approved by the

Mahidol University Central Institutional Review Board (COA No. MU-CIRB 2019/126.2604).

2.2 The screening procedures

There were 2 screening tests in this study. First, the handedness of participants was evaluated by the Edinburgh Handedness Inventory [8] that is 10 questions asked for the preferred hand for each activity in daily life. Only right-handed persons were recruited in this study. Second, the Thai mental state examination (TMSE) was used to screen the cognitive functions in all participants [9]. This task consists of 30 questions covering in 6 cognitive domains including orientation (6 points), registration (3 points), attention (5 points), calculation (3 points), language (10 points), and recall (3 points). The total score is 30 points. Only participants who got score more than or equal of 23 would be recruited for the EEG experiment. Because of a TMSE score < 23 usually indicates cognitive impairment [10].

2.3 EEG acquisition

The EEG system used in current study is Neuroscan version 4.3 (Compumedics Neuroscan, USA). The biopotential pickup was used the silver/silver chloride electrodes attached on an EEG cap. The EEG cap was made of an elastic spandex-type fabric with 31 electrodes that arrange according to the international 10-20 system [11] including FP1, FP2, Fz, F3, F4, F7, F8, FT7, FC3, FCz, FC4, FT8, T3, T4, T5, T6, TP7, TP8, C3, Cz, C4, CP3, CPz, CP4, P3, Pz, P4, O1, Oz, and O2 electrode sites. The additional 4 electrodes were placed over both orbits for detecting eye movement. The reference electrodes were applied over mastoid regions. The average power of both mastoid areas (A1+A2)/2 was used as reference. Pre-recording filter was set as band-pass at 0.1-60 Hz and notch filter was opened at 50 Hz. Analog-to-digital (A/D) rate was set at 500 Hz. Before EEG recording, EEG gel was applied to each pore of EEG cap to reduce the electrical impedance less than 5 kOhms.

This experiment was conducted at Somdet Chaopraya Institute of Psychiatry. All participants had to sit in a large armchair with head support in a silent room with temperature at 25 °C. The computer screen would set in front of participants. Before starting experiment, the protocol was clearly explained to participants. Participants or caregivers of patients with schizophrenia had to sign the informed consent form if they agreed to join this study.

The EEG was recorded during eyes-open for 5 minutes and during performing a cognitive task.

During eyes-open session, participants would be advised to minimize their movement and look at cross sign at the computer screen. After that, they were allowed to rest for 1 minute before the next phase of EEG recording that was the EEG recording during Go/NoGo task.

2.4 Cognitive task

The cognitive-state EEG recording was recorded with the Go/NoGo task. In this task, participants had to press a button in Go condition and inhibit the response in NoGo condition. Therefore, the Go/NoGo task is aimed to explore the inhibitory control that mainly involves the frontal lobe functions [12]. This task has been used in our previous research [13].

The STIM2 software (Compumedics Neuroscan, USA) was used for generating this cognitive task. The stimulus in this task is an image of number from 0 to 9. The image would be presented for 200 milliseconds (ms) and the inter-stimulus interval was set at 1,300 ms. Total number of stimulus were 200 trials consisted of 60% of Go and 15% of NoGo trials. Go condition was set as a series of number 1 followed by number 0 while the NoGo condition was other series of number except for a series in Go condition. The estimated duration of this task was around 5 minutes. The behavioral parameters for comparison consisted of accuracy to Go condition (%), accuracy to Nogo condition (%), and reaction time to Go condition (ms).

2.5 EEG analysis

Before computerized EEG analysis, the EEG data would be carefully read for detecting brain wave abnormalities especially for the presence of epileptiform discharge. Any participant who had abnormal EEG data was rejected from further EEG analysis and be informed to meet a neurologist in the hospital for further investigation.

After checking the quality of the raw EEG data, the EEG file would be undergone quantitative analysis. First, the continuous EEG file would be cut into a small EEG segment with 2,000 ms interval. The EEG length of 2,000 ms provides at least 300 short EEG segments for averaging with resolution of 0.5 Hz. Then, any EEG segments with artifacts were removed with the artifact rejection at $\pm 80 \mu\text{V}$. The baseline correction was set at the first point of each EEG epoch and the post-recording filters were set at 0.3 to 30 Hz. Next, all EEG segments would be averaged in the frequency domain using the fast Fourier transform (FFT) for converting the EEG data from time to frequency domain. The brain activities

after FFT were presented as the absolute power (μV^2) of four main frequency bands including delta (0.5-4 Hz), theta (4.5-8 Hz), alpha (8.5-13 Hz), and beta waves (13.5-30 Hz). The mean absolute power and standard deviation (SD) (μV^2) was presented from an individual electrode over the main brain regions including frontal (F), central (C), parietal (P), and temporal (T) areas.

Apart from the numerical value, the EEG data would be shown in the 2-dimensional brain model called topographic brain mapping (TBM) by Neuroscan software. The TBM presented the brain wave powers from each electrode with the color scale that red tone represents the higher power while the blue tone represents the lower power. The overall summary of experimental procedures was shown in figure 1.

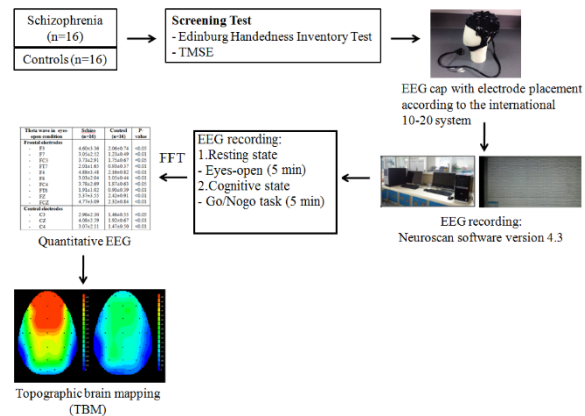


Figure 1. The experimental procedures

2.6 Statistical analysis

The IBM Statistical Package for the Social Sciences (SPSS) software was used for statistical analysis. The independent t-test was used to compare the absolute power of EEG and the cognitive performance between patients with schizophrenia and healthy controls. The significant difference was set as P-value < 0.05 .

3. RESULTS

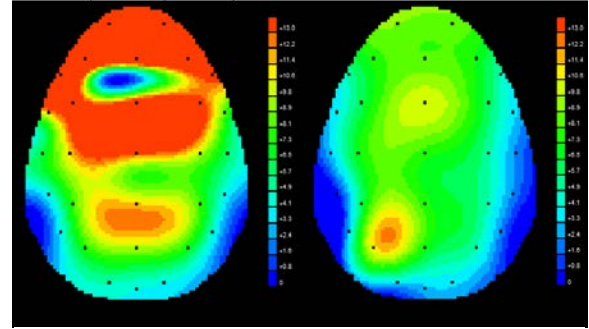
3.1 The visual inspection of raw EEG data

The raw EEG data reading did not show any brain abnormalities in both groups. Therefore, all EEG data were appropriate for further quantitative analysis.

3.2 The qEEG data during eyes-open condition

The qEEG analysis during eyes-open condition between patients with schizophrenia and healthy

controls was shown in 4 main frequency bands consisted of delta, theta, alpha, and beta activities. The frontopolar (FP) and occipital (O) electrodes were not included for qEEG analysis due to a lot of signal artifacts on those electrodes. Our results showed that patients with schizophrenia were significantly greater absolute powers especially for delta, theta, and alpha powers than control group. While the altered beta power was significantly detected only over F8 sites (0.72 ± 0.37 and 0.52 ± 0.31 in schizophrenia and control groups respectively). The results of delta, theta, and alpha powers in eyes-open condition between two groups were shown in table 2, 3, and 4 respectively. Moreover, the TPM of delta, theta, and alpha power between two groups in eyes-open condition were shown in figure 2, 3, and 4 respectively.



(A) Schizophrenia group (B) Control group

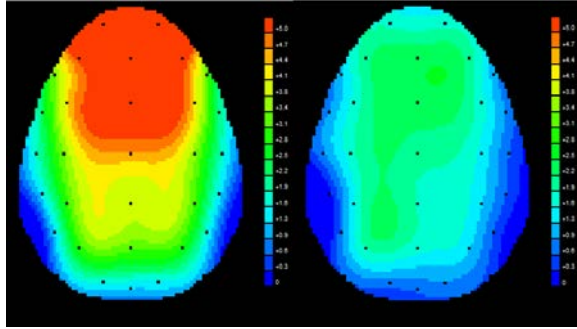
Figure 2. The TBM of delta wave in eyes-open condition compared between schizophrenia (A) and control groups (B).

Table 2. The mean delta power \pm SD (μV^2) in eyes-open condition between 2 groups.

Delta wave in eyes-open condition	Schizo (n=16)	Control (n=16)	P-value
Frontal electrodes			
- F3	17.97 \pm 19.47	8.03 \pm 3.28	<0.05
- F7	16.63 \pm 19.60	6.42 \pm 2.65	<0.05
- FC3	11.56 \pm 8.56	6.28 \pm 2.05	<0.05
- FT7	8.09 \pm 6.18	4.73 \pm 1.44	<0.05
- F4	17.20 \pm 17.51	8.33 \pm 3.99	<0.05
- F8	13.91 \pm 13.06	4.82 \pm 1.73	<0.01
- FC4	10.78 \pm 7.89	8.32 \pm 7.73	0.27
- FT8	6.70 \pm 4.18	4.25 \pm 1.64	<0.05
- FZ	17.27 \pm 16.16	8.43 \pm 3.16	<0.05
- FCZ	12.73 \pm 8.19	7.72 \pm 2.25	<0.05
Central electrodes			
- C3	8.08 \pm 4.34	5.35 \pm 1.57	<0.05
- CZ	11.77 \pm 9.56	6.79 \pm 1.97	0.05
- C4	7.94 \pm 3.85	5.77 \pm 2.05	0.05
Parietal electrodes			
- CP3	6.43 \pm 2.91	4.65 \pm 1.48	<0.05
- CPz	10.13 \pm 7.81	6.51 \pm 2.18	<0.05
- CP4	6.68 \pm 2.70	5.02 \pm 1.82	0.05
- P3	6.48 \pm 3.67	4.29 \pm 1.26	<0.05
- Pz	8.68 \pm 7.97	5.68 \pm 1.83	0.27
- P4	6.14 \pm 3.44	4.60 \pm 1.45	0.11
Temporal electrodes			
- T3	5.19 \pm 2.66	3.75 \pm 1.42	0.06
- T5	3.35 \pm 1.82	2.25 \pm 0.82	<0.05
- T4	4.47 \pm 1.72	3.94 \pm 2.32	0.20
- T6	3.73 \pm 2.59	2.42 \pm 0.67	0.10
- TP7	3.41 \pm 1.63	2.29 \pm 0.70	<0.05
- TP8	3.45 \pm 1.35	3.06 \pm 2.16	0.10

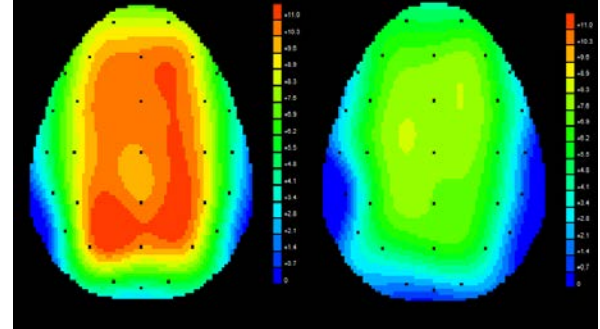
Table 3. The mean theta power \pm SD (μV^2) in eyes-open condition between 2 groups.

Theta wave in eyes-open condition	Schizo (n=16)	Control (n=16)	P-value
Frontal electrodes			
- F3	4.60 \pm 3.36	2.06 \pm 0.74	<0.05
- F7	3.05 \pm 2.52	1.23 \pm 0.49	<0.01
- FC3	3.73 \pm 2.91	1.75 \pm 0.67	<0.05
- FT7	2.01 \pm 1.65	0.93 \pm 0.37	<0.01
- F4	4.88 \pm 3.48	2.16 \pm 0.82	<0.01
- F8	3.03 \pm 2.04	1.05 \pm 0.44	<0.01
- FC4	3.78 \pm 2.69	1.87 \pm 0.63	<0.05
- FT8	1.91 \pm 1.02	0.90 \pm 0.39	<0.01
- FZ	5.37 \pm 3.55	2.42 \pm 0.91	<0.01
- FCZ	4.77 \pm 3.09	2.32 \pm 0.84	<0.01
Central electrodes			
- C3	2.96 \pm 2.30	1.46 \pm 0.55	<0.05
- CZ	4.08 \pm 2.59	1.92 \pm 0.67	<0.01
- C4	3.07 \pm 2.11	1.47 \pm 0.50	<0.01
Parietal electrodes			
- CP3	2.57 \pm 2.08	1.24 \pm 0.47	<0.01
- CPz	3.35 \pm 2.12	1.57 \pm 0.52	<0.01
- CP4	2.67 \pm 1.93	1.27 \pm 0.47	<0.05
- P3	2.51 \pm 2.10	1.09 \pm 0.39	<0.05
- Pz	2.84 \pm 2.06	1.35 \pm 0.44	<0.05
- P4	2.46 \pm 2.07	1.07 \pm 0.37	<0.05
Temporal electrodes			
- T3	1.47 \pm 1.19	0.73 \pm 0.30	<0.01
- T5	1.12 \pm 0.82	0.55 \pm 0.24	<0.05
- T4	1.47 \pm 0.90	0.75 \pm 0.32	<0.01
- T6	1.42 \pm 1.60	0.51 \pm 0.19	<0.01
- TP7	1.17 \pm 0.89	0.54 \pm 0.19	<0.05
- TP8	1.23 \pm 0.78	0.58 \pm 0.20	<0.01



(A) Schizophrenia group (B) Control group

Figure 3. The TBM of theta wave in eyes-open condition compared between schizophrenia (A) and control groups (B).



(A) Schizophrenia group (B) Control group

Figure 4. The TBM of alpha wave in eyes-open condition compared between schizophrenia (A) and control groups (B).

Table 4. The mean alpha power \pm SD (μV^2) in eyes-open condition between 2 groups.

Alpha wave in eyes-open condition	Schizo (n=16)	Control (n=16)	P-value
Frontal electrodes			
- F3	3.70 \pm 3.18	1.71 \pm 0.89	<0.05
- F7	2.63 \pm 2.42	1.07 \pm 0.59	<0.01
- FC3	3.46 \pm 2.88	1.49 \pm 0.77	<0.05
- FT7	2.07 \pm 1.73	0.97 \pm 0.55	<0.05
- F4	3.93 \pm 3.18	1.81 \pm 1.01	<0.05
- F8	2.56 \pm 1.73	0.99 \pm 0.55	<0.01
- FC4	3.53 \pm 2.87	1.66 \pm 0.87	<0.05
- FT8	1.99 \pm 1.18	0.96 \pm 0.57	<0.01
- FZ	4.23 \pm 3.53	1.94 \pm 1.08	<0.05
- FCZ	4.15 \pm 3.57	1.91 \pm 1.06	<0.05
Central electrodes			
- C3	3.30 \pm 2.77	1.63 \pm 0.98	<0.05
- CZ	4.03 \pm 3.54	1.75 \pm 0.92	<0.05
- C4	3.64 \pm 3.15	1.70 \pm 1.14	<0.05
Parietal electrodes			
- CP3	3.31 \pm 3.10	1.68 \pm 1.24	<0.05
- CPz	4.03 \pm 3.71	1.76 \pm 1.21	<0.05
- CP4	3.66 \pm 3.82	1.60 \pm 1.13	<0.05
- P3	3.62 \pm 3.70	1.74 \pm 1.55	0.10
- Pz	3.94 \pm 4.10	1.86 \pm 1.46	0.06
- P4	3.60 \pm 3.95	1.47 \pm 1.09	<0.05
Temporal electrodes			
- T3	1.75 \pm 1.51	0.97 \pm 0.53	0.06
- T5	1.78 \pm 1.41	0.85 \pm 0.63	0.05
- T4	1.80 \pm 1.11	0.89 \pm 0.48	<0.01
- T6	2.32 \pm 3.16	0.75 \pm 0.55	<0.05
- TP7	1.59 \pm 1.46	0.78 \pm 0.41	<0.05
- TP8	1.83 \pm 1.52	0.78 \pm 0.47	<0.01

3.3 The behavioral performance and qEEG data during Go/Nogo tasks

The behavioral performance in Go/Nogo task is used for evaluating the inhibitory control. Our results found that patients with schizophrenia were significantly lower score of Go accuracy than healthy controls. The behavioral performance in Go/Nogo task between two groups was shown in table 5.

Table 5. The behavioral performance in Go/Nogo task compared between patients with schizophrenia and controls.

Go/Nogo task performance	Schizo (n=16)	Control (n=16)	P-value
Accuracy to Go (%)	76	93	<0.01
Reaction time to Go (ms)	441.57	414.13	0.39
Accuracy to NoGo (%)	94	97	0.93

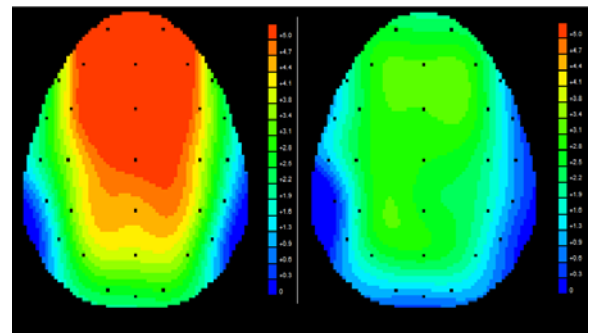
The qEEG analysis during Go/Nogo task between patients with schizophrenia and controls was shown in 4 main frequency bands. Similar to qEEG changes in resting-state, patients with schizophrenia were significantly greater theta powers than healthy controls in all electrodes. The TBM of theta wave in Go/Nogo task was shown in figure 5. However, the qEEG changes in delta and alpha bands in schizophrenia group was found over few electrodes while the altered beta power was significantly observed only over F8 sites (0.94 \pm 0.62 and 0.65 \pm 0.59 in schizophrenia and control groups respectively). The results of delta, theta, and alpha powers in Go/Nogo task between two groups were shown in table 6, 7, and 8 respectively.

Table 6. The mean delta power \pm SD (μV^2) in Go/Nogo task between 2 groups.

Delta wave in Go/Nogo task	Schizo (n=16)	Control (n=16)	P-value
Frontal electrodes			
- F3	13.67 \pm 10.85	10.34 \pm 4.52	0.22
- F7	15.91 \pm 18.98	7.41 \pm 3.66	0.09
- FC3	11.16 \pm 6.31	8.62 \pm 3.02	0.36
- FT7	7.92 \pm 4.76	5.11 \pm 1.65	<0.05
- F4	13.54 \pm 10.08	10.65 \pm 4.06	0.46
- F8	10.85 \pm 8.74	6.57 \pm 3.05	<0.05
- FC4	10.97 \pm 5.81	9.24 \pm 3.18	0.54
- FT8	6.62 \pm 2.67	5.27 \pm 1.89	0.10
- FZ	14.44 \pm 9.95	11.13 \pm 3.84	0.32
- FCZ	13.13 \pm 5.98	10.93 \pm 3.36	0.21
Central electrodes			
- C3	8.91 \pm 3.89	7.66 \pm 2.56	0.29
- CZ	12.34 \pm 5.45	9.72 \pm 2.89	0.14
- C4	9.11 \pm 3.07	7.99 \pm 2.45	0.26
Parietal electrodes			
- CP3	7.50 \pm 2.46	6.84 \pm 2.06	0.42
- CPz	10.62 \pm 4.67	8.66 \pm 2.58	0.15
- CP4	8.08 \pm 2.33	7.08 \pm 2.17	0.21
- P3	7.42 \pm 2.60	6.27 \pm 1.89	0.16
- Pz	9.29 \pm 4.68	7.37 \pm 2.11	0.27
- P4	7.42 \pm 3.11	6.23 \pm 1.82	0.19
Temporal electrodes			
- T3	5.39 \pm 2.31	4.43 \pm 1.36	0.25
- T5	3.92 \pm 2.04	3.37 \pm 1.00	0.34
- T4	4.75 \pm 1.69	3.92 \pm 0.82	0.08
- T6	4.01 \pm 1.76	3.26 \pm 1.01	0.15
- TP7	3.80 \pm 1.61	2.90 \pm 0.75	0.05
- TP8	3.89 \pm 1.50	3.31 \pm 0.87	0.19

Table 7. The mean theta power \pm SD (μV^2) in Go/Nogo task between 2 groups.

Theta wave in Go/Nogo task	Schizo (n=16)	Control (n=16)	P-value
Frontal electrodes			
- F3	4.12 \pm 2.16	2.51 \pm 0.84	<0.05
- F7	3.03 \pm 2.13	1.51 \pm 0.69	<0.01
- FC3	3.37 \pm 1.59	2.05 \pm 0.73	<0.01
- FT7	1.94 \pm 0.88	1.05 \pm 0.37	<0.01
- F4	4.35 \pm 2.46	2.56 \pm 0.77	<0.05
- F8	2.69 \pm 1.54	1.36 \pm 0.59	<0.01
- FC4	3.51 \pm 1.91	2.10 \pm 0.71	<0.05
- FT8	1.78 \pm 0.75	1.08 \pm 0.44	<0.01
- FZ	5.25 \pm 2.94	2.94 \pm 0.96	<0.01
- FCZ	4.49 \pm 2.17	2.81 \pm 0.96	<0.05
Central electrodes			
- C3	2.68 \pm 1.24	1.68 \pm 0.59	<0.01
- CZ	3.82 \pm 1.75	2.24 \pm 0.78	<0.01
- C4	2.97 \pm 1.48	1.66 \pm 0.58	<0.01
Parietal electrodes			
- CP3	2.34 \pm 1.16	1.40 \pm 0.49	<0.01
- CPz	3.17 \pm 1.46	1.76 \pm 0.59	<0.01
- CP4	2.56 \pm 1.33	1.43 \pm 0.52	<0.01
- P3	2.29 \pm 1.25	1.25 \pm 0.56	<0.01
- Pz	2.65 \pm 1.32	1.47 \pm 0.51	<0.01
- P4	2.32 \pm 1.32	1.24 \pm 0.49	<0.01
Temporal electrodes			
- T3	1.46 \pm 0.68	0.78 \pm 0.27	<0.01
- T5	1.25 \pm 0.78	0.66 \pm 0.22	<0.01
- T4	1.39 \pm 0.70	0.84 \pm 0.30	<0.01
- T6	1.14 \pm 0.74	0.70 \pm 0.37	<0.01
- TP7	1.07 \pm 0.58	0.57 \pm 0.15	<0.01
- TP8	1.08 \pm 0.61	0.68 \pm 0.23	<0.05



(A) Schizophrenia group (B) Control group

Figure 5. The TBM of theta wave in Go/Nogo task compared between schizophrenia (A) and control groups (B).

Table 8. The mean alpha power \pm SD (μV^2) in Go/Nogo task between 2 groups.

Alpha wave in Go/Nogo task	Schizo (n=16)	Control (n=16)	P-value
Frontal electrodes			
- F3	3.26 \pm 2.94	2.01 \pm 1.18	0.13
- F7	2.46 \pm 2.09	1.41 \pm 0.88	0.07
- FC3	3.02 \pm 2.62	1.74 \pm 1.04	0.08
- FT7	2.09 \pm 1.65	1.19 \pm 0.73	0.06
- F4	3.43 \pm 2.72	2.17 \pm 1.35	0.11
- F8	2.35 \pm 1.81	1.44 \pm 1.08	0.12
- FC4	3.14 \pm 2.37	1.97 \pm 1.23	0.09
- FT8	1.97 \pm 1.28	1.31 \pm 0.99	0.15
- FZ	3.79 \pm 3.30	2.27 \pm 1.36	0.10
- FCZ	3.72 \pm 3.22	2.26 \pm 1.38	0.10
Central electrodes			
- C3	2.83 \pm 2.51	1.67 \pm 1.04	0.10
- CZ	3.51 \pm 2.92	1.97 \pm 1.15	0.06
- C4	3.12 \pm 2.40	1.79 \pm 1.11	0.05
Parietal electrodes			
- CP3	2.94 \pm 2.93	1.57 \pm 0.97	0.09
- CPz	3.38 \pm 2.85	1.79 \pm 1.06	<0.05
- CP4	2.99 \pm 2.38	1.58 \pm 0.91	<0.05
- P3	3.58 \pm 4.27	1.67 \pm 1.29	0.12
- Pz	3.23 \pm 3.03	1.71 \pm 1.04	0.07
- P4	3.13 \pm 3.06	1.47 \pm 0.82	0.13
Temporal electrodes			
- T3	1.91 \pm 1.49	1.03 \pm 0.60	<0.05
- T5	1.98 \pm 2.07	1.07 \pm 0.63	0.15
- T4	1.62 \pm 1.01	1.06 \pm 0.67	0.08
- T6	1.73 \pm 1.34	1.06 \pm 0.73	0.09
- TP7	1.72 \pm 1.52	0.80 \pm 0.33	0.06
- TP8	1.48 \pm 1.10	0.97 \pm 0.67	0.12

4. DISCUSSION

This study could demonstrate the different qEEG data in patients with schizophrenia, compared to healthy controls. Patients with schizophrenia showed greater absolute powers in delta, theta, and alpha bands than controls during eyes-open EEG recording. Interestingly, the altered brain waves' power was mainly detected over frontal electrodes. The increment of delta and theta waves found in current study were in line with an EEG study in patients with schizophrenia [2]. In contrast, the alpha power was also increased in this work that was contrary to previous studies [14]. The different results of alpha wave may be explained by the high variation of clinical spectrum in patients with schizophrenia.

The EEG recording during Go/Nogo task was also showed the similar neural patterns with resting-state eyes-open session. The increased delta, theta, and alpha powers were observed in patients with schizophrenia, compared to healthy controls. However, when compared to resting-state, the qEEG

difference between two groups was not obviously changed in cognitive-state EEG recording, particularly in delta and alpha bands. This finding may be explained by cognitive processing that could alter brain wave patterns [15]. Thus, the different qEEG profile in patients with schizophrenia during Go/Nogo task may be the summation between disease pathology and cognitive processing leading to more complex EEG change. Taken together, the resting-state EEG recording is more prefer than cognitive-state EEG recording to reveal the abnormal neural activities in schizophrenia.

The theta wave that obviously changed in both resting- and cognitive-state EEG recording as well as in almost electrode sites should be used for potential marker of disease. However, the increased slow brain waves could be demonstrated in various neurological and psychiatric diseases [3-5]. Thus, the greater slow brain wave activities were not specific marker of schizophrenia, but may be used as a severity marker of disease. Previous study showed that increased theta wave was found to associate with structural brain pathology and more clinical symptoms related to frontal lobe dysfunction called the negative symptoms of schizophrenia [16]. This finding indicated that increased theta power could be used as a severity marker of schizophrenia.

Regarding cognitive task, patients with schizophrenia was lower accuracy rate for Go condition than healthy controls indicated the poor attention control in schizophrenia. However, the accuracy for Nogo condition that is the measurement of inhibitory control was not significantly different between two groups. This result was similar to previous studies that showed the impaired frontal lobe functions measured by neuropsychological tasks in patients with schizophrenia [17-19]. Therefore, the evidence of frontal lobe dysfunction was revealed in this study by qEEG analysis and impaired performance in Go/Nogo task.

There were some limitations in this study. For examples, the emotional state and stress level of participants were not formally evaluated that both stress and emotion might affect the EEG data. In addition, the clinical information on disease and medication were not included in current analysis.

5. CONCLUSION

This study demonstrated the increment of brain waves' power especially for theta wave in patients with schizophrenia. This result was consistent to our hypothesis. The altered neural activities were mainly

observed in resting-state EEG recording and frontal electrodes. Therefore, the suitable EEG marker for schizophrenia should be focused on the theta band during resting-state EEG recording. Further analysis of qEEG data with clinical parameters in patients with schizophrenia are also recommended.

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REFERENCES

- [1] Bhugra D. The global prevalence of schizophrenia. *PLoS Med.* 2005; 2(5):e151.
- [2] Boutros NN, Arfken C, Galderisi S, Warrick J, Pratt G, Iacono W. The status of spectral EEG abnormality as a diagnostic test for schizophrenia. *Schizophr Res.* 2008; 99(1-3):225-237.
- [3] Siripornpanich V, Visudtibhan A, Kotchabhakdi N, Chutabhakdikul N. Delayed cortical maturation at the centrotemporal brain regions in patients with benign childhood epilepsy with centrotemporal spikes (BCECTS). *Epilepsy Res.* 2019; 154:124-131.
- [4] Yadollahpour A, Mirzaiyan M, Rashidi S. Quantitative EEG for early and differential diagnosis of bipolar disorders: a comprehensive review of the literature. *Int J Ment Health Addiction.* 2017; 15:387-393.
- [5] Barry RJ, Clarke AR, Johnstone SJ. A review of electrophysiology in attention-deficit/hyperactivity disorder: I. Qualitative and quantitative electroencephalography. *Clin Neurophysiol.* 2003; 114(2):171-183.
- [6] Dimitrov M, Nakic M, Elpern-Waxman J, Granetz J, O'Grady J, Phipps M, Milne E, Logan GD, Hasher L, Grafman J. Inhibitory attentional control in patients with frontal lobe damage. *Brain Cogn.* 2003; 52(2):258-270.
- [7] de la Torre JC, Barrios M, Junqué C. Frontal lobe alterations in schizophrenia. *Eur Arch Psychiatry Clin Neurosci.* 2005; 255:236-244.
- [8] Oldfield RC. The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia.* 1971; 9:97-113.
- [9] Train the Brain Forum Committee. Thai mental state examination (TMSE). *Siriraj Hosp Gaz.* 1993; 45:661-674.
- [10] Tachapaitoon A, Kumthornthip W, Tosayanonda O. Thai mental state examination in stroke patients. *J Thai Rehabil.* 2000; 9 (3): 120-124.
- [11] Jasper HH. The ten-twenty electrode system of the International Federation. *Electroencephalogr Clin Neurophysiol.* 1958; 10:371-375.
- [12] Simmonds DJ, Pekar JJ, Mostofsky SH. Meta-analysis of Go/No-go tasks demonstrating that fMRI activation associated with response inhibition is task-dependent. *Neuropsychologia.* 2008; 46(1):224-232.
- [13] Chetsawang J, Nudmamud-Thanoi S, Kraiwattanapirom N, Siripornpanich V, Unharasamee W, Chetsawang B. The effect of methamphetamine-induced neurodegeneration and psychiatric disorders on cognitive impairment in methamphetamine abusers in Thailand. *J Pub Health Dev.* 2019; 17(1):15-29.
- [14] Newson JJ, Thiagarajan TC. EEG frequency bands in psychiatric disorders. a review of resting state studies. *Front Hum Neurosci.* 2019; 12:521.
- [15] Roohi-Azizi M, Azimi L, Heysieattalab S, Aamidfar M. Changes of the brain's bioelectrical activity in cognition, consciousness, and some mental disorders. *Med J Islam Repub Iran.* 2017; 31:53.
- [16] Sponheim SR, Clementz BA, Iacono WG, Beiser M. Clinical and biological concomitants of resting state EEG power abnormalities in schizophrenia. *Biol Psychiatry.* 2000; 48(11):1088-1097.
- [17] Yamada M, Ueda K, Namiki C, Hirao K, Hayashi T, Ohigashi Y, Murai T. Social cognition in schizophrenia: similarities and differences of emotional perception from patients with focal frontal lesions. *Eur Arch Psychiatry Clin Neurosci.* 2009; 259(4):227-233.
- [18] Orellana G, Slachevsky A. Executive functioning in schizophrenia. *Front Psychiatry.* 2013; 4:35.
- [19] Nishimura Y, Takizawa R, Muroi M, Marumo K, Kinou M, Kasai K. Prefrontal cortex activity during response inhibition associated with excitement symptoms in schizophrenia. *Brain Res.* 2011; 1370:194-203.



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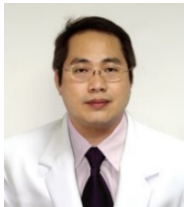
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