

EEG Differences Between Eyes-Closed and Eyes-Open Conditions at the Resting Stage for Euthymic Participants

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Most prior research examined differences in the EEG frequency bands between eyes-closed and eyes-open conditions at the resting state as a baseline; without counter checking on the mental health state of the subjects; the depressive symptoms were often not assessed or controlled during the experiment. We examined EEGs of euthymic participants (who were free from the psychiatric symptoms) for the above two conditions at the resting state. A population of participants with healthy levels of depression, anxiety, and stress symptoms ($n = 50$) has been examined with the Patient Health Questionnaire-9 (PHQ-9) and Depression Anxiety Stress Scale-21 (DASS-21). The powers of the alpha rhythm, interpreted as relaxation waves, were higher during eyes-closed compared to eyes-open condition ($P = 0.0\dots$) in all brain regions (32 EEG channels). The prefrontal cortex was characterized by higher delta, theta, and beta powers during eyes-open periods at the resting state, as compared with eyes-closed ones.

Keywords: EEG, eyes-open, eyes-closed conditions, euthymic subjects, baseline, EEG frequency bands.

INTRODUCTION

Numerous prior studies have examined differences between eyes-closed and eye-open conditions in the resting state at data acquisition with EEG, to determine the appropriate baseline readings for the protocol development. The majority of this research was focused on the alpha frequency band under the above-mentioned conditions. Specifically, the alpha activity in EEGs is dominant in normal individuals during an eyes-closed resting condition [1–4]. Also, studies reported that the alpha power is significantly reduced within the posterior cortical regions during eyes-open condition [5–9]; consequently, this activity is suppressed by visual stimulation. Therefore, such information can be used as an indicator to differentiate between the visual and non-visual data inputs through EEG [6, 9, 10]. In general, the eye-closed condition is recommended

as a baseline resting state in EEG measurements for different experimental designs of EEG studies, especially those involving no tasks with visual stimulation [11].

For eyes-open studies, Barry et al. [11] found that delta and theta activities during this condition showed greater reductions in the frontal and lateral brain regions. According to the same report, beta activity that comes after the alpha-wave band also was reduced at transition from eyes-closed to eyes-open conditions in the posterior and right hemisphere regions. Therefore, these authors [11] suggested that the eye-closed condition could serve as a convenient arousal baseline, while the eyes-open condition could serve as the respective activation baseline. It was concluded that eyes-closed and eyes-open conditions cannot serve as equivalent baseline ones. Another study by Barry et al. [12] with children demonstrated decreased powers of delta and theta waves and an increased power of the beta band at a higher alpha activity during the eyes-closure [12].

Of note, prior studies of various resting-state conditions have not examined psychiatric symptoms of the participants involved in the experiment, to ensure the stage of participants' mental health.

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The brain signals are sensitive and varied if the participants suffer from some kind of mental health-care issues; this may create a discrepancy of data acquisition for the brainwave study. It was reported that about 20-40% of EEG findings in depressed participants differ noticeably from those in the healthy control [13, 14]. The main difference between healthy and depressed persons was found in the alpha frequency band. According to Henriques and Davidson [15], depressed participants demonstrated lesser left-sided activation (increase in the alpha power) than healthy control participants. In depression, the asymmetry in EEG activity was reported over frontal regions [16–19], and this was further concreted in another study [20]. It was reported that major depression disorder (MDD) patients demonstrate a reduction of the left frontal activation and an increased global alpha power relative to the controls. These findings were interpreted as a reduced approach on motivation and generalized cortical deactivation, respectively [20]. Conversely, Fingelkurts et al. [21] reported that depressed participants had a higher alpha-band power, extensively distributed beta activity, and decreased delta activity, as compared to the non-depressed participants. On the other hand, another report from Begic et al. [22] described the decreased alpha-rhythm power but increases in the delta, theta, and beta powers over frontal regions in depressed participants. There were also reports on a greater synchronization of delta oscillations [23] and a greater power of delta activity found in bipolar disorder patients [24]. Depressive symptoms may impact the resting-state EEG measures under both eyes-closed and eyes-open conditions. In summary, earlier works suggested that depressed patients have noticeable variations of EEG activity compared with the respective parameters in healthy participants. The reports showed that an affective state of the participants is an important confound for brainwave signals. Therefore, it is important to verify the mental stage of the participants before the measurements of their EEG signals for different brainwave studies.

We examined both eyes-closed and open conditions at the resting state of the participants identified as emotionally healthy (euthymic) subjects. This study enabled us to obtain stable EEG signals from the euthymic participants for changes in the whole-brain signals, to serve as a baseline before moving on to depressive-syndrome EEG analysis. Participants were screened for depressive

symptoms with the Patient Health Questionnaire-9 (PHQ-9) [25] and Depression Anxiety Stress Scale-21 (DASS-21) [26]. The study was focused on investigating the most significant EEG frequency band out of the entire range under the above conditions during the 2-min-long resting state for euthymic participants.

METHODS

Participants. The participant group included a total of 50 volunteers (university students, 30 males and 20 females) recruited from the undergraduates of the Faculty of Engineering and Science in the university. The mean (\pm s.d.) age was 22.7 ± 1.47 years (range 19-25) Participants were first screened with the Patient Health Questionnaire-9 (PHQ-9) and Depression Anxiety Stress Scale-21 (DASS-21) to ensure they are free from depression, anxiety, and stress during EEG recording under eyes-closed and open conditions at the resting stage.

Mental Health Screening. Participants with no prior psychiatric history were eligible for the study procedures. Depression screening measures provided an indication of the severity of depression symptoms and assess the severity within a given time period (7 to 14 days). In this research, the Patient Health Questionnaire-9 (PHQ-9) [25] and Depression, Anxiety, and Stress Scale-21 (DASS-21) [26] were used to determine the mental health status for each individual. Only participants with normal values on the PHQ-9 and DASS-21 scores were enrolled. These two questionnaires are in the public domain and relatively easy to be administered. The questionnaires were given to the participant before starting the EEG experiment. These two questionnaires have been estimated to possess a high validity and reliability and are commonly used in clinical settings [27]. The PHQ score range was from 0 to 27, as each item was scored from 0 (not at all) to 3 (nearly every day). The PHQ scores 5, 10, 15, and 20 represented mild, moderate, moderately severe, and severe depression, respectively [25]. A score below 10 was the threshold for inclusion in our study.

The DASS-21 consists of 21 questions related to the daily living, depression, anxiety, and stress of an individual. The DASS-21 is widely used by clinicians in the United Kingdom and is also characterized by high reliability and validity [26]. The DASS scores range from 0 (did not apply to me at all) to 3 (applied to me very much or most

of the time). The depression scores of 10, 14, 21, and 28 represent normal, mild, moderate, severe, and extremely severe states. The anxiety scores of 8, 10, 15, and 20 and the stress scores of 15, 19, 26, and 34 are categorized as normal, mild, moderate, severe, and extremely severe, respectively. In this study, the participants with depression scores below 14, anxiety scores below 10, and stress scores below 19 were categorized as healthy participants and, thereby, eligible for the participation in the study.

Electroencephalography Acquisition. Upon arrival, participants were given an information sheet, signed the consent form, and completed the screening questionnaires. The experiment was conducted in a controlled environment. The study included a conventional EEG registration with NCC Medical 32-channel bipolar electroencephalograph. EEGs were recorded at 32 scalp loci reference to vertex (Cz), complying the International 10–20 electrode placement system. Each participant was seated comfortably and followed the protocol to relax for two minutes before starting of the studies. The EEG recording consisted of two 2-min-long sessions with the eyes closed and open at the resting state. The resting stage in this study is referred to the

participant who was allowed to take a rest for 2 min before starting of the experiment, to relax the mind and pay attention to the experiment during EEG recording for not doing other tasks.

Data Acquisition. EEG signals were digitized at 128 sec^{-1} with a low-frequency filter of 0.5 Hz, a high-frequency filter of 40 Hz, and a notch filter of 50 Hz. The EEG data were then calculated by fast Fourier transform (FFT) analysis to obtain the results in the absolute EEG band power (μV^2) at each electrode within the following bands, delta (1–4 Hz), theta (4–7 Hz), alpha (8–12 Hz), and beta (12–40 Hz). The observed regions included Fp1, Fp2, F3, F4, F7, F8, C3, C4, P3, P4, T3, T4, T5, T6, O1, and O2. The EEG data of each frequency is presented in the graphs in this paper to compare their mean powers and standard errors for eyes-closed and eyes-open conditions. Figure 1 illustrates the scalp loci positions together with generally accepted summary functions of each brain region.

Statistical Analysis. The paired *t*-test was used to evaluate the significance of differences between eyes-closed and eyes-open conditions for each EEG frequency band; $P < 0.05$ was considered as an indication of significance. The data were analyzed with SPSS (ver. 11.5. (SPSS Inc., USA).

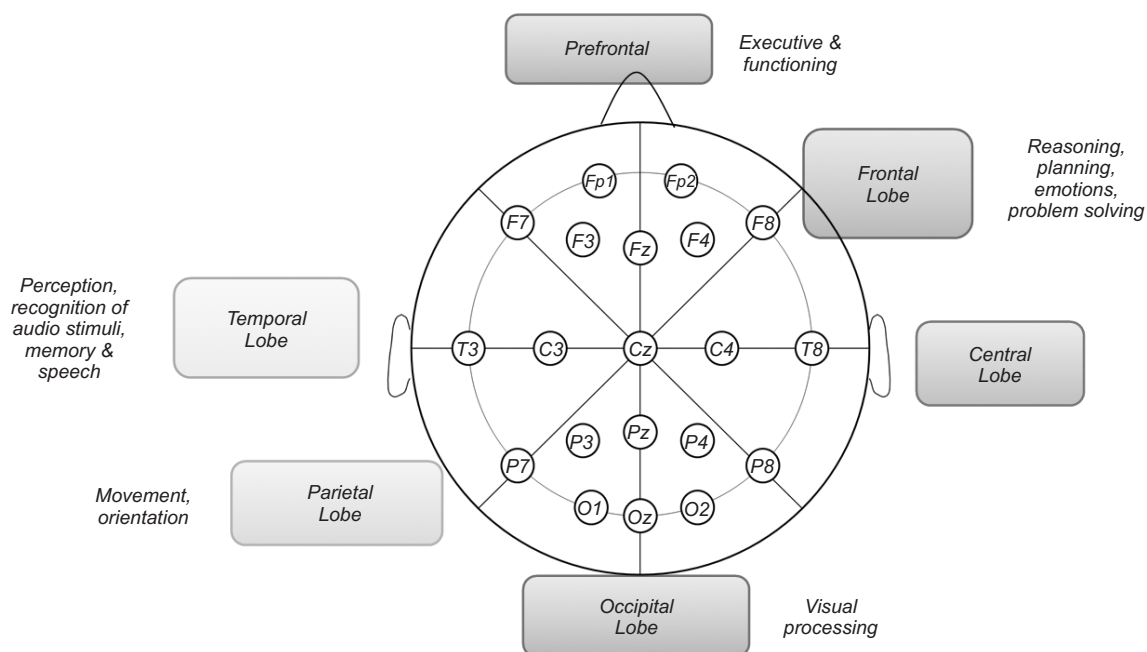


Fig. 1. International 10-20 electrode placement system.

RESULTS

Participant Demographics. The focus in our study was to compare the EEG findings at eyes-closed and eyes-open conditions in the resting stage for verified euthymic participants. The selection of participants in this study is clearly filtered, and only those with the questionnaire scores of the Patient Health Question-9 (PHQ-9) score below 10, depression score of the DASS below 14, anxiety score below 10, and, finally, stress score below 19 were included in the normal category. The mean PHQ-9 score (\pm s.d.) in our sampling was 4.42 ± 2.27 (\pm s.d.), while the mean DASS-21 scores in this sampling for depression, anxiety, and stress were 4.48 ± 2.84 , 7.00 ± 5.73 , and 8.72 ± 5.19 , respectively.

Powers of the EEG Bands (0–30 Hz) for Comparison for Eyes-Closed and Eyes-Open Conditions in the Resting Stage. The delta power band (1–4 Hz) is illustrated in Fig. 2 that displays a very profound reading at Fp1 and Fp2 (prefrontal area) under eyes-open condition. Generally, the delta power reading within this region was above $200 \text{ k}\mu\text{V}^2$, as compared to eyes-closed condition. The same outcome was observed for the frontal region (from F3 to F8) where the reading for voltage the power for eyes-open condition is slightly higher than that for eyes-closed. For other brain regions, the EEG power band readings for both conditions did not significantly differ from each other. The result was similar for the statistical analysis outcome where the delta power was found to be significantly lower during the eyes-closed state

at F_{p1} ($t(49) = -6.573, P = 0.0\dots$), F_{p2} ($t(49) = -7.16, P < 0.01$), F_3 ($t(49) = -2.554, P = 0.014$), F_4 ($t(49) = -5.724, P = 0.0\dots$), F_7 ($t(49) = -4.79, P = 0.0\dots$), and F_8 ($t(49) = -6.304, P = 0.0\dots$). In this study, the delta power increased profoundly at the prefrontal and frontal areas under eyes-open condition. This was associated with results of the recent study where the delta frequency appeared to be related to cortical plasticity in wakefulness and sleep [28]. The delta EEG frequency was proposed to be related to activation of cognitive and emotional processes. Therefore, the delta frequency should be increased at the frontal, central and posterior sites during the cognitive loading [29]. This probably was the reason of a higher delta power at the prefrontal and frontal areas during eyes-open condition, as certain cognitive processes were activated with the functioning visual input. Besides, there was a report on the delta range within the frontal-central-posterior and occipital regions affected by the emotional process [30]. Guntekin and Basar [29] also concluded that the reduction in the delta rhythm could be a general electrophysiological marker for cognitive dysfunctions (Alzheimer’s disease, MCI, bipolar disorder, schizophrenia, and alcoholism) [29]. This was an essential reason to recruit the euthymic participants in the study. It was also found that the female participants had relatively higher delta activities in comparison with those in male participants during visual stimulation [31, 32]. We have a total of 20 females in this investigation, which could be considerably contributed to the obtained results.

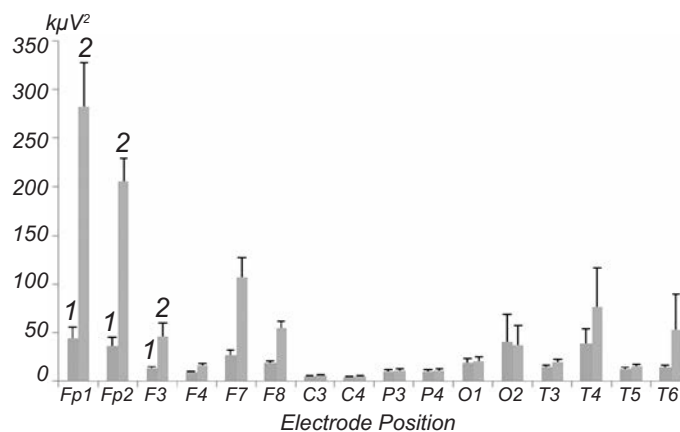


Fig. 2. Mean absolute power of the delta band under eyes-closed and eyes-open resting conditions. Error bars represent standard errors of the mean.

The next low-frequency brainwaves after delta are theta oscillations (4–8 Hz) (Fig. 3). Under eyes-open condition, the theta power (above $38 \text{ k}\mu\text{V}^2$) was noteworthy higher at Fp1 and Fp2 compared to that under eyes-closed condition. Besides that, channels P3, P4, O1, and O2, i.e. the posterior and occipital areas, had a higher theta power under eye-closed condition than that at eyes-open. The global mean of the theta power was $12.41 \text{ k}\mu\text{V}^2$ for eyes-closed and $14.21 \text{ k}\mu\text{V}^2$ for eyes-open. On the other hand, statistical analysis for the theta power band showed significantly lower values at F_{p1} ($t(49) = -5.254, P = 0.0\dots$) and F_{p2} ($t(49) = -5.542, P = 0.0\dots$) but higher ones at C_3 ($t(49) = 2.256, P = 0.029$), C_4 ($t(49) = 2.395, P = 0.021$), P_3 ($t(49) = 3.692, P = 0.001$), P_4 ($t(49) = 4.202, P = 0.0\dots$), O_1 ($t(49) = 3.66, P = 0.001$), O_2 ($t(49) = 3.178, P = 0.003$), T_3 ($t(49) = 2.511, P = 0.015$), and T_5 ($t(49) = 3.654, P = 0.01$) for eyes-closed condition compared to eyes-open. The theta power increased drastically at the frontal and prefrontal areas but decreased at the central, posterior, occipital, and temporal areas during eyes-open condition at the resting state.

This result was consistent with findings of Barry et al. [11] who reported on a global reduction of theta activity under eyes-open condition; it was suggested that this situation was associated with stimulus processing (especially at the posterior regions) and accompanied by an increased theta power in the frontal hemisphere regions [11]. Other studies reported that the theta power during the resting/sleeping state decreases with age [33–35]. Older children may also have a lower theta power than younger children, and this was interpreted as a sign of brain maturation [36]. In

our study, euthymic participants were teenagers and young subjects, from 19 to 25 years old. The theta power increases over the frontal and central regions during the cognitive processes and during the performance of a variety of the tasks, where working memory, calculation, and even musical imagining are involved [37]. The theta activity is known to be affected by emotional processing [38] and is associated with neuropsychiatric disorders, depression in particular [39–40]. We believe that the euthymic participants in this study would give a clear baseline for brainwaves before other future studies.

The alpha rhythm (8–12 Hz) at channels P3, P4, O1, O2, T5, and T6 under eyes-closed condition boosted up to $29 \text{ k}\mu\text{V}^2$ and above (Fig. 4). The highest alpha power was observed at channel P4 under eyes-closed condition ($35.62 \text{ k}\mu\text{V}^2$). The global mean of the alpha-range power during eyes-closed state was $20.0 \text{ k}\mu\text{V}^2$ vs. $5.08 \text{ k}\mu\text{V}^2$ for eyes-open. The alpha power during eyes-open condition was relatively low; at all channels it was below $10 \text{ k}\mu\text{V}^2$. The alpha-frequency power was significantly higher within all brain regions under eyes-closed condition, as compared to eyes-open condition ($P = 0.00\dots$).

This result was consistent with previous studies[11], where alpha activity was shown to be regularly suppressed by visual stimulation, but our results are more uniform. The alpha rhythm is dominant in normal individuals under eyes-closed resting condition. The widespread alpha-band reduction at transition from eyes-closed to eyes-open conditions was also found in 8- to 12-year-old children [12]. In prior research, it was reported that alpha resynchronization with the

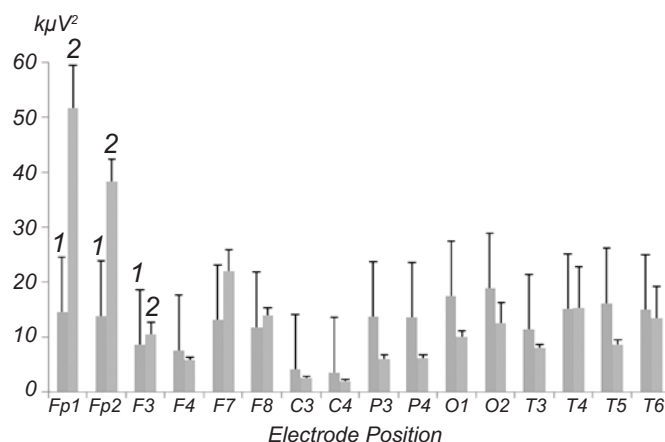


Fig. 3. Mean absolute power of the theta band under eyes-closed and eyes-open resting conditions.

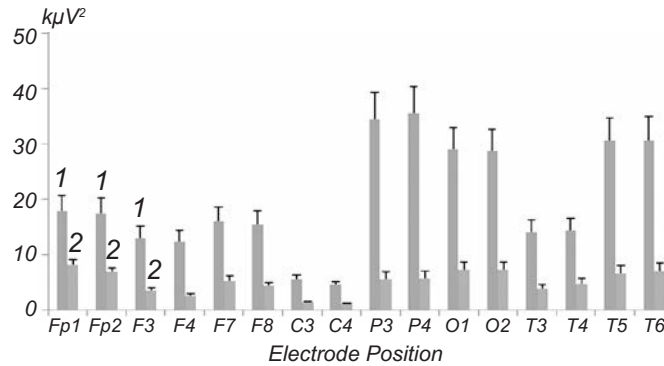


Fig. 4. Mean absolute power of the alpha band under eyes-closed and eyes-open resting condition.

action of a visual input was generally considered a reflection of functional connections of the visual system activating the entire cortex [41]. Neuper and Pfurtscheller [42] reported that the alpha power in the resting state may be interpreted as an index of relative cortical inactivity, while alpha-power suppression usually reflects active cognitive processing [42].

The beta-range power obtained the lowest readings among all other frequency powers, on average, for both eyes-closed and eyes-open conditions. According to Fig. 4, both the highest and the lowest beta powers occurred during eyes-open condition, where the highest power (10 kμV²) was at Fp1, and the lowest beta power (below 2 kμV²) was at C3 and C4. The global mean beta power for eyes-closed condition was 6.47 kμV², and that for eyes-open situation was 5.76 kμV². The difference between the global mean powers for both conditions was insignificant. According to statistical analysis, the beta power significantly decreased for eyes-closed condition at prefrontal F_{p1} ($t(49) = -2.441$, $P = 0.018$) and F_{p2} ($t(49) = -2.453$, $P = 0.018$). At the same time, this index significantly increased at F_4 ($t(49) = 2.926$, $P = 0.005$), C_3 ($t(49) = 3.601$, $P = 0.001$), C_4 ($t(49) = 3.691$, $P = 0.001$), P_3 ($t(49) = 5.275$, $P = 0.0...$), P_4 ($t(49) = 5.312$, $P = 0.0...$), T_3 ($t(49) = 2.731$, $P = 0.009$), T_5 ($t(49) = 3.897$,

$P = 0.0...$), and T_6 ($t(49) = 2.587$, $P = 0.013$). The beta-range power was relatively low, as compared to that of other frequency bands.

The beta-band activity is believed to be related to increased attention [43], sensorimotor behavior [44], language processing [45], and memory [46]. Therefore, the beta power was relatively low under resting conditions, as there was minimum activation of the processes mentioned above. The shift of the beta power from posterior to prefrontal sites was observed at the transition from eyes-closed to eyes-open condition. Such shifting of the beta power was compatible with previous research reports, which proposed that the beta-shifting topography reflects an increase in the level of activation related to higher-order processing and integration of visual inputs [11].

According to the results described above, channels Fp1 and Fp2 demonstrated higher power values at the delta, theta, and beta frequencies during eyes-open condition. The alpha power was an exception; it increased profoundly under eyes-closed condition. During eyes-closed condition, channels P3, P4, O1, and O1 showed higher powers of theta-, alpha- and beta-frequency oscillations compared to eyes-closed condition. Also, channels C3 and C4 always showed the lowest EEG power among all other channels, which was below 5.5 kμV². In general, the

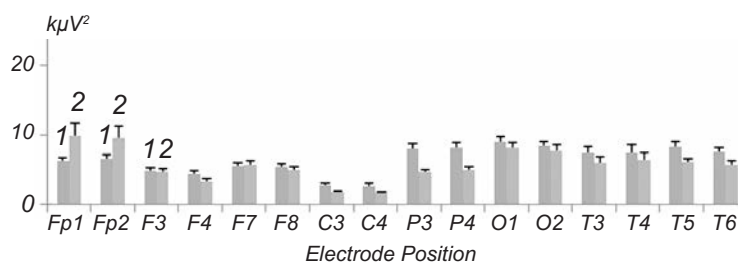


Fig. 5. Mean absolute power of the beta band under eyes-closed and eyes-open resting conditions.

prefrontal area demonstrated higher delta, theta, and beta powers during eyes-open situation compared to eye-closed condition, may be due to activation of the cognitive processes related to activation of the visual system. The prefrontal cortex is associated for executive and cognitive functions with the visual cortical regions [47]. In contrast, the alpha power was higher at the prefrontal area during eyes-closed condition, where the alpha power is dominant at suppression of the visual system. The posterior and occipital cortical lobes are characterized by higher theta, alpha, and beta powers with the eyes closed, while the central lobe always showed the lowest EEG power of those ranges.

Thus, we described the differences in all frequency EEG ranges for both eyes-closed and eye-open conditions in the resting state for euthymic participants. For eyes-closed condition, the alpha band power was observed to be higher significantly throughout all brain regions. Conversely, the delta-frequency power increased at the prefrontal and frontal regions under eyes-open condition. This was the same for the theta frequency; its power increased within the prefrontal region during eyes-open condition. Among all, the beta-frequency band showed a much lower power compared to other EEG rhythms bands in both eyes-closed and eyes-open conditions at the resting stage.

The limitation of our study was that the dimension of the examined participant group was not very large. A greater population is expected to be recruited in the respective study to strengthen the results for future research with detection of depression-associated brainwaves.

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This research was in agreement with the existing international ethical standards and obtained ethical consent approval from the respective Committee in the University Tunku Abdul Rahman. Participation was voluntarily based, and written informed consent was obtained from all participants.

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