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ORIGINAL ARTICLE

Quantitative EEG Changes and Their Relation to Clinical Characteristics in Patients with Migraine

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Abstract

Purpose: This study aimed to identify quantitative EEG changes in migraine patients as compared to a control group, and to explore the relationship between these changes and the clinical characteristics of migraine patients.

Materials and Methods: In this study, a total of 38 participants were recruited from the neurophysiology unit at Ghazi Al-Hariri Hospital. Among them, 18 were healthy individuals with no history of chronic headaches or neurological diseases, and the remaining 20 were diagnosed migraine patients. To provide a clearer understanding of the sample size, the migraine patients were further divided into two groups: ictal and inter-ictal, based on the presence or absence of headaches during the testing. EEG recordings were conducted for 10 minutes each with eyes closed and eyes open conditions. Subsequently, absolute power values for Delta, Theta, Alpha, and Beta brain waves were calculated in each group.

Results: The quantitative EEG analysis revealed a significant decrease in Theta and Beta waves, following a descending pattern from the control group to inter-ictal migraine patients and then to ictal migraine patients. Conversely, Alpha waves exhibited an ascending pattern, increasing from the control group to inter-ictal and ictal migraine patients. When comparing the absolute power of Alpha waves between patients with migraine without aura (M_{woA}) and migraine with aura (M_{wA}), the results demonstrated that during closed-eye conditions, Alpha waves were higher in M_{wA} than in M_{woA}. However, under open-eye conditions, the Alpha wave amplitude significantly decreased in M_{wA} compared to M_{woA}, during both ictal and inter-ictal phases.

Conclusion: Neurophysiological abnormalities have been identified in the brains of migraine patients. Comparing quantitative EEG results between migraine patients with aura and those without aura, it was found that Alpha waves were more responsive to EEG tasks in migraine patients with aura, both during inter-ictal and ictal phases.

Keywords: Quantitative Electroencephalogram; Migraine without Aura; Migraine with Aura; Absolute Power.

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1. Introduction

Migraine is a chronic intermittent primary headache disorder that has a significant impact on public health and individual well-being. Its global prevalence ranks it as the second leading cause of disability, affecting approximately 12% of the worldwide population [1]. Manifesting recurrent episodes of moderate to severe unilateral headaches, migraine is often accompanied by distinct symptoms such as nausea, photosensitivity, phonophobia, and disruptions in sensory processing [2, 3].

The etiology of migraine has been a subject of ongoing scientific inquiry. Originally considered a neurovascular anomaly, current theories suggest that a sequence of neural events initiates pain and subsequent nerve activation [4]. A growing understanding highlights the involvement of dysfunctions in the hypothalamic-hypophysial axis in the pathogenesis of primary headache syndromes, with initial migraine symptoms possibly indicating transient hypothalamic abnormalities [5]. This neural dysfunction affects both peripheral and central components of the trigemino-vascular system, leading to the release of inflammatory mediators that sustain and propagate pain. Calcitonin Gene-Related Peptide (CGRP), a crucial neuropeptide, significantly contributes to trigeminal nerve dynamics [6].

The Headache Classification Committee of the International Headache Society has standardized the clinical classification and diagnosis of migraine [7]. Among the various subtypes, two predominant forms warrant attention:

Migraine without aura: Prevalent in two-thirds of cases, this subtype engenders unilateral headache episodes with durations spanning four hours to three days. Pulsating pain of moderate to severe intensity, often coupled with manifestations like nausea, photophobia, and phonophobia, characterizes this presentation.

1. Migraine without aura: This subtype, prevalent in two-thirds of cases, involves unilateral headache episodes lasting from four hours to three days. These episodes are characterized by pulsating pain of moderate to severe intensity, often accompanied by symptoms like nausea, photophobia, and phonophobia.
2. Migraine with aura: Representing one-third of migraine cases, this subtype includes premonitory signs preceding the headache phase. Aura manifestations encompass speech impairment, dizziness, visual disturbances, sensory abnormalities, and, occasionally, loss of consciousness. Following the aura, headaches occur, accompanied by further migraine symptoms. The mechanism of Cortical Spreading Depression (CSD) is considered the underlying electrophysiological basis [7].

The Electroencephalogram (EEG), a non-invasive tool, records spontaneous cerebral electrical activity through scalp electrodes [8]. Offering accessible and secure monitoring, EEG analysis involves the examination of discrete frequency bandwidths that correspond to distinct neural states and cognitive functions [9-11].

Several key EEG frequency ranges are identified within the spectrum:

- Delta wave (0.5 to 3.9 Hz): Predominant during sleep and specific continuous-attention tasks.
- Theta wave (4 to 7.9 Hz): Associated with drowsiness, sleep onset, and cognitive inhibition.
- Alpha wave (8 to 12.5 Hz): Predominant in posterior cerebral regions during eye closure and mental relaxation, decreasing with eye-opening and cognitive engagement.
- Beta wave (12.6 to 30 Hz): Prominent in children and young adults, often associated with heightened cognitive activity and anxiety.
- Gamma wave (30 to 80 Hz): Thought to indicate coordinated neural engagement during focused motor or cognitive tasks.

Quantitative EEG involves the mathematical analysis of digital EEG data, providing parameters for comparative assessments [12]. Unlike conventional EEG analysis, which relies on visual inspection, quantitative EEG offers a more refined approach.

Spectral analysis is a dominant methodology for quantifying EEG data. It involves breaking down complex EEG signals into constituent frequencies and calculating oscillation amplitudes (power) for each frequency range. The cumulative power within each frequency band, known as the power spectrum, offers a metric indicating overall activity within the band [12, 13].

Previous studies have aimed to uncover quantitative EEG changes in individuals with migraine. Notably, Vellieux *et al.* [13] compared the relative power of delta, theta, alpha, and beta bands across various transient neurological deficit disorders, including migraine. Clemens *et al.* [14] examined EEG spectrum data in untreated migraine without aura subjects. Bjork *et al.* [15] explored absolute and relative power, along with asymmetry, within delta, theta, and alpha bands across different cerebral regions. Simultaneously, efforts have focused on identifying clinical differences between migraine subtypes [16-18].

Due to its significant impact on quality of life, migraine holds a crucial position among primary headache disorders. Therefore, a thorough investigation into its underlying pathology and associated quantitative EEG changes is essential. The insights gained from such research have the potential to lead to innovative treatment approaches, ultimately improving therapeutic outcomes for affected individuals.

2. Materials and Methods

2.1. Patients and Control

The study was conducted at the neurophysiology department of Ghazi Al-Hariri Hospital in Baghdad and took place from October 1, 2022, to May 1, 2023. The control group consisted of 18 healthy individuals (12 females and six males) who had no history of chronic headaches or neurological disorders. Their ages ranged from 20 to 34 years, with a mean age of 26.82±3.66. The patients' group included 20 migraine patients referred from the neurology department of Baghdad Teaching Hospital. Their ages ranged from 20 to 55 years, with a mean age of 29.45±8.44. Inclusion criteria involved both male and female patients diagnosed with migraines according to the International Classification of Headache Disorders, Third Edition (ICHD-3). Exclusion criteria included patients with acute or chronic neurophysiological disorders, malignancy, prior craniotomies, or the use of neuroactive substances. All patients provided verbal consent after receiving a detailed explanation of the protocol. Ethical approval was obtained from the ethical committee of the College of Medicine at the University of Baghdad.

2.2. Methods

The methodological framework of the present study included several key procedures: history taking, EEG recording, and quantitative EEG analysis using the Fast Fourier Transform.

At the beginning of patient interaction, a thorough history was gathered, covering essential social information such as age, gender, marital status, and occupation. Additionally, inquiries were made about the timing of headache occurrence, its frequency, duration, and accompanying symptoms such as blurred vision, numbness, tingling, weakness, difficulties with concentration, speech impairments, or loss of consciousness. Subsequently, patients were divided into two distinct groups: group I (ictal) comprised individuals experiencing active headaches during the EEG recording, while group II (inter-ictal) consisted of those who were not experiencing pain at the time of recording.

EEG recording was conducted using a Natus EEG machine and Nicoletone N EEG software version v5.95.1.17. A total of 21 electrodes were accurately positioned on the scalp according to international (10-20 System) standards, ensuring precise electrode placement between auricular landmarks and spanning the anterior-posterior dimension from the nasion to the inion.

Spectral analysis through the Fast Fourier Transform was performed on 4-second epochs that were free from artifacts. Absolute band power (UV^2) was determined by averaging power across frequency bins within the Delta (0.5–3.9 Hz), Theta (4–7.9 Hz), Alpha (8–12.5 Hz), and Beta (12.6–30 Hz) frequency ranges.

Calculation of average regional values encompassed occipito-prietal (P3-O1, P4-O2), temporal (T3-T5, T4-T6), and fronto-central (F3-C3, F4-C4) regions. This yielded quantitative EEG metrics for analysis, as shown in Figure 1, which includes both (a) a Fast Fourier Transform (FFT) analysis for migraine patients and (b) a Fast Fourier Transform (FFT) analysis for the control group.

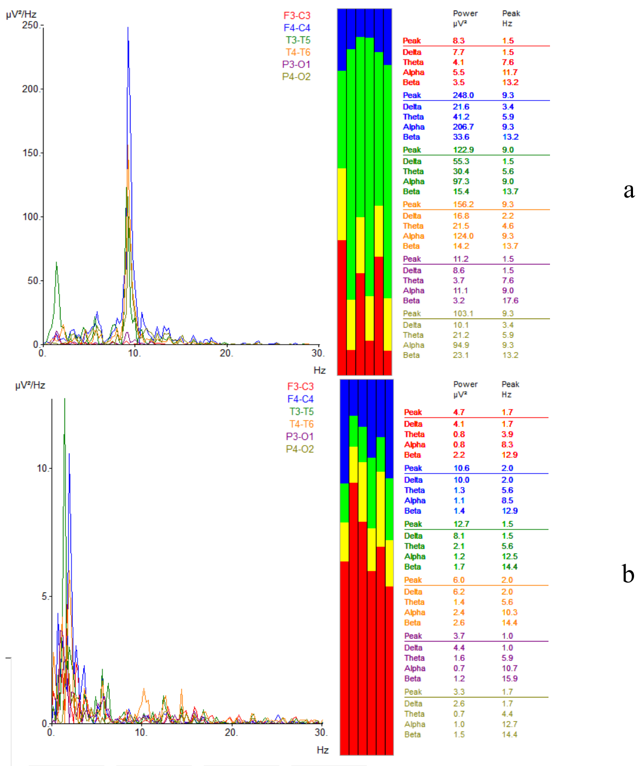

Figure 1. (a) A fast Fourier transform (FFT) analysis for migraine patients. (b) A fast Fourier transform (FFT) analysis for control

2.3. Statistical Analysis

Data manipulation and analysis were conducted using IBM SPSS Statistics (Statistical Package for Social Sciences) version 20. Descriptive statistics were employed to present numerical data, including means and standard deviations (mean±SD), while nominal data were presented using frequency and percentage calculations.

To investigate differences in means among the inter-ictal, ictal, and control groups in terms of demographic and clinical attributes, a one-way ANOVA test was performed.

Calculation of absolute power for each wave (mean, median, and SD) was carried out using the MATLAB statistical tool. The Kruskal-Wallis test, an extension of the Mann-Whitney U test that allows comparisons among more than two independent groups, was used as a nonparametric alternative to the one-way ANOVA.

The significance threshold was set at $p \leq 0.05$, where $p > 0.05$ indicated non-significance and $p \leq 0.001$ indicated high significance.

3. Results

The demographic profiles of the study participants are illustrated in Table 1. The sample consists of 20 migraine patients, categorized into 10 ictal and 10 inter-ictal cases, along with 18 healthy controls. An analysis of the data reveals that there are no significant differences in terms of age, gender distribution, presence or absence of aura, headache history, frequency, duration, or severity across the groups. However, a notable distinction is observed in the years of education, with a statistically significant variance between the patient and control groups (p-value = 0.001).

Table 1. Demographic and clinical information of the study groups

		Ictal (n=10) (Mean, SD)	Interictal(n=10) (Mean, SD)	Control (n=18) (Mean, SD)	P-value
Age (years)		31.7±10.47	27.2±7.37	26.82±3.66	0.20
Gender (No&%	**Male**	7(35%)	6(30%)	11(31.4%)	0.82
	Female	13(65%)	14(70%)	24(68.6%)	
Years of education		10.25±3.88	11.20±3.29	16.00±0	0.001*
MwA (No & %)		5(25%)	6(30%)	-	0.37
MwoA		15(75%)	14(70%)		
Headache history(years)		7.22±7.92	5.30±3.88	-	0.50
Headache frequency (month)		8.78±3.49	7.50±3.77	-	0.45
Headache duration(hours)		3.78±0.83	3.20±1.47	-	0.31
Pain severity (0-10)		7.78±1.09	8.10±1.28	-	0.56

3.1. Quantitative EEG Analysis

The analysis of EEG recordings with eyes open revealed a descending pattern in the powers of both delta and theta waves (Figure 2), decreasing from the control group to the inter-ictal phase and further to the ictal phase. Statistical significance was observed in the powers of delta and theta waves ($p = 0.005, 0.02$), respectively, while the ascending trajectory of alpha wave power exhibited statistical significance from the control group to the inter-ictal and ictal phases ($p = 0.001$). In contrast, beta wave power displayed a descending pattern from the control group to the inter-ictal and ictal groups, supported by a statistically significant p-value ($p = 0.005$).

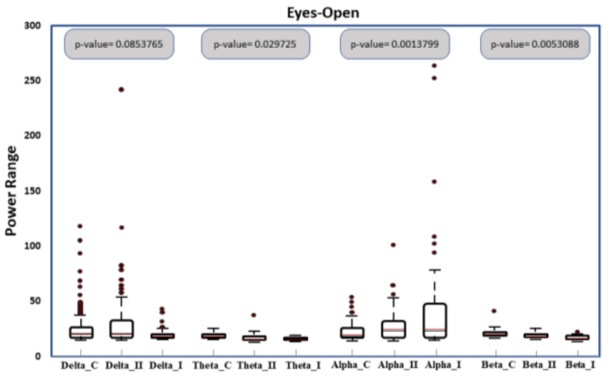

Figure 2. represents the Absolute power (UV)² of delta, theta, alpha, and beta waves for all of I for (ictal), II for (interictal), and C for (control) when the eyes were opened

When the eyes were closed, both delta and theta wave powers showed a decrease from the control group to the inter-ictal phase and further to the ictal phase. Statistical significance was observed in the powers of delta and theta waves ($p = 4.6 * 10^{-5}, 0.02$), respectively. In contrast, alpha wave power exhibited an increased power density in both ictal and inter-ictal migraine patients, with the difference being statistically significant ($p = 1.1 * 10^{-6}$). As for the beta wave, a significant decline was evident from the control group to the inter-ictal and ictal migraine patients ($p = 0.01$) (Figure 3).

3.2. Pain Duration, Frequency, and Severity Comparison between M_{WoA} and M_{WA}

A comparative analysis between migraine patients with and without aura revealed higher pain frequency and severity in the migraine without aura group. Notably, there was no discernible disparity in pain duration between the two groups (Figures 4, 5, and 6).

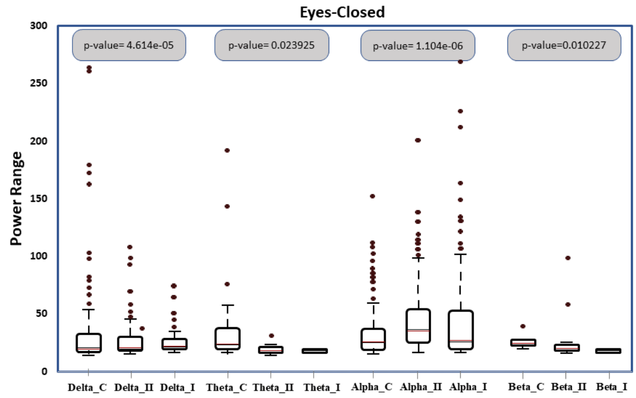

Figure 3. This Represents the Absolute power (UV)² of delta, theta, alpha, and beta waves for all of I for (ictal), II for (interictal), and C for (control) when the eyes were closed

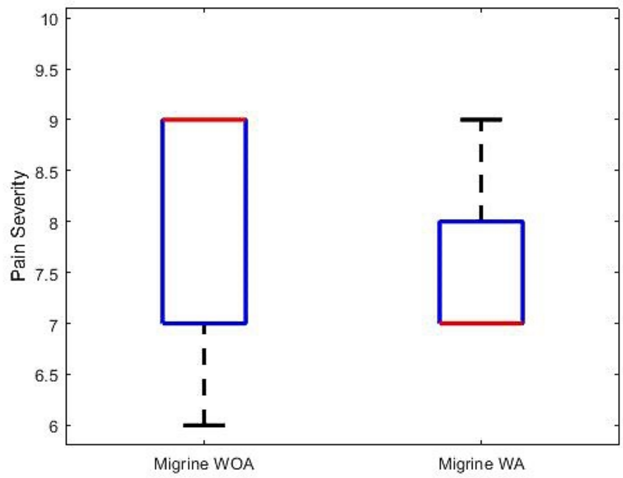

Figure 4. Comparing pain severity between migraine patients with aura and without aura

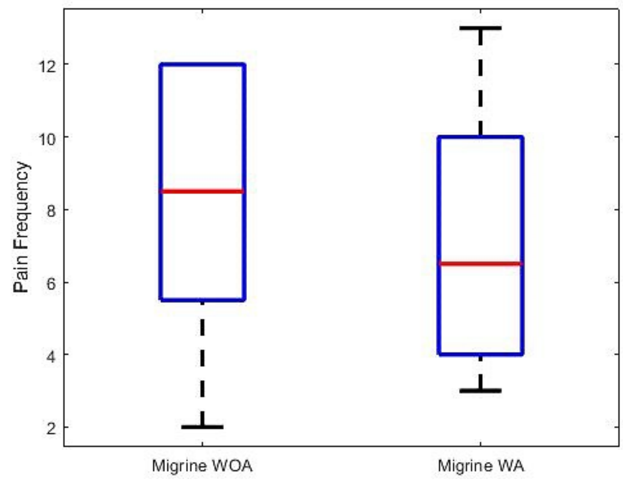

Figure 5. Comparing pain frequency per month between migraine patients with aura and without aura

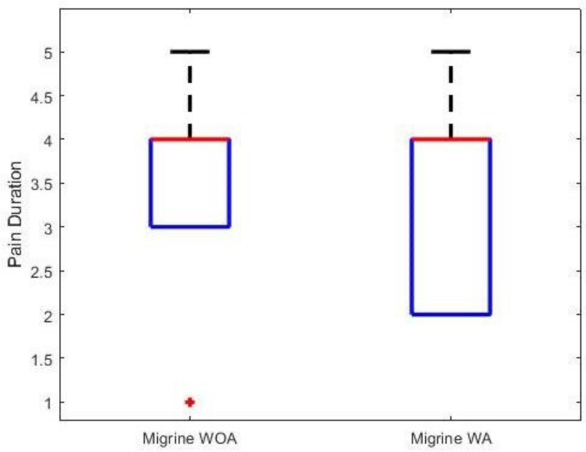

Figure 6. Comparing pain duration in hours between migraine patients with aura and without aura

3.3. Alpha Wave Power in M_{WoA} and M_{WA}

In the examination of alpha wave power, the closure of the eyes led to increased power density in patients with aura, showing a significant P-value during the ictal phase (p = 0.007) (Figure 7 a, b). Conversely, under eyes-open conditions, there was a significant reduction in alpha wave power in M_{WA} during both the ictal and inter-ictal phases, with P-values of 0.005 and 0.0002, respectively (Figure 8 a, b).

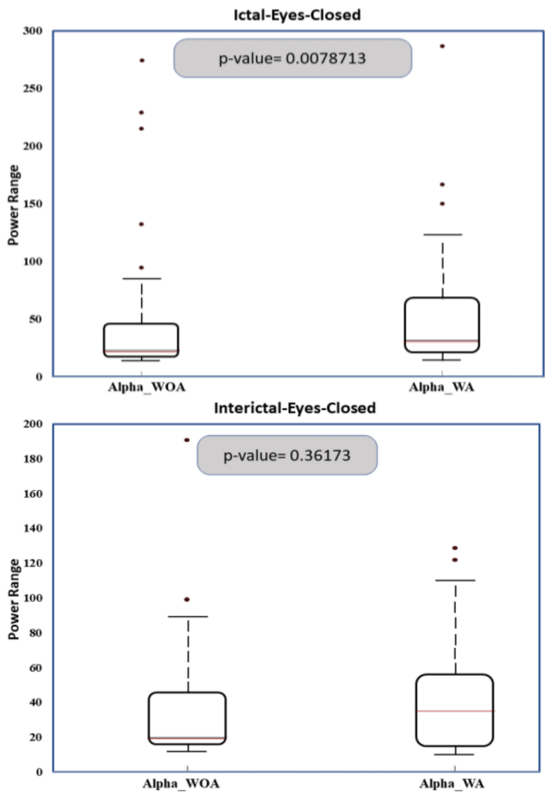

Figure 7. Absolute power (UV)² of the alpha wave between migraine with and without aura during eyes closed in (a) Ictal and (b) inter-ictal phase

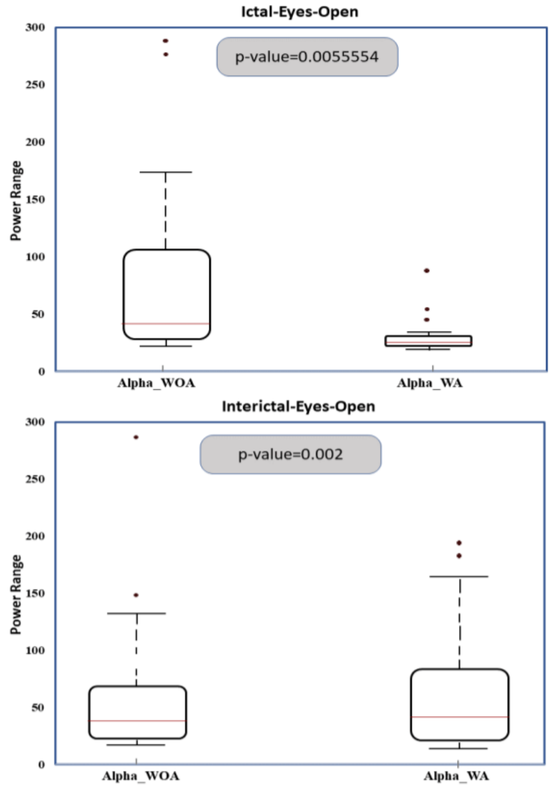

Figure 8. Absolute power (UV)² of the alpha wave between migraine with and without aura during eyes opened in (a) Ictal and (b) inter-ictal phase.

4. Discussion

Migraine, ranked as the second most prevalent disabling disorder, affects approximately 12% of the global population [1]. It is further categorized into migraine with aura (M_{WA}) and migraine without aura (M_{OA}).

The present study aimed to explore quantitative EEG changes in individuals with migraine during both ictal and inter-ictal phases, in comparison with a cohort of healthy controls. Additionally, we sought to investigate potential associations between quantitative EEG alterations and clinical characteristics, such as pain severity, duration, and frequency, in patients with migraine with aura and migraine without aura.

Regarding the quantitative EEG changes observed in migraine patients, a discernible trend emerged in which the absolute power of slow waves (delta and theta) and beta waves exhibited a significant decrease, following a descending pattern from controls to inter-ictal migraine patients, and subsequently to the ictal phase. Conversely, alpha waves demonstrated a statistically significant increase, exhibiting an ascending pattern from controls to inter-ictal and then ictal phases, particularly during pain attacks.

Numerous investigations have been conducted to quantify EEG changes in migraine patients. For instance, one study employed relative power calculations across four EEG frequency bands, revealing a significant elevation in alpha relative power and a concurrent decrease in beta relative power in migraine patients [13]. Similarly, a study analyzing EEG spectrum data in untreated migraine individuals found heightened alpha power, particularly in the right occipital region [14].

Contrasting results have been reported in other research. Authors examining absolute and relative power, as well as asymmetry within specific frequency bands, observed significantly elevated relative theta activity in migraine patients [15].

In our study, a comparison between migraine patients with aura (M_{wA}) and those without aura (M_{woA}) revealed that while M_{woA} patients experienced more frequent and severe headaches, these differences were not statistically significant.

It is noteworthy that previous studies by Rasmussen BK and Olesen J. found that headaches were less severe and shorter-lasting in M_{wA} than in M_{woA} [16], while Antonio Russo and colleagues observed a higher frequency of attacks in M_{woA} patients compared to M_{wA} patients [17]. Additionally, Vani A. Mathru and colleagues reported abnormal extra-trigeminal pain processing correlated with pain intensity and severity in migraine patients with frequent headache episodes [18], consistent with our findings.

Interestingly, our study demonstrated that during headache attacks (ictal phase), the alpha wave exhibited significantly higher power in M_{wA} compared to M_{woA} when the eyes were closed. Conversely, when eyes were open, the alpha wave displayed a significant decrease in M_{wA} patients during both the ictal and inter-ictal phases.

These findings align with research by Perez-Munoz and Andrea, indicating higher alpha wave activity during closed-eye records among migraine sufferers, suggesting potential implications for alpha activity as a cerebral marker for migraines [19]. Coppola G. and colleagues noted cortical hyper-reactivity to sensory stimulation in migraine patients, with greater cortical response observed in MA compared to MO [20], thereby reinforcing our study's outcomes.

A growing body of evidence implicates the brainstem in the pathogenesis of both M_{woA} and M_{wA}. One study identified hyper-perfusion in the brainstem during M_{wA} attacks [21], an area previously associated with attacks in M_{woA} groups [22], or in both M_{wA} and M_{woA} [23]. Furthermore, studies have documented abnormal macrostructure and functional activity in various subcortico-cortical regions, including the somatosensory and neurolimbic areas, periaqueductal gray matter, hypothalamus, thalamus, trigemino-thalamic tract, and visual cortex [24-30].

Although numerous studies have explored structural brain changes in migraine patients, the significance of these alterations in the biology of migraines remains incompletely understood. Nonetheless, the presence of such changes suggests that migraine may contribute to progressive anatomical modifications in the brain, potentially playing a role in disease development and associated disability.

Furthermore, our study contributes to the growing body of evidence implicating the brainstem and various subcortico-cortical regions in the pathogenesis of migraines. Understanding these neurological substrates and their functional alterations may guide future research into targeted treatments for migraine patients.

Despite the valuable insights gained from this study, it is essential to acknowledge its limitations, including time constraints and a relatively small sample size. Future research endeavors involving larger cohorts of migraine sufferers are warranted to validate and expand upon our findings, potentially leading to more precise diagnostic tools and therapeutic strategies for this debilitating disorder.

5. Conclusion

Our study unveiled distinct quantitative EEG patterns in migraine patients compared to healthy controls, specifically indicating reduced slow (delta and theta) and beta waves among migraine patients, alongside heightened alpha waves during the ictal phase. When considering clinical aspects, migraine without aura (M_{woA}) exhibited increased headache frequency and severity in contrast to migraine with aura (M_{wA}). Interestingly, M_{wA} patients displayed enhanced alpha wave reactivity during both inter-ictal and ictal phases, potentially indicating an augmented cortical response. These findings contribute to a deeper understanding of quantitative EEG dynamics in migraines and provide insights into their relationship with clinical characteristics.

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