Detection of Differences between Migraine and Tension-Type Headache from Electroencephalogram Signals

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Abstract

Tension-Type Headache (TTH) and migraine are common disorders all over the world. Some patients with a diagnosis of TTH have clinical symptoms, which are usually seen in migraine. Thus, distinguishing between TTH and migraine can be difficult. Confusion in the diagnosis of migraine and TTH has increased interest in this topic. To eliminate this problem, electroencephalogram (EEG) signals were obtained from healthy volunteers, migraine patients and patients diagnosed with TTH. These signals were analyzed by means of time axis to quantify the differences between healthy, migraine and TTH patients. The obtained features were statistically analyzed to determine whether or not there was any difference between the groups. As a result, it was found that the features obtained from EEG signals can distinguish the migraine and TTH groups successfully.

1. Introduction

Migraine is a common disorder of neurovascular-origin that appears as a pain that can last for an instant or for weeks [1]. It is seen in 15%-20% of males and 23%-29% of females in the world [2]. A migraine patient can have an attack once or twice a month on average [1]. The most common symptom is severe headache and symptoms such as nausea, vomiting, photophobia (hypersensitivity to light), osmophobia (hypersensitivity to smell), and phonophobia (hypersensitivity to voice). Some migraine patients have sensitivity to light or smell that can be felt in the short term; this situation is known as migraine with aura (MwA) [3]. MwA is a new type of migraine is less commonly seen than the other types of migraine. There is no clear conclusion about what causes MwA. However, at least two brain chemicals (serotonin and dopamine) are thought to play a role. Migraine without aura (MwoA) is called simple migraine and is characterized by diffuse or unilateral throbbing headache in the brain. Symptoms are seen intermittently. MwA and MwoA have been shown to possess a genetic factor [4].

The most important factor in the diagnosis of migraine is careful and detailed listening to the patient's description of his/her complaints. Depending on these factors, the medical history of the patient, the age at onset, location, characteristics, accompanying symptoms, and neurological dysfunction of the pain are all important for the diagnosis [5]. There is no specific device that can definitively diagnose this disorder. Diagnostic devices such as magnetic resonance imaging, brain tomography and EEG are used for making a diagnosis. Although the EEG method seems to have lost its significance compared to other devices, it is still widely used in neurology clinics [6]. Because, EEG is non-invasive and harmless, this method is used frequently in practice. Also, there are studies which used EEG signals for the diagnosis of migraine [7-9].

TTH typically occurs in the frontal or occipital region of the brain and is characterized by mild to moderate bilateral pressure or squeeze pain [10]. Unlike migraine, there are no symptoms of nausea or vomiting, but there may be photophobia or phonophobia. TTH is a "featureless" headache, which means that it is diagnosed especially in case of the absence of migraine symptoms in headache types [11]. However, some patients diagnosed with TTH also have clinical symptoms, which are usually seen in migraine. Thus, to distinguish between TTH and migraine can be difficult [12,13]. Unfortunately, there are no comprehensive, useful studies to determine specific diagnostic criteria for TTH [13].

TTH is the most common headache type in the world. Despite advances to understand the complex mechanisms of the pathogenesis of TTH, a clear indication of what is unique to TTH has not as yet been found. There are very few studies on TTH compared to migraine. As a result, the pathophysiology of the disorder is not fully understood. TTH is an important headache type because it is more common in society [14]. For this reason, identifying the distinctive features of TTH should be a priority task.

It was stated in some literature studies that the EEG signals is used to diagnosis of the migraine. Due to the sensitivities of migraine patients to light, it is assumed that migraine can be detected from EEG signals during photic stimulus. In addition, although the EEG gives quantitative information for diagnosis of migraine, distinguishing of between the migraine patients and healthy individuals from EEG signals is still a problem [15]. There are feature extraction and classification studies in the literature to diagnose migraine from EEG signals. In some studies, EEG signals obtained from migraine patients and healthy individuals were analyzed using Wavelet Transform (WT) [16], Short Time Fourier Transform (STFT) [17], Hilbert Transform [18], cross correlation [19], Welch method [20], Autoregressive methods [21] and Fast Fourier Transform [22]. In classification studies, Support Vector Machines [21] and Neural Networks [23] were used usually. Despite there are considerable number of studies to diagnosis of migraine, it appears that new techniques are needed to determine the association of migraine and EEG signals.

Another problem increased the interest in this topic is that making mistakes for diagnosis of migraine with TTH. However, there have been limited studies on this topic in the literature. In a study, non-linear analysis of signals recorded from temporal

muscles using surface EMG was used to obtain new diagnostic criteria for determination of TTH and migraine patients [24]. Many studies have been in the form of statistical analysis of categorical variables based on the stories of patients, level of serum biomarkers, or transient threshold assessment to distinguish two separate stimuli applied in the same region [25,26].

To the best of our knowledge in recent times, studies on this subject are very few, and there are limited EEG signal processing studies. Therefore, in this study, EEG signals were obtained from healthy volunteers, migraine patients and patients diagnosed with TTH. These signals were analyzed by means of time axis to quantify the differences between healthy, migraine and TTH patients. The obtained features were examined to determine whether there was any difference between the statistically analyzed groups.

2. Materials and Methods

The EEG is a widely used medical test device that detects abnormal electrical activity in the brain. Important advances in the neuro science, effective signal processing algorithms and clinical-focused diagnostics and research have made it easier to switch between personal health practices. It is clear in the literature that EEG will be a promising future for monitoring the health of daily life. The Ag / AgCl electrodes, which can easily be attached to the person and can be easily applied by the person himself / herself, are the most common electrodes for recording the EEG signals from the skin of the head in clinical context. However, proper skin preparation and electrolyte application must be performed to ensure that a high-quality EEG signal is obtained [27].

The EEG signals have a complex structure and are difficult to interpret. The visual analysis of these signals is inadequate, as they are interpreted by a specialist physician in the field, as they are both time-based and have long-term records. In order to overcome this disadvantage, EEG signals must be analyzed with appropriate signal processing methods [28].

2.1. Data Acquisition

In this study, EEG signals were obtained from 39 patients with TTH diagnosis, 30 migraine patients and 21 healthy volunteers in the Neurology Department of Kayseri Training and Research Hospital. Most migraine patients in the study are MwoA patients. Migraine and TTH volunteers were diagnosed according to the International Headache Society (IHS) guidelines. The results of the evaluations are as follows: those with a chronic illness (hypertension, diabetes, chronic liver, kidney, lung disease hematologic disease, etc.), chronic migraine and episodic headache, prophylactic treatment, ischemic risk factor, hematologic disease, Patients with an acute or chronic infectious condition and those taking antibiotics, intracranial space-occupying lesions, malignancies, pregnancy stories, anemia or polycythemia within the last 1 year, surgical operations in the past 6 months were not included in the study. In addition, alcohol and cigarette smokers, individuals who take anticoagulants and anti-inflammatory treatment, systemic corticosteroids, individuals who have systemic inflammatory disease were excluded.

Volunteers were identified according to the inclusion and exclusion criteria. The records were obtained as bipolar with electrodes placed according to the 10-20 system as shown in Fig. 1. The data were sampled with 200 Hz sampling frequency and obtained from 16 channels.

The EEG signals were recorded with a photic stimulus. The frequency of the flash light used as an actuator is selected as 10 Hz. The records were taken approximately 4-5 minutes in total, with resting state with eyes open for the first 2 minutes, followed by a 10 second flash stimulus, followed by 10 seconds resting state with eyes open and last rest for about two minutes.

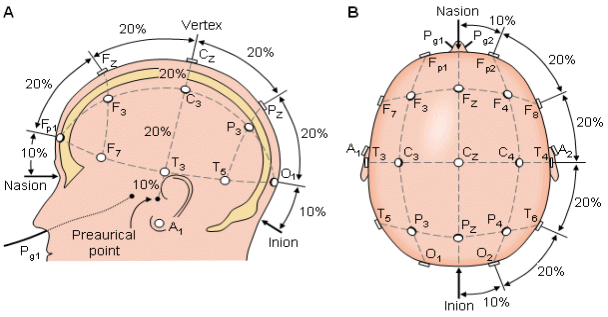

Fig. 1. The international 10-20 system [29].

Table 1 lists the channel names of the 16-channel EEG. In Fig. 2, the names of the regions where the electrodes are placed for 10-20 system are given.

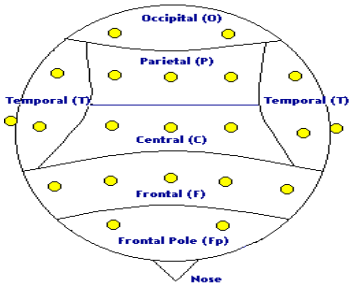

Fig. 2. International 10-20 Electrode Placement System [30]

Table 1. Channels and positions

Channel number	Bipolar electrode position	Channel number	Bipolar electrode position
1	Fp1-F7	9	Fp2-F4
2	F7-T3	10	F4-C4
3	T3-T5	11	C4-P4
4	T5-O1	12	P4-O2
5	Fp1-F3	13	Fp2-F8
6	F3-C3	14	F8-T4
7	C3-P3	15	T4-T6
8	P3-O1	16	T6-O2

2.2. Method

Stages of study is given in Fig. 3. Firstly, the EEG signals were filtered with a low pass butterworth filter at filter order 5, with a cutoff frequency of 30 Hz. The purpose of this filtering is to reduce the effect of electrooculography signals because, the eyes are open during recording. So, the result of the analysis will be more accurate. In this study, all the EEG channels are studied. Features were obtained from the filtered signals selecting certain intervals of signals and calculating the

correlation coefficient. The relation between the two data is determined as features because the correlation coefficient describes relation between signals as numerical value the best. When the studies in the literature are examined, it is seen that the EEG signals obtained from the migraine patients were analyzed using frequency domain features. In this study, the reason for the extracting of the correlation coefficient as a feature is that, EEG signals obtained from migraine and TTH patients have not been studied in time domain much for evaluation of these two diseases. For this reason, correlation analysis was performed to understand whether the photic stimulation on the time axis would cause a change in the signal or not. Statistical analysis results were interpreted to understand whether the correlation feature is considered a selective feature to distinguish migraine and TTH. The extracted features are as follows:

• *First feature*: Correlation between the first 10 second duration EEG signals and 10 second duration of during photic stimulus.

• *Second feature*: Correlation between the 10 second duration of photic stimulus and after the photic stimulus 10 second duration signal.

• *Third feature*: Correlation between the last 10 seconds duration of the signal and 10 seconds duration of during the photic stimulus.

In this study, the correlation feature is used because it allows us to interpret the similarity of the data. Thus, the similarity of EEGs of migraine, TTH and healthy individuals will be discussed.

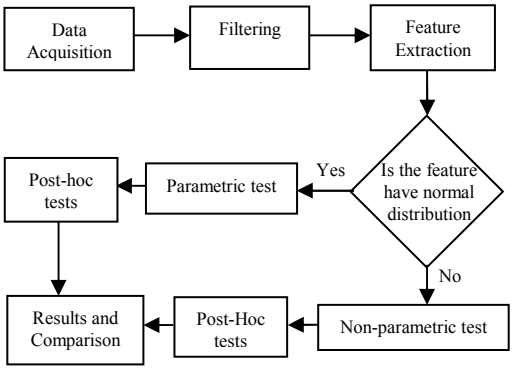

Fig. 3. Flowchart of work

Cross correlation is a method of estimating the degree to two series correlated. Consider two signal x(n) and y(n) where n=0,1,2...N-1. The cross correlation $r_{xy}(k)$ at shift or lag parameter k is defined as Equation 1 [31].

$$r_{xy}(k) = \sum_{n=-\infty}^{\infty} x(n)y(n-k) \qquad k = 0,\pm1,\pm2,..... \tag{1}$$

In the first equation, when y(n) = x(n) is called autocorrelation and it provides measure of self-similarity. For any k, normalized cross-correlation coefficient can be examined as equation 2. r_{xx} and r_{yy} are autocorrelation for time series [31].

$$c_{xy}(k) = \frac{r_{xy}(k)}{\sqrt{r_{xx}(0)r_{yy}(0)}} \tag{2}$$

$$-1 \le c_{xy}(k) \le +1 \tag{3}$$

As seen in equation 3, the correlation coefficient get value between minus one and one, if correlation coefficient close to one, then two signals are similar (they almost overlap) and if the correlation coefficient is close to zero, the signals are very different (orthogonal as the matter of fact). If the correlation coefficient is close to minus one, the signals are similar (opposite direction) [31].

3. Results

In this study, for each of the 16 EEG channels, 3 features (16x3 = 48 feature set) were calculated. Statistical analysis was carried out to determine whether or not the features are different in EEGs obtained from migraine, TTH, and healthy individuals. Firstly, normal distribution was determined using the Kolmogorov-Smirnov and Shapiro-Wilk methods for the obtained features in the groups. The reason for applying these tests is to decide whether to use parametric or non-parametric methods for statistical analysis. If the data have normal distribution, the variances are homogeneous, and the subjects are independent of each other, parametric methods should be selected. Parametric methods are stronger and more flexible than non-parametric methods. However, this does not mean that parametric methods should always be preferred. If parametric methods are applied to the data but the data does not satisfy any of the three conditions specified, it is wrong to accept the results obtained as correct [32]. The results of the Kolmogorov-Smirnov and Shapiro-Wilk tests show that the features obtained from some channels of EEG records don't have normal distribution. According to this, parametric tests were applied to normal features and non-parametric test for non-normal features. The Kruskal-Wallis test was selected for non-normal features and one-way ANOVA for normal features. Only statistically significant features were given in the tables. The results of these statistical analysis methods are shown in Table 2 and Table 3 for features calculated with a significant value between the migraine, TTH and healthy groups. The F value in Table 2 is obtained by dividing the average of squares between groups by the average of squares within groups. The F-value gives information about the distinction of the features between the groups [32].

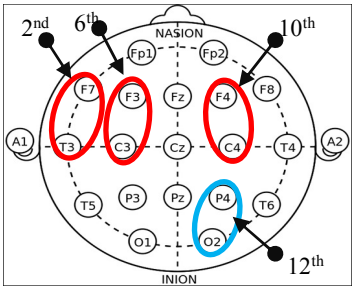

Fig. 4. The channels whose features are statistically significant

Table 2. One-Way ANOVA test

Feature	Channel	F	Significant (p)
Second feature	10	4.308	0.017
First feature	12	3.333	0.040

Table 3. Kruskal-Wallis test

Feature	Channel	Chi-Square	Significant (p)
Second feature	2	6.480	0.039
Third feature	6	9.014	0.011

Significant differences between migraine, TTH patients and healthy subjects were obtained by parametric and nonparametric tests are shown in Tables 2 and 3. Post-hoc tests are applied how to find the differences between two groups in pairs. Therefore, post-hoc analysis should be done to compare migraine and TTH diseases or to compare TTH patients and health subjects. In parametric methods, post-hoc tests were done using ANOVA method. In non-parametric methods, groups were analyzed using the Mann-Whitney U test in duplicate. The results of these methods are given in Table 4 and Table 5. Unlike Table 2 and Table 3, all the results with or without significance are given in Table 4 and Table 5.

Table 4. One-way ANOVA post–hoc test

Feature	Channel	Groups	Significant (p)
Second feature	10	TTH-Migraine	0.046
		TTH-Healthy	0.924
		Migraine- Healthy	0.034
First feature	12	TTH-Migraine	0.729
		TTH-Healthy	0.167
		Migraine- Healthy	0.034

Table 5. Mann-Whitney U test

Feature	Channel	Groups	Significant (p)
Second feature	2	TTH-Migraine	0.231
		TTH-Healthy	0.007
		Migraine- Healthy	0.295
Third feature	6	TTH-Migraine	0.146
		TTH-Healthy	0.089
		Migraine- Healthy	0.002

4. Conclusions and Discussions

In this study, we aimed to determine whether the signal processing techniques applied to EEG signals could be used for the determination of migraine and tension type headache, which constitute a large part of primary headache types. This issue has been studied because there are not enough works in the literature. In literature, some of migraine studies using EEG signals are shown in Table 6. To the best of our knowledge, migraine and TTH cannot be classified using EEG signals. Determination of migraine and TTH is very important because these diseases greatly affect the socio-economic life of the individual. EEG is used for the diagnosis of many brain disorders or for investigation by researchers. It is a commonly used method in neurology clinics. There are many studies in the literature which use EEG to diagnose migraine, but there is no study on how to distinguish migraine from TTH by using signal processing from EEG signals. For this reason, in this study, we tried to find features from the EEG signals which can be used primarily to determine migraine, TTH and healthy individuals. The EEG signals were obtained by applying 10 Hz photic stimulation to the volunteers. Cross-correlation values were calculated, and we examined whether these values have significant differences between the three groups. When Table 4 and Table 5 are examined, a significant difference between TTH and migraine ($p = 0.046<0.05$) was obtained for the second feature (correlation between the signal during photic stimulus and the signal during after photic stimulus for 10-second duration). This indicates that photic stimulation differs significantly in the EEG signals obtained from migraine and TTH patients. The second feature obtained from the TTH and healthy subjects shows a significant difference ($p = 0.007<0.05$). The channels in which the features are statistically significant are shown in Fig. 4. The majority of channels with a statistically significant feature were obtained in the frontal region. This suggests that the frontal region may help to distinguish migraine from TTH. Migraine patients and healthy individuals were determined by all features calculated from EEG signals. This supports the studies in the literature. The difference between migraine patients and TTH patients was obtained only in the first feature. It is not enough to distinguish two diseases. In future work, we will aim to increase the number of volunteers and to use several signal processing methods with various classifiers, to reveal the differences between migraine and TTH.

Table 6. Literature review

Ref.	Subject	Method	Stimuli	Results
[15]	normal and migraine adults	STFT	5 to 20 Hz photic	more dispersed frequency signal in migraine patients
[20]	17 heathy subjects 9 migraines 5 pregnant women	Welch, Modified Covariance	No	$p<0.05$
[23]	16 MwoA patients 15 control subjects	WT	No	$p<10^{-4}$
[33]	30 migraine patients 30 healthy subjects	Independent Component Analysis	4 Hz photic	Classification success rate increased by 5%
[34]	50 migraine patients (children) 50 TTH patients (children)	Sex, age, abnormality rates etc. features	2, 5, 6, 8, 10, 13, 16, 18, and 21 Hz photic	$p<0.05$
[35]	11 migraine patients (women)	Alpha band phase synchronization	3, 6, 9, 12, 15, 18, 21, 24, and 27 Hz flash	p=0.0001 90:9% accuracy
proposed	39 TTH patients 30 migraine patients 21 healthy subjects	Correlation analysis	10 Hz photic	$p<0.05$

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