

## ELECTROENCEPHALOGRAM AND VISUAL EVOKED POTENTIAL CHANGES Study IN PATIENTS PRESENTED WITH PRIMARY HEADACHES

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### **ABSTRACT:**

#### **Background:**

A headache is pain anywhere in the region of the head or neck. The most common types of primary headaches are migraines and tension-type headaches. They have different characteristics. Migraines typically present with pulsing head pain, nausea, photophobia (sensitivity to light) and phonophobia (sensitivity to sound). Tension-type headaches usually present with non-pulsing "band like" pressure on both sides of the head, not accompanied by other symptoms. Other very rare types of primary headaches which included, Cluster headaches, Trigeminal autonomic cephalgia and Chronic daily headaches.

#### **Objectives:**

The aim of this study to evaluate the role of visual evoked potential and electroencephalography in patients presented with primary headaches (migraine and non-migraine) and to determine the frequency of these abnormalities and to investigate the relationship between other variables such as age, gender, type of headache.

#### **Material and Methods:**

This study was a cohort study in which a total of (450) subjects, into (150) with primary headache (male and female) and this was included in this study, 128 with migraine headache, 22 with non-migraine headache and 300 were normal, as control group. The electrophysiological tests were done at the neurophysiology unit of Mirjan Teaching hospital in Babylon City, during the period from 28 / October/ 2014 until 22 / May/2015. Electroencephalography and Visual evoked potential were performed for the patients and control in parallel. We recorded Latency, waves morphology and amplitude in migraine with and without aura and non-migraine included, tension, cluster, trigeminal autonomic cephalgia and chronic daily headaches.

#### **Results:**

This study reveals that involvement of the migraine are more than that of the non-migraine in headache patients when compared with control group and when compared between the migraine and non-migraine headache patients. The most common EEG changes in headaches patients were diffuse slowing and spike wave of back ground activity, in such a way that 54 (42.2%) migraine patients had abnormal EEG changes, in comparison to 4 (18.2%) of non-migraine patients. Visual evoked potential (VEP) was dependable marker for central nervous system affection in primary headache (migraine and non-migraine) and the most common abnormalities were prolonged latency and amplitude is stay in normal ranged (5-10)  $\mu$ .volt.

#### **Conclusion:**

This study stated that EEG, the significant abnormal findings in patients with migraine headaches are more than patients with non-migraine headaches. The abnormal EEG findings in migraine patients were found mainly during hyperventilation and photic stimulation. Epileptic discharge were found in about of the whole migraine patients represented by spike and wave, polyspike and sharp waves respectively, 25.69%, 12.69%, 12.69%. In VEP, regarding the latency of P75, N100 and P 145 there were significantly higher in patients with headache in compared to the control group, while there were no significant changes related to the amplitude..

### **INTRODUCTION:**

Headache is defined as a pain arising from the head or upper neck of the body. The pain originates from the tissues and structures that surround the brain because the brain itself has no nerves that give rise to the sensation of pain (pain fibers) (1). Headaches can radiate across

the head from a central point or have a pinching vise-like quality. They can be sharp, throbbing or dull, appear gradually or suddenly and last for multiple days or less than an hour (2).

All headaches are considered primary headaches or secondary headaches. Primary headaches are

not associated with other diseases. Examples of primary headaches are migraine headaches. Typically the headache affects one half of the head, is pulsating in nature, and lasts from 2 to 72 hours. Associated symptoms may include nausea, vomiting, and sensitivity to light, sound, or smell. The pain is generally made worse by physical activity (3).

Migraines are believed to be due to a mixture of environmental and genetic factors. About two-thirds of cases run in families. Changing hormone levels may also play a role, as migraines affect slightly more boys than girls before puberty, but about two to three times more women than men (4,5). The risk of migraines usually decreases during pregnancy. The exact mechanisms of migraine are not known. It is, however, believed to be a neurovascular disorder (6). The primary theory is related to increased excitability of the cerebral cortex and abnormal control of pain neurons in the trigeminal nucleus of the brainstem (7).

Migraines can also cause tingling or numbness of the skin. People with severe migraines also have nausea, vomiting and light sensitivity. Medications, certain foods, smells, loud noises and bright lights can all trigger a migraine headache (8).

Visual symptoms and photophobia are common features of migraine, but are not exclusively confined to attacks. Hypersensitivity to environmental light (9) and grating patterns of definite spatial frequency have been demonstrated to persist even between attacks (10,11).

Hypersensitivity to visual stimuli might be related to the faster low-level visual processing that has been described in migraineurs with aura (12).

Migraine is a primary headache disorder and may occur with or without aura (13).

, tension headaches is the most common type of primary headache. The pain can radiate from the lower back of the head, the neck, eyes, or other muscle groups in the body. TTH account for nearly 90% of all headaches (14).

, and cluster headaches is a rare type of primary headache. sometimes called 'suicide headaches'. They occur in clusters, often every day for a number of days or even weeks. Then they disappear for months on end. They are uncommon, and tend to occur particularly in adult male smokers. They are severe, one-sided headaches, which are really very disabling (they prevent regular activity). People often describe them as the worst pain they have ever felt (15).

Daily headache can occur as a CTTH, but it is often a combination of tension-type and migraine (16).

Most often, this type of combination or mixed headache develops in a person who initially had typical episodic migraine but in whom, over several years, a chronic daily or almost-daily headache develops (17).

Trigeminal autonomic cephalalgia (TAC) is primary headache syndromes characterized by severe short-lasting headaches accompanied by paroxysmal facial autonomic symptoms (18).

#### **AIM OF THE STUDY:**

This study was undertaken in order to evaluate the role of visual evoked potential and electroencephalography in patients presented with primary (migraine and non-migraine) headache and to determine the frequency of these abnormalities and to investigate the relationship between other variables such as age, gender, type of headache and clinical signs.

#### **SUBJECTS AND METHODS:**

This study was carried out through the period from October 2014 to May 2015, in the brain alone planning and optic nerve, as well as in consultation nervous in Mirjan Hospital in the city of Babylon. By using the history, as a cross section observational study, we select (150) patients with primary headache, in addition to (300) healthy control subjects. underwent EEG and VEP study with age and sex matched healthy control group should be selected for this study. all of them met the criteria of episodic headache (migraine with, without aura & non migraine) according to the international classification of headache disorder.

Subjects:

#### **Two groups of subjects were studied:**

##### **The control group:**

This group comprised thirty hundred healthy volunteers, (135 males and 165 females) ranging in age from (9 to 67) years, with a mean age of (30.40±7.38) years.

##### **The patients group:**

One hundred and fifty headache patients were selected all types of primary headache in Mirjan Teaching Hospital, they were (43 males and 107 females) ranging in age from (7 to 69) years with a mean age of (31.23±12.38) year.

##### **Methods:**

All the subjects were approved for:

- Electrophysiological tests:
- Visual evoked potential (VEP).
- Electroencephalography (EEG).

##### **Visual Evoked Potentials (VEPs) Study:**

Visual Evoked Potential test was carried out in a dark, quiet room, with the subjects sitting comfortably on a chair, and advised not to move or blink continuously during the test in order to decrease muscle contraction artifacts from eyes and skeletal muscles which blur the evoked

potential waves, thus it is of paramount importance to avoid such artifact.

#### **Instrumentation:**

Using in this study Evoked Potential machine, serial no.GH 17 H9NW315431B, model 171S, (Italy) was used for electrophysiological analysis of the VEP using the VEP program. The VEP system include four channel preamplifiers which are connected to plasma screen as a photo-stimulator source.

#### **Procedure:**

Recording Visual Evoked Potentials:

The subject is call him to sit on the chair while made recording and told him to see in same level of the red point sited in the center of the screen, and the space between his state and the screen is fixed at rate equal to 100 cm.

The patient should asked him to cleaning and lesser his hair then asked him to sleep on the bed then begin applying gel on the surface of electrodes ( to made skin impedance slighter ) on the subsequent positions : on the right side from the beside of the head and about five centimeters from frontal side placed the three electrodes (F7,T3,T5) ,in the anther side(left side) placed the three other electrodes (F8,T4,T6) ,and then placed the five electrodes from the right side also, in frontal side (Fp1,F3,C3,P3,O1) ,and then placed the five electrodes from left frontal side (Fp2,F4,C4,P4,O2) .At the end all of these electrodes were connected to the referential inputs by electrode cables.

#### **Stimulation:**

The full-field checkerboard pattern reversal (black and white checker board pattern), displaying at a rate of 3.5 reversals/ second (Hz). Mean luminance of the screen was fixed at 60-cd/m and contrast level of 100%. With visual angle of 16 (degrees) subtended by the stimulus field. The checkerboard size was selected according to the visual acuity of the subject between 60-90 (minutes). Each eye was stimulated separately by covering the other eye with a gauze patch (Monocular testing). VEP tests were filtered and amplified by the VEP computer program, and averaged of 200 runs according to response clearance. The amplifier band width was 0.1 – 100 Hz, with amplifier sensitivity of 2  $\mu$ V and sweep speed of 500 msec/Div (18). Two series of examination of each eye were done to ensure reproducibility of the traces and results of VEP. During the test, the fixation point of the eye was kept on a target on the center of the screen (red dot), the subjects eye lids were fully opened to allow maximum amount of face and neck muscles, avoiding swallowing, moving tongue, speaking and frequent blinking, in order to minimize the artifacts during the recording procedure (Figure 1).



**Figure(1): Electrodes placement( montage) used in pattern reversal VEP test & 10-20 international Electrodes placement system.**

#### **Electroencephalography (EEG) study:**

Electroneurodiagnostics is the study and recording of electrical activity in the brain and nervous system. Tests are performed by technologists who record information on paper or computer, and the results are then interpreted by a specially trained physician.

Brain cells continually send messages to each other that can be picked up as small electrical impulses on the scalp. The process of picking up and recording the impulses is known as an EEG.

The billions of nerve cells in your brain produce very small electrical signals that form patterns called brain waves. During an EEG, small electrodes and wires are attached to your head. The electrodes detect your brain waves and the EEG machine amplifies the signals and records them in a wave pattern on graph paper or a computer screen . A normal EEG means that you have a normal pattern of brain D wave activity. An abnormal reading means that abnormal patterns of brain activity are being produced and picked up.

#### **EEG Procedure:**

Electrical impulses in the brain are evaluated using an EEG. The test measures this electrical activity through several electrodes placed on your scalp. An electrode is a conductor through which an electric current can pass safely. The electrodes transfer information from your brain through wires to an amplifier and a machine that measures and records the data. The test is administered at a hospital, at your healthcare provider's office, or at a laboratory by a specialized technician. The test usually involves the following steps:

You will be asked to lie down on your back in a reclining chair or on a bed. The technician will measure your head and use a pencil to mark

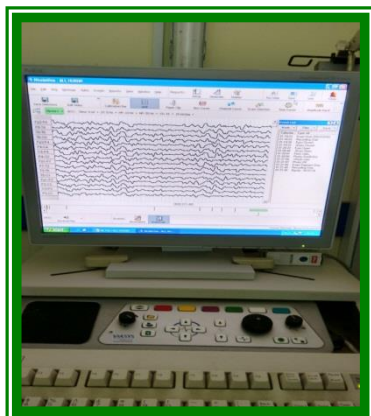
where electrodes will be attached to your scalp. These spots are then scrubbed with a special cream that helps the electrodes get a high-quality reading .

The technician will put a sticky gel adhesive on 16 to 25 electrodes and will place these electrodes at various spots on your scalp. The electrodes look like flat metal disks (Figure 2).



**Figure (2): Electrodes placement ( montage) used in pattern reversal Electroencephalography (EEG).**

Once the test begins, the electrodes send electrical impulse data from your brain to the recording machine. This machine converts the electrical impulses into visual patterns that can be seen on a screen and are saved to a computer. On the screen, the electrical impulses look like wavy lines with peaks and valleys. As show in figure (3).



**Figure (3): Photograph for the EEG system.**

You may be directed by the technician to do certain things while the test is in progress, such as lie still, close your eyes, breathe deeply or quickly, or look at stimuli like a flashing light or a picture.

The EEG usually takes 30 to 60 minutes. After the test is complete, the technician will remove the electrodes. During the test, very little

electricity is passed between the electrodes and your skin. The electrodes do not send any sensations, and you will feel little to no discomfort.

### RESULTS:

In this study is show the overall mean age of patients with headache and control were  $(31.23 \pm 12.38)$  and  $(30.40 \pm 7.38)$  years old, respectively, the distribution of patients and control by sex, (28.7%) and (47.3%) of patients and control were males, as show in the Figure (4).

In this study is show the differences between patients with headache and control by EEG Changes there was significant difference between patients and control by EEG, Patients with headache were 30 times more likely to have abnormal EEG, in the (Table 1).

In this study is shows the differences of patients with headache types and control during hyperventilation and photic stimulation of EEG. 24%, 14.66%, 1%, 1%, as show in the figure (5).

Table (2) shows the Mean Differences of VEP amplitude Parameter by Patients with Headache and Control Groups. There were significant mean differences of VEP Amplitude RT and LT by study groups. Table (3) shows the Differences of Patients with Headache and Control Groups by VEP latency and waves morphology. There were significant differences of Patients with Headache and Control Groups by RT Latency Positive1, RT Latency Negative1, LT Latency Positive1, LT Latency Negative1, RT Latency Positive2, and wave Morphology. Case group were 6, 2, 19, 3, 13 and 24 times to have abnormal right latency 1 positive and negative and left latency 1 positive and negative, right latency 2 positive and abnormal wave morphology, respectively.

In this study is shows distribution of patients by types of headache. (71.30%), (13.3%), (10.0%), (2.7%), (2.0%) and (0.7%) of the patients had migraine without aura, migraine with aura, tension headache, cluster headache, chronic headache and TAC headache, respectively, as show in the figure (6).

In this study is shows The distribution of different EEG abnormalities in different types of migraine. Spike 25.96%, poly spike 12.96%, sharp 12.96%, slow 48.14%, as show in the figure (7). In this study show the distribution of different EEG abnormalities in different types of Non-migraine. Spike 0.0%, poly spike 0.0%, sharp 4.54%, slow 13.63%, as show in the figure (8).

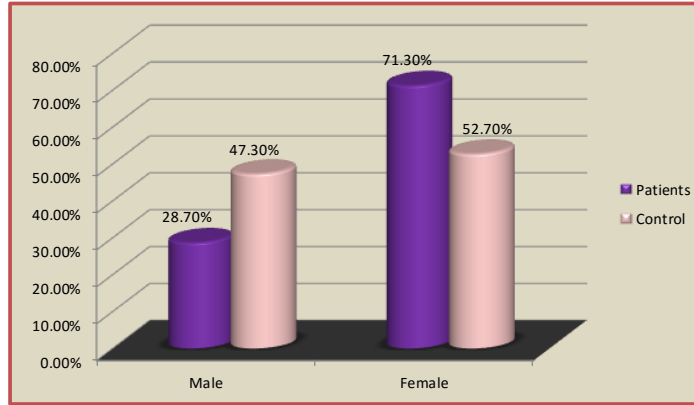


Figure (4): Distribution of patients and control by sex.

Table (1): Differences of Patients with Headache and Control by EEG Findings.

Variable	Study Groups		$\chi^2$	P Values	Odds Ratio (95% C.I.)
	Patients headache (%)	Control			
EEG Normal	92 (61.3)	294 (98.0)	110.20	<0.001*	30.89 (12.91-73.92)
EEG Abnormal	58 (38.7)	6 (2.0)			

\*p value  $\leq 0.05$  is significant  
 EEG = Electroencephalography  
 $\chi^2$  = Chi-Square , C.I. = Confidence Interval

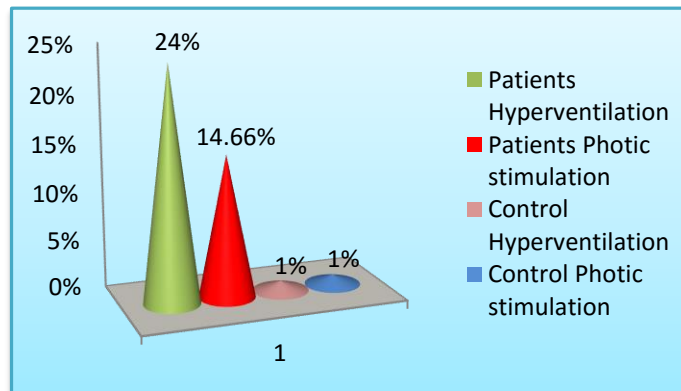


Figure (5): differences of patients and control during hyperventilation & photic stimulation.

Table (2): Mean Differences of VEP amplitude by Patients with Headache and Control Groups.

Variable	Study groups	Mean	S.D	t-test	P value
VEP Amplitude RT ( $\mu$ volt)	Case	7.47	2.25	8.622	<0.001*
	Control	6.22	0.80		
VEP Amplitude LT ( $\mu$ volt)	Case	6.75	1.60	2.876	0.004*
	Control	6.37	1.15		

\*p value  $\leq 0.05$  is significant



VEP = Visual Evoked Potential  
 RT = Right, LT = left  
 S.D = Standard deviation

**Table (3): Differences of Patients with Headache and Control Groups by VEP latency and Waves Morphology.**

Variable	Study Groups		$\chi^2$	P values	Odds Ratio (C.I. 95%)
	Case (%)	Control (%)			
<b>RT Latency Positive1</b> Normal < 75 (m.sec) Abnormal $\geq$ 75 (m.sec)	103 (68.7) 47 (31.3)	281 (93.7) 19 (6.3)	49.938	<0.001*	6.749 (3.783-12.037)
<b>RT Latency Negative1</b> Normal < 110 (m.sec) Abnormal $\geq$ 110 (m.sec)	107 (71.3) 43 (28.7)	262 (87.3) 38 (12.7)	17.344	<0.001*	2.771 (1.696-4.527)
<b>LT Latency Positive1</b> Normal < 75 (m.sec) Abnormal $\geq$ 75 (m.sec)	79 (52.7) 71 (47.3)	287 (95.7) 13 (4.2)	121.79	<0.001*	19.841 (10.45-37.69)
<b>LT Latency Negative1</b> Normal < 110 (m.sec) Abnormal $\geq$ 110 (m.sec)	102 (68.0) 48 (32.0)	261 (87.0) 39 (13.0)	23.148	<0.001*	3.149 (1.948-5.092)
<b>RT Latency Positive2</b> Normal < 145 (m.sec) Abnormal $\geq$ 145 (m.sec)	130 (86.7) 20 (13.3)	99 (33.0) 201 (67.0)	115.24	<0.001*	13.19 (7.78-22.39)
<b>LT Latency Positive2</b> Normal < 145 (m.sec) Abnormal $\geq$ 145 (m.sec)	127 (84.7) 23 (15.3)	265 (88.3) 35 (11.7)	1.197	0.274	0.729 (0.414-1.286)
<b>Wave Morphology</b> Normal Abnormal	120 (80.0) 30 (20.0)	297 (99.0) 3 (1.0)	53.123	<0.001*	24.75 (7.413-82.635)

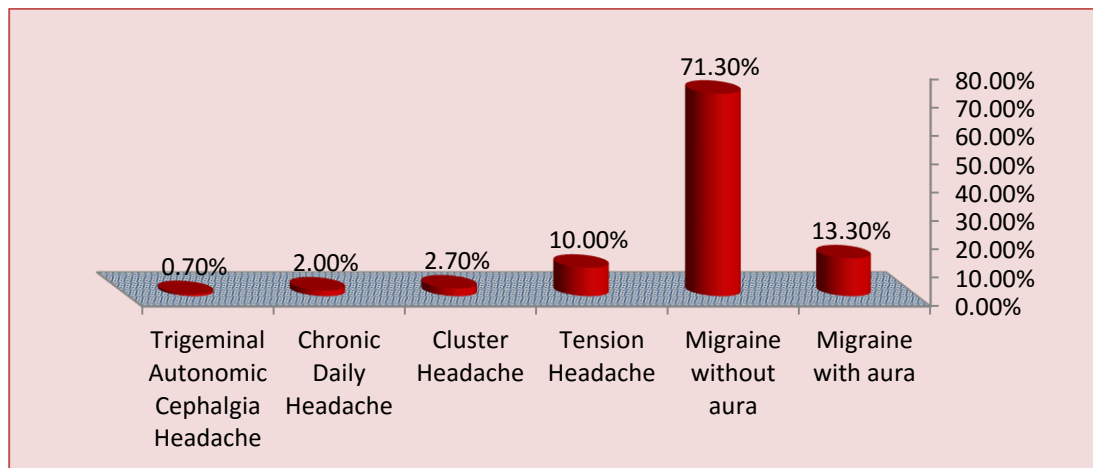
\*p value  $\leq$  0.05 is significant,

\*\*reference group

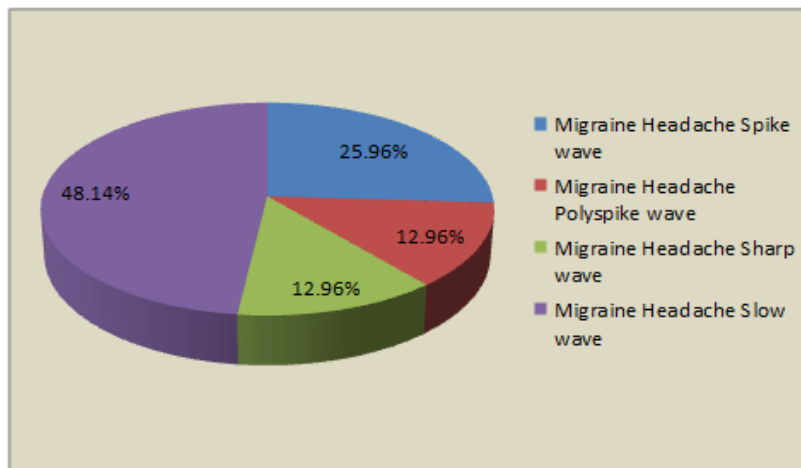
RT = Right, LT = Left

$\chi^2$  = Chi-Square

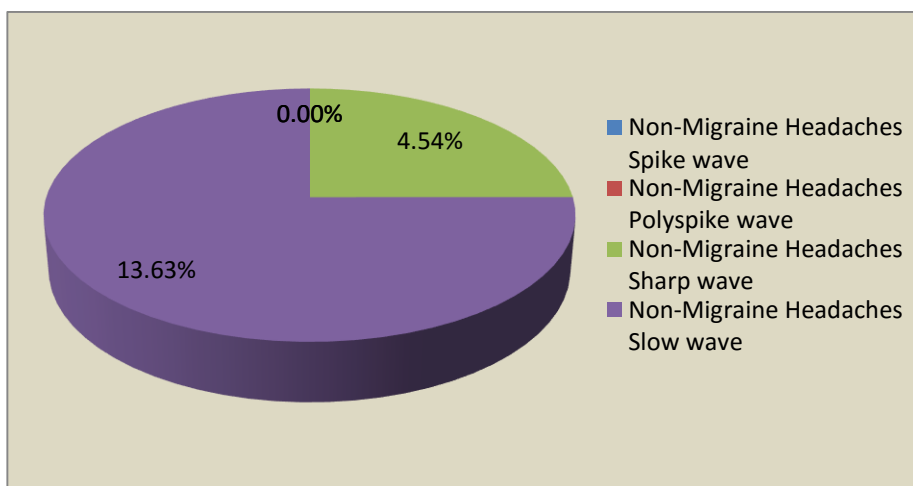
C.I. = Confidence Interval



**Figure (6): Distribution of Patients by types of Headache.**



**Figure (7):** The distribution of different EEG abnormalities in different types of migraine.



**Figure (8):** The distribution of different EEG abnormalities in different types of non-migraine.

### **DISCUSSION:**

Concerning the gender distribution, we have found that migraine is more common in females than males in different age groups at ratio of about 2.3:1. We found in figure (4) that female (47.30%) was susceptible to infected headache more than male (28.70%) in compared to control group. These findings are agreed with (20) who found females 2:1 for headache, as well as with other studies of (21) and also agreed with (22) who found that female to male ratio is about 3:1, but (23) found female to male ratio 3:2, so that there is a significant preponderance in females over males, this may be attributed to hormonal changes that occur in females mainly estrogen (24). we found higher incidence of migraine without aura, then followed by migraine with aura, tension headache, cluster headache, chronic daily headache, trigeminal autonomic cephalgia (TAC). (66.0%), (13.3%), (10.0%),

(2.7%), (2.0%) and (0.7%). This agreement with (Stephen L. Hauser, MD, 2006) who found Migraine without aura is more common than migraine with aura in our study group with ratio of 2:1.

Also agreement with (25) who found the most common types of primary headaches are migraines and tension-type headaches.

Also agreed with (26) who found Of the 94% who consulted their primary care physicians for headache, 76% had migraine and 18% had migrainous headache. Few patients had tension-type headache.

higher frequency of EEG abnormalities in headache patients than in control though the difference was statistically significant (odds ratio = 30.89; C.I. (12.91-73.92)), patients with headache were 30 times more likely to have abnormal EEG. We found 58 of 150 (38.7% abnormal EEG) in patients with

headache, while in control group we found 6 of 300 (2% abnormal EEG). The abnormalities found in EEG study was spike wave, poly spike, sharp wave and slow wave. we found in figure (5) that patients with headaches more effected during the hyperventilation and photostimulation phase than control, (24%) H-response, (48.14%) PS in patients, while (1%) H-response, (1%) PS in control . This agreed with (27) who found increased in hyperventilation and photic stimulation variability (and/ or asymmetry) in the headache-free phase. Also comparable to the study by (28,29) who found The incidence of EEG abnormalities reported above varies from 13-60% depending on the interpretation during HV in migraineurs, the diagnostic standards used and the inclusion of mixed conditions. Also with (30) who found that Prominent photic driving at high flash frequencies (H-response) in migraine patients is the most consistently reported difference between headache patients and controls this similar to the findings of EEG abnormalities in headache were originally described by (31). In the figure (6) the most common EEG abnormalities in migraine headaches group were epileptic and paroxysmal discharges including spike, poly spike, sharp and slow waves. Spike wave was seen in 14 (25.96%) patients & poly spike wave complex in 7 (12.96%) patients & sharp wave in 7 (12.96%) patients & slow wave in 26 (48.14%) patients who have migraine headache, this study which agreed with (32,33) who have found paroxysmal high voltage abnormal slow wave activity in a number of patients and proposed the term dysrhythmic migraine for this group. This study are comparable to the study done by (34) who found slow waves are the most common abnormalities (52.64%) seen followed by sharp waves (42.10%) and spikes (5.26%) in descending order these abnormalities (slow wave, sharp wave and spike) are seen more in migraine with aura. Also These are comparable to the study done by (35) who found that slow waves are the most common abnormality. And also comparable to the Iranian study (36) who found slow waves in 70% of patients, sharp waves in 29% and spikes in 8.4%. These abnormalities were found mainly in occipital region and disagree to the study done by (37)

who found that among 64 migraineurs, 73.4% were abnormal EEG and they found that 27% have slow wave, spikes and sharp waves in 46.6%. in 22 patients who have non-migraine tension headache, sharp wave (4.54%), slow wave (13.63%). Also agreed with (38) who found epileptiform EEG abnormalities in 11% in both migraine and tension headaches. we found the P75 and N100 significantly longer in the study group than the control group ( $p = 0.001$ ). P145 latency was found to be longer in patients with longer duration of disease. Case group were 6, 2, 19, 3, 13 and 24 times to have abnormal right latency positive1 and negative and negative, right latency positive 2 and wave morphology than control group, respectively. N100 latency was found to be significantly longer in patients with aura than the patients without aura ( $p = 0.178$ ). this study was agreed with (39,40) who found higher VEP P1 latencies adult and pediatric patients with migraine, this abnormal VEPs suggested the presence of cerebral hyperexcitability in these patients, increased sensitivity to light and other stimulants resulting from neuronal hyperexcitability has been shown to cause light intolerance in even painless peroids(41,42) were found similar VEP latencies its higher in patients of migraine. Also agreed with another study (43) who found The N75 and P100 latencies were found to be significantly longer in the study group than the control group ( $p = 0.014$  and  $p = 0.034$ , respectively). non-significant amplitude difference between the patients of headache and control mean values table(2). Can be explained by the high variability of the amplitude recorded in the subjects, however, it has been shown that amplitude difference measurement is probably not prove to be very useful clinically (44).

In addition to the latency abnormalities, the evaluation of amplitude and waveform morphology can provide useful information in the diagnosis and assessment of patient e.g. prolonged latency can occur in both migraine and non-migraine headache, however, in headache, VEP amplitude is usually normal whereas in compressive and ischemic lesion, the amplitude may be higher and VEP waveform was directed to a more natural form.

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