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The Study Of Visual Evoked Potential In A Sample Of Iraqi Migraine Patients With Psychotherapy.

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ABSTRACT

In general headaches are classified into whether not accompanied by other disorders and hence termed primary or otherwise being secondary to other illness. Migraine headache is one of these types that are considered primary. Typical presentation of migraine headache is that of a pulsating kind that involves one side of the head and continues for a period ranging from 2 up to 27 hours. Sometimes headache is accompanied by a number of other symptoms such as sensitivity to smell, sound or light, nausea and vomiting. To evaluate visual evoked potential parameters, N75, P100 and N75-P100 in migraine patients in relation to type of migraine whether common or classical with psychotherapy. The present study included 88 patients with migraine, 21 males and 67 females. The age range of participants was form 10 to 43 years. The study was conducted at the neurology unite at Al-Diwaniyah teaching hospital, Al-Diwaniyah province, Iraq. Collection of information and laboratory work started on January 2017 and extended up to May 2018. Data included age, gender, duration of illness, frequency of attacks and photophobia According to presence or lack of aura, patients were classified into those with common and those with classical migraine. Evoked potential parameters included N75 and P100 of both right and left eyes for each individual. Mean N75-P100 was significantly higher in patients with migraine compared to that of control subjects, 16.22± 7.54 ms versus 7.62± 2.29 ms (P<0.0001). The best cutoff value of N75-P100 was >10.7 µV which exhibit an area under the curve AUC of 0.866 (95% confidence interval of 0.830 to 0.897) and highly significant *P*-value (<0.001). The sensitivity of this cutoff value was 74.20% and the specificity was 96.00%. N75 show no significant correlation to any of the clinical characteristics of the study group. P100 showed significant positive correlation with age of the patient, whereas, N75-P100 amplitude showed significant negative correlation with age, being significantly higher in women than men, 17.11 ±7.58 µV versus 11.71 ±5.47 µV, respectively, (P<0.001) and in classic than common subtype, 21.51±6.51 µV versus 13.82 ±6.71 µV, respectively, (P<0.001). The best predictor of migraine headache among visual evoked potential parameters is N75-P100 amplitude which is in addition significantly higher in women and in classic type of migraine.

Keywords: Visual evoked potential, N75, P100, psychotherapy, migraine

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INTRODUCTION

In general headaches are classified into whether not accompanied by other disorders and hence termed primary or otherwise being secondary to other illness. Migraine headache is one of these types that are considered primary. Typical presentation of migraine headache is that of a pulsating kind that involves one side of the head and continues for a period ranging from 2 up to 27 hours. Sometimes headache is accompanied by a number of other symptoms such as sensitivity to smell, sound or light, nausea and vomiting. Physical activity often makes symptoms worse [1]. The etiology behind migraine is thought to be interplay among a number of genetic and environmental factors. It has been shown that about 67% of cases are familial. Hormonal factors have been suggested to play a role since majority of adult cases are women (the rate in women is 2 to 3 times higher than men); however, before puberty the incidence is the same or slightly higher in boys [2]. In addition, it has been shown that the risk of migraine is often less in pregnant ladies. The definite pathophysiology behind migraine headache is still not well defined; however, it is highly suggestive that the disease is due some vascular pathology [3].

The principal suggestion is related to elevated excitability of the cerebral cortex and abnormal regulation of neurons relaying pain sensation in the trigeminal nucleus. Numbness or tingling of the skin can also associate migraine headache. Severe migraines may be also associated with nausea, vomiting and light sensitivity in some individuals. Certain foods, medications, loud noises, smells, and bright lights may all stimulate a migraine headache. Photophobia and visual symptoms and are frequent associates of migraine headache; however, they do not exclusively accompany attacks. Increased sensitivity to environmental light source and lattice patterns of certain spatial frequency have been shown to continue even between assaults. Increased sensitivity to light stimuli could be attributed to the more rapid low-level visual processing which has been shown in patients with migraine with aura. Clinically speaking migraine may be classified into a type that is often preceded by “aura” (the classic one) and a type that is commonly not accompanied by aura symptoms (the common type). Aura may come in the form of unpleasant smell or abnormal light sensation that usually precedes and hence warns the patient about the incoming headache attack. A number of studies have shown that migraine with aura is accompanied by increased risk of cerebrovascular accidents. Substantial genetic and neuroimaging evidence in favor of a link between migraine with aura and ischemic stroke has been recently presented in a review article on migraine and stroke. Moreover, infarcts that are subclinical have been attributed to migraine [15], [16], [17].

Throughout the last 10 years different research workers have shown significant alterations of bioelectrical activity in the visual cortex of patients with migraine at time of the migraine cycle. More strictly speaking, “cortical visual evoked potentials (VEPs)” are utilized to study the mass activity of the neurons in the visual cortex. Majority of VEP studies have demonstrated that the brain of patients with migraine with or without aura shows “an interictal deficit of habituation during stimulus repetition, and by its ictal normalization” [4]. However, this finding was rejected by some authors. The aim of the present study was to compare VEP findings between patients with classic migraine and patients with common migraine with psychotherapy and relate these findings to age and gender of participants [21].

METHODOLOGY

The present study included 88 patients with migraine, 21 males and 67 females. The age range of participants was form 10 to 43 years. The study was conducted at the neurology unite at Al-Diwaniyah teaching hospital, Al-Diwaniyah province, Iraq. Collection of information and laboratory work started on January 2017 and extended up to May 2018. Data included age, gender, duration of illness, frequency of attacks and photophobia According to presence or lack of aura, patients were classified into those with common and those with classical migraine. Evoked potential parameters included N75 and P100 of both right and left eyes for each individual. Statistical analysis was carried out using statistical package for social sciences (SPSS) version 23. Numeric data were presented as mean and standard deviation, whereas, nominal data were presented as number and percentages. P-value was considered significant at a level of equal or less than 0.05 [18], [19].

RESULTS

Mean age of patients with migraine enrolled in this study was 26.69 ±7.57 years and that of control subjects was 27.35 ±6.65 years with statistical matching (P=0.511). There were 15 male and 73 female patients

with migraine and control subjects were statistically matched to patients with respect to gender (P=0.901), 21 male and 107 female control subjects. Mean duration of disease was 3.56 ±3.64 years and it ranged from 2 months to 20 years. The frequencies of migraine headache attacks were highly variable with a median of 5 and an interquartile range (IQR) of 3. The group of patients was composed of the following: 88 patients with common migraine accounting for (68.8%) and 40 patients with classic migraine accounting for (31.2 %). Photophobia was seen in 103 patients (80.5%); 25 (19.5%) patients suffered from bilateral involvement; 47 (36.7%) patients had right eye photophobia and 56 (43.8%) patients had left eye involvement, as shown in table 1. Mean parameters of visual evoked potential (VEP) are shown in table 2 which revealed no significant difference in mean P100 between migraine patients and control subjects, 107.90± 7.54 ms versus 108.29± 4.86 ms (P=0.547); however, mean N75-P100 was significantly higher in patients with migraine compared to that of control subjects, 16.22± 7.54 ms versus 7.62± 2.29 ms (P<0.0001). In order to find the N75-P100 cutoff value that can predict a migraine diagnosis, receiver operator characteristic curve analysis was carried out as shown in figure 1 and table 3. The best cutoff value of N75-P100 was >10.7 µV which exhibit an area under the curve AUC of 0.866 (95% confidence interval of 0.830 to 0.897) and highly significant P-value (<0.001). The sensitivity of this cutoff value was 74.20% and the specificity was 96.00%. N75 show no significant correlation to any of the clinical characteristics of the study group. P100 showed significant positive correlation with age of the patient, whereas, N75-P100 amplitude showed significant negative correlation with age, being significantly higher in women than men, 17.11 ±7.58 µV versus 11.71 ±5.47 µV, respectively, (P<0.001) and in classic than common subtype, 21.51±6.51 µV versus 13.82 ±6.71 µV, respectively, (P<0.001), as shown in table 4 and figures 2 and 3 [19], [20].

Table 1: Characteristics of the study and control groups

Characteristic	Migraine Patients n = 128	Control subjects n = 88	*P*
Age, Mean ±SD	26.69 ±7.57	27.35 ±6.65	0.511
Gender, M/F	15/73	21/107	0.901
Duration of migraine	3.56 ±3.64; 2 months -20 years		
Frequency of attack; Median (IQR)	5 (3)		
Type of migraine; common/ classic	88/ 40		
Photophobia			
Single eye; n (%)	103 (80.5)		
Both eyes; n (%)	25 (19.5)		
Right eye; n (%)	47 (36.7)		
Left eye; n (%)	56 (43.8)		

n: number of cases; SD: standard deviation; M:male; F: female; IQR: interquartile range.

Table 2: Comparison of VEP parameters between control and study groups

Characteristics	Migraine *n* = 256 eyes	Control *n* = 176 eyes	*P*
N75; mean ± SD (ms)	81.99± 14.73	----	----
P100; mean ± SD (ms)	107.90± 7.54	108.29± 4.86	0.547
N75-P100 (µV)	16.22± 7.54	7.62± 2.29	<0.001

SD: standard deviation

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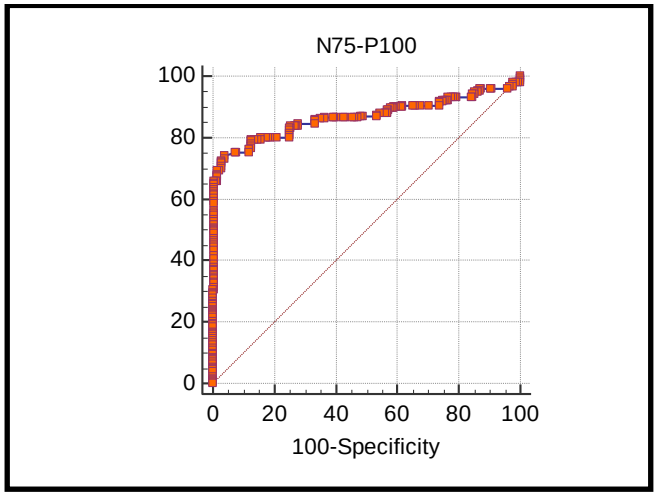

Figure 1: Receiver operator characteristic (ROC) curve to calculate N75-P100 cutoff value

Table 3: ROC curve characteristics

Characteristic	Value
Cutoff	>10.7 µV
AUC (95% CI)	0.866 (0.830 to 0.897)
P	<0.001
Sensitivity	74.20%
Specificity	96.00%

AUC: area under the curve; CI: confidence interval

Table 4: Correlation between VEP parameters and clinical characteristics of the study group

Characteristic	N75		P100		N75-P100	
	r	*P*	r	*P*	r	*P*
Age	-0.061	0.332	0.147	0.018	-0.210	0.001
Gender	0.033	0.598	-0.040	0.522	0.266	<0.001
Frequency	-0.018	0.780	-0.117	0.061	0.019	0.762
Duration	-0.081	0.198	-0.069	0.274	0.091	0.146
Type of migraine	-0.040	0.525	-0.122	0.051	0.474	<0.001
Photophobia	0.098	0.118	-0.039	0.533	0.046	0.465

r: correlation coefficient

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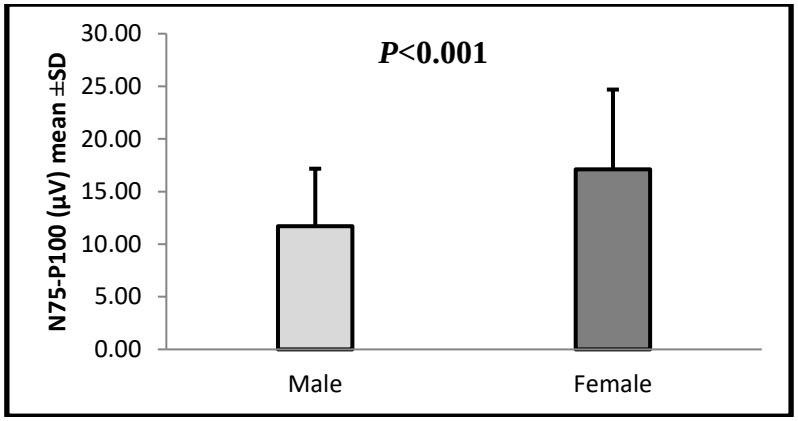

Figure 2: Mean N75-P100 according to gender

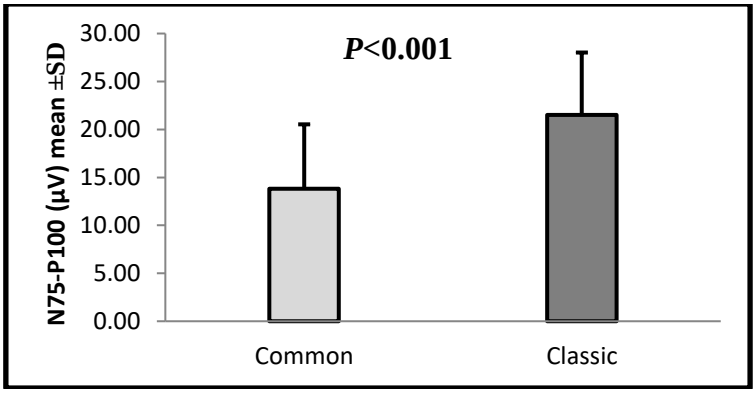

Figure 3: Mean N75-P100 according to migraine type

DISCUSSION

In the current study we were able to identify a cutoff value of N75-P100 amplitude that can predict migraine headache with high sensitivity and specificity. In addition, it was shown that N75 and P100 time intervals were not significantly different in patients with migraine when compared to control subjects with Psychotherapy. "VEP is an electrical signal recorded from the scalp over the visual cortex after light-evoked (pattern reversal or diffuse flash) stimulation of the retina". The preferred form of stimulation is Pattern reversal (often a reversing white to black and black to white checkerboard) [14]. The traditional waveform evaluated for pattern-reversal VEP is the N75-P100-N135. The N indicates a negative waveform, and the P indicates a positive waveform. The number after the letter represents the time in (milliseconds) of the average happening of the peak (eg, P100 is the positive peak naturally occurring about 100 ms). P100 is the most frequently evaluated feature of the conventional waveform. Amplitude and Latency are other significant parameters of the VEP. Latency is the time needed for the signal to reach the visual cortex beginning from the retina. "The amplitude or difference from the trough of N75 to the peak of P100 represents the strength of the signal reaching the visual cortex in relation to how many functional retinal ganglion cells are present" [5], [6].

In the current study, N75-P100 was significantly higher in women than in men and also in classic type than in common type. The pathophysiological establishment of various aura phenotypes and associated differences in visual evoked potential profiles is till now not clear. "Cortical spreading depression (CSD)" is supposed to be the pathophysiological factor behind migraine aura. CSD is a wave that is electrochemical and it usually begins in the hind regions of the brain and spreads forward at around 3 mm/min, accompanied by dual phase cerebral blood flow alterations [7]. In a number of brain imaging researches carried out during migraine assaults, despite not in all, [8] the metabolic and vascular alterations associating the migraine aura spread more forward in patients with complex neurological signs and hemiplegia than in those with mere visual changes. Getting rid from CSD is largely determined by intact neurovascular coupling to provide the raised energy requirement and to regain ion gradients via the pump of Na^+/K^+ ATPase [9]. Neurovascular coupling is altered in

migraine patients with Psychotherapy, at time of continuous visual stimulation, between attacks, particularly in migraine with aura subtype [10], [11]. There is also acceptable proof from functional neuroimaging and biochemical studies that monoaminergic, especially serotonergic, transmission from the brainstem to the cortex and thalamus is disturbed in migraine patients with Psychotherapy [12]. Finally, a lot of information from different laboratories has demonstrated that the "mitochondrial energy reserve and ATP" levels are profoundly decreased in the brain of patients with migraine between assaults [13]. The above discussion my provided explanation for the significantly higher N75-P100 amplitude in patients with classic migraine, that has been observed in the present study. In conclusion, the best predictor of migraine headache among visual evoked potential parameters is N75-P100 amplitude which is in addition significantly higher in women and in classic type of migraine.

REFERENCES

[1] Lulli, M.P., Farinelli, I., Simeoni, S., De Filippis, S., Patacchioli, F.R., Martelletti, P. (2007). *Genetics of migraine and pharmacogenomics: some considerations*. The journal of headache and pain, Vol 8, No. 6, pp. 334-9.

[2] Wray, S.H. (1995). *Mijovic-Prelec, D. and Kosslyn, S. M. Visual processing in migraineurs*. Brain, Vol. 118, pp. 25-35.

[3] Weatherall, M.W. (2015). *The diagnosis and treatment of chronic migraine*. Therapeutic Advances in Chronic Disease. Vol 6, No. 3, pp. 115-123.

[4] Spector, J.T., Kahn, S.R., Jones, M.R., Jayakumar. M., Dalal, D., Nazarian, S. (2010). *Migraine headache and ischemic stroke risk: an updated meta-analysis*. Am J Med, Vol 123, pp. 612–624.

[5] Kurth, T., Slomke, M.A., Kase, C.S. (2005). *Migraine, headache, and the risk of stroke in women: a prospective study*. Neurology, Vol 64, pp. 1020–1026.

[6] Kurth, T. (2010). *The association of migraine with ischemic stroke*. Curr Neurol Neurosci Rep, Vol 10, pp. 133–139.

[7] MacClellan, L.R., Giles, W., Cole, J. (2007). Probable migraine with visual aura and risk of ischemic stroke: the stroke prevention in young women study. Stroke, Vol 38, pp. 2438–2445.

[8] Etminan, M., Takkouche, B., Isorna, F.C., Samii, A. (2005). *Risk of ischaemic stroke in people with migraine: systematic review and meta-analysis of observational studies*. BMJ, pp. 330:63.

[9] Donaghy, M., Chang, C.L., Poulter, N. (2002). *European Collaborators of the World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception*. Duration, frequency, recency, and type of migraine and the risk of is chaemic stroke in women of childbearing age. J Neurol Neurosurg Psychiatry. Vol 73, pp. 747–750.

[10] Mawet, J., Kurth, T., Ayata, C. (2015). *Migraine and stroke: in search of shared mechanisms*. Cephalalgia, Vol 35, pp. 165–181.

[11] Tietjen, G.E. (2004). *Stroke and migraine linked by silent lesions*. Lancet Neurol, Vol 3, p. 267.

[12] Stovner, L.J., Zwart, J.A., Hagen, K. (2006). *Epidemiology of headache in Europe.* European Journal of Neurology, Vol 13, No. 4, pp. 333-45.

[13] Kruit, M.C., VAN Buchem, M.A., Hofman, P.A. (2004). M*igraine as a risk factor for subclinical brain lesions*. JAMA, Vol 291, pp. 427–434.

[14] Lay, C.L., Broner, S.W. (2009). *Migraine in women*. Neurologic Clinics, Vol 27, No. 2, pp. 503-11.

[15] Bartleson, J.D., Cutrer, F.M. (2010). *Migraine update. Diagnosis and treatment*. Minn Med, Vol 93, No. 5, pp. 36-41.

[16] Dodick, D.W., Gargus, J.J. (2008). *Why migraines strike*. Sci. Am. Vol 99, No. 2, pp. 56-63.

[17] Cullom, D.R., Chang, B., Friedberg, A.M., and Rapuano, C. (2004). *The Wills Eye Manual, Office and Emergency Room Diagnosis and Treatment of Eye Disease*. J.B. Lippincott Company.

[18] Hay, K.M., Mortimer, M.J., Barker, D.C., Debney, L.M., and Good, P.A. (1994). *1044 women with migraine: theeffect of environmental stimuli*. Headache, Vol 34, pp. 166-168.

[19] Wilkins, A.J., Nimmo-Smith, M.I., Tait, A., McManus, C., Della Sala, S., Tilley, A., Arnold, A., Barrie, M., Scott, S. (1984). *A neurological basis for visual discomfort*. Brain, Vol 107, pp. 989-1017.

[20] Marcus, D.A., Soso, M.J. (1989). *Migraine and stripe-induced visual discomfort*. Arch Neurol, Vol 46, pp. 1129-1132.

[21] Thase, M.E. (1997). *Treatment of major depression with psychotherapy or psychotherapy-pharmacotherapy combinations*, Archives of general psychiatry, Vol 54, No. 11, pp. 1009-1015.