Original Article

Lack of habituation of visual-evoked potential in the interictal period is not a consistent neurophysiological marker of migraine: A cross-sectional analytical study

Ankita Rani[1], Ramkumar Sugumaran[1], Sunil K. Narayan[1]

[1]Department of Neurology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India.

ABSTRACT

Objectives: Migraine is a frequent incapacitating neurovascular illness characterized by severe headache bouts. Individuals suffering from migraine appear to process auditory and visual information differently from those without migraine. The visual-evoked potential (VEP) is a commonly used standardized test to measure excitability in the occipital cortex. Patients with migraine exhibit amplification rather than habituation of stimulus-induced brain responses, between attacks. Our objective is to compare the amplitude of P_{100} and the latencies of N_{75}, P_{100}, and N_{145} (N and P represent negative and positive peaks, respectively, with average latency being subscripted with the alphabet) in the fourth block between migraine patients and controls and to determine the various clinical factors associated with the P_{100} mean amplitude and latency differences between the first and the fourth block in migraine patients.

Materials and Methods: The study compared 20 migraine patients (with or without aura) and 20 apparently healthy subjects with no history of migraines or secondary headaches, focusing on the habituation of the VEP. Four blocks of 200 responses were recorded during the headache-free period, and the latencies and amplitudes of N_{75}, P_{100}, and N_{145} components were analyzed.

Results: There was a statistically significant ($P < 0.05$) decrement in the P100 amplitude in the fourth block when compared to the first block in both eyes in the controls as well as migraine patients. In addition, there was no statistically significant difference between controls and migraine sufferers in the P_{100} amplitude of the fourth block in either eye. The N_{145} latency in the fourth block was shorter in both eyes in migraine patients compared to controls ($P < 0.05$). The mean P_{100} amplitude difference between the first and fourth block correlated negatively with age and positively with headache frequency, while there was a moderate negative correlation with headache duration. The mean P_{100} latency difference between the first and fourth block correlated positively with age and negatively with headache frequency, while there was a moderate positive correlation with headache duration.

Conclusion: In our study, VEP habituation was not lacking in migraine patients which means that habituation of the P_{100} wave was noted in migraineurs. The VEP reveals neurological changes due to ischemia injury or neurotransmitter imbalances. Migraine alters cortical excitability, but it is unclear if these changes are due to altered excitatory connections, damaged inhibitory networks or subcortical pre-activation. Our findings suggest that at least during the interictal period, lack of habituation cannot be employed as a consistent neurophysiological marker of migraine across laboratories.

Keywords: Migraine, Headache, Visual-evoked potential, Habituation, Potentiation

INTRODUCTION

Migraine is a widespread neurovascular disorder with a high prevalence resulting in socioeconomic, personal, and other repercussions. The International Headache Society classifies migraine headaches as with or without an aura. In 82% of cases, patients experience the visual symptoms of migraineous aura, which include scotoma, a central or paracentral blind spot, stars, zigzags, and flashes of light.[1] According to studies, migraineurs exhibit alterations in their evoked potential even when they are not experiencing headaches.[2] The brain's sensitivity to migraine attacks appears to be mostly dependent on cortical excitability during migraine interictal periods. Patients with migraines exhibit amplification rather than habituation of stimulus-evoked brain responses between attacks. The main structures involved in the pathogenesis of migraine are the brainstem, trigeminovascular system, and cerebral cortex. It is unclear whether the change in habituation is caused by higher or lower cortical pre-activation levels. Increased or decreased cortical excitability may contribute toward the

pathogenesis. Mainly two theories prevail to explain the cortical excitability in migraineurs, which are the theory of hypoexcitability and the theory of hyperexcitability. Authors, who support the idea of decreased pre-activation in migraineurs, emphasize lower initial P_{100} amplitude during repetitive stimulation[3] while some studies[4] showed the migraineurs being characterized by an increase in neuronal excitability. There has been substantial research into the biochemical and neurophysiological abnormalities that lead to migraine attacks, but the inconspicuous element that causes the disorder, which, if present, should also be visible during a period of pain-free time, is the underlying dysfunction.[5] Visual-evoked potentials (VEPs) are a functional option that smoothens the path of assessment of the visual pathway. Pattern-reversal VEPs can be used to explore the two parallel routes that carry visual information: The luminance and contour processing pathways. These pathways are hypothesized to be differentially affected in migraine.[6] The mass activity of visual cortex neurons is inferred from cortical VEPs. In a previous pattern reversal (PR)- VEP study, during the interictal stage, potentiation substituted the normal habituation pattern in migraineurs.[7] The visual cortex appears to exhibit habituation of the VEP as a physiological phenomenon when it malfunctions during episodes of migraine. Cortical activity is habituated and potentiated by chemically regulated connections that come from the brainstem and may use transmitters such as serotonin, noradrenaline, dopamine, histamine or acetylcholine.

Through the assessment of VEP in migraine patients in between attacks and comparison with normal patients, this study aims to gain insight into the pathophysiology of migraine. The brain's vulnerability to migraine attacks appears to be mostly determined by the cerebral cortex's excitability during the interictal state of migraine. Besides, no previous studies have analyzed the various clinical factors associated with the P_{100} mean amplitude and latency differences between the first and the last block in migraine patients on consecutive VEP stimulations. This will be important in determining the clinical factors that are associated with the lack of VEP habituation in migraine patients. This study helped us to know the cortical excitability by analyzing the habituation of VEP in between attacks, which can be used as an objective measurement of prophylactic treatment response. Furthermore, it can be used to compare the efficacy of various migraine prophylactic drugs, thereby aiding in better treatment outcomes.

MATERIALS AND METHODS

Study setting and design

The study was conducted in the outpatient clinic of the Department of Neurology, after obtaining Institutional

Ethics Committee approval (JIP/IEC/2021/0247), and consent was taken from each participant before the study. A total number of 40 participants (20 migraine patients and 20 normal individuals), aged 18–60 years, were recruited for the study. Two groups were studied, namely, the case group and the control group. In the case group, participants were chosen for the study if they had been diagnosed with a migraine headache, with or without aura, according to the third edition of the International Classification of Headache and had no other neurological disorder. Patients must have a headache frequency of <15 episodes per month (episodic migraine). Furthermore, patients must be headache-free for at least one week before the VEP study. Patients with H/O migraine disorders other than episodic migraine, any severe systemic illness such as acute or chronic renal failure, uncontrolled systemic hypertension/DM, malignancy, previous cervical spine surgery or craniotomy, heart disease, psychiatric illness, epilepsy, cerebrovascular diseases, and pregnant and lactating women were excluded from the study. Patients on prophylactic medication and other non-steroidal anti-inflammatory drugs were also included in the study. Healthy subjects, who had not been diagnosed with migraine headaches with or without aura and with no other secondary causes of headaches, were included in the control group. According to a prior study by Vijayalakshmi *et al.*,[2] and based on Open epi version 3.1, it was suggested that a sample size of 20 patients was required, with 10 patients in each group, to achieve an 80% power and a 95% confidence interval for comparing migraine patients and controls. This was based on the assumption that there would be a group difference of 2.6 and a standard deviation (SD) of 2.6 in migraine patients and 1.1 in controls in the P_{100} amplitude in the fourth block. However, since the sample size was small, we included a feasible sample size of 40 with 20 patients in each group.

Instruments used

The VEP test was performed using the Nihon Kohden ENMG/EP measuring system machine. After washing their hair, the patients were advised not to apply any oil or hair spray before the test. Patients with refractory errors were instructed to put on their regular glasses. The subjects were instructed not to move or blink frequently during the VEP test to reduce muscle contraction artifacts from the subject's eyes and skeletal muscles, which distort the evoked potential waves. The VEP test was conducted in a dark, silent room with the subjects sitting comfortably on a chair.

The Oz (recording electrode), Fz (reference electrode), and FPz (ground electrode) were placed according to the 10–20 placement system. The television set (PR Stimulator) was placed 1 m from the subject's nasion. The preamplifier was wired up to the electrodes. The low-pass filter was set at 100 Hz

and the high-pass filter at 1 Hz with sweep speed, duration, and sensitivity at 50 ms/div, 30 ms, and 5 µV, respectively. The number of epochs was 200, and the amplification ranged from 20,000 to 100,000. The electrode impedance was kept below 3 kΩ. With PR stimuli, a black and white checkerboard with an 80% contrast, and a spatial frequency of 2 cycles per degree was used. The alternating checker-board pattern was utilized as the visual stimuli in the PR stimulation technique, which was binocularly presented on a video screen with a fixation point for full field at >8°. The pattern was 8 × 8 min in size, and the stimulus frequency was 1 Hz. The subjects were instructed to fix their gaze at the center of the screen. The stimulus was given continuously for approximately 12.8–13 min. This 12.8-min time was broken up into four 3.2-min blocks, 200 epochs on average make up each block. The peak latency and peak-to-peak amplitude of both the positive and negative waves were assessed after the response was recorded and displayed on the monitor. The VEP results were interpreted by a person blinded to the diagnosis.

Outcomes

The primary outcome was to compare the amplitude of P_{100} in the fourth block between migraine patients and controls. The secondary outcomes were, first to compare the latencies of N_{75}, P_{100}, and N_{145} in the fourth block between migraine patients and controls; secondly, to determine the various clinical factors associated with the P_{100} mean amplitude and latency differences between the first and the fourth block in migraine patients.

Statistical methods

Demographics were described using mean, SD, frequency, and percentage. We verified data distribution through visual analysis of the Q-Q plot. We found that sample data followed the normal distribution; hence, we adopted parametric tests for comparisons. For comparing continuous data between groups, an independent *t*-test was performed, and for categorical variables, a Chi-square test was performed. To examine the link between the dependent variable and independent variables in correlation and regression, Pearson's correlation and multiple regressions were used. $P < 0.05$ was the threshold for significance. Statistical analysis was performed using data analysis in Microsoft Office 21 and R Studio version 4.2.2.

RESULTS

A total of 40 subjects were included in the study out of which 20 subjects were recruited as controls and 20 subjects with migraine were recruited as cases. The mean age of the patients was 34.4 ± 8.72 years and that of controls was 26.45 ± 5.45. The mean frequency of the headache in migraine patients was 7.7 ± 4.01 episodes per month, and the duration

of the headache was 6.65 ± 1.93 h. Baseline characteristics and demographic features were compared between cases and matched controls [Table 1].

The amplitude of P_{100} in the fourth block decreased in both eyes of the controls compared to the first block [Table 2a], which was statistically significant ($P = 0.003$ [left side]; $P = 0.002$ [right side]). Similar to this, there was a statistically significant ($P < 0.001$) drop in the amplitude of P_{100} in the fourth block compared to the first block in both eyes of the migraine patients [Table 2a]. The N_{145} latency in the fourth block was shorter in both eyes in migraine patients compared to controls ($P = 0.01$) [Table 2b]. However, there was no statistically significant difference between migraine patients and controls in the amplitude or latency of P_{100} in the fourth block in either eye [Table 2c and d].

The amplitude decreases progressively from block one to block four [Table 2e] in both the control and migraine patients, while there is no significant difference between the two groups.

Multiple regressions were run to predict the mean difference of P_{100} latencies between the first and the fourth block from age, gender, frequency of migraine attacks, duration of disease, and clinical features of headache that included distribution, character, the severity of headache, photophobia, phonophobia, and nausea/vomiting. The statistical prediction of P_{100} latencies based on these variables is non-significant, $F(11, 8) = 1.389482$, $P = 0.32$, $R^2 = 0.656$ [Table 3]

The mean difference of P_{100} amplitude between the first and the fourth block was also used as a dependent variable for multiple regression analysis with independent variables the same as mentioned for the mean difference of P_{100} latencies. The statistical prediction of P_{100} amplitudes based on these variables is also non-significant, $F(11, 8) = 0.616526$, $P = 0.77$, $R^2 = 0.4587$ [Table 4].

There was a negative correlation between age and mean P_{100} amplitude difference between the first and fourth block (Pearson's r = −0.08497, $P < 0.001$) [Figure 1a] and a positive correlation with headache frequency (r = 0.07438, $P < 0.001$) [Figure 1b]. However, there was a moderate negative correlation present between headache duration and mean P_{100} amplitude difference (r = −0.45682, $P < 0.001$) [Figure 1c]. The mean P_{100} latency difference between the first and fourth block correlated positively with age (r = 0.07086, $P < 0.001$) [Figure 1a] and negatively with headache frequency (r = −0.19043, $P < 0.001$) [Figure 1b] while there was a moderate positive correlation with headache duration (r = 0.33583, $P < 0.001$) [Figure 1c and Table 5].

DISCUSSION

We recruited 20 controls and 20 patients (Female [12]: Male [8]) with migraine; 85% of those patients reported migraine without aura. Photophobia (45%) and nausea (55%)

Table 1: Demographic features.

Characteristics	Case group (*n*=20)	Control group (*n*=20)	*P*-value
Age* (in years)	34.4±8.72	26.45±5.45	0.004
Gender (%)			
Male	8 (40)	12 (60)	0.134
Female	12 (60)	8 (40)	0.134
Distribution (%)			
Holocranial	8 (40)		
Hemicranial	11 (55)		
Occipitonuchal	1 (5)		
Character (%)			
Throbbing	16 (80)		
Stabbing	1 (5)		
Steady	3 (15)		
Frequency* (episodes/month)	7.7±4.01		
Duration* (in years)	2.005±0.23		
Timing* (in hours)	6.65±1.93		
Severity (%)			
Mild	2 (10)		
Moderate	13 (65)		
Severe	5 (25)		
Symptoms (%)			
Photophobia	9 (45)		
Phonophobia	8 (40)		
Nausea	11 (55)		
Migraine with aura (%)	3 (15)		
Migraine without aura (%)	17 (85)		
Medication (%)			
Prophylactic	8 (40)		
SOS	10 (50)		
No medication	2 (10)		

*Values given as (Mean±standard deviation), all other values given as a number (%), SOS: as needed

were the most common symptoms accompanying migraine. A majority (80%) of the patients reported throbbing pain and 65% had moderate pain. The 55% of the total patients recruited reported unilateral pain while 40% had holocranial pain. The 40% of the patients were on prophylactic medications.

In our study, subjects with migraine showed P_{100} amplitude habituation as compared to controls, which contradicts findings from other studies published.[1,2,7] Both controls and migraineurs exhibited habituation. This can be due to methodological differences. For instance, in the current study, which we designed to evaluate habituation, the stimulation rate and the number of averaged responses on which measures were performed were modest. In addition to this, it was found that VEP parameters vary as a function of spatial frequency.[8,9] An increase in spatial frequency results in a reduction of P_{100} amplitude. It has been shown that as the spatial frequency increases, visual sensitivity gradually declines. This can be attributed to the eye's optical quality or the higher levels of visual processing (beyond the lateral geniculate nucleus) responsible for VEP production. In addition, it is suggested that sensitivity loss at high spatial frequency may result from

quantal variations in light. This might be one of the reasons behind the discrepancy in the results. Furthermore, most of our patients were already on migraine prophylactic drugs and did not have migraine attacks in the recent past before the study. This result contradicts claims made in several other review articles that the lack of habituation in interictal migraineurs is a neurophysiological characteristic and the most repeatable finding.[2,7] A few trials with either negligible or no variation in the amplitude of the P_{100} wave were found to have similar outcomes to our study.[10-15]

When the VEP is recorded continuously for a long period (18–20 min), latency may increase while amplitude decreases. Such a prolongation of latency was noted in both migraine patients as well as in controls. However, the mean change in latencies between the migraine patients and controls was non-significant for the N_{75} and P_{100} waves, while the difference was highly significant for the N_{145} wave. Numerous studies that found a non-significant prolongation of P_{100} latency reported similar outcomes.[11-15] The VEPs can show changes in neurological function brought on by ischemic injury, aberrant neurotransmitter levels or both. The prolonged P_{100} latency

Table 2: (a) Comparison analysis chart showing the comparison of P100 amplitude in the control group and migraine patients (b) comparison of N75 and N145 latencies in the fourth block between migraine patients and control, along with the comparison of (c) P100 amplitude and (d) P100 latencies in the fourth block between migraine patients and controls. (e) The amplitude of P100 across the blocks is also shown.

(a) Comparison of P100 amplitude in the control group and migraine patients					
P100 amplitude (mV) in the control group					
Side	**Pair**	**N**	**Mean±SD**	**t value**	**P value**
Left side	1st block	20	8.041±3.574		
	4th block	20	7.443±3.176	3.32329969	p=0.003
Right side	1st block	20	8.272±3.666		
	4th block	20	7.595±3.103	3.17235365	P=0.002
P100 amplitude (mV) in the migraine patients					
Side	**Pair**	**N**	**Mean±SD**	**t value**	**P value**
Left side	1st block	20	8.417±3.403		
	4th block	20	6.944±3.127	5.15	p<0.001
Right side	1st block	20	8.496±3.502		
	4th block	20	6.822±3.210	5.13674493	p<0.001

(b) Comparison of N75 and N145 latencies (ms) in the 4th block between the migraine patients and controls					
Variables	**Side**	**Group**	**N**	**Mean±SD**	**P value**
N75	Left side	Migraine patients	20	71.425±6.983	
		Controls	20	70.725±5.5712	p=0.728
	Right side	Migraine patients	20	71.350±6.8712	
		Controls	20	69.100±5.3376	p=0.255
N145	Left side	Migraine patients	20	135.300±9.8052	
		Controls	20	147.175±19.7406	p<0.01
	Right side	Migraine patients	20	134.700±11.9950	
		Controls	20	148.600±18.4124	p<0.01

(c) Comparison of P100 amplitude (mV) in the 4th block between the migraine patients and controls					
Side	**Group**		**N**	**Mean±SD**	**t value**	**P value**
Left side	Migraine patients		20	6.944±3.127		
	Controls		20	7.443±3.176	-0.5344568	p=0.59
Right side	Migraine patients		20	6.822±3.210		
	Controls		20	7.595±3.103	-0.796752	p=0.43

(d) Comparison of P100 latencies (ms) in the 4th block between the migraine patients and controls				
Side	**Group**	**N**	**Mean±SD**	**P value**
Left side	Migraine patients	20	103.100±8.202	
	Controls	20	104.175±7.765	p=0.67
Right side	Migraine patients	20	104.600±8.144	
	Controls	20	100.275±22.829	p=0.43

(e) Amplitude of P100wave (mV) from 1st block to 4th block			
Side		**Mean values**	
		Controls	**Migraine patients**
Left side	1st block	8.1	8.4
	2nd block	7.7	7.7
	3rd block	7.6	8.1
	4th block	7.4	6.9
Right side	1st block	8.2	8.4
	2nd block	7.8	7.6
	3rd block	7.7	7.6
	4th block	7.5	6.8
SD: Standard deviation			

Table 3: Regression analysis of dependent variable P100 mean latency difference between the first and the fourth block.

Domain score	Standard coefficients			95.0% Confidence interval for B	
	Beta	t	Sig.	Lower bound	Upper bound
Age	−0.05034	−0.81711	0.437521	−0.192424582	0.091735349
Gender	−1.00539	−0.83776	0.426483	−3.772797126	1.762020128
Education	−0.8394	−0.77664	0.459713	−3.331737936	1.652937443
Frequency of migraine attacks	−0.32774	−1.44805	0.185634	−0.849668501	0.194185093
Duration of disease	−0.35923	−0.98443	0.353737	−1.200720422	0.482259568
Distribution	0.350881	0.320269	0.75697	−2.175536035	2.87729772
Character	0.342078	0.375058	0.717365	−1.761151708	2.445308399
Severity	2.371828	1.902379	0.093624	−0.503227246	5.24688394
Photophobia	−1.21196	−0.43323	0.676295	−7.663087067	5.239160923
Phonophobia	2.718994	1.078377	0.312304	−3.095308309	8.533296967
Nausea/ Vomiting	2.616298	1.952173	0.086701	−0.474203387	5.706799043

Sig.: Statistical significance

Table 4: Regression analysis of dependent variable P100 mean amplitude difference between the first and the fourth block.

Domain score	Standard coefficients			95.0% confidence interval for B	
	Beta	t	Sig.	Lower bound	Upper bound
Age	0.036708	0.560068	0.590767	−0.114433234	0.187849892
Gender	−1.77814	−1.39284	0.201154	−4.72205046	1.165767213
Education	−0.14299	−0.12436	0.904095	−2.79428045	2.508308314
Frequency of migraine attacks	−0.21345	−0.88652	0.401202	−0.768660477	0.341768171
Duration of disease	−0.21586	−0.55608	0.593366	−1.111019672	0.679297672
Distribution	−0.20165	−0.17303	0.866929	−2.889200475	2.485893681
Character	0.427279	0.440386	0.671314	−1.810091079	2.664649281
Severity	1.358621	1.02438	0.33563	−1.699800426	4.417042227
Photophobia	0.473907	0.159245	0.877423	−6.388657938	7.336471589
Phonophobia	0.02131	0.007945	0.993855	−6.163818094	6.206438142
Nausea/vomiting	−0.29581	−0.20748	0.840815	−3.583413316	2.991802029

Sig.: Statistical significance

Table 5: Correlation of different variables with the P100 mean amplitude and latency differences between the first and the fourth block.

Characteristics	Parameter of P100 wave	Pearson coefficient (r)	P-value
Age (in years)	Amplitude	−0.08497	<0.001
	Latency	0.070861	<0.001
Frequency (episodes per month)	Amplitude	0.074376	<0.001
	Latency	−0.19043	<0.001
Duration (in years)	Amplitude	−0.45682	<0.001
	Latency	0.33583	<0.001

may be brought on by the long-term repercussions of assaults, which include cerebral ischemia and edema. However, we included individuals in our study who had been suffering from migraine for only two years, which may be the cause of the non-significant lengthening of the P_{100} latency [Table 1]. In addition, 85% of the participants in our survey claimed to have migraine without aura. Since only 15% of migraineurs with aura were recruited in our study, a subgroup analysis was not statistically feasible. However in a study, migraine sufferers with an aura, in particular, were found to have greater P_{100} latency.[10]

A common occurrence in the neural system, habituation has intricated spatially and functionally dependent mechanisms. It is proposed that the cerebral cortex is regulated by excitatory interneurons that receive input from thalamocortical neurons, inhibitory intra-cortical interneurons, and subcortical connections in the brainstem involving neurotransmitters such as histamine, noradrenaline, serotonin, and dopamine. These mechanisms typically guard against cortical overstimulation.[16,17] Serotonin has extensive sensory cortex innervation, tonic pacemaker activity, and modulatory effects on cortical information processing.[18] A 1 Hz reversal rate was used in the current study, and habituation appeared to be evident in both the controls and the migraineurs. Although there is mounting evidence that migraines modify cortical excitability, it is unclear whether these alterations are the result of changed excitatory connections, damaged inhibitory networks or altered subcortical preactivation.[19] The inconsistent results in
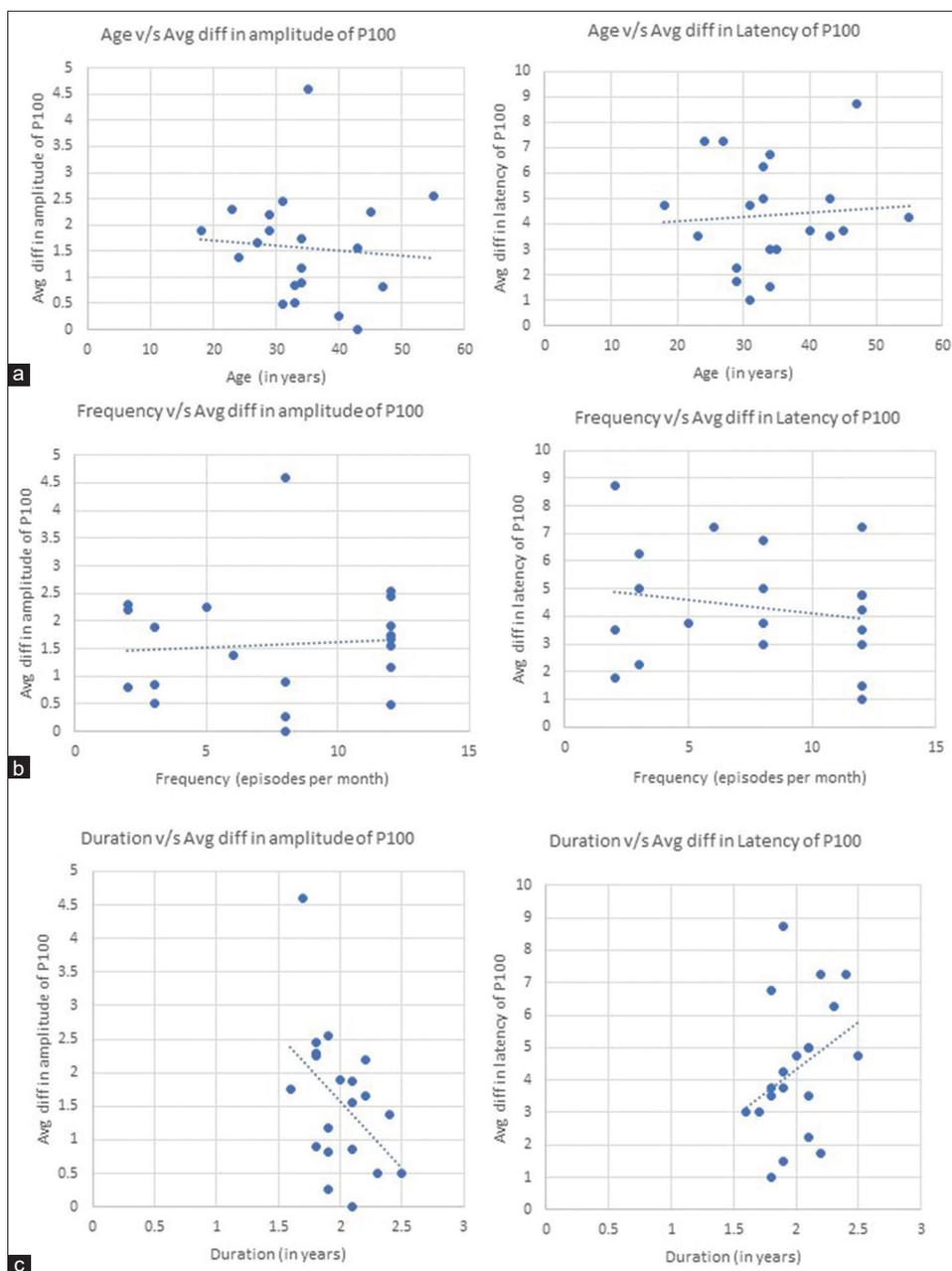
Figure 1: Correlation graphs showing (a) negative correlation graph between age and mean difference (block one–block four) of P100 amplitude (Left) and positive correlation graph between age and mean latency difference (block one–block four) of P100 latency (Right). (b) Positive correlation graph between frequency of headache and mean difference (block one–block four) of P100 amplitude (Left) and negative correlation graph between frequency of headache and mean difference (block one–block four) of P100 latency (Right). (c) Negative correlation graph between duration of migraine and mean difference (block one–block four) of P100 amplitude (Left) and positive correlation graph between duration of headache and mean difference (block one–block four) of P100 latency (Right).

earlier VEP amplitude studies were initially thought to be due to habituation[2], but this explanation now seems less likely in light of the current findings. Several investigations have indicated that migraineurs do not exhibit a lack of habituation.[6,8,20-23]

In our study, we found that the duration of migraine is strongly associated with the mean P_{100} amplitude difference. This may imply that the severity and duration of migraines over time may be a risk factor for impaired visual cortex function. In

addition to this, duration is also moderately associated with the mean P_{100} latency difference. We found that VEP amplitude habituation increased with migraine frequency. The average P_{100} latency difference was found to be decreasing with an increase in frequency. This is possibly due to the shorter time between attacks in patients with a high frequency of the condition.

There was no discernible relationship between age and the P_{100} wave parameter. This might be a result of the smaller sample size and dispersed age data plot.

In our study, no correlation was observed between VEP and photophobia. It may be possible that photophobia depends more on subcortical than cortical visual pathways.[22,24] These findings confirm the association between the severity of migraine clinical presentation and the behavior of neurophysiological responses.

This study has a few strengths and limitations. The primary strength of the study is its adequate sample size. Another strength is the inclusion of healthy controls for proper comparison between the two groups. The stimulation rate and low number of averaged responses on which measurements were performed in the present study, in which we aimed to evaluate habituation, are probably the primary limitations of the investigation. Second, most of our patients were already on migraine prophylactic drugs and did not have migraine attacks in the recent past before the study.

CONCLUSION

Our study results suggest that, at least in the interictal stage, lack of habituation cannot be used as a reliable neurophysiological migraine marker in different laboratories. The disparate findings in previous research are probably due to methodological discrepancies such as the stimulation rate, the number of averaged responses, and the patient recruitment strategy. It seems that migraineurs' habituation behavior is not always hindered, but rather is affected in a subtle way that depends on stimulating stimuli. To properly understand the varying results of VEP habituation studies in migraineurs and the effects of the migraine cycle, particularly the pre-ictal phase, a long-term study is required. Drug-naïve people and those who have recently had episodes must be the subjects for future research.

Ethical approval

The research/study approved by the Institutional Review Board at Jawaharlal Institute of Postgraduate Medical Education and Research, number JIP/IEC/2021/0247, dated November 20, 2021.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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