Evaluation of Brainstem Auditory Evoked Potentials in Migraine Individuals

Vijayalakshmi TN[1], Ratna Manjushree Jayaraman[2], Bhanu[3], Heber Anandan[4]

ABSTRACT

Introduction: Migraine is the most commonly encountered primary headache condition in practice. Studies have shown that migraineurs are charactecterized by changes in the evoked potentials even during headache free period. This study was indented in knowing about the pathophysiology of migraine and brain stem auditory evoked potentials in migraine patients in comparison with normal persons.

Material and Methods: 30 subjects of the age group of 20 to 50 years fulfilling the criteria of migraine as per the IHS criteria in the study group. Thirty age and gender matched normal individuals were included in the control group. All the subjects were tested during the headache free period. One ear is tested at a time. Other ear is masked with white noise. Each ear is tested continuously for a period of 15 minutes. 15 minutes period is divided into 4 blocks of 2000 trials each.

Results: There was a very highly significant decrease in the amplitude of the fourth block in the controls, where as in the migraine patients, there was a very highly significant increase in the amplitude of the fourth block. When the amplitude of the fourth block of the migraine patients was compared with the amplitude of the fourth block of the controls, there was a very highly significant increase in the amplitude in the migraine patients.

Conclusion: These results suggest that migraine patients not only have habituation deficit but also have potentiation of BERA waves during continuous period of stimulation in the headache free period.

Keywords: Habituation, potentiation, Brainstem auditory evoked potentials, migraine, latency, amplitude

INTRODUCTION

Migraine is the most commonly encountered primary headache condition in practice. Sohmer Feinmesser[1] were the first to publish auditory brainstem response recorded with surface electrodes in humans. Jewett and Williston described description and interpretation of waves arriving from brainstem due to auditory stimulus. Evoked potentials are useful in the study of neurophysiology (Shagass C).[2] The methods of electro neurophysiology are particularly appropriate for the study of migraine pathophysiology because they are atraumatic and able to detect functional abnormalities (Ambrosini.A et al.).[3] Brainstem auditory evoked potential (BAEP) recording is a physiological technique for evaluation of auditory pathway. The electrical activities from the activation of the eighth nerve, cochlear nucleus, tracts and nuclei of the lateral lemniscus and inferior colliculus are recorded (Chiappa KH et al).[4] The presumed correlation of each peak with specific brainstem structures creates clinical interest (Julie V Patterson et al).[5] This study was indented in knowing about the pathophysiology of migraine and brain stem auditory evoked potentials in migraine patients in comparison with normal persons

MATERIAL AND METHODS

A Cross sectional comparative study was conducted in the Institute of Physiology and Experimental medicine, Madras Medical College, Chennai. Informed consent from the patients and ethical committee approval were obtained. Subjects with migraine with or without aura at least for a period of 6 months, not taking any drugs for migraine on a regular basis and with normal respiratory, cardiac, renal and hepatic functions were included in the study group. Thirty subjects fulfilling the criteria of migraine as per the IHS (International Headache Society) criteria from the outpatient department of the Institute of Neurology, Madras Medical College, Chennai were include. Subjects between 20-50 years with normal hearing were included in the control group. Subjects with any co-morbid like ear disease, diabetes mellitus, hypertension, anemia, any other neurological illness and those who are on medication which affects hearing are excluded from the study. The participants were subjected to clinical examination. Subjects with normal Rinne's and Weber's and pure tone audiometry were included in the study. BERA was tested during the headache free period. The apparatus set up for measuring Brainstem Evoked Response Audiometry are set up as per Guide line 9A: Guidelines on Evoked potential by American Society of Clinical Neurophysiology. The stimulus in the form of clicks is transmitted via a transducer placed in the head phone to the ear. The electrodes required for BERA measurement are placed in the corresponding sites of scalp following the international 10-20 Electrode placement system. High quality EEG electrodes are used. Surface electrodes are preferred because it is painless and there are lower chances of infection. For better placement of electrodes, the hair must be oil free. The patient was instructed to have shampoo bath before coming for investigation. Active and ground electrodes are placed on the ipsilateral and contralateral mastoid process respectively (Lau S K and William) after the skin has been cleaned. The electrode on the vertex acts as the reference. Filter selectively restricts the frequency domain of a signal. Since the biological signals are very small (5 to 50 micro volts), variable degree of amplification (up to 500,000) is needed equal

[1]Assistant Professor, Institute of Physiology and Experimental Medicine, Madras Medical College, [3]Professor (retd.), Department of Neurology, Madras Medical College, [2]Associate Professor, Department of Physiology, Tirunelveli Medical College, [4]Senior Clinical Scientist, Dr. Agarwal's Healthcare Limited, Tamilnadu, India

Corresponding author: Heber Anandan, Dr. Agarwal's Healthcare Limited, No.10, South By-pass Road, Vannarpettai, Tirunelveli – 627003, Tamilnadu, India

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to the range of Analog to Digital converter. signal averaging technique is used to clarify the responses and enables to get the uncontaminated measure of the sound evoked electrical activity. A 10 millisecond epoch after the stimulus is generally averaged for BAEP studies. At least 1000-2000 trials are averaged to get a good quality recording. One ear was tested at a time. Other ear was masked with white noise. Each ear was tested continuously for a period of 15 minutes. The 15 minutes period was divided into 4 blocks of 3.8 minutes each. Each block was an average of 2000 trials. The amplitude, latency, inter peak latency and the A/R (amplitude ratio) of the study group was compared with the control group.

STATISTICAL ANALYSIS

SPSS version 21 was used for the statistical analysis. Statistical analysis was done using independent samples T- Test and paired T-Test.

RESULTS

On comparison of the age, weight and height and gender of the patients and controls, there was no statistically significant difference making them comparable

Decrease in the amplitude of wave V of BERA was seen in the 4th block when compared to the 1st block in both the ears of the control group which was very highly significant ($p<0.0001$). Decrease in the amplitude of wave 1 of BERA was seen in the 4th block when compared to the 1st block in both the ears of the control group which was very highly significant ($p< 0.0001$). Amplitude ratio (A/R) of BERA between the 1st block and the 4th block of both the ears shows a significant ($P < 0.05$) decrease in the 4th block in the control group (Table-1,2)

Increase in the amplitude of wave V of BERA was seen in the 4th block when compared to the 1st block in both the ears in migraine patients which was very highly significant ($p<0.0001$). Increase in the amplitude of wave 1 of BERA in the 4th block when compared to the 1st block which was not statistically significant in both the ears in migraine patients. Amplitude ratio (A/R) of BERA between the 1st block and the 4th block of both the ears shows a significant ($P<0.05$) increase in the 4th block in migraine patients (Table-3,4).

Wave V of block 4 showed a very highly significant increase ($p<0.0001$) in migraine patients when compared to the controls in both the ears. There was a progressive increase in the amplitude of wave V of BERA from the 1st block to the 4th block in the migraine patients whereas there is a progressive decrease in the amplitude from 1st block to 4th block in the control group in both the ears. The amplitude of the 1st block in migraine patients

Pair	N	Mean	SD	t-value	P-Value
Wave V Block 1 Vs	30	1.039	0.577	5.653	
Wave V Block 4	30	0.535	0.330		<0.0001
A/R 1 Vs A/R 4	30	1.201	0.834	2.933	
	30	0.939	0.585		0.006
Wave I Block 1 Vs Wave I	30	1.015	0.540	4.321	
Block 4	30	0.645	0.363		<0.0001

Table-1: Comparison of BERA amplitude (mv) of the Left ear in the Control group

Pair	N	Mean	SD	t-value	P-Value
Wave V Block 1 Vs Wave V	30	1.099	0.558	8.908	
Block 4	30	0.559	0.359		<0.0001
A/R 1 Vs A/R 4	30	1.430	0.895	2.152	
	30	1.267	0.918		0.040
Wave I Block 1 Vs Wave I	30	0.929	0.516	6.795	
Block 4	30	0.543	0.371		<0.0001

Table-2: Comparison of BERA amplitude (mv) of the Right ear in the Control group

Pair	N	Mean	SD	t-value	P-Value
Wave V Block 1 Vs Wave V	30	0.849	0.389	-7.037	
Block 4	30	1.469	0.595		<0.0001
A/R 1 Vs A/R 4	30	1.149	0.884	-2.592	
	30	2.987	4.587		0.015
Wave I Block 1 Vs Wave I	30	1.111	0.805	-0.283	
Block 4	30	1.144	0.925		0.779

Table-3: Comparison of BERA amplitude in (mv) of the Left ear in the Migraine patients

	N	Mean	SD	t-value	P-Value
Wave V Block 1 Vs Wave V	30	0.899	0.332	-7.276	
Block 4	30	1.583	0.629		<0.0001
A/R 1 Vs	30	1.046	0.804	-2.043	
A/R 4	30	3.999	7.839		0.046
Wave I Block 1 Vs	30	1.153	0.669	-0.293	
Wave I Block 4	30	1.195	0.505		0.871

Table-4: Comparison of BERA amplitude (mv) of the Right ear in Migraine patients

Side	Wave V	Group	N	Mean	Std. Dev	t-Value	P-Value
Left	Block 4	Migraine patients	30	1.469	0.5946	7.520	<0.0001
		controls	30	0.535	0.3301		
Right	Block 4	Migraine patients	30	1.583	0.6290	7.749	<0.0001
		Controls	30	0.559	0.3594		

Table-5: Comparison of wave V amplitude (mv) in the 4th block between the migraine patients and controls

is lower than the amplitude of the first block in the controls in both the ears. The ratio of wave V to wave 1 (A/R) also showed an increase in the migraine patients from the 1st block to the 4th block whereas there is a decrease in the amplitude ratio in the control group in both the ears. No significant change in the BERA latency was observed in both the ears when migraine patients were compared with the controls (Table-5).

DISCUSSION

The results show that there is habituation in the controls whereas there is potentiation in migraine patients. Similar studies were done by Ambrosini et al.[3], Schoenen et al[6,7]; Maertens de Noordhiut et al[8]; Bocker et al[9]; Kropp et al[10]; Wang et al[11,12]; Afra et al[13], Wang and Schoenen[14]; Ozkul et al,[15] who have said that migraineurs are characterized interictally by lack of habituation or even potentiation of cortical evoked potentials during repetitive stimulation. Habituation is well known in normal volunteers (Lutzenbrgr et al).[16] Two studies have explored auditory evoked potential habituation in migraine. In the study done by Wang et al.[17], found that there was potentiation during the 70 dB, but not during the 40 dB stimulation whereas in another study done by Sand and Vingen in[18] found no significant habituation deficit in migraineurs at 40, 55 and 70 dB. In our study we used 60 db and found habituation in normal subjects and potentiation in migraine patients. There was no significant difference in latency and inter peak latency between the migraine patients and the controls regarding the latencies and inter peak latencies. This result was consistent with the study done by Sand T, Vingen et al.[18] who have said that the latency and inter peak latency were normal during the interictal period. In this study it was found that the amplitude of wave V of the first block of the migraine patients is lower than the amplitude of the first block of the controls. This was similar to the study done by Schoenen et al.[7], Wang et al.[11] in which they have said that the amplitude of the first block of the migraine patients was lower than the amplitude of the first block in the controls due to the reduced pre activation of the sensory cortices in migraine patients. Amplitude reduction to a sustained stimulus of equal intensity is called habituation and it has protective effect from sensory over stimulation (Thompson et al.)[19] and lactate accumulation (Sappey-Mariner et al.).[20] Habituation in the central nervous system has been studied in neuronal circuits of varying complexities (Sokolov[21], Thompson et al.[19], Kandel et al.[22]). There is a circumstantial evidence that habituation and potentiation of cortical activity depend on the so called state – setting, chemically addressed connections that originate in the brain stem and involve serotonin, dopamine, noradrenaline, acetylcholine or histamine as transmitters (Mesulam).[23] In the Aplysia Gill withdrawal reflex, habituation is controlled by serotonergic neurons (Kandel).[22] In a study by (Ozkul and Bozlar)[15], they found that the interictal habituation deficit disappears when treated with specific serotonin reuptake blocker fluoxetine. Whatever the exact cause of abnormal cortical information processing in migraine might be, the lack of habituation during repetitive stimulation may have deleterious consequences on the metabolic homeostasis in the brain parenchyma. In headache free interval, migraineurs present subtle cognitive dysfunctions that may contribute to the burden of the disorder. Whether these learning deficits are related to the habituation deficit in cortical information processing shown with electrophysiological methods remain to be demonstrated. Such a relationship would not be surprising, as the phenomenon of habituation is considered to play a pivotal role in the learning processes.

CONCLUSION

There is potentiation in the wave V of BERA generated by inferior colliculus during the continuous period of stimulation of 15 minutes in migraine patients showing potentiation. There is increase in the amplitude of wave 1 of BERA generated by eighth nerve in the fourth block in migraine patients which is not statistically significant. There is a significant increase in the A/R (amplitude ratio) in the fourth block when compared to the first block in migraine patients. There was no significant difference in the latency of the BERA waves in migraine patients when compared to the controls. The present study has shown that there is habituation deficit or rather potentiation in migraine patients which could affect brain metabolism. More studies are needed to find out the precise nature of CNS dysfunction in migraine and to determine whether the cortical physiological patterns allow, the identification of subgroups of migraineurs in whom correlations can be established with specific genotypes, responses to prophylactic agents or interictal cognitive dysfunctions.

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