

## EVALUATION OF BRAINSTEM AUDITORY EVOKED POTENTIAL IN MIGRAINE PATIENT

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### ARTICLE INFO

Received: 2<sup>nd</sup> Jun 2015

Revised: 4<sup>th</sup> Aug 2015

Accepted: 12<sup>th</sup> Aug 2015

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**Keywords:** *Migraine, Aura, Brainstem auditory evoked potential, Wave Latency, Interpeak Latency*

### ABSTRACT

**Background:** Migraine is worldwide common, chronic, Neurovascular disorder, characterized by attacks of severe headache and an Aura involving neurologic symptoms. Its pathogenesis was incompletely understood whether of cortical or brainstem origin. **Aim:** The present study was undertaken to investigate brainstem auditory functions in Migraine patients. **Materials and Methods:** The subjects were recruited based on International Headache Society classification for Migraine. Subjects with episodes of headache for at least 2yrs, 2 attacks per month in last quarter year were included in the study. Forty subjects (16 Migraine with Aura & 24 cases – Migraine without aura) & forty age / sex matched controls were selected. Brainstem auditory evoked potential was recorded using 4-Channel polygraph (Neuro perfect plus). Electrodes were placed according to 10 – 20 electrode placement system. Auditory stimulus in the form of click sound is delivered through the headphones. Clicks were delivered at a rate of 8-10 /sec. The intensity of the stimulus is set at 30db. About 100 averages were recorded. BAEP waveforms - Wave I, III & V latencies and the interpeak latencies were measured. The results were analysed statistically using student's 't' test. **Results:** BAEP recording shows significant prolongation in latencies of Wave I, III & V and the Interpeak latency (IPL) I-III, III-V & I-V in Migraine with aura. In Migraine without aura, there was significant prolongation of Wave I, III & V and III-V & I-VIPL ( $P < 0.05$ ). **Conclusion:** Prolongation suggests that there is involvement of brainstem structures in Migraine, thus BAEP can be used as an effective tool in evaluation of Migraine.

### INTRODUCTION

Headache is one of the most frequently encountered Neurological symptom.<sup>[1]</sup> Headache is caused by irritation of pain sensitive Intracranial structures like Dural sinuses, intracranial portions of Trigeminal, Glossopharyngeal, Vagus and upper Cervical nerves; large arteries and venous sinuses. The structures which are insensitive to pain are Brain parenchyma, Ependymal lining of ventricles and the Choroid plexus.<sup>[2]</sup>

Painful stimuli arising from the brain tissue above the Tentorium cerebelli are transmitted via Trigeminal nerve whereas impulses from posterior fossa are conveyed by Glossopharyngeal, vagus and upper two cervical nerves.<sup>[2]</sup> Headache disorders can be classified into Primary Headache disorder and Headache secondary to structural brain disease.

Primary Headaches are disorders in which headache and associated features occur in the absence of exogenous cause. Migraine, Tension type headache and Cluster headache are most common Primary headache syndromes.<sup>[3]</sup>

Migraine is the disorder of the brain characterized by complex sensory dysfunction.<sup>[4]</sup> It is an Episodic headache disorder and second most common type of primary headache.<sup>[2,3]</sup> Migraine occurs at any age either at childhood, adolescent or adult life, more common in

Females than Males in the ratio of 3:1. 60% of patients have positive Family history.<sup>[5]</sup>

Migraine has a great impact on mental, physical, functional and socioeconomic aspects of patient's life.<sup>[6]</sup> Migrainous have higher lifetime risk of Depressive disorder, Panic disorder, Generalized Anxiety disorder, phobias and Suicide attempts than the normal subjects.<sup>[7]</sup>

The Diagnosis of Migraine was based on headache characteristics and associated symptoms, which is subjective.<sup>[2]</sup> Routine Clinical Examination also appears to be normal in Migraine patients. So, Electrophysiological and Psychophysical tests have been carried out in Migraine patients.<sup>[6]</sup>

Migraine attacks originate due to abnormal Nociceptive Neuromodulator centers especially the Monoaminergic sensory control systems located in the Brainstem. Neuro-otological symptoms like vertigo, phonophobia, tinnitus, and unsteadiness and hearing loss are also common in Migraine. There is a mild bilateral and reversible auditory & vestibular hypofunction during Migraine attack. So, Brainstem auditory evoked potential (BAEP) can be done to assess the function of Brainstem structures traversed by auditory pathways.

BAEPs are the potentials recorded from the Ear and scalp in response to brief auditory stimuli that assess the

conduction through the auditory pathway from the auditory nerve up to Midbrain.<sup>[8]</sup> Transduction of acoustic stimulus by the hair cells create an electrical signal that appear as evoked potential and is carried through the auditory pathway to the brainstem and from there to the cerebral cortex.<sup>[9]</sup>

BAEPs are recorded within 10ms after the acoustic stimulus. Stimulus is delivered to one ear via headphones while the contralateral ear is masked with continuous white noise.<sup>[10]</sup> The stimulus is usually a square wave pulse. If the electrical square pulse causes the diaphragm of the earphone to move toward the patient's ear then condensation click is produced. Reversing the polarity produces rarefaction click. The amplitude of the waveforms is affected by the type of the stimulus.<sup>[11]</sup>

Five waveforms are recorded within 10ms of auditory stimulus. Wave I originates from the peripheral portion of the eighth cranial nerve, Wave II arises from cochlear nucleus, Wave III from superior olivary nucleus, Wave IV originates from the lateral lemniscus and Wave V from inferior colliculi.<sup>[9]</sup> The interpeak latencies measured are I-III, III- V & I- V. They are measured as the distance between the peaks of both waves. I-III IPL represents conduction from the eighth nerve into the core of the lower pons. III - V IPL represents conduction from the lower pons to the midbrain. I- V IPL measures conduction from the proximal part of 8<sup>th</sup> cranial nerve upto the Midbrain.<sup>[10]</sup>

Hence, Brainstem Auditory Evoked Potential was done in Migraine patients to better understand the pathogenesis of Migraine and to utilize this test for Diagnosis and Effective management of Migraine.

## MATERIALS AND METHODS

**Study design:** This study, a case control study

**Place of research:** The study was conducted in the Research laboratory, Department of Physiology, Thanjavur Medical College & Hospital, Thanjavur.

**Duration of study:** The study period extended from August 2013 to June 2014.

**Ethical approval:** Ethical Committee approval was obtained from the institution before commencing the study. The nature of the study was explained to the subjects, an informed written consent was obtained from the subjects prior to the study.

**Inclusion criteria:** The subjects were recruited from the Out-patient clinic of Department of Neuromedicine.

**Grouping:** The study group : comprises of 40 Migraine patients who were selected according to International Headache Society Diagnostic Criteria<sup>[3]</sup> and subdivided into 16 patients – Migraine with Aura and 24 patients – Migraine without Aura (4 males and 36 females).

Out of 40 controls, 6 males and 34 females of age group 19 to 55yrs with no history of headache, healthy controls were selected for the study.

Patients in the age group of 19 to 52 yrs diagnosed as Migraine with episodes of headache for at least 2yrs and at least 2 attacks per month in the last quarter year were included in the study.

**Exclusion criteria:** Subjects with Neurological diseases, ENT, Systemic diseases and auditory deficits were excluded.

**Methodology:** A detailed history of Headache duration, frequency and history suggestive of aura and history to rule out other types of headache were noted.

**Methods:** Brainstem auditory evoked potential was recorded using 4-Channel polygraph (Neuro perfect plus). Electrodes were placed according to 10 – 20 electrode placement system. Channel 1 is placed at Cz - Ai (ipsilateral ear ) and Channel 2 is placed at Cz - Ac ( contralateral ear ). Ground electrode is placed about 20% from the Nasion– Fz position. Auditory stimulus in the form of click sound is delivered through the headphones. Clicks were delivered at a rate of 8-10 /sec. The intensity of the stimulus is set at 30db. About 100 averages were recorded. BAEP waveforms - Wave I, III & V latencies and the interpeak latencies were measured.

**Statistical analysis:** the statistical analysis was done by using Statistical package SPSS version 20. The statistical analysis was done using unpaired student't' test. Values were expressed as mean with standard deviation. P value less than 0.05 was considered as statistically significant.

## RESULTS

**Table 1: Comparison of Brainstem Auditory Evoked Potential Mean values in cases (Migraine with aura ) &Control group**

Parameters (msec)	Migraine with Aura	Control	P value
	Mean ± SD	Mean ± SD	
Wave I	1.272±0.293	1.1222±0.23	0.044
Wave III	3.9381 ± 0.62	3.4323±0.64	0.009
Wave V	6.3444±1.40	5.6510±0.92	0.033
I – III IPL	2.6625±0.58	2.2797±0.58	0.028
III – V IPL	2.5906±0.57	2.2420±0.46	0.020
I – V IPL	5.2556±1.05	4.4888±0.82	0.005

BAEP study results showed significant prolongation in latencies of Wave I, III & V with P value <0.05 in Migraine patients when compared with controls. Also, the interpeak latencies I- III, III- V & I- V were significantly prolonged in study group, Migraine with aura than the controls (Table 1). In Migraine without Aura III- V & I- V IPL were significantly prolonged. (Table 2)

**Table 2. Comparison of Brainstem Auditory Evoked Potential Mean values in cases ( Migraine without aura ) &Control group**

Parameters (msec)	Migraine without Aura	Control	P value
	Mean ± SD	Mean ± SD	
Wave I	1.39±0.359	1.1222±0.23	0.000
Wave III	3.79 ± 0.56	3.4323±0.64	0.029
Wave V	6.33± 0.82	5.6510±0.92	0.004
I – III IPL	2.39± 0.42	2.2797±0.57	0.411
III –V IPL	2.56± 0.52	2.2420±0.46	0.014
I – V IPL	4.95±0.67	4.4888±0.82	0.022

## DISCUSSION

In the present study, Brainstem auditory Evoked Potential parameters were evaluated in Migraine patients with and without Aura and in control group. Migraine can best be explained as a 'Brain state' in which the cellular and vascular functional changes occur at the same time due to dysfunction of subcortical structures, brainstem and diencephalic nuclei that modulate sensory inputs. These nuclei act as a 'Migraine Mediator' whose dysfunction will lead to abnormal perception and activation of Trigeminal Vascular System(TVS) which then activate the central structures.

Thus, Migraine is mainly due to TVS activation generated within the brain without a peripheral sensory input. Migraine is the central sensory processing disorder, there is dysfunction of descending brainstem pain modulatory system. The hyperexcitability of the nociceptive circuitry downstream is responsible for this central sensitization in Migraine patients.<sup>[12]</sup>

BAEP study reports showed significant prolongation of Latencies and Interpeak latencies in Migraine when compared with controls.

D Kaushal, S Sanjay Munjal, M Modi, N Panda<sup>[13]</sup> Evaluated BAEP in 25 Migraine patients. They reported prolongation in wave I, III & V latencies and I-III & I-V interpeak latencies and revealed that prolongation was due to involvement of Brainstem structures as well as activation of brainstem in Migraine patients. These results were in accordance with our present study.

Anil K Dash et al.,<sup>[14]</sup> Studied audiovestibular functions in Migraine patients with and without vertigo. BAEP results revealed that there was significant prolongation in latencies of wave I, III & V and interpeak latencies I-III, III-V & I-V. This study concluded that BAEP abnormalities are the earliest indicator of impending auditory involvement in patients with Migraine. These results were consistent with our present study.

Laila EL Mosly et al.,<sup>[7]</sup> Evaluated the effect of Migraine on quality of life in females and associated changes in evoked potentials. They measured BAEP in 30 Migraine patients and reported that there was prolongation of wave III & wave V latency and I-III & I-V interpeak latency due to hyperexcitability of the cerebral cortex but no significant change in III - V interpeak latency both during an attack and in the interictal phase. These results were similar with our present study.

Firat Y et al.,<sup>[15]</sup> Measured auditory brainstem responses in pediatric population during the period of an attack and asymptomatic period of Migraine. There was prolongation of wave V and I - V Interpeak latency in Migraineurs. These changes were due to transient impairment of auditory brainstem function in Migraine patients. These results were in accordance with our present study. Drake ME et al.,<sup>[16]</sup> Measured BAEP in 50 common Migraine cases. They found that there was significant prolongation of I - V and III- V interpeak latency in Migraine patients. This study suggests that prolongation was due to dysfunction of brainstem centers and possibly related to endorphin or serotonin neurotransmission.

Sherifa A Hamed, Amal Mohammed Elatter<sup>[17]</sup> Evaluated vestibular function in 58 Migraine patients (with and

without aura) and reported prolongation in wave III latency and I-III, III -V & I - V interpeak latencies. This study suggests that in Migraine, there is permanent vestibular damage either peripheral or central vestibular pathways. Similar results were observed in our study. Yang Y, Li P, Ye HC<sup>[18]</sup> Explored personality test and BAEPs in 30 Migraine patients. They reported that the latencies of wave I, III & V and the Interpeak latencies of III- V were prolonged and related this prolongation to brainstem dysfunction. Similar results were observed in our study.

Zgorzalewicz M et al.,<sup>[19]</sup> This study evaluated BAEP in children and adolescents with primary headaches. They reported significant prolongation in latencies of wave III in Migraine children when compared with TTH. This study suggests that brainstem contributes to the pathophysiology of Migraine. Bayazit Y et al.,<sup>[20]</sup> Studied BAEP in 20 Migraine patients, they reported abnormal BAEP findings in seven patients with increased latency of waves I, III & V and the interpeak latency III-V. They concluded that cochlear vestibular symptoms can be seen in Migraine patients. Thus there is dysfunction of neuronal excitability in Migraine, due to defective neurotransmitter signaling and cerebral bioelectrical dysrhythmia.

## CONCLUSION

The present study results show that there is involvement of the Brainstem in Migraine patients. Thus, Auditory brainstem evoked responses can be considered as useful, non-invasive, reliable & diagnostic technique and earliest indicator of impending auditory involvement in migraine patients.

**Limitations:** This study does not compare the duration of the disease with the changes in the Brainstem auditory evoked potential study and the role of Neuromodulatory centers in the brainstem in pathophysiology of Migraine.

**Acknowledgement:** Special thanks to The Dean, Thanjavur Medical College

**Conflict of interest:** No conflicts of Interest

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