EVALUATION OF AUDITORY BRAIN STEM EVOKED RESPONSEIN MIGRAINEPATIENTS

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CERTIFICATE

This is to certify that this dissertation titled **"EVALUATION OF AUDITORY BRAIN STEM EVOKED RESPONSE IN MIGRAINE PATIENTS''** is a bonafide record of work done by **Dr.P.MATHI SELVI.,** during the period of her Post graduate study from 2014 to 2017 under guidance and supervision in the Department of Physiology, Chengalpattu Medical College and Hospital, Chengalpattu – 603 001 in partial fulfillment of the requirement for **M.D. PHYSIOLOGY** degree Examination of The Tamil Nadu Dr. M.G.R. Medical University to be held in April 2017.

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DECLARATION

I declare that the dissertation entitled **"EVALUATION OF AUDITORY BRAIN STEM EVOKED RESPONSE IN MIGRAINE PATIENTS"** submitted by me for the degree of M.D. is the record work carried out by me during the period of **March 2015 to February 2016** under the guidance of **Dr.A.ANITHA, M.D., DCH.,** Head of the Department of Physiology, Chengalpattu Medical College, Chengalpattu. This dissertation is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the University regulations for the award of degree of M.D., Physiology (Branch V) examinations to be held in April 2017.

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INSTITUTIONAL ETHICAL COMMITTEE

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The Members of the committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

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Evaluation of Auditory Brainstem Evoked Response In Migraine Patients

ORIGINALITY REPORT

%16	%11	%12	%6
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Nuwer, M.R.. "IFCN recommended standards for brain-stem auditory evoked potentials. Report of an IFCN committee", Electroencephalography and Clinical Neurophysiology, 199407 Publication	%1
2	www.ispub.com Internet Source	%1
3	ispub.com Internet Source	%1
4	www.acns.org Internet Source	%1
5	cdn.intechopen.com Internet Source	%1
6	Submitted to Northeast Iowa Community College Student Paper	%1
7	Andrew J Gitter. "AAEM minimonograph #16:	

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LIST OF ABBREVIATION

WHO	-	World Health Organization
IHS	-	International Headache Society
CGRP	-	calcitonin –gene related peptide
5HT	-	5-Hydroxy tryptamine
FHM	-	Familial Hemiplegic Migraine
MIDAS	-	Migraine Disability Assessment Score
EP	-	Evoked potential
VEP	-	Visual Evoked Potential
MRI	-	Magnetic Resonance Imaging
BERA	-	Brain Stem Evoked Response Audiometry
BAEP	-	Brainstem Auditory Evoked Potential
SLR	-	Short Latency Response
AVCN	-	Anterior ventral cochlear nucleus
PVCN	-	Posterior ventral cochlear nucleus
DCN	-	Dorsal cochlear nucleus
dB	-	Decibel
dBHL	-	Hearing level
dBSL	-	Sensory level
SPL	-	Sound pressure level
Hz	-	Hertz
IPL	-	Inter peak latency
AEP	-	Auditory Evoked Potential
ABR	-	Auditory Brainstem Evoked Responses
mv	-	Micro volts
ms	-	Milliseconds

INTRODUCTION

Virtually every one experiences occasional headache at some time in their life. WHO ranks headache as one of the top ten disabling disorder for the two genders & the fifth most disabling disorder for women.(1)

Ancient humans have experienced headaches and evidence of remedies torelieve headache. Pain can be traced back as early as 7000BC. In 1200C BEbers Papyrus outlines a ritual for relieving head ache. The Egyptians also attributed the cause of headache as the work of an evil spirit for those experiencingwarmth in the head, the application of moistened mortar to the head was suggested. The Greeks were the next to espouse willow bark as a treatment forpain. Hippocrates (4th or 5th century BC) recommended the extract of willow bark for headache pain.

It is estimated that Globally the percentage of adult population with active headache disorder are46% for headache in general 11% for migraine,42% for tension type headache &3% for chronic daily headache[1] Prevalence of headache in India is 63.9 % with female preponderance.

In 1992 epidemological studies by Richard Lipton, Walter, Stewart, and their colleagues have tremendously expanded our understanding of headaches and the recognition of the impact on patients' lives and society in general.

The American Migraine Prevalence and Prevention (AMPP) study (AMPP 2004-2009) has provided many answers about headache patients, including their treatments, lives, and problems and continues to offer insight into the management of the headache.

In 2013 [2] the International Headache Society (IHS) updated its classification,as follows

- Primary Headache disorder
- Secondary Headache disorder.

Primary headache are those in which headache and its associated features are the disorder itself, whereas secondary headache are those caused by exogenous disorder.

Common causes of headache

- Primary type – **migraine**, tension, cluster, idiopathic, exertional
- Secondary type – systemic infection, head injury, vascular disorder, subarachnoid hemorrhage, brain tumor.

MIGRAINE

Migraine is the most commonly encountered primary headache condition in practice. It is a headache plus syndrome with numerous other accompaniments and associations. The term migraine is derived from the Greek word Hemi&kranion.

EPIDEMIOLOGY

WHO ranks migraine as one of the top 20 leading neurological causes ofdisability. It is estimated that 12% of world's population suffer from migraineand in India, of 1200 million population there are 150-200 million migraineurs under treatment. The prevalence of migraine is about 20% in female and 6% in males[4] More common in females than males in the ratio of 3:1. Three-fourth of Adult migraine patients are females[5]. Studies have shown that women are more likely to have migraine without Aura with peak incidence in third decade[6]

A study from a headache clinic (**Ravishankar K 1997**)[(7)] has shown theprevalence as out of 1000 patients analyzed in the study , 86% had primary headache and 55% of these patients who had primary headache, had migraine that fulfilled the IHS criteria.

National statistics reveal that 31% of migraineurs lose at least one day ofwork and 76% lose at least one day of house hold activities every three

months.51% report that work or school productivity is reduced by half and maydecrease even more as the pain intensifies

HISTORY

Hippocrates in around 400B.C stated that visual disturbances can precede a migraine such as flashing light or blurred vision. Aretaeus of Cappodocia (AD 81_138) was the first todistinguish migrainefrom general headache, noting migraine's unilaterality[8], periodicity, and the associated symptom of nausea. Aretaeus divided all diseases into acute and chronic. For headache, he described headaches of short duration, lasting a few days, as cephalalgia. The term "cephalea" referred to headaches which lasted longer. Because of migraine's one-sided occurrence, Aretaeus named it Heterocrania, meaning "half-a-head."

During the 2nd century AD, Galen (131_201)was credited with describing migraine as Hemicrania,[9]and explained that counter-irritation as a treatment for headache, when he proposed the use of the electric torpedo fish applied to the forehead. This form of therapy foreshadowed the use of Electrotherapy by Duchenne (1806_1875) and the transcutaneous electric stimulator (TENS) introduced in the late 20th century for all types of chronic pain.

The use of trephination for headache treatment was described by Paul of Aegina(625_690) who practiced in ancient Alexandria. The procedure

involved removing a circular portion of the skull, was believed to disturb the evil spirits which werecausing the headache pain and allow them to escape through the wound.

Avicenna(980-1037) noted that headache location could vary between frontal,occipital, or generalized, and that one-sided headaches could be provoked by smells. He used cashews as a remedy for headache as well asother neurological and psychiatric disorders.

Abulcasis(935-1013) recommended therapy for headache was extreme, applying a hot iron to the head of the individual with headaches. Another headache intervention that he suggested was an incision made to the temple and application of garlic to the wound.

Maimonides (1135- 1204) recognized various triggers of headache, including extremes of cold and heat, caused bychanges in barometric pressure. For headache treatment, Maimonides recommended that those suffering from a “strong midline headache, secondary to thick blood or internal coldness” couldbenefit from consumption of undiluted wine eitherduring or after a meal. The warming effect of thewine would help, and also would thin the blood.

The monograph Hemicrania was written by CharlesLepois (1563_1633). This work focuses on the author’sown headaches, which were only relieved by sleep orvomiting. He found relief with consumption of large amounts of fluids. In this treatise, Lepois notes that his headaches are triggered

by changes in weather. He also described an association between one-sided headaches and epilepsy.

DEFINITION:

Migraine is defined as a complex neurological disorder that ischaracterized by recurrent episodes of head pain, autonomic, neurological andgastrointestinal symptoms. Migraine attacks typically last between 4 and 72 hours with freedom from pain between attacks.

CLASSIFICATION OF MIGRAINE

I. Common Varieties

Migraine without Aura

Migraine with Aura

Childhood Migraine

II. Uncommon Varieties

Basilar type Migraine

Familial Hemiplegic Migraine

Migrainous infarction

II. According to International Headache Society (IHS 2013)[(2)], migraine is classified as

- headache with aura
- headache without aura.

Migraine sufferers experience considerable disability and have areduced quality of life, which over the years can affect their work, family lifeand routine life style. Attacks cause severe impairment requiring rest in 53 %of sufferers.

Migraine affects the individual's quality of life and develops a significant burden on the society. The economic burden can be direct or indirect .Direct cost is the treatment cost while indirect cost is due to the loss of productivity and absenteeism. The extent of disability is measured in terms of days lost from the school, office work and household work.

PRECIPITATING FACTORS

1. Emotional stress
2. Too much or too little sleep,
3. Menstruation,
4. Alcohol remains a common trigger of migraine
5. Chocolates
6. Missing or delaying a meal

7. Food that contain tyramine can trigger attacks in predisposed patients.(hard cheeses, vinegar, yogurt, or any product that ishighly fermented)
8. Chocolates
9. Odors, particularly pungent ones
10. Bright light and exercise

SYMPTOMS OF MIGRAINE:

1) Hypersensitivity to sound
2) Hypersensitivity to light
3) Nausea sensation and vomiting
4) Eyes become red and patient perceives of burning eyes
5) Loss of appetite
6) Throbbing pain in half of head
7) Patient wishes to stays all alone and feels comfortable in silent and dark room.
8) Depression and irritability, numbness or weakness in an arm or leg.

TABLE: - 1 DIAGNOSTIC CRITERIA

According to the International-Headache-Classification--ICHD-III-2013(2)-Beta, the following table shows the diagnostic criteria for migraine with and without aura.

MIGRAINE WITHOUT AURA DIAGNOSTIC CRITERIA	**MIGRAINE WITH AURA DIAGNOSTIC CRITERIA**
A. At least five attacks fulfilling criteria B_D B. Headache attacks lasting 4_72 hours (untreated or unsuccessfully treated) C. Headache has at least two of the following four characteristics: 1. Unilateral location 2. Pulsating quality 3. Moderate or severe pain intensity 4. Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs) D. During the headache, at least one of the following:	A. At least two attacks fulfilling criteria B and C B. One or more of the following fully reversible aura symptoms: 1. Visual 2. Sensory 3. Speech and or language 4. Motor 5. Brainstem 6. Retinal C. At least two of the following four characteristics: 1. At least one aura symptom spreads gradually over at least 5 minutes, and/or two or more

1. Nausea and/or vomiting 2. Photophobia and phonophobia E. Not better accounted for by another ICHD-III diagnosis	symptoms occur in succession 2. Each individual aura symptom lasts 5 to 60 minutes 3. At least one aura symptom is unilateral 4. The aura is accompanied, or followed within 60 minutes, by headache D. Not better accounted for by another ICHD-IIIdiagnosis, and transient ischemic attack has been excluded

PATHOPHYSIOLOGY

Headache is caused by irritation of pain sensitive Intracranial structures like dural sinuses, intracranial portions of Trigeminal, Vagus, Glossopharyngeal, and upper cervical nerves, large vessels and venous sinuses. The structures which are insensitive to pain are Brain parenchyma, Ependymal lining of ventricles and the Choroid plexus[10]. 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[10].

The key structures involved in primary headache appears to be

1. The large intracranial vessels and duramater.

2. The peripheral terminals of the trigeminal nerve that innervate thesestructures.

3. The caudal portion of the trigeminal nucleus which extends into thedorsal horns of the upper cervical spinal cord and receives input fromthe first and the second cervical nerve roots (trigemino cervical complex).

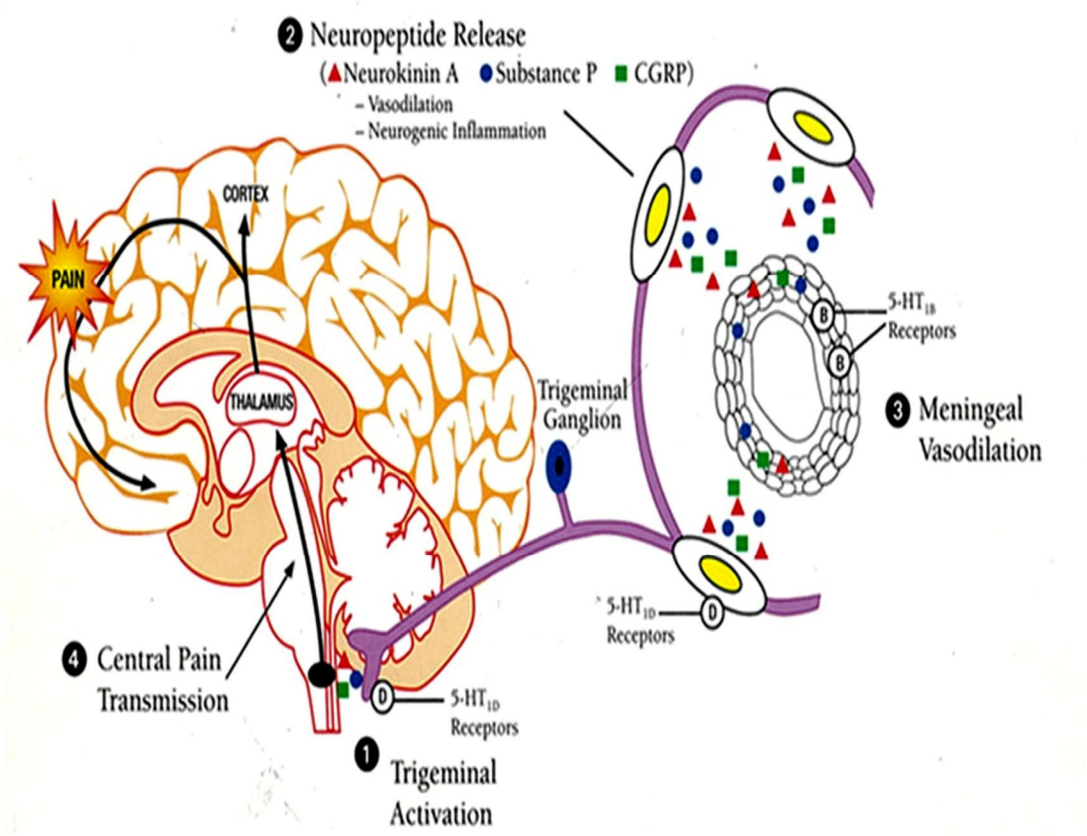
4. The pain modulatory systems in the brain that receive input from trigeminal nociceptors.[11]

PATHOGENESISOF MIGRAINE:

In migrainepathophysiology neuronal and vascular components are very relevant. The structures which are involved are the brain stem, cerebral cortex and the central components of the trigeminovascular system.

During a attack of migraine the temporal artery get enlarged and stretch the the nerve present around the artery which release chemicals that cause inflammation, pain, and further enlargement of the artery which produces the pain.

FIGURE:- 1 PATHOGENESIS OF MIGRAINE



Sympathetic nervous system gets activated in patients with migraine. The sympathetic nervous systemwhich is a part of autonomic nervous system that is responsible for control of stress and pain. Nausea, vomiting and diarrhea occurs because of the increased sympathetic activity. It also delays stomach emptying and thereby prevents oral medications from entering the intestine and being absorbed. The impaired absorption of oral medications is a common reason for the ineffectiveness of medications taken to treat migraine headaches. The increased sympathetic activity also contributes to the sensitivity to light and sound sensitivity as well as blurred vision

Cortical spreading Depression:

It is a complex phenomenon. Where neurons are generally involved, astrocytes may play an important role. Astrocytes regulate the extracellular environment, normalizing regions of low magnesium or regions of abnormal quantities of glutamate and potassium. Therefore, astrocytic dysfunction can lead to regions of the brain being more hyperexcitable than usual. Changes in bloodflow that are seen in aura may also be seen in migraine without aura, and why the changes that occur during aura are often far more extensive than the clinical manifestations of the aura. During CSD there is an increase in intracellular calcium, and glial cells communicate via calcium waves, probably causing a phenomenon similar to that seen in neuronal CSD.

One form of hemiplegic migraine involves abnormalitiesthat are only expressed in astrocytes, and it is likelythat a great deal of migraine pathology is astrocytic rather than neuronal. However, the fundamental hyperexcitability of the cerebral cortex of migraineurs can be documented with a variety of studies

Migraine pain may be due to activation of the trigeminovascular pain pathway. This is comprised of trigeminal sensory afferent neurons that innervate cranial tissues, in particular the large cerebral arteries andthe meninges. It is suggested that the neuronal influence leads to alterations in blood flow. Most of these blood flow changes described in migraine are

probably secondary to many of the functional events that occur during a attack of migraine.

It is likely that ‘cortical spreading depression’ is associated with the release of a variety of chemicals in the meninges, which activates cranial meningeal nociceptors of first-order trigeminal neurons. The subsequent pulsatile nature of the headachemay be due to activated trigeminal nociceptors on extracranial arteries, or perhaps these activated trigeminal nociceptors in the meninges are reacting tonormal CSF pulsations which would otherwise be insensate. This meningeal activation also leads to meningeal inflammation, which includes duralplasma protein extravasation and a sterile meningeal inflammatoryresponse.

The symptoms of a severe migraineattack are strikingly similar to the symptoms of an attack of meningitis, and this is understandable giventhe similarity of meningeal inflammation of migraineand meningeal inflammation of meningitis.

Indeed, in both cases sufferers complain of a pulsatile headache, nausea, photophobia, neck stiffness, and pain uponeye movements. Vasodilatation alone will not account for the pain of migraine. Vasoactive intestinal peptide is a neurotransmitter involved in parasympathetic activation,but is not a trigger of a migraine attack, blood flow changes

observed in migraine are likelyreflections of the metabolic changes that are a consequenceof this cortical activation.

In a migraine attack, there is an initial hyperemia of the brain, which is then followed by a prolonged period of oligemia. Calcitonin gene-related peptide (CGRP) is widely expressed in multiple cell types, and certainly throughout the central and peripheral nervous system. Likelymost relevant to migraine is its abundance in sensory nerve terminals of intracerebral and extracranial blood vessels. With trigeminal nerve activation there is an antidromic release of CGRP. When CGRP was infused intomigraineurs, it produced a migraine-like headache Nitric oxide (NO) is also involved in migrainepathogenesis. Glyceryltrinitrate infusions reliably trigger migraine attacks.

Genetic factors;

Familial factors are believed to play an important part in migraine and genetic studies have constituted significantly. Migraine is known to be 50% more common among first degree relatives of sufferers than in matched controls[12]. Higher rate of concordance for monozygotic twins than dizygotic twins & this effect is more in females than males[5]. Migraine is clearly genetically complex with a non-mendelian mode of inheritance and mutationlikely in multiple genetic loci. In migraine patients the cause for neurologic symptom is mainly due to mutation in a Brain calcium- channel

gene.It was found that in brain and in inner ear a defective calcium channel will lead to reversible hair cell depolarization and auditory and vestibular symptoms.

By studying families with familial Hemiplegic Migraine (FHM) migraine genes was identified. Studies also showed that Familial Hemiplegic migraine revealed involvement of ion channels & when there is alteration in membrane excitability it predisposes to migraine.

FHM 1 is caused by mutation that involves the cav2 .1(p/q) type voltage gated calcium channel CACNAIA gene will produce FHM 1 (13). 50% FHM is mainly due to mutation. Mutation in Na+K+ ATPase ATP IA2 gene, designated FHM2 is responsible for about 20% of FHM. FHM 3[11].is mainly due to mutation that occurs in the Neuronal voltage gated sodium channels SCNIA (Harrison's17th Edition).

Evidence from Neurophysiology

Trigeminal nerve activities and subsequent changes in the cerebral vasculature are widely acknowledged to be key steps in the pathology of an attack, associated with a neurogenic inflammation with release of 'calcitonin-gene related peptide (CGRP)', Neurokinis A' & 5 HT. These substances when released may cause irritation of trigeminal nerve afferents. The role of these neuropeptides such as CGRP has also been explored[14]. CGRP is known to be released during migraine attacks & CGRP receptor antagonists are under

investigation as migraine treatments[14]. However, it is not only the nociceptive afferent pathways that mediate a migraine attack.

Disruption of the natural modulation of other sensory pathways by cerebral structures is also relevant[15]. The resultant Sensory sensitivity can take many forms. Sensory stimuli may act as Migraine triggers[16]. Sensory stimuli can also execute a migraine attack once initiated, so that the sufferer will show behavioural responses in the form of avoidance[17]. In addition some individuals describe symptoms such as photophohia. Exacerbation of head ache by light can occur in individuals suffering with migraine who have preserved non-image forming visual pathways but not in those with no optic nerves or eyes. Presence of migraine photophobia was associated with the presence of cicardian light induced rhythms. In an animal study it was found that thalamic processing of nociceptive and other inputs have a role in mediating migrainous symptoms.

Role of thalamus comes from recent work identifying third-order thalamic neurons as a possible site of action for CGRP receptors. Antagonist administration caused reduction in spontaneous firing rate of cells in the ventropostero medial nucleus of the thalamus[18]. Hyper excitability is mainly in the sensory system.

Evidence from Channelopathies:

Ion channel function is critical in the regulation of tissue excitability. Channelopathies are a group of disorders that have been shown to be caused by ion channel dysfunction[19]. The group includes for example, hypo & hyperkalaemic periodic paralysis and also the various forms of episodic ataxia. Migraine shares several clinical features with known channelopathies such as an episodic nature with characteristic triggers. Additionally many channelopathies exhibit migraine attacks as a part of the phenotype. Examples include episodic ataxia type II[20]& the CADASIL syndrome. These are part of a group of single gene disorder for which pathogenic genetic mutation are known, that they have a strong association with migraine.

Evidence from Imaging:

Models of migraine pathophysiology acknowledge that the brainstem plays an important key role in the genesis of migraine. Chronic migraine is due to rostral brainstem vascular malformation[14]. Brainstem activation has been shown on PET scanning in typical spontaneous & induced Migraine without Aura[22]. Furthermore the activated brainstem areas encroach upon the location of the vestibular nuclei as identified in previous lesion-based structural Magnetic resonance imaging (MRI / Studies)[23]

NEUROTRANSMITTERS:

Role of Serotonin

It has been found that neurotransmitter serotonin plays an important role in migraine. In the brain, serotonin normally regulates the vascular smooth muscle tone of meningeal blood vessels[24]. It has been found that a relative deficiency of serotonin may constitute to the development of migraine[25]. Tryptans are designed to selectively stimulate sub population of 5 HT receptors. Tryptans are agonists of 5 HTIB, 5 HTID & 5 HTIF receptors[11].

Role of Dopamine

Dopaminergic stimulation produces migraine symptoms. There is dopamine receptor hypersensitivity in migraineurs which is demonstrated by giving dopaminergic agonist at doses that do not affect normal subjects. Dopamine receptor antagonists are effectivetherapeutic agents in migraine.

DIAGNOSIS:

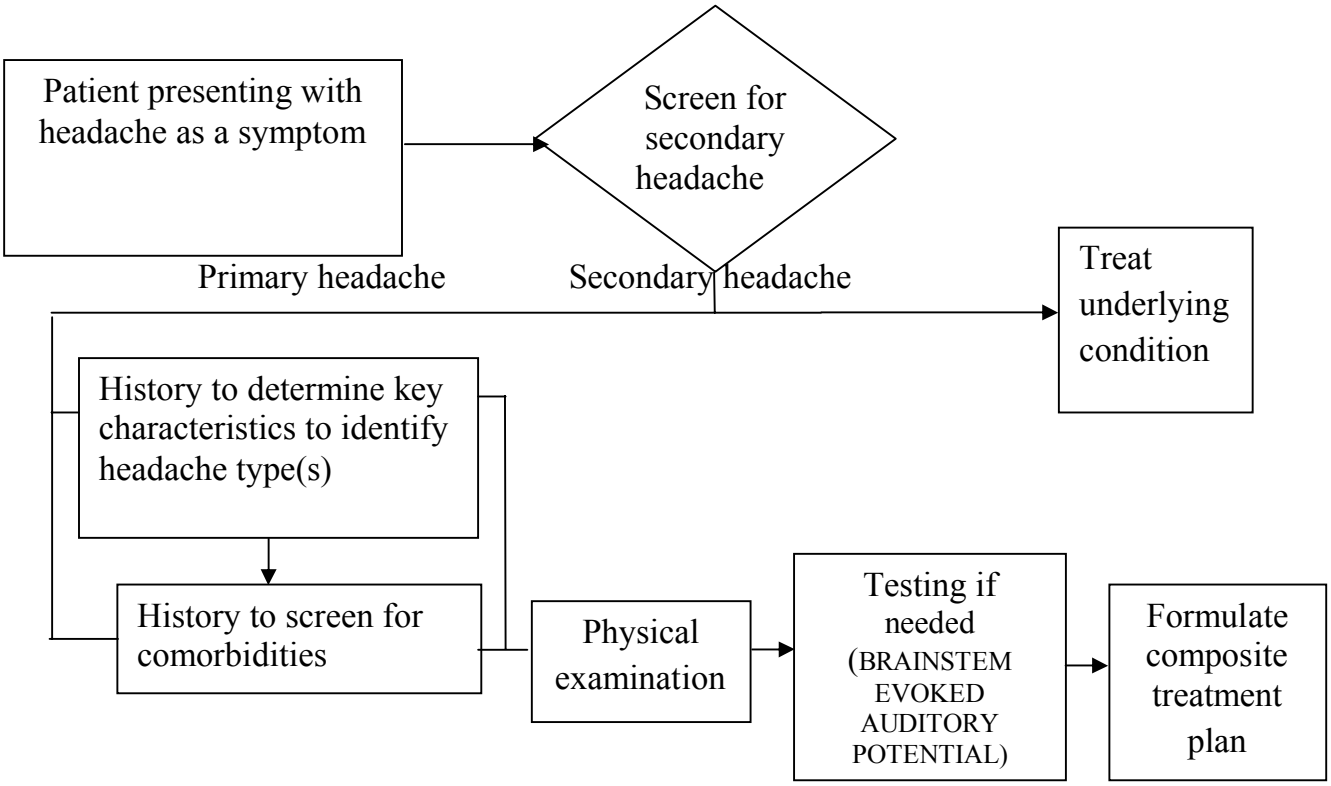
The pain of migraine is commonly unilateral, but can be bilateral. In children, it is usually bilateral.Although the quality of pain is often pulsatile, it maybe pressure-like or stabbing, even in cases where it is initially pulsatile. Light and sound sensitivity ensues, there may be intolerance to light and sound, or these stimuli might amplify the pain of the attack. A characteristic feature of a migraine is that it worsens with movement. All of these factors shape the behavior of migraineurs during an attack. If permitted, they often

preferto lie in bed on a few pillows and remain still in a quiet, dark, cool environment[10].

Despite the high prevalence of migraine the diagnosis rate remains unclear. Neuroimaging studies have found that the hypothalamus is activated early in a migraine attack during the prodrome. Therefore, the hypothalamus may very well supplant the dorsalpons as the "migraine generator." Other imaging studies suggest differences in grey and white matter, cortical thickness, and functional connectivity between the brains of migraineurs and controls. It is unclear if many of these changes occur as a direct resultof migraine attacks or whether these changes precedethe onset of migraine and simply predispose to it. Thus neuroimaging tests such as MRI, PET scanning are not necessary to diagnose migraine, but may be used to find other causes of headaches in those whose examination and history do not confirm a migraine diagnosis.It is believed that a substantial number of people with the condition remain undiagnosed.

Studies have shown that migraineurs are characterized by changes in the evoked potentials during headache period. During the past 30 years, evoked potential have been intensely studied in migraine patients. The methods of electro neurophysiology are particularly appropriate for the study of migraine pathophysiology because they are atraumatic and able to detect functional abnormalities[26].

FIGURE:- 2 DIAGNOSIS OF MIGRAINE



EVOKED POTENTIAL (EP):-

Evoked potentials are one of the common techniques in neurophysiology in the past half century [27]. EPs are reliable, sensitive, objective measures of nervous system function. They are sensitive enough to detect abnormalities even when the physical examination is normal.

Evoked potentials refer to surface electrical activity recorded from the surfaces of the scalp in response to specific and adequate stimulus. These waveforms are maximized by thecomputer to a point where their latency and voltage can be measured.

MIGRAINE AND EVOKED POTENTIALS

Brain stem auditory evoked potentials[28]

BAEPs are the electrical potentials recorded from the ear and scalp in response to brief sound stimulus to assess the conduction of the impulse through the auditory pathway up to the midbrain.

Principle of Auditory Evoked Potential [30]

The evoked response Audiometry is based on the principle that the Bio Electric Response evoked by a sound stimulus always occurs after the same time interval. Auditory stimulus in the form of clicks or pure tune is used to assess the **AuditoryPathway**. When sound wave reaches cochlea, it is converted into an electric impulse and then travels from the cochlea to the auditory cortex through the following pathway.

Spiral ganglia in the cochlea

↓

ventral and dorsal cochlear nucleus in the brain stem

↓

superiorolivary complex in mid brain

↓

Lateral Lemniscus in the mid brain

↓

Inferior colliculus in the mid brain

Medial Geniculate Body

BAEPs appear following transduction of the acoustic stimulus by the ear cells create an electrical signal that is carried through the auditory pathway to the brain stem and from there to the cerebral cortex.

The Auditory evoked transient response can be recorded up to 500 milliseconds from the time of onset of the sound stimulus.

Brain stem auditory evoked potentials [28]

Auditory evoked potential of the first 10 milliseconds is called early phase of transient response or short latency response (SLR)[31].when an auditory stimulus is given series of potential can be recorded in the first 10ms corresponding to the activation of peripheral, pontomedullary, pontine, and midbrain portion of auditory pathways . Short latency is also known as Brainstem Evoked Response Audiometry (BERA) or Brainstem Auditory Evoked Potentials (BAEP), since it records the auditory evoked potential when the auditory stimulus is traversing through the brainstem region.

Advantages of BAEP :-

1) Identification of the site of lesion in retro-cochlear pathologies. The retrocochlear pathologies are a big area from the spiral ganglion of the cochlear nerve to the midbrain (level of inferior colliculus). BAEP test helps to delineate the approximate area in

the retro- cochlear pathway here the lesion is present. This helps in diagnosing like acoustic neuroma.

2) Detection of deafness in the difficult –to- test patients like infants and mentally retarded or malingering subjects. This test can be carried out correctly even in deeply sedated and anaesthetized patients.

3) Objectively in determining the nature of deafness (whether sensory or neural) in difficult –to- test patients, especially when the patients cannot follow or respond adequately to tests.

4) Study of central auditory disorders - Evoked response audiometry has been found to be of use in separating diseases of the auditory cortex from diseases of the more peripheral organs.

Anatomical and physiological basis of brain stem auditory evoked response audiometry[32]

The displacement of the tympanic membrane produced by the sound pressure wave is transmitted to the oval window through the inner ear ossicles. This produces movement of the perilymph and secondarily of the endolymph, which is contained in the ductus cochlearis and also includes the basilar membrane, spiral organ, and the tectorial membrane. The spiral organ contains hair cells that, when displaced by the movement of the tectorial membrane,

produces auditory potentials. The receptor potential leads to the release of the neurotransmitters, which trigger action potentials in the dendrites of the ascending nerve fibers of the cochlear nerve. The basal portion of the basilar membrane is activated by high frequency sound whereas sounds of low frequency generate receptor potentials in the apical portion of the cochlea. The click, which is most commonly used stimulus to produce BAEPs contains mainly high –frequency components and therefore mainly activates the basal cochlear portion. The cochlear nerve neurons are bipolar, situated in spiral ganglia and their dendrites go to hair cells and axons to the cochlear nucleus. The cochlear nucleus has three sub- nuclei:

1. TheAnterior ventral cochlear nucleus (AVCN)
2. The Posterior ventral cochlear nucleus (PCVN)
3. The Dorsal cochlear nucleus (DCN)

The AVCN output is through the ventral acoustic striae forming the bulk of trapezoid body to terminate in the superior olivary nuclei and inferior colliculus. The neurons in the AVCN discharge at short latency to acoustic stimuli with a pattern like that of eighth nerve.The PVCN output mostly goes through ventral and middle acoustic striae to terminate in the superior olivary nuclei and inferior colliculus.

Dorsal cochlear nucleus terminates in the superior olivary nucleus and contralateral inferior nucleus through dorsal striae. The discharges from these neurons are different from AVCN by having a longer latency.

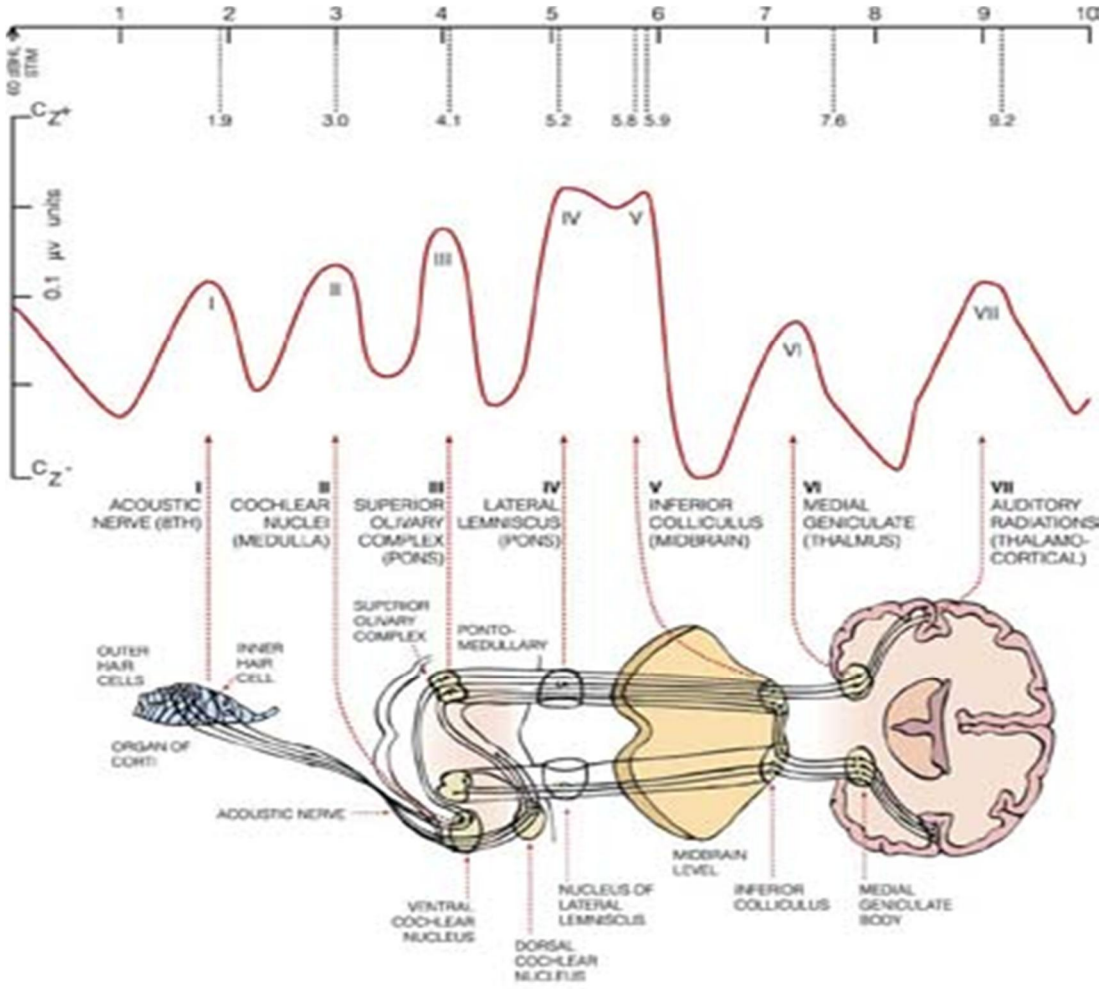
Basalportion in pons superior olivary nuclear complex consists of medial and lateral components cochlear nucleus terminates in it .The medial components receives the input from both ipsilateral and contralateral AVCN which are excitatory. The lateral superior olivary nucleus also receives ipsilateral excitatory inputs from AVCN and PVCN and inhibitory inputs from contralateral AVCN and PVCN via trapezoid body. Olivary nuclei are the first site in auditory pathways where neurons are affected in a nonlinear manner to binaural stimulation.

The inferior colliculi and the lateral lemniscal nuclei converge the input from contralateral cochlear nucleus and superior olivary nucleus. From inferior colliculi the impulse travels to medial geniculate body and then to auditory cortex. Orderly orientation of the neurons in dorsal cochlear, medial superior olivary, and lateral superior olivary nuclei results in summation of synaptic potentials to result in high amplitude electrical fields.

As the auditory impulses traverse through the different stations in the auditory pathway, it undergoes some degree of processing at each of the stations. Passage of the impulse through this pathway generates an electrical activity which can be monitored by placing a surface electrode on the vertex of

the scalp. On graphical recording, this electrical activity presents a wave – form with discrete peaks, the character of which is dependent upon the functional and structural integrity of the above mentioned pathways.

FIGURE:-3Anatomical and physiological basis of brain stem auditory evoked response



Terminologies used in evoked potential study[29]

Hearing level (dB HL)

This scale refers to the number of decibels of intensity compared to the threshold of hearing in a group of normal subjects. Zero on this scale is defined as the threshold at which a normal subject can just perceive 50% of the stimuli.

Sensory Level (dB SL)

On this scale zero is defined as the point at which the individual can barely appreciate the stimuli.

Physical Definition (dB pe SPL)

Physical measurement of sound pressure levels used at the zero dB reference level. There is a pressure of 20uPa which equals 0.002dyn/cm2. The zero dB pe SPL turns out to be approximately equal to – 32 dB HL. 22

Individual Equipment scale

Individual equipments have their own dial setting in terms of dB, which should be correlated with HL or SL. For deciding the click intensity in a patient, dB SL is measured and the stimulus delivered 60-70 dB higher.

Normal BAEP

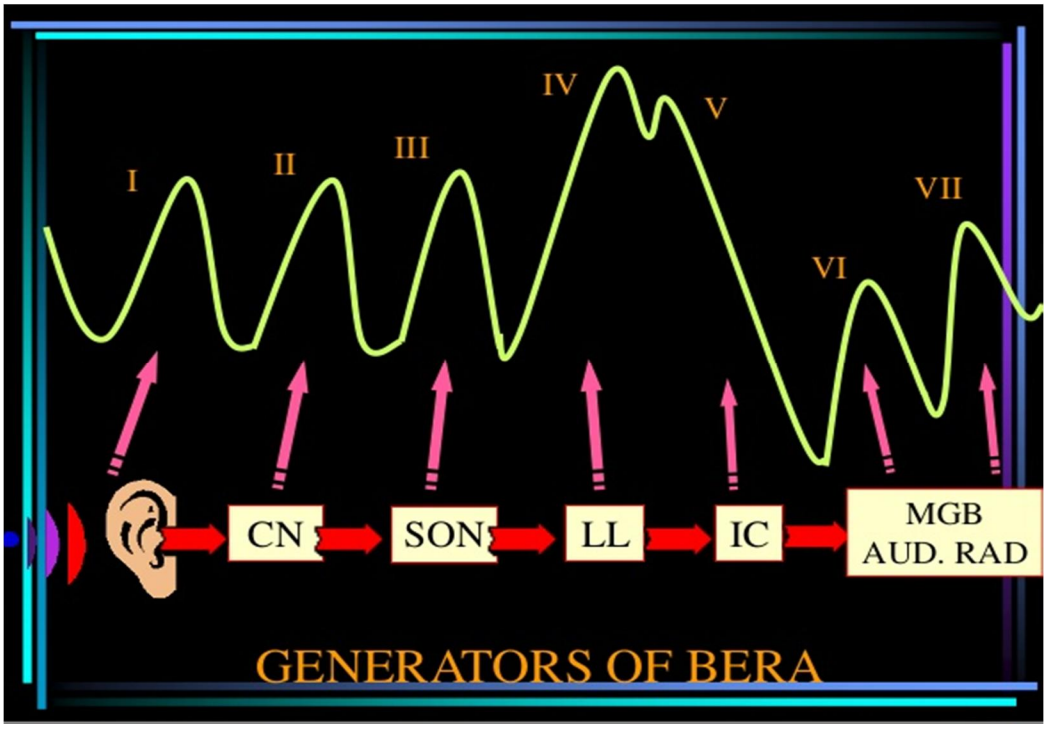
Classical BAEP consists of '5-8 vertex' positive peaks which are labeled using 'Roman numbers.' The **first five** peaks are of clinical

importance. The troughs immediately following the peaks are designated by a prime mark eg, the trough of wave I is designated as I'.

TABLE:-2 Generators of BAEP waveforms

Wave form	Generators
I	Eighth cranial nerve
II	Cochlear nucleus
III	Superior olivary nucleus
IV	Lateral lemniscus
V	Inferior colliculus

FIGURE:- 4 GENERATORS OF BERA



Wave formrecognition

Wave 1

This is the first prominent up going peak in the ipsilateral ear recording channel. It is reduced or absent from the contralateral ear recording channel. It appears 1.4 ms after the stimulus. The amplitude of this wave can be increased by using horizontal montage, external canal needle electrode, nasopharyngeal electrode, increasing stimulus intensity or decreasing the stimulus rate. Patients with central nervous system problems only, should have a preserved wave I since it originates from VIII nerve.Conversely, the patients with significant peripheral hearing impairment may have a very poorly formed or absent wave I but relatively normal wave II-V.

Wave II

Wave II is poorly defined in some adults and most neonates. It sometimes appears as a small peak following wave I. It may appear in the down going slope of wave I or in the up going slope of wave III. It is more prominent in contralateral channel recording where it has a slightly prolonged latency compared to ipsilateral. Sometimes the fusion of waves II and III results in M-shaped II-III complex.

Wave III

It has a prominent up going peak. It is smaller and appears earlier in the contralateral channel. Some normal subjects have a bifid wave III. Bifid wave III may be related to the condensation or rarefaction clicks.

Wave IV

This wave is identified as the peak just preceding the wave V. So once wave V is identified, it is not difficult to recognize wave IV. Sometimes the wave IV and wave V becomes superimposed leading to difficulties in identification of the waves. A distinct and separately identifiable wave IV is present in only 50-60% of subjects. In other cases the wave IV cannot be identified separately.

Wave V

It is the most reliable and easily identifiable wave in the BAEP tracing. The hallmark of wave V is that there is a sharp negative (downward) deflection immediately following the peak. (The wave V usually appears at 5.6-5.85 milliseconds in normal subjects when the BAEP test is done at 50-60 dB suprathreshold level. Though the amplitude of the BAEP waves is variable, yet it is usually the target and the most robust of the five BAEP waves)

Measurement and normal values of BAEPs

The following variables are studied

1. Absolute latency and amplitude
2. Inter peak latencies (IPLs)
3. Amplitude ratio of wave V/I
4. Inter ear inter peak differences

Absolute latencies and amplitudes

Absolute latency is measured as the distance from the beginning of the first wave to peak .The amplitude is measured as the height from peak to trough of that wave. The difficulty is encountered when the wave forms are poorly formed. The recommended method for latency comparison is to superimpose the major ascending and descending limbs of waves of two sides against a strong source of light.

Inter peak latency

The commonest inter peak latencies employed in clinical practice are I-V, I-III, and III-V.

I - V IPL

Normal value is 4.5ms. It is a measure of conduction from proximal VIII nerve through pons to midbrain. This IPL is slightly shorter in young female and longer in older male. Normal right to left asymmetry should not exceed 0.5 ms.

I - III IPL

Normal value is about 2.5ms.It measures conduction from VIII nerve across subarachnoid space into the core of lower pons. The I-III IPL can be increased in any diffuse process that affects the generation of these waves.

III-V IPL

The normal value is about 2.4ms. It measures conduction from lower pons to midbrain.

V/I amplitude ratio

Since wave I is generated outside and wave V inside, these can be compared to determine the relationship of expected amplitude. Wave V/I can be expressed either as ratio or percentage. The amplitude ratio is normally between 50% and 300%. The amplitude ratio may be influenced by filter setting and click intensity, therefore, comparison with the normal values of the respective laboratory is essential. When the amplitude ratio V/I is lower than 50% then there will be a small wave V, and may be consistent with a central impairment. Very high V/I amplitude ratio (300%) suggests small amplitude of wave I, which may be due to peripheral hearing impairment.

Inter ear latency difference

The difference in the absolute latency of a particular wave in between the two ears should not be more than 0.5 ms, provided the same suprathreshold sound stimulus has been presented to the two ears

TABLE:- 3 BAEP Normal values

Wave (latency ms)	Chiappa et al (1979)	Misra and Kalita
I	1.7 + 0.15	1.67 + 0.17
II	2.8 + 0.17	2.78 + 0.21
III	3.9 + 0.19	3.65 + 0.22
IV	5.1 + 0.24	5.0 + 0.30
V	5.7 + 0.25	5.72 + 0.3
VI	7.3 + 0.29	7.2 + 0.48
I-III IPL	2.1 + 0.15	1.99 +0.25

Variations inBAEP

BAEP abnormalities may include the following

1. Absence of wave forms
2. Amplitude ratio abnormalities
3. Abnormal absolute or inter peak latencies
4. Right to left asymmetry

In most normal individuals waves I-V are seen. Sometimes in normal subjects, wave IV may form a wave IV-V complex. In such a situation, if there is absence of wave IV it does not indicate an abnormality.It is also difficult to

distinguish wave II in some normal subjects. When all the waves are absent, it is (I-V) is abnormal. When wave I is recordable and not the succeeding waves, it is abnormal. Similarly recordable wave I and III but unrecordable wave IV and V is also abnormal.

Factors affecting BERA recording

Technical factors

Stimulus rate

This is the number of clicks presented to the ear per second. The recommended rate is 10- 40 clicks per second. Very high stimulus rates such as 80 or 100 clicks per second change the latency and amplitude of the BERA waves. Usually, the amplitude decreases and the latency increase if the stimulus rate is high.

Stimulus phase or polarity

The phase of the click stimulus may be two types, viz. condensation phase and rarefaction phase. The transducer which produces the click sound has a diaphragm which vibrates. When the diaphragm moves towards the ear drum, the phase is called condensation phase. When the diaphragm moves away from the ear drum, it is called rarefaction phase. For routine BAEP studies, use of rarefaction phase is recommended, mainly because it produces better resolution of the BAEP waves. However, the latency and amplitude of wave V is not much altered by the phase of sound stimulus.

Intensity of the sound stimulus

For routine BAEP studies, the intensity of the click stimulus of 60 dB suprathreshold is recommended i.e. 60dB above the hearing threshold of the ear being tested.on lowering the intensity of the click stimulus there is an increase in the absolute latencies and there is a decreases in the amplitude of the BAEP waves. Since the amplitude and latency of the BAEPwaves are dependent upon the intensity of the click sound used, same intensity should be used not only in both the ears of the same patient but also in all patients such that the results are easily comparable.

Binaural / Monaural stimulation

In clinical studies only a monaural stimulation is recommended, i.e. one ear at a time should be tested. Presenting stimulus to both ears together increases the amplitude of the wave III, IV, V but not wave I.

Filter characters of the machine

The BAEP machine should be so adjusted that it records only between a fixed ranges of frequencies. The lower limit of this frequency range, called low frequency filter should be 100Hz or 150 Hz and the higher frequency filter is usually kept at either 3000 or 5000 Hz. To interpret the BAEPaccurately and to compare it with the normative data, fixed or standard and correct filter settings should be used. Altering the filter settings will

change the amplitude ratios of the waves and introduce unwanted artifacts into the BAEP tracing.

Nature of the sound used

The sound stimulus used is a click sound. The click sounds are generated as square wave pulses each of which are of 0.1 millisecond duration. When BAEP test is being done for neurological diagnosis, it is essential that all the BAEP waves are clearly recorded. Hence sound stimuli (clicks only) are delivered at 50-60 dB above hearing threshold since this evokes neat and robust easily recognizable wave peaks.

Confounding variables

Age

Interpeak latency (IPL) I-V is slightly longer by 0.1-0.15 ms in older individual compared to younger individuals[35]

Gender

Womens have a shorter latency and higher amplitude of BAEP .The I-V interpeak latency is shorter by 0.1 ms in females when compared to males.[35]

Temperature

The absolute latency and IPL are prolonged on lowering the body temperature. A 0.17 ms increase in wave V latency on 1 degree Celsius

reduction of body temperature has been reported. At 32.5 degree Celsius BAEP waves are distinctly abnormal and at 27 degree Celsius the wave forms disappear[36].

Among all the evoked potentials, BAEP's is commonly used because it is a more reliable electrophysiological method and it is a non-invasive procedure to evaluate the function of brainstem structures which is travested by acoustic pathways. Assesment of the acoustic pathway by BAEP's which plays a very important role in the description of pathophysiology of primary headache especially migraine. This study was done to evaluate the involvement of Brain stem structures in migraine patients.

REVIEW OF LITERATURE

MIGRAINE

One of the oldest ailments known to mankind.is migraine. In around 400B.C Hippocrates stated that migraine is preceded by visual disturbances which we call aura. Aretaeus was credited for his migraine discovery who described one sided headache later it was Galenus who pointed connection between stomach and brain due to vomiting

Abu Bakr Mohamed pointed association between Migraine and Hormones. `In 1950 Harold Wolff proposed that blood vessel abnormalities were associated with migraine. Migraine has a great impact on physical, mental, functional &socioeconomic aspects of patient's life[37]. Migraineurs have higher life time risk of Panic disorder depressive disorder, generalized anxiety disorder, phobia and suicide attempts than the normal subjects.[38]If migraine is diagnosed the next important step is to evaluate theextent of the patient disease and disability.

The migraine disability assessments say (MIDAS Questionnaire) by Innovative Medical Research 1997 is used validated easy to use tool. Patients were asked to answer questions, & accordingly they are divided into 4 grades.

Grade 1- Minimal or infrequent Disability; 0-5

Grade II –Mild or infrequent Disability; 6-10

Grade III- Moderate Disability: 11-20

Grade IV-Severe Disability :> 20

CONFOUNDING VARIABLES AND MIGRAINE

In a study done by **Stewart et al** [4] a mailed survey was done to evaluate the age and sexspecific incidence in 120000 US subjects. The incidence of migraine is maximum in the ages of 20 and 24 in women and ages 15&19 in males. Migraine is highly prevalent in the population, with the cumulative prevalence being 43% in femalesand 18% in males. In young children migraine ismore prevalent in males, but by puberty females predominate.

Rasmussen BK, Olen[6] conducted studies by randomly selecting 3000 males and 1000 females aged 40 years from Danish population by mailed questionnaire regarding migraine and it was found that the prevalence of any type of migraine was 18%. Out of these, 12% are male & 24% are females. The male female ratio is approximately 1:2 & has shown that females are more likely to have migraine without aura with peak incidence in third decade

Bigal et al[39] in his study has stated that obesity has been recognized to be a significant risk factor for the transformation of episodic attacks into a

chronic form of migraine Higher BMIs will increase the risk of all chronic headaches, and they are positively correlated with headache frequencyand disability.When overweight subjects subsequentlyreduce their BMI, it often leads to a reduction in headache frequency. Bariatric surgery for those who are morbidly obese is often recommended.

COMPLICATION:

Peatfield et al. 1981[40] stated that the migrainous aura is visual in 82% **Rasmussen and Olesen, 1992**[6] found that the migrainous aura is visual in 90% of cases, and it was also found that hypersensitivity to light is mostly present in migraine attacks . People who get migraines often describe the pain as one sided pain severe headache disorder. During migraine attack, the patient becomes very sensitive to light and sound.

Thaker et al[41] studied the association of migraine with vertigo and it was found that out of 344 cases of vertigo, 19 had headache characteristic of migraine. The spectrum ranges from a transient reversible dysfunction to a more permanent destruction and includes involvement of both peripheral and central vestibular system.

Parker[42]-reported that there is a strong association between migraine and vertigo results of his study showed reversible hair cell depolarization leading to auditory and vestibular symptoms is due to the defective calcium channels, primarily expressed in brain and inner ear..

Laila E Mosley[38] stated that migraineurs have higher life time risk of Panic disorder depressive disorder, generalized Anxiety disorder, phobia and suicide attempt than the normal subjects. Nofal found that migraine has a great impact on physical, mental, functional & socioeconomic aspects of patient's life.

PATHOGENESIS OF MIGRAINE-

Bhowmik et al[43] found that certain triggering factors such a missing ameal, hypoglycemia, increased tension, lack of sleep , menstruation, hormones, or smoking, alcohol etc causes vascular disturbance. A vascular disturbance is thought to cause migraine.

Golla and Winter described a particular response of migraine patients to light stimulation. This consisted of the exaggeration of the response itself to a wider range of stimulus frequencies, in comparison with normal subjects. Certain factors can trigger migraine in persons who are prone to develop headaches called migraine triggerers

On the onset of menstruation the blood estrogen level decreases in some woman which is a trigger for migraine attack. On fasting there is hypoglycaemia which precipitates migraine attack. Therefore, prolonged fasting should be avoided by migraine sufferers.

Kelman 2007: Martin et al 2006[44] Sensory stimuli may act as Migraine triggers Sensory stimuli can also execute a migraine attack once initiated, so that the sufferer will show behavioural responses in the form of avoidance

Noseda et al 2010[17] In addition some individuals describe symptoms such as photophohia. Exacerbation of head ache by light can occur in individuals suffering with migraine who have preserved non-image forming visual pathways but not in these with no optic nerves or eyes. Presence of migraine photophobia was associated with the presence of cicardian light induced rhythms. In an animal study it was found that Thalamic processing of nociceptive and other inputs have a role in mediating migrainous symptoms.

Coleston1994[45] suggested that in migraineurs the abnormalities reported reflect dysfunctions at the cortical level, but precortical visual processing may also be impaired

(LipkinAF, Jenkins HA)[31] **& (VIERRE et all 1996)** observed that woman developed recurrent episodes of sudden sensorineural hearing loss, occurring with migraine headaches and found out that it is an unusual complication of migraine, which probably arises from a reversible vasoconstriction of the cochlear blood vessels. Spasm of the cochlear vessels is responsible for reversible hypoxic injury and temporary hearing loss.

Ambrosini. A et al. 2003[26] said that in migraine patients the cereberal cortex has a reduced preactivation excitability level thus causing habituation deficit

Summ et al 2010[46] Role of Thalamus comes from recent work identifying third-order thalamic neurons as a most important site for CGRP receptors. Antagonist administration caused reduction in spontaneous firing rate of cells in the ventropostero medial nucleus of the thalamus.

Lance et al obtained circulatory alterations in migraine by stimulating locus coeruleus in cats and monkeys. Based on this other authors studied brainstem function by means of a technique called BERA experience to have migraine without aura with peak incidence in third decade.

Robert W. Baloh MD, 1997[47] suggested that reversible hair cell depolarization with auditory and vestibular symptom is due to the defect in calcium channels present in brain and inner ear.In families with migraine headaches and neurologic symptoms this hypothesis is under investigation.

Iadecola – 2002 proposed that Trigeminal nerve activities and subsequent changes in the cerebral vasculature are widely acknowledged to be key steps in the pathology of an attack, associated with a neurogenic inflammation with releasing a large amount of ‘calcitonin-gene related peptide (CGRP), Neurokinis- A & 5 HT. These substances when released may cause irritation of Trigeminal nerve afferents.

Goadshy et al 2009[21] The role of these Neuropeptides such as CGRP has also been explored. CGRP is known to be released during migraine attacks. Godsky 2008 CGRP receptor antagonists are under investigation as migraine treatments. Nociceptive afferent pathways mediate a migraine attack.

Goadshy & Holland 2009[15] Disruption of the natural modulation of other sensory pathways by cerebral structures is also relevant. The resultant sensory sensitivity can take many forms.

BAEP IN MIGRAINE-

Stockard et al. 1971[35], Allison et al. 1983 suggested that women have a higher amplitude shorter latency of BAEP. The I-V IPL is shorter by 0.1 ms in female compared to male.

Laila EL Moslyet al[38] 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. In migraine patients the abnormalities reflect not only dysfunctions at the cortical level, but it is found that precortical visual processing is also impaired.

Newer et al. 1994[49] Studies revealed that there is prolongation of I-V interpeak latency in older adults by 0.1-0.15ms. Wanget al 1996 conducted a study and observed that in migraine patients there is interictal electrophysiological abnormality which is intensity dependent of Auditory evoked cortical potential

Anil K Dash et al., studied audiovestibular functions in migraine patients with and without vertigo. BAEP results revealed that there was increase in I, III and V latencies and interpeak latencies I-V, III-V & I-III. This study concluded that auditory involvement is the earliest indicator in migraine patients and this was found by BAEP abnormalities.

Dorfman et al (1981)[36] found that the absolute latency and IPL are prolonged on lowering the body temperature. A 0.17 ms increase in wave V latency on 1 degree Celsius reduction of body temperature has been reported. At 32.5 degree Celsius BAEP waves are distinctly abnormal and at 27 degree Celsius the wave forms disappear

Kaushal et al[52] who evaluated BAEP in 25 migraine patients. The results revealed prolongation in latencies I, III & V latencies and interpeak latencies I-III & I- V and it was stated that prolongation was due to involvement of Brainstem structures as well as activation of brainstem in migraine patients.

The methods of electro neurophysiology are particularly appropriate for the study of migraine pathophysiology because is a more reliable method and it is a non-invasive procedure to evaluate the function of brainstem structures which is travested by auditory pathways. Among all the evoked potentials, BAEP potentials is commonly used because neurophysiological examination by means of auditory evoked potential enable us to make neurophysiological assesment of the auditory pathway which plays a very important role in the description of pathophysiology of primary headache especially migraine.

This study was done to evaluate the involvement of Brain stem structures in migraine patients. Review of literature highlights the fact that auditory pathway is definitely involved in migraine patho physiology but the extent of involvement with concordance evidence of duration was inconclusive. So the aim of the present study is to evaluate BAEP in migraine patients at the earliest to detect the subclinical involvement of the nervous system.

AIM AND OBJECTIVES

AIM:

"To evaluate the Auditory Brain Stem Evoked Response in Migraine Patients and to compare it with normal subjects

OBJECTIVE;

1. To evaluate 'Auditory Brain Stem Evoked Response' in migraine patients.

2. To compare the latency and interpeak latency of BAEP waves between migraine and normal subjects.

MATERIALS AND METHODOLOGY

Study design: Case control study

Control – Normal Subjects

Case – Subjects Fulfilling the Criteria Of Migraine As Per International Headache Society

Period of study:

One year (2015 to 2016)

Place of study:

Department of PHYSIOLOGY
Chengalpat Medical College, Chengalpat

Selection of subjects - Sixty subjects participated in the study

Study group

Thirty subjects fulfilling the criteria of migraine as per the HIS (International Headache Society)[1] from the outpatient department of the Institute of Neurology, Chengalpat Medical College, Chengalpat.

Age group: 20-50 years of both sexes.

Control group

Thirty age and gender matched normal subjects were included in the study for comparison with the study group. All the participants were informed about the study, oral and written consent were obtained. Permission from the Institutional ethical committee was also obtained

Inclusion Criteria for Study Group

- Age group 20 to 50 yrs / both gender
- Migraine With Or Without Aura at least For a Period of 6 Months
- Patient With Normal Respiratory/Cardiovascular/Hepatic Function
- Patients with normal hearing and normal vision.

Inclusion Criteria for Control Group:

- Age group between 20-50-yrs
- Subjects with Normal Hearing and Normal Vision

Exclusion Criteria:

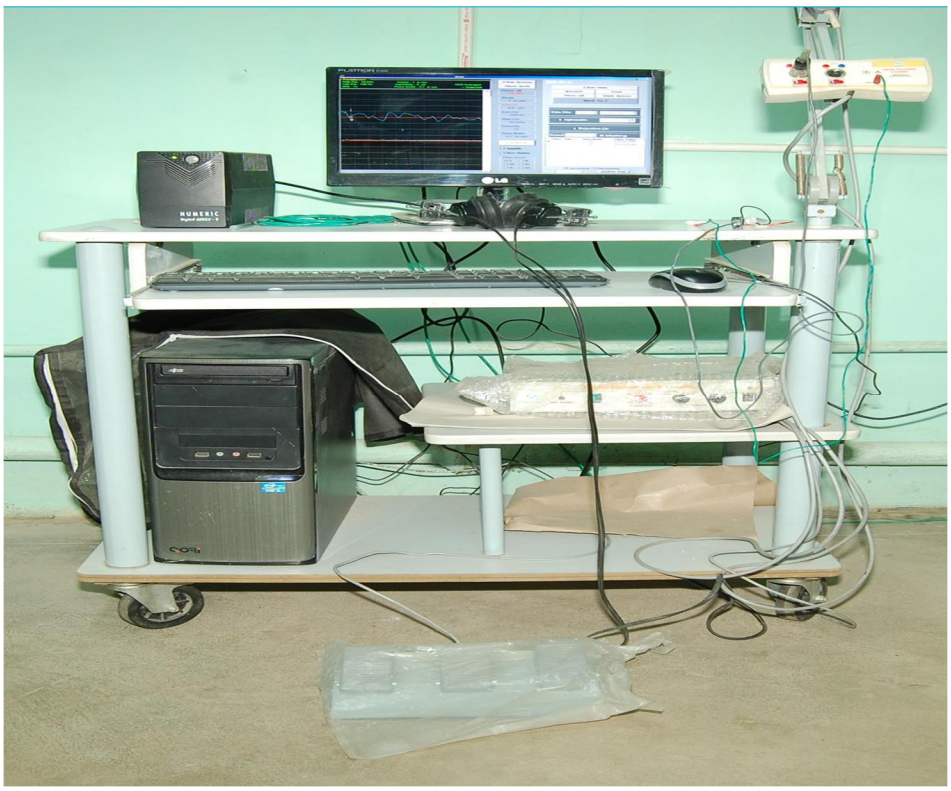
- Known Hypertensive
- Diabetes Mellitus
- Ear Diseases

- Anaemia
- Known Smoker / Alcoholic / Any medication
- Any Other Neurological Illness
- Those who are on medications which affects hearing

Clinical Examination

Routine clinical examination was performed. Rinne's, weber and pure tone audiometry was conducted. Following that BERA was done byusing 'NEUROPERFECT EMG-2000(EMG/NCV/EP' System.

FIGURE:-5 'NEUROPERFECT EMG-2000(EMG/NCV/EP' System



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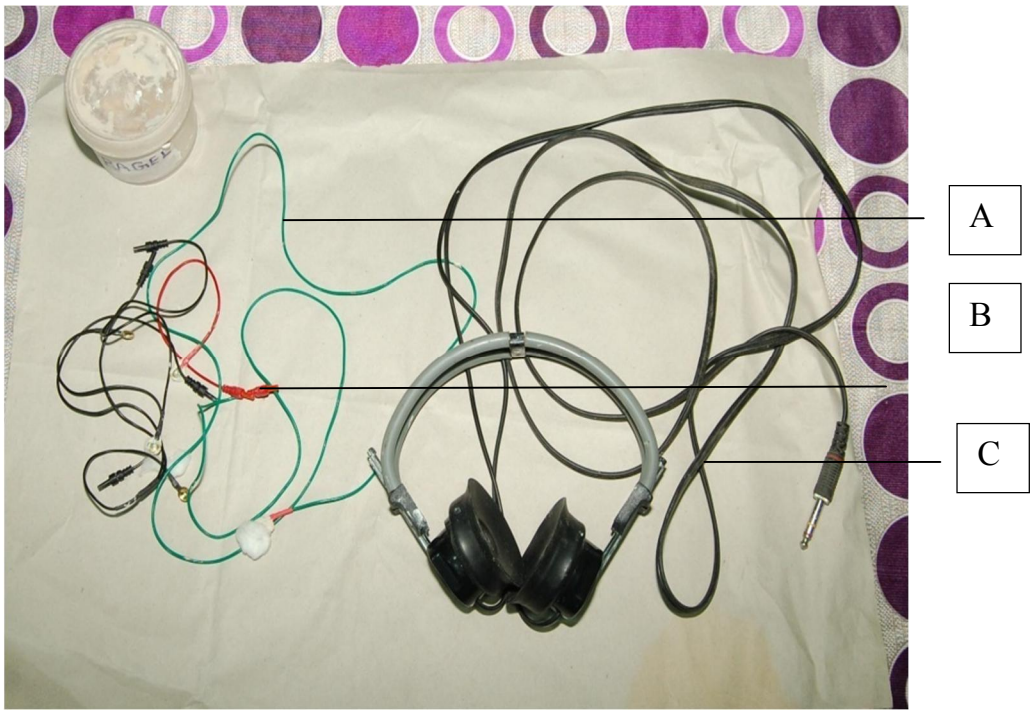


A-GROUND ELECTRODE

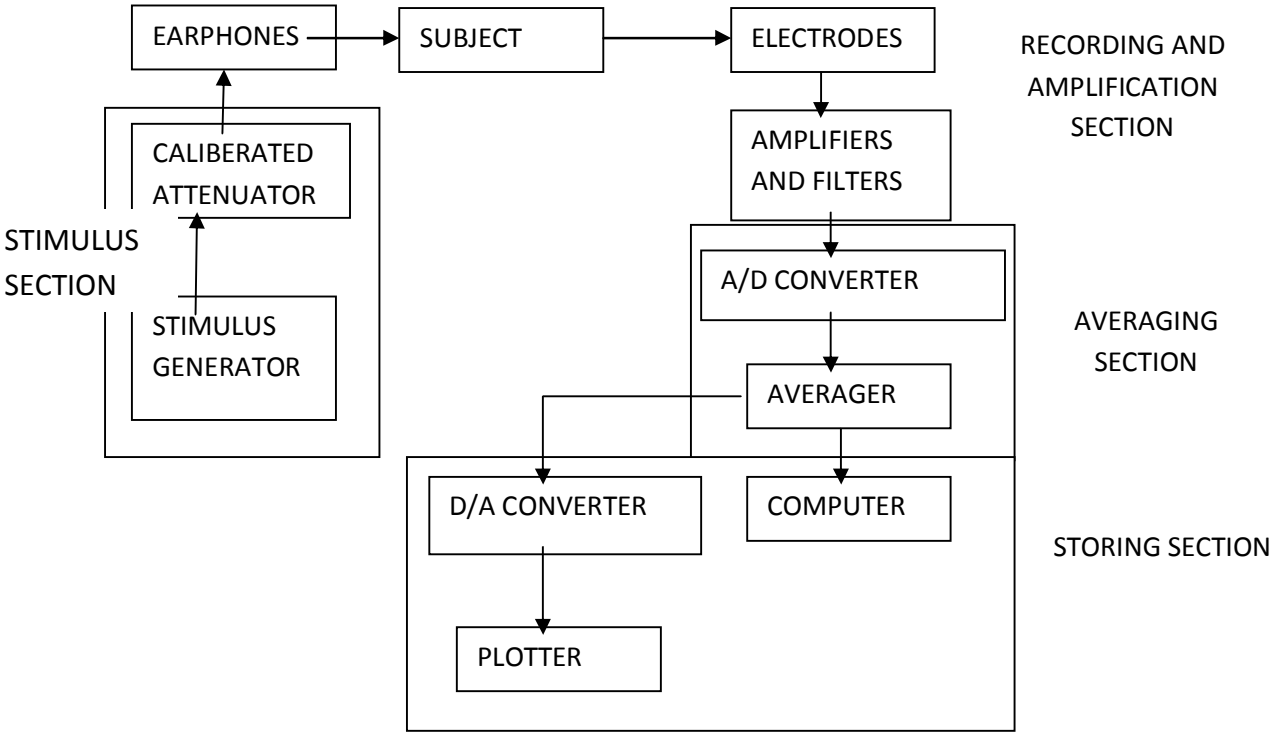
B-RECORDING ELECTRODE

C-HEAD PHONE

BAEP

The apparatus set up for measuring Brainstem Evoked Response Audiometry are set up as per the "Recommended standards for the clinical practice of Evoked potentials; introduced in Guide line 9A: Guidelines on Evoked potential by American Society of Clinical Neurophysiology.

FIGURE:-6 The basic apparatus for recording of auditory brainstem evoked responses (ABR) is illustrated



1. Pulse generators:

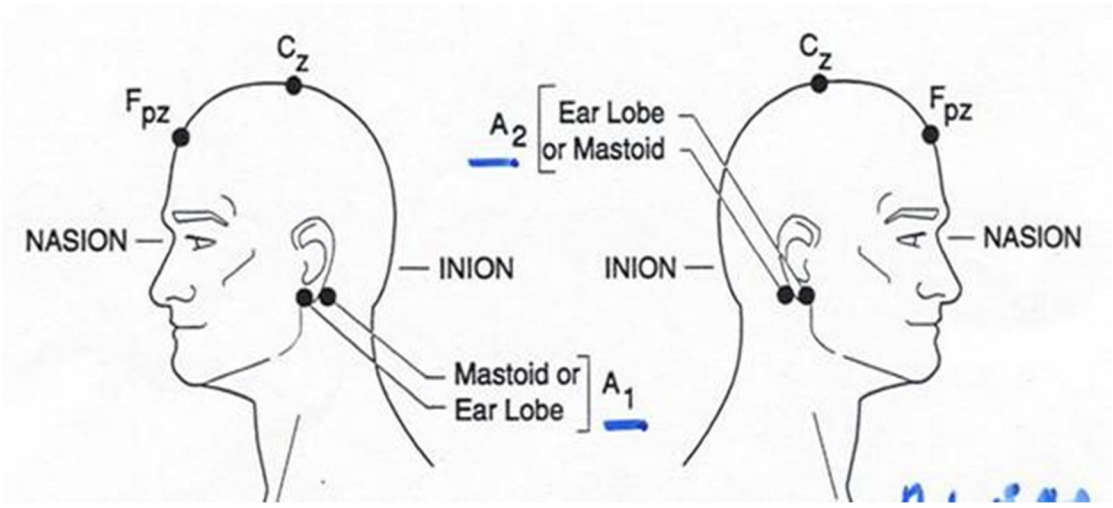
Ear phone or head phone has a transducer which transmits the stimulus in the form of clicks.

2. Recording Electrodes

The electrodes required for BAEP measurement are placed in the corresponding sites of scalp following the international 10-20 Electrode placement system. High quality EEG electrodes are used. Both needle and surface electrodes can be used for recording BAEPs. Surface electrodes are preferred because it is painless and there are lower chances of infection. For

better placement of electrodes, oil must not be applied.On the day of investigation patient is asked to have a thorough shampoo bath. 1 cm disc electrodes filled with conducting jelly or paste is preferred. The electrical impedance should be kept below 5 kilo ohms. If the impedance is too high, the skin is cleaned again with acetone and the surface electrode is reapplied together with electrolyte jelly or EEG paste. Active and ground electrodes are placed on the ipsilateral and contralateral mastoid process respectively (**Lau S K and William)**[30]after the skin has been cleaned. The electrode on the vertex acts as the reference.

FIGURE:7ELECTRODE PLACEMENT



3. Filter

Filter is a device, which selectively restricts the frequency domain of a signal. The filter band pass is the frequency range of a signal, which is transmitted through the filter. The frequency range in which the signal is rejected is known as stop band. Filtering of neurophysiological signals is

required for eliminating the noise and optimizing the recording. Filtering is also useful for bringing out the characteristics of the waveforms.

The low frequency filter removes the slowly changing low frequency components and allows the higher frequencies to pass through. Therefore, the low frequency filter is also known as high pass filter. Similarly, the high frequency filter eliminates the rapidly changing high frequency components and allows the low frequency components to pass through. Hence the high frequency filters are known a low pass filters.

Filter setting for BERA is as follows

Low-cut filter: 10- 100 Hz

High-cut filter: 3000 Hz

4. Amplifier

Since the biological signals are very small (5 to 50 micro volts), variable degree of amplification (up to 500,000) is needed equal to the range of Analog to Digital converter. The electrode impedance includes intrinsic impedance of the electrodes and the impedance of electrode – skin interface. For the measurement of any electrical activity say for example, the action potential generated in central nervous system, nerve or muscle, must flow through the electrode into the amplifier and return to the patient through the ground lead. Electrode impedance results in drop of the amplitude of action

potential. This attenuated action potential reaches the amplifier. To reduce this attenuation, the impedance of the amplifier must be much greater than the electrode impedance. According to the recommended standards of the Guideline 9 (A) the differential input impedance of the amplifier must be at least 100 mega ohms. This minimizes the waveform distortion and improves noise rejection. Unequal electrode impedance imbalances the electrode amplifier input, converting some of the noise into a differential signal, which is amplified to the same extent as the neurophysiological signal.

5. Signal averager

The process of measuring the electrical activity in the brain in response to sound stimulus presented to the ear, is a very complicated and cumbersome process. This is so because, some degree of random and spontaneous electrical activity is continuously occurring within the brain. A recording of this random electrical activity is called electroencephalography (EEG). The electrical activity set up in the brain, in response to a sound stimulus, mingles up and mixes with the random and spontaneous electrical activity occurring within the brain and gets obscured. The magnitude of the electrical activity evoked by a sound stimulus is only 1/100 of that of spontaneous random electrical activity (Background potential). To separate these two types of electrical activity, a process called “signal averaging” is done. This is based on the fact that, evoked electrical activity is time specific and occurs at a fixed point of time after the sound stimulation, whereas, the random electrical activity is not time

specific and occurs at random. Hence, if the electrical activity generated by a very large number of separate sound stimuli at a specific point of time is added together, only the electrical activity evoked by sound stimulus will keep on adding, whereas, the background potential occurring at random without any time specificity will cancel each other. Thus this signal averaging technique is used to clarify and not amplify 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. Two to three repetitions are done and superimposed to check for reproducibility. The latency values measured in the separate repetitions should agree with each other within 0.1millisecond or less. The amplitude values should agree with each other within 10%.

6. Electrical safety

In recording BERA, measures must be taken to assure the patients safety. The grounding and the chassis leakage current of all instruments connected to the patient are located in the same room as the patient must be periodically tested. Equipment should be designed to prevent inadvertent shock power –on, power –off and failures.

Running the test

One ear was tested at a time. Other ear was masked with white noise. Click stimuli of intensity 70dB above normal hearing threshold, at the rate of 10sec and 0.1 msec duration were presented monoaurally The other ear was masked by White noise-40Db HL.

Statistical analysis:

The BAEP parameters such as latency, and inter peak latency of the study group was compared with the control group by using SPSS version 18.

FIGURE:-8 RECORDING OF BAEP BY USING' NEUROPERFECT EMG-2000(EMG/NCV/EP' SYSTEM

RESULTS

Out of 60 subjects who participated in the study, 30 were control group and 30 are migraine subjects. BAEP was done, latency and interpeak latency was taken for analysis

The data were statistically analyzed and their significance derived using independent samples T-Test and paired T-Test.

P value < 0.05 was considered significant.

P value <0.01 was considered highly significant.

P value < 0.001 was considered very highly significant

TABLE: 4 CONFOUNDING VARIABLE

PARAMETERS	CONTROL	MIGRAINE	P VALUE
Age	31.20 ±7.15	34.03 ±10.33	0.222
Height	157.10 ±5.53	153.67 ± 4.95	0.014
Weight	57.07 ±6.19	56.57 ± 5.01	0.732
Gender	1.80 ±0.41	1.93 ±0.25	0.133
BMI	22.73 ±2.35	23.77 ± 2.57	0.109

p≤0.05 is significant; p≤0.01 is highly significant; p≤0.001 very highly significant.

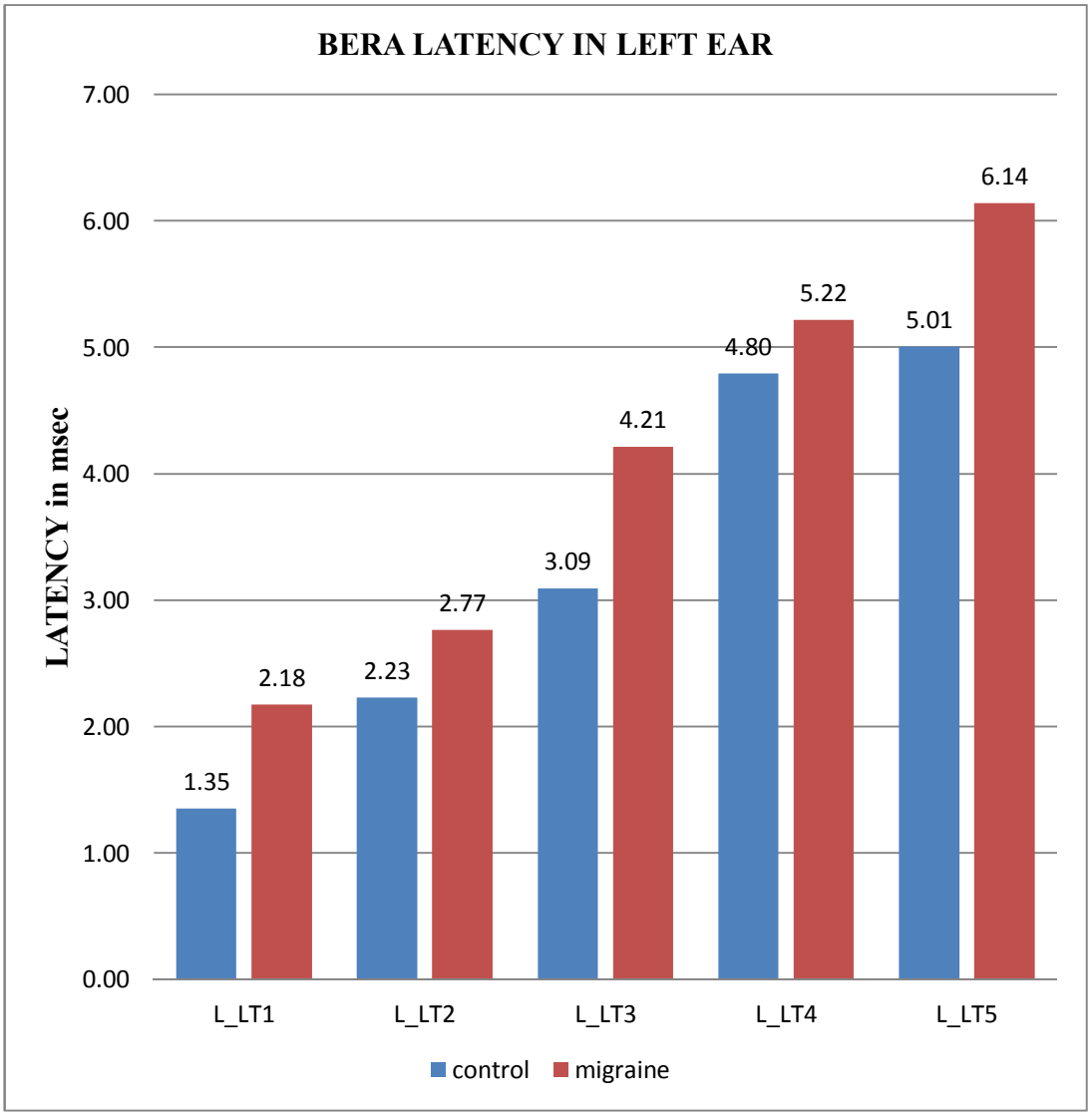
Table 4. shows no statistically significant difference in both control and study groups regarding age distribution, height, weight, gender and body mass index.

TABLE: 5 BAEP LATENCY IN LEFT EAR

PARAMETER	**CONTROL n=30**	**MIGRAINE PATIENTS n=30**
Lat 1	1.35 ± 0.40	2.18 ± 0.23
Lat 2	2.23 ± 0.56	2.77 ± 0.43
Lat3	3.09 ± 0.37	4.21 ± 0.29
Lat4	4.80 ± 0.18	5.22 ± 0.34
Lat5	5.01 ± 0.31	6.14 ± 0.29

The mean latency of BAEP waves of control group was compared with migraine patients and it was found to be prolonged.

FIGURE 9 SHOWS COMPARISON OF BAEP LATENCY IN LEFT EAR



The graph shows mean latency of control and migraine cases.Latency is prolonged in migraine compared to controls

TABLE: 6 COMPARISON OF BAEP LATENCY OF THE LEFT EAR

PARAMETER	CONTROL n=30	MIGRAINE PATIENTS n=30	P VALUE
Lat 1	1.35 ± 0.40	2.18±0.23	**0.000**
Lat 2	2.23± 0.56	2.77±0.43	0.000
Lat3	3.09± 0.37	4.21±0.29	0.000
Lat4	4.80± 0.18	5.22±0.34	**0.000**
Lat5	5.01±0.31	6.14±0.29	**0.000**

$p \leq 0.05$ is significant; $p \leq 0.01$ is highly significant; $p \leq 0.001$ very highly significant.

This tables shows prolongation of latency of BAEP of left ear of migraine patients compared to control group and this is statisticaly significant.

Table: 7 INTER PEAK LATENCY IN LEFT EAR

PARAMETER	CONTROL n=30		MIGRAINE PATIENTS n=30	
Latency(msec)	Mean	S.D	Mean	S.D
Lat 1-3	1.74	0.58	2.04	0.43
Lat 1-5	3.66	0.47	4.12	0.34
Lat 3-5	1.91	0.48	1.93	0.44

The comparison of inter peak latencies between control and migraine patients in left ear

FIG: 10 INTERPEAK LATENCY IN LEFT EAR

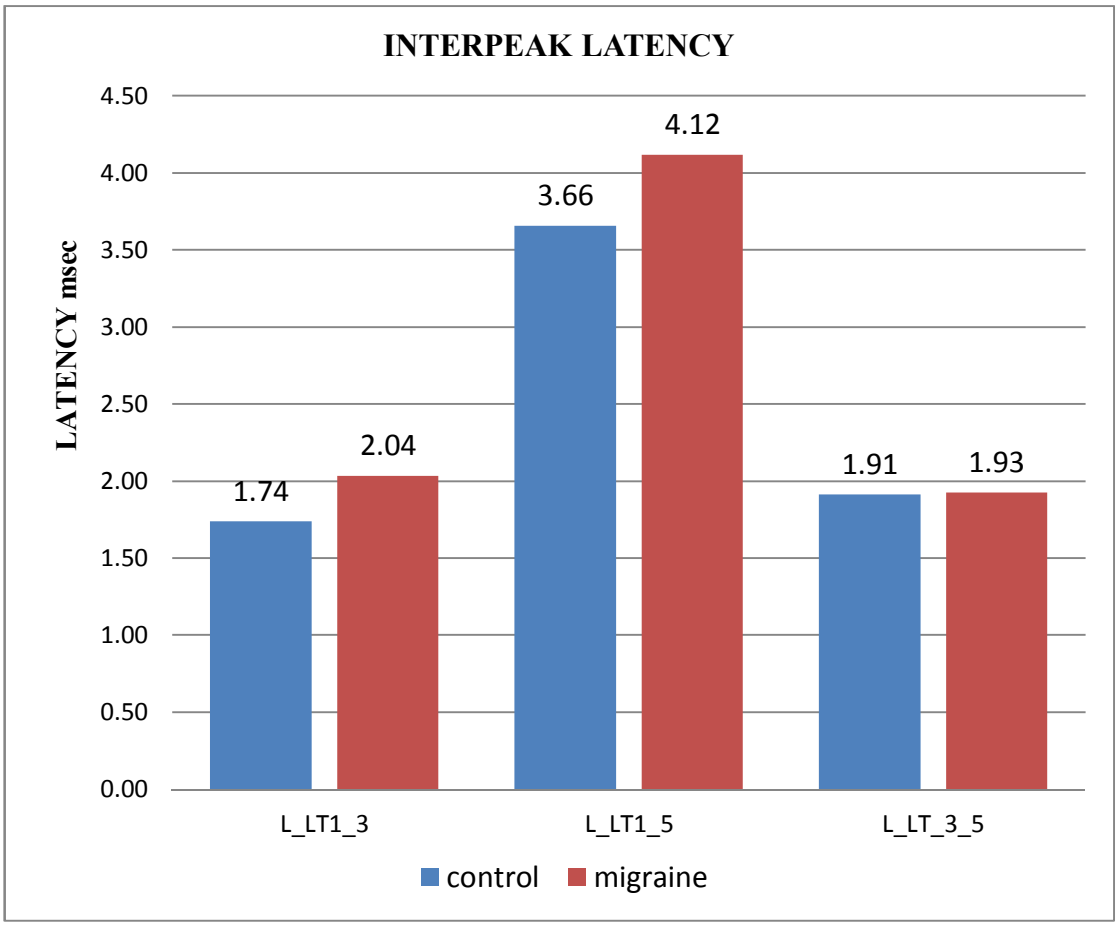


Figure 10. shows interpeak latency(I-III,I-V,III-V) in left ear.The graph shows the mean interpeak latency is prolonged in migraine compared to controls

TABLE :8 COMPARISON OF INTERPEAK LATENCY OF THE LEFT EAR.

PARAMETER	CONTROL n=30	MIGRAINE PATIENTS n=30	P VALUE
Lat 1-3	1.74±0.58	2.04±0.43	**0.029**
Lat 1-5	3.66±0.47	4.12±0.34	**0.005**
Lat 3-5	1.91±0.48	1.93±0.44	0.904

$p \leq 0.05$ is significant; $p \leq 0.01$ is highly significant; $p \leq 0.001$ very highly significant.

The comparison of interpeak latencies between control and migraine patients showed highly statistical significance in interpeak latencies I-III and I-Vin left ear.

TABLE:9 BAEP LATENCY IN RIGHT EAR

PARAMETER	CONTROL n=30	MIGRAINE PATIENTS n=30
Lat 1	1.48±0.28	1.65±0.22
Lat 2	2.71± 0.23	2.87±0.26
Lat 3	3.42± 0.18	3.78±0.45
Lat 4	4.68±0.22	4.79±0.29
Lat 5	5.49±0.37	5.92±0.32

The mean latency of control group and migraine patients shows statistical significance. Latencies are prolonged in migraine patients when compared to control.

FIG:11 BAEP LATENCY IN RIGHT EAR

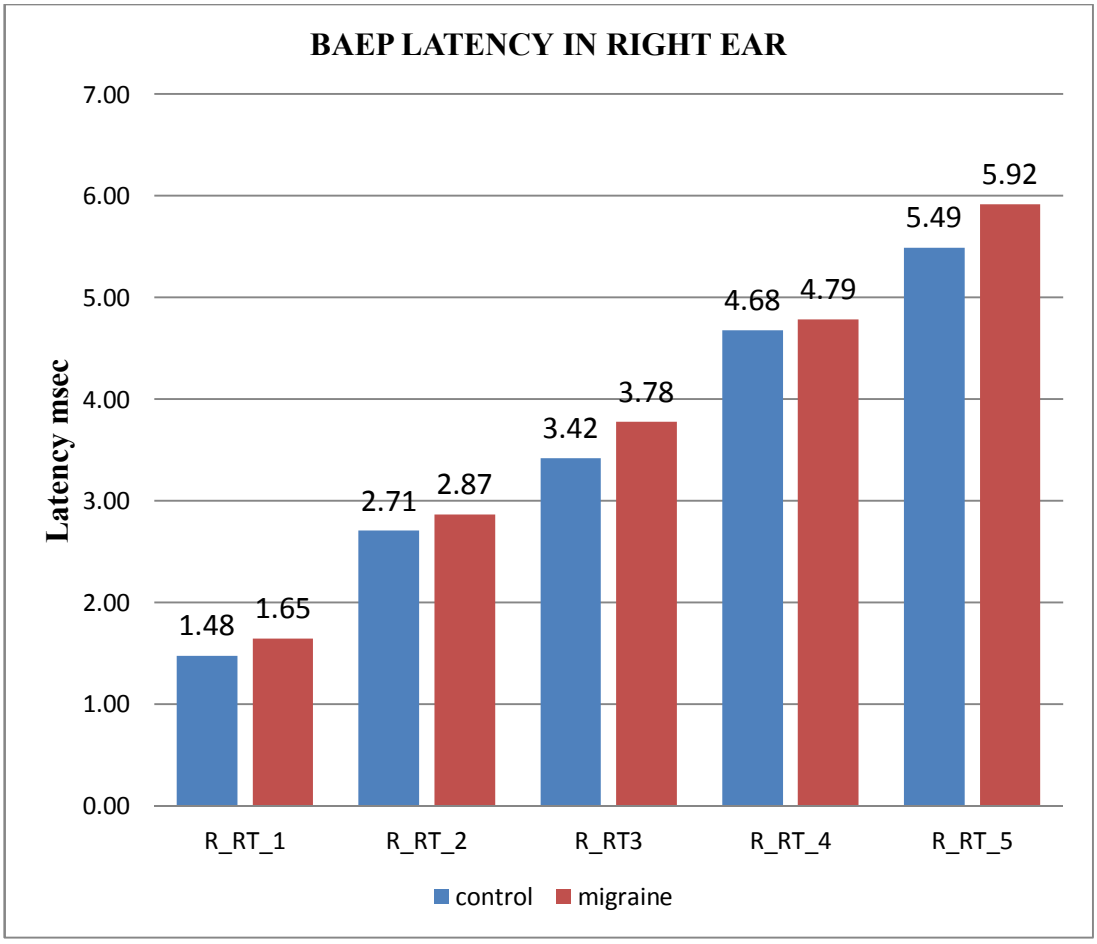


Fig.11 shows BAEP latency in Right ear.The graph shows mean latency of control and migraine cases. Latency is prolonged in migraine compared to controls

TABLE :10 COMPARISON OF BAEP LATENCY IN RIGHT EAR

PARAMETER	CONTROL n=30	MIGRAINE PATIENTS n=30	P VALUE
Lat 1	1.48± 0.28	1.65±0.22	0.011
Lat 2	2.71±0.23	2.87± 0.26	0.016
Lat 3	3.42±0.18	3.78± 0.45	**0.006**
Lat 4	4.68± 0.22	4.79±0.29	0.081
Lat 5	5.49± 0.37	5.92±0.32	**0.001**

$p \leq 0.05$ is significant; $p \leq 0.01$ is highly significant; $p \leq 0.001$ very highly significant.

This table shows prolongation of latency of left ear of migraine patients compared to control group and this is statisticaly significant

TABLE:11 INTERPEAK LATENCY IN RIGHT EAR

PARAMETER	CONTROL n=30	MIGRAINE PATIENTS n=30
Lat 1-3	2.03±0.36	2.42±0.68
Lat 1-5	3.81±0.55	4.36±0.57
Lat 3-5	2.07±0.37	2.15±0.57

Thecomparison of interpeak latencies between control and migraine patients showed statistical significancein right ear.

TABLE:12 COMPARISON OF INTERPEAK LATENCY RIGHT EAR

PARAMETER	CONTROL n=30		MIGRAINE PATIENTS n=30		P Value
Lat 1-3	2.03	0.36	2.42	0.68	0.007
Lat 1-5	3.81	0.55	4.36	0.57	**0.000**
Lat 3-5	2.07	0.37	2.15	0.57	0.83

$p \leq 0.05$ is significant; $p \leq 0.01$ is highly significant; $p \leq 0.001$ very highly significant.

The comparison of interpeak I-III,I-V,III-V latencies between control and migraine patients showed statistical significance in Right ear. Latency I-V **($p \leq 0.001$**) is very highly significant.

FIG:12 INTERPEAK LATENCY IN RIGHT EAR

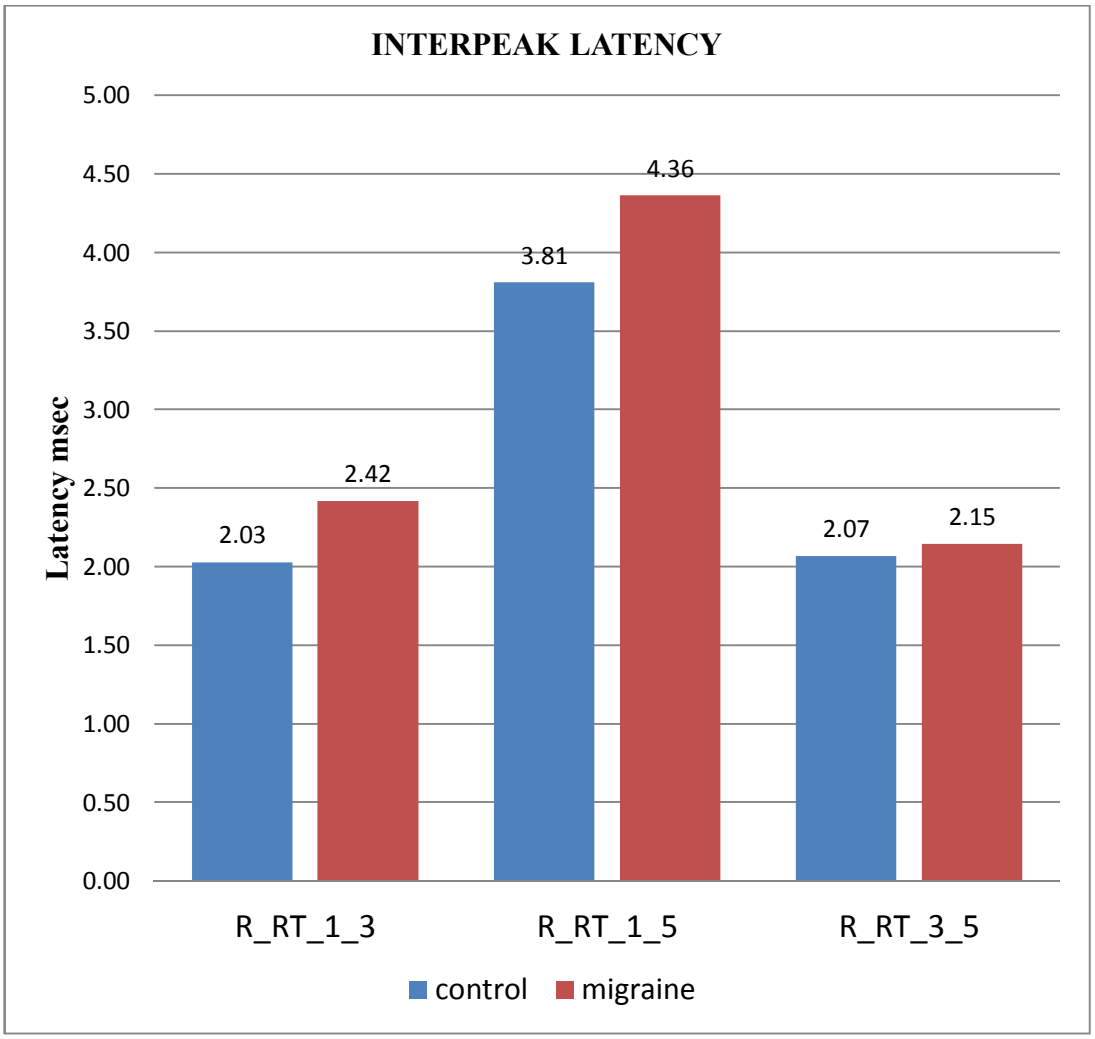


Fig 12 shows BAEP latency in Right ear.The graph shows mean interpeak latency of control and migraine cases. interpeak latency is prolonged in migraine compared to controls

DISCUSSION

In the present study, Brainstem auditory Evoked Potential parameters were evaluated in migraine patients in order to find out whether cortex or brainstem is involved in migraine patients.

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.

The study was done with 30 migraine patients and 30 controls with NEUROPERFECT EMG-2000-BAER- Both the controls and the migraine patients were stimulated with click stimuli of intensity 70Db above normal hearing threshold at the rate of 10sec and 0.1 msec duration were presented monoaurally and the other ear was masked monoaurally by white noise.

Results were interpreted with respect to the latency and interpeak latency of both ears and compared between the migraine and normal subjects.

In our study there was no statistically significant difference in age, sex & BMIbetween control and study group ruling out the confounding variables regarding Biophysical profile.This study coincides with the study done by Stockard et al 1979 which states that central auditory conduction is largely independent of subjects biophysical profile.

Brain Stem Evoked Response Audiometry (BAEP)

In this study, there is significant prolongation of latencies (all latencies) and interpeaklatencies (I-III & I-V) of BAEP waves in migraine when compared with controls. Wave I-III is generated by the auditory branch of cranial nerve VIII and lower part of brain and Wave IV & V generated by upper brain.

In the present study there is prolongation of latencies in both ears.lt is supported by previous studies done by Kaushal et al who evaluated BAEP in 25 Migraine patients. The results revealed prolongation in latencies I, III & V latencies and interpeak latencies I-III & I-Vand it was stated 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.

Interpeak latency I-V represents conduction from the proximal part of the eighth nerve through pons to the mid brain. In this study there is

significant prolongation of I-V interpeak latency observed in migraine patients compared with controls.

Similarily Bayazit Y et al .,studied BAEP in 20 migraine patients and reported abnormal BAEP findings in seven patients with increased latency of waves I , III & V and the interpeak latency 1-5. They concluded that cochlear vestibular symptoms can be seen in migraine patients and is due to defective neurotransmitter signaling and cerebral bioelectrical dysrhythmia.

(Schlake H.P.etal, 1990).concluded that in migraine patients (including basilarmigraine) peak latencies were pathologically delayed. Statistical analysis did not show any significant difference in regard to peak latencies and interpeak latencies between migraine patients and controls.

Table6&8 shows the comparison of absolute latency & interpeak latency between migraine and control group for left earandthere is significant difference between absolute latencies of migraine and control groups. However no significant difference is observed between migraine and control groups for III-V interpeak latencies ($p>0.05$).

Table7&9 shows the comparison of absolute latency & interpeak latency between migraine and control group for right ear and there is significant difference between absolute latencies of migraine and control groups. Similarly significant results are obtained for interpeak latencies between migraine and study groups.

However no significant difference is observed between migraine and control groups for III-V interpeak latencies ($p>0.05$)

However, side differences of all peaks (except peak IV, VI) were significantly increased in migraine patients as compared to controls. Results indicated a slight butpermanent impairment of brainstem function in migraine.

Kuritzky A et al, 1981observed plasma serotonin level are essentially decreased during migraine attacks. Latency parameters values follow the variations in the serotonin levels.

The serotonergiccontrolsystem, a dualhormone-neurotransmitter with numerous types of receptors.Serotonin is known as one of the most importantneurotransmitters.In the brain serotonin regulates the vascular smooth muscle tone of meningeal blood vessels.This amine structured neurotransmitterlevel is influenced in migraine

A.F. Lipkins et al.reported sudden sensorineural hearing loss in a patient during migraine attacks. Functional neuroimaging studies in patients with migraine during pain attacks had shown the activation of brainstem.

Interpeak latency III-V reflexes the conduction from the lower pons to the mid brain. There is no prolongation of interpeak latencies III-V significant between study and control group for III-V interpeak latency.

In this present study BAEP reports showed significant prolongation of interpeak latency of wave I-III &I-V but no prolongation is observed in the interpeak latency of wave III-V in migraine when compared with controls. This result is supported by previous studies done by Firat Y et al who 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 temporary loss of auditory brainstem function in patientsmigraine. These results were in accordance with our present study.

Laila EL Mosly et al., Evaluated the role of Migraine on standard of life in females and associated changes in evoked potentials. They measured BAEP in 30 Migraine patients and reported that there was prolongation of latency III-V and I-V & I-III interpeak latency due to hyperexcitability of the cerebral cortex but no significant change in 3-5interpeak latency both during an attack and in the interictal phase. These results were similar with our present study.

Anil K Dash et al., studied audiovestibular functions in migraine patients with and without vertigo. BAEP results revealed that there was significant prolongation in latencies of wave I, III & IV and interpeak latencies I-III, III-V & I-V. This study concluded that BAEP abnormalities are the earliest indicator of imminent acoustic involvement in migraine subjects. These results were consistent with our present study.

Sherifa A Hamed, Amal Mohammed Elatter evaluated vestibular function in 58 patients with migraine both 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 -Explored personality test and BAEPs in 30 Migraine patients. They reported that the latencies of wave I, III &V and the Interpeak

latencies of 3-5 were prolonged and related this prolongation to brainstem dysfunction. Similar results were observed in our study.

ZgorzalewiczM et al., [14] 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.

Drake ME et al., 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. Present study also shows that during an attack of migraine brainstem structures play an active role leading to prolongation of interpeak latencies which supports the' Brainstem activation theory of migraine'. [14]

CONCLUSION

Thirty migraine patients both male and female and thirty age matched healthy controls attending Neurology outpatient department participated in the study during the attack of migraine. BAEP was done after obtaining ethical committee clearance and informed consent by using NEUROPERFECT EMG-2000.

From the present study the following conclusions are made

- There is prolongation of latency I, III and V which is statistically significant waves generated from lower brain stem structures mediating defective neurotransmitter signaling

- Prolongation of interpeak latency of I-III and I-V is also statistically significant and it reveals that the prolongation is due to involvement of upper brain stem structures causing bioelectrical dysrhythmia

- Increase in all peaks during migraine attack follows the variation in serotonergic control system substantiating that brain stem structures play an active role during the attack of migraine.

- Prolongation of interpeak latency supports the imminent acoustic involvement and brain stem activation theory of migraine.

- BAER can be used as an effective non-invasive, reliable, and diagnostic technique and earliest indicator of impending auditory involvement in migraine patients making neurophysiological evaluation of the auditory pathway&early intervention even in migraine patients without aura.

SUMMARY

This study was conducted to assess the brain stem auditory evoked potentials in migraine patients for a continuous period of 10 milliseconds during head ache period. 30 migraine patients both male and female and 30 age matched healthy controls attending neurology outpatient department participated in the study. After obtaining ethical committee clearance and informed consent BAEP was done using NEUROPERFECT EMG-2000. The results were statistically analysed and tabulated for discussion. It was found that there is involvement of brain stem in migraine patients.

Latencies I, II, III, IV, V were prolonged indicating defective brainstem neurotransmitter signaling.

Interpeak latency I – V, I – III, prolongation supported the serotonergic control system dysfunction taken for analysis.

So study proves that there is involvement of brain stem structures during migraine attacks evidenced by the extension of interpeak latencies of waves in BAER

This study does not compare the duration of the disease with the changes in the BAER and the quantification of neurotransmitter signaling. BAER can be used as an effective non-invasive, reliable, and diagnostic

technique and an earliest indicator of impending auditory involvement in migraine patients enabling to intervene even before in migraine patients without aura

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PROFORMA FOR CONDUCTING THE STUDY ON BRAIN STEM AUDITORY EVOKED POTENTIAL CHANGES IN MIGRAINE PATIENTS

1. Name :
2. Age :
3 Sex :
4. Address :
5. Duration of the disease :
6. Any other associated illness
    (i) History of diabetes mellitus :
    (ii) History of hypertension
    (iii) History of any ear disease :
7. History of drug intake
8. Family history :
9. General examination
10. Investigations
    (i) Rinne's and Weber's test :
    (ii) Pure tone audiometry
    (iii) Brain stem auditory evoked :

Potential

11. Date of conduct of experiment :

MIDAS QUESTIONNAIRE

INSTRUCTIONS:

Please answer the following questions about allheadaches you have had over the last 3 months. Write zero if you did not do theactivity in the last 3 months.

1. On how many days in the last 3 months did you miss work or schoolbecause of your headache?.....days

2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches (do not include days you counted in question 1 where you missed work or school)?.....days

3. On how many days in the last 3 months did you **not** do household work because of your headaches?.....days.

4. How many days in the last 3 months was your productivity in householdwork reduced by half or more because of your headaches (do not includedays you counted in question 3 where you did not do householdwork)?.....days.

5. On how many days in the last 3 months did you miss family, social, or leisure activities because of your headaches?.....days.

   A. On how many days in the last 3 months did you have a headache?(if aheadache lasted more than one day , counted each day)……..days

B. On a scale of 0-10, on average how painful were these headaches?(Where 0 = no pain at all, and 10 = pain as bad as it can, be)…….

- Migraine Disability Assessment Score
- (Questions 1-5 are used to calculate the MIDAS score)

Grade 1- Minimal or infrequent Disability; 0-5

Grade II –Mild or infrequent Disability; 6-10

Grade III- Moderate Disability: 11-20

Grade IV-Severe Disability :> 20 (Innovative Medical Research 1997)

PATIENT CONSENT FORM

STUDY DETAIL :

"EVALUATION OF AUDITORY BRAIN STEM EVOKED RESPONSE IN MIGRAINE PATIENTS"

STUDY CENTRE:

DEPARTMENT OF PHYSIOLOGY & NEUROLOGY OP, CHENGALPATTU MEDICAL COLLEGE & HOSPITAL, CHENGALPATTU.

PATIENT NAME: **AGE:** **SEX:**

IDENTIFICATION NUMBER:

I confirm that have understood the purpose of procedure for the above study.

I have the opportunity to ask question and all my questions and doubts have been answered to my satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw anytime without giving any reasons, without my legal rights being affected.

I understand that my investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arrives from the study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team.

I hereby give consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic test.

Signature of investigator

Signature/Thumb impression of participant

Date:
Place:

Participant's address:

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு : தலைவலி நோயாளிகளுக்கும் சாதாரண மனிதர்களுக்கும் ஆன செவித்திரன் செயல்பாட்டில் மூலைத்தண்டு வட பங்கின் பரினாமம்.

ஆய்வு செய்யப்படும் இடம் :

பங்கு பெறுபவரின் பெயர் :

பங்கு பெறுபவரின் வயது : பங்கு பெறுபவரின் எண்:

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விபரங்கள் எனக்கு விளக்கப்பட்டுளளது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கின்றேன். எந்த காரணத்தினாலோ எந்த சட்டச்சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவை இல்லை என அறிந்து கொள்கிறேன். இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் சாட்சியாளரின் கையொப்பம்

இடம்: இடம்:

தேதி: தேதி:

Medicaid Systems Neuro Lab.& Deptt of Audiology & Neuro Sciences

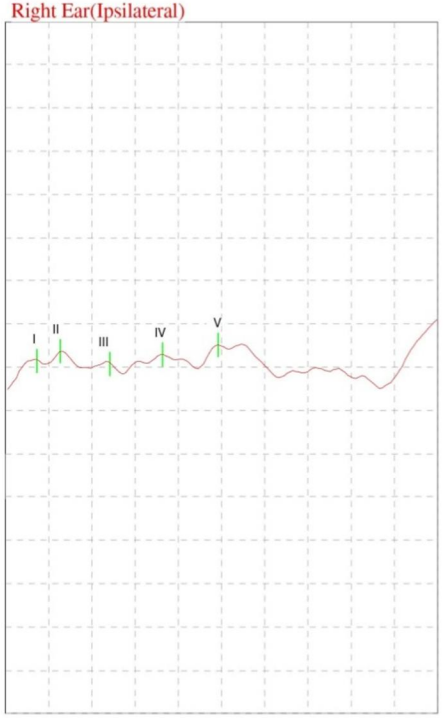
389, Industrial Area.,Phasev-II, Ram Darbar chd, Chandigarh.
Phone :- 652706

Medicaid

BERA

19 SELVAM 23 yrs/Male Refd. By : Date : 09/05/2016

Right Ear(Ipsilateral)



N= 1010
1 µV
1 m sec
70 dB

Left Ear(Contralateral)

Right

S.No.	Rec. Site	Lat I (ms)	Lat II (ms)	Lat III (ms)	Lat IV (ms)	Lat V (ms)	(I-III) (ms)	(I-V) (ms)	(III-V) (ms)	Ia (µV)	Va (µV)	Va/Ia
1	Fz-Cz	--	--	--	--	--	1.7	4.2	2.5	--	--	--

Left

S.No.	Rec. Site	Lat I (ms)	Lat II (ms)	Lat III (ms)	Lat IV (ms)	Lat V (ms)	(I-III) (ms)	(I-V) (ms)	(III-V) (ms)	Ia (µV)	Va (µV)	Va/Ia
1	Fz-Cz	0.7	1.3	2.4	3.6	4.9	1.7	4.2	2.5	--	--	--

Test Comments

Note: The results may be clinically correlated

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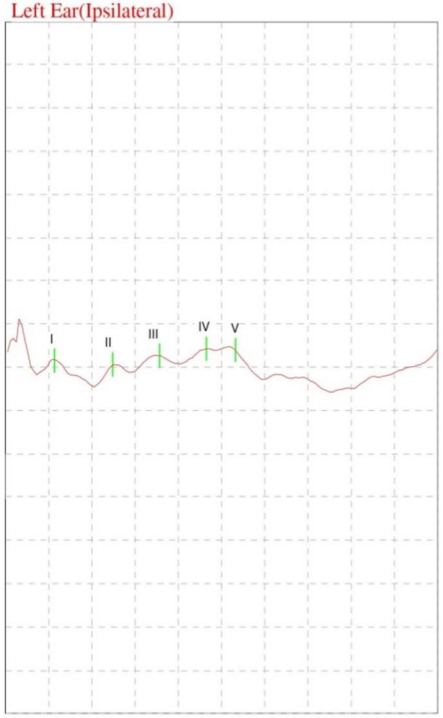
BERA

19 SELVAM 23 yrs/Male Refd. By : Date : 09/05/2016

Left Ear(Ipsilateral)



N= 1010
1 µV
1 m sec
70 dB

Right Ear(Contralateral)

Left

S.No.	Rec. Site	Lat I (ms)	Lat II (ms)	Lat III (ms)	Lat IV (ms)	Lat V (ms)	(I-III) (ms)	(I-V) (ms)	(III-V) (ms)	Ia (µV)	Va (µV)	Va/Ia
1	Fz-Cz	1.1	2.5	3.5	4.6	5.3	2.4	4.2	1.8	--	--	--

Right

S.No.	Rec. Site	Lat I (ms)	Lat II (ms)	Lat III (ms)	Lat IV (ms)	Lat V (ms)	(I-III) (ms)	(I-V) (ms)	(III-V) (ms)	Ia (µV)	Va (µV)	Va/Ia
1	Fz-Cz	--	--	--	--	--	--	--	--	--	--	--

Test Comments

Note: The results may be clinically correlated

MASTER SHEET

BERA - CONTROL GROUP LATENCY (ms)

						LEFT								RIGHT							
Sl. No.	Age	Gender	Ht	Wt	BMI	LT I	Lt II	Lt III	Lt IV	Lt V	I-III	I-V	III-V	RT I	Rt II	Rt III	Rt IV	Rt V	I-III	I-V	III-V
1	27	2	149	45	20	1.65	2.77	3.2	4.77	5.1	1.55	3.45	1.9	1.42	3.08	3.48	4.6	5.08	2.06	3.67	1.6
2	28	2	156	60	24	1.42	2.9	3.1	4.98	5.21	1.68	3.79	2.11	1.43	3.02	3.4	4.9	5.44	1.98	4.02	2.04
3	25	2	156	55	22	1.6	2.56	3.2	4.81	5.4	1.6	3.8	2.2	1.42	2.98	3.6	4.69	5.48	2.19	4.06	1.88
4	32	2	155	62	25	1.69	2.5	3.1	5.06	4.3	1.41	2.61	1.2	1.4	2.73	3.94	4.29	6.15	2.52	4.73	2.21
5	45	2	146	60	28	1.56	3.08	3.1	4.98	5.1	1.54	3.54	2	1.42	2.5	3.69	4.56	5.4	1.69	3.4	1.71
6	24	2	159	56	22	1.42	2.5	3.2	4.73	5	1.78	3.58	1.8	1.42	3.02	3.4	4.73	6.21	2.19	4.79	2.81
7	24	2	153	43	18	1.9	2.5	2.5	4.69	5.3	0.6	3.4	2.8	1.42	2.5	3.52	4.42	5.23	1.56	3.27	1.71
8	20	2	148	58	26	1.2	2.3	3.5	4.81	5.23	2.3	4.03	1.73	1.42	2.98	3.6	4.5	5.23	1.6	3.23	1.63
9	38	2	155	54	22	1.2	1.5	3.1	4.77	5.3	1.9	4.1	2.2	1.6	2.6	3.48	4.77	5.69	1.48	3.68	2.21
10	28	2	150	50	22	1.65	1.2	3.2	4.98	5.22	1.55	3.57	2.02	1.42	2.5	3.48	4.56	5.21	1.67	3.4	1.73
11	25	2	153	58	24	1.5	2.8	3.1	4.5	4.5	1.6	3	1.4	1.42	3.06	3.4	4.52	6.06	2.52	4.65	2.66
12	33	2	156	62	25	1.3	2.56	3.35	4.9	5.2	2.05	3.9	1.85	1.42	2.85	3.4	4.9	5.21	2.9	3.56	1.81
13	40	2	154	64	27	1.65	2.5	3.35	4.81	5.2	1.7	3.55	1.85	1.73	2.65	3.6	5.06	5.48	2.44	4.06	1.88
14	38	2	160	60	23	0.3	2.5	3.4	4.5	4.7	3.1	4.4	1.3	1.42	2.5	3.4	4.52	6.06	2.52	4.65	2.66
15	40	2	156	53	21	1	1.3	2.3	4.56	5.2	1.3	4.2	2.9	1.42	3.08	3.4	5.08	5.73	2.29	4.08	2.33
16	41	2	159	56	22	1.3	2.5	3.2	4.73	4.5	1.9	3.2	1.3	1.77	2.6	3.1	4.72	6.21	2.19	4.72	3.11
17	32	2	158	48	19	0.3	2.1	3.1	4.81	5.23	2.8	4.93	2.13	2	2.8	3.6	4.5	5.23	1.6	3.23	1.63
18	20	2	162	58	22	1.65	2.1	3.35	4.97	5.21	1.7	3.56	1.86	1.5	2.77	3.2	4.56	5.21	1.67	3.4	2.01
19	29	2	155	48	20	1.65	2.77	3.1	4.77	4.9	1.45	3.25	1.8	1.42	3.08	3.21	4.6	5.08	2.06	3.67	1.87
20	35	2	158	50	19	1.56	2.1	3.1	4.95	4.5	1.54	2.94	1.4	2	2.7	3.4	4.58	5.42	1.69	3.41	2.02
21	24	2	160	58	22	1.65	2.5	2	4.81	5.1	0.35	3.45	3.1	1.42	2.5	3.2	5.06	5.48	2.44	4.06	2.28
22	44	2	150	57	25	1.5	2.56	3.35	4.9	5.1	1.85	3.6	1.75	1.42	2.7	3.2	4.9	5.21	2.29	3.56	2.01
23	28	2	160	59	23	0.3	1.3	3.2	4.81	4.5	2.9	4.2	1.3	1.04	2.1	3.6	4.5	5.23	1.6	3.23	1.63
24	35	2	156	58	23	1.42	2.5	3.2	4.73	5.2	1.78	3.78	2	1.42	2.77	3.5	4.72	6.21	2.19	4.72	2.71
25	22	1	166	64	23	1.3	1.5	3.1	4.5	5.21	1.8	3.91	2.11	1.4	2.5	3.1	4.5	5.21	1.85	3.21	2.11
26	31	1	164	65	24	1.3	1.5	3.1	4.81	5.1	1.8	3.8	2	2	2.73	3.2	4.5	5.15	1.81	3.15	1.95
27	28	1	167	67	24	1.5	1.3	3.1	5.08	4.5	1.6	3	1.4	1.3	2.23	3.6	5.01	5.54	2.16	4.02	1.94
28	25	1	167	68	24	1.3	2.5	3.6	4.56	5.21	2.3	3.91	1.61	1.2	2.32	3.65	4.53	5.23	1.81	3.45	1.58
29	38	1	160	60	23	1.5	1.5	3.42	4.5	5.21	1.92	3.71	1.79	1.42	2.6	3.2	4.5	5.21	1.85	3.21	2.01
30	37	1	165	56	20	1.3	2.77	2.2	5.07	4.8	0.9	3.5	2.6	1.42	2.8	3.1	5.01	5.53	2.15	4.02	2.43

BERA - MIGRAINE PATIENTS LATENCY (ms)

						RIGHT								LEFT							
Sl. No.	Age	Gender	Ht	Wt	BMI	Rt I	Rt II	Rt III	Rt IV	Rt V	I-III	I-V	III-V	Lt I	Lt II	Lt III	Lt IV	Lt V	I-III	I-V	III-V
1	25	2	156	53	23	1.42	2.77	4.32	4.8	5.95	2.9	4.29	1.63	1.9	2.8	4.3	5.1	5.87	2.4	3.97	1.57
2	48	2	146	57	27	1.42	3.08	4.33	4.4	5.96	2.9	4.53	1.67	2.2	2.9	4.4	5	5.97	2.2	4.1	1.57
3	35	2	159	63	25	1.42	3.08	3.55	4.45	5.9	3.03	4.48	2.35	1.9	2.99	4.5	5.2	5.8	2.6	3.9	1.3
4	28	2	153	56	24	1.42	3.08	3.75	4.4	5.8	3	4.4	2.1	2.1	2.72	4	5.4	5.9	1.9	4.6	1.9
5	20	2	155	50	20	2	3.08	4.22	4.8	5.8	2.8	4.23	1.45	2	3.1	4.1	5.1	6.1	2.1	4.1	2
6	21	2	149	54	23	1.42	2.51	3.85	4.9	5.6	3.01	4.4	2	2	2.6	4.5	5	6.1	2.5	4.1	1.6
7	50	2	157	55	22	1.96	2.77	3.8	4.8	5.7	2.3	4.3	2	2.9	2.9	4.2	5.3	5.8	1.3	2.9	1.6
8	45	2	156	56	22	2	3.08	3.4	5.08	5.95	1.9	4.2	2.3	2.5	3.1	4.1	5.5	6.1	1.6	4.2	2
9	38	2	150	66	29	1.42	2.52	3.6	4.69	5.8	1.5	4.6	3.1	2.3	3.1	4.2	5.4	5.9	1.9	3.6	1.7
10	20	2	154	54	22	1.81	2.6	4.25	4.98	5.8	2.9	4.43	1.9	2	2.5	4.5	5.6	5.9	2.5	4	1.4
11	26	2	156	56	22	1.42	3.08	3.85	5.08	5.52	2.4	5.8	3.4	2.1	3	4.6	5.3	6	2.5	4.2	1.4
12	35	2	142	50	24	1.65	3.08	3.69	4.98	5.85	2.8	4.1	1.9	2.1	2.9	4.3	5.7	6.5	2.2	4.4	2.2
13	45	2	150	55	24	1.42	2.85	3.5	4.8	5.81	1.8	5.1	3.3	2.3	3	3.5	5.2	6.3	1.2	4	2.8
14	32	2	153	54	23	1.42	3.08	4.42	5.08	6.21	3.9	4.79	2	2	2.9	3.9	5.01	6.5	1.9	4.5	2.6
15	50	2	148	60	27	1	2.56	3.77	4.81	6.3	2.1	4.1	2	2.2	2.8	4.1	5.8	6.1	1.9	4.1	2
16	35	2	159	63	29	1.42	2.51	4.77	4.79	5.91	3.49	3.44	1.43	2.1	2.9	4.3	5	5.9	2.2	3.8	1.6
17	45	2	150	55	24	2	3.08	3.7	4.56	5.91	1.3	3.3	2	2.1	3.1	3.9	5.1	6.3	1.8	4.2	2.4
18	32	2	153	54	23	1.81	2.6	4.8	4.9	6.2	3.3	4.7	1.4	2	2.5	4.5	5.3	6.1	2.5	4.3	1.6
19	50	2	148	60	27	1.42	2.77	3.7	4.7	5.9	1.7	4.2	2.5	2.1	2.9	4.7	4.3	5.9	2.6	4	1.2
20	35	2	159	63	25	2	3.08	3.3	4.5	5.5	1.6	4.4	2.8	2.2	2.3	4.1	5.4	6.4	1.9	4.4	2.3
21	46	2	158	58	24	1.42	2.85	3.35	5.08	6.2	1.93	4.78	2.8	2.5	3.1	4.1	5	6.1	1.6	4.2	2
22	21	2	147	56	25	1.65	3.08	3.85	5.08	6.2	2.5	4.4	1.9	2.5	1.6	3.5	5.2	6.1	1	3.9	2.6
23	22	2	153	55	23	2	3.08	3.8	5.08	6.1	2.76	4.96	2.3	2.4	2.2	4.2	5.5	6.7	1.8	4.3	2.5
24	40	2	150	58	25	1.42	2.51	3.08	5.08	5.75	2	4.6	2.6	2.3	3.8	4.1	5.5	6.8	1.8	4.5	2.7
25	20	2	155	45	18	2	3.08	3.81	4.98	5.81	2.1	4.2	2.1	2.3	2.3	4.6	5.2	6.9	2.3	4.6	2.3
26	23	2	155	53	21	2	3.06	3.3	4.5	6.2	1.1	2.8	1.7	2	1.9	4.6	5.1	6.1	2.6	4.3	1.5
27	35	2	158	56	22	1.72	2.77	3.1	4.2	5.9	1.9	3.8	1.9	2	3.1	4.1	5.8	6.1	2.1	4.1	2
28	34	2	156	51	20	1.79	2.5	3.08	4.1	5.9	2.5	4.9	2.4	2.4	2.9	4.1	5.3	6	1.7	4.2	1.9
29	42	1	165	63	23	2	3.08	3.8	5.1	6.2	3.2	3.9	0.9	1.8	2.3	4.3	4.5	5.9	2.5	4.1	1.6
30	23	1	160	68	27	1.71	2.77	3.75	5.1	6.4	2.2	4.8	2.6	2.1	2.8	4.1	4.7	6.1	2	4.3	2