CAN LATER PEAKS OF VEMP AND N3 POTENTIAL HELP IN UNDERSTANDING VESTIBULO - COCHLEAR RELATIONSHIP?

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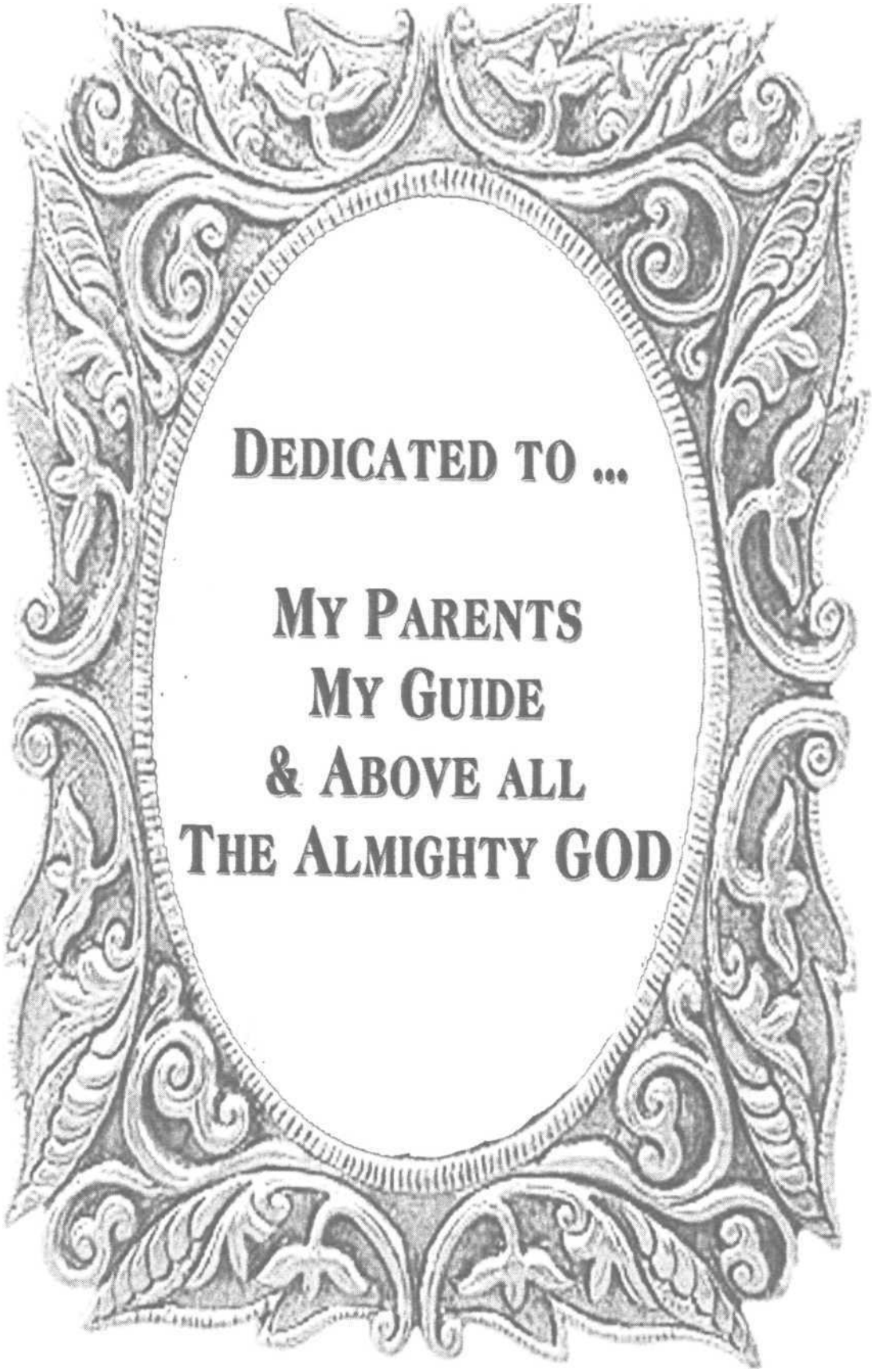
DEDICATED TO ...
MY PARENTS
MY GUIDE
& ABOVE ALL
THE ALMIGHTY GOD

CERTIFICATE

This is to certify that this dissertation entitled ***"Can later peaks of VEMP and N3 potential help in understanding Vestibulo-cochlear relationship?"*** is the bonafide work submitted in part fulfillment for the degree of Master of Science (Audiology) of the student (Registration No. 05AUD002). This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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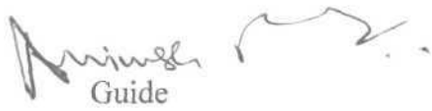

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DECLARATION

This is to certify that this dissertation entitled *"Can later peaks of VEMP and N3 potential help in understanding Vestibulo-cochlear relationship?"* is the result of my own study under the guidance of Mr. Animesh Barman, Lecturer, Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted in any other university for the award of any diploma or degree.

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April, 2007

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Acknowledgements

I could write for hours,
Use the finest words in Webster's,
Fill pages upon pages with verse -
Only two words are needed,
Two words are everything I want to say:

Thank you.

I am indebted to my dissertation guide Mr. Animesh Barman, Lecturer , Department of Audiology for introducing me to the subject, and for in constant guidance and encouragement throughout.

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"The mediocre teacher tells. The good teacher explains. The superior teacher demonstrates. The great teacher inspires". Thanks to all the teachers for inspiring me to achieve the pinnacle of success.

Mere collection of data is of little use without proper analysis. Many thanks are due to Vasanthalakshmi madam for her help in analyzing the data.

I recognize help of numerous case subjects for my dissertation.

The one that I look up to,
The one that I run to, when I have a problem.
The one that I talk to,
Your the one best friend that was always there for me.
Dearest, Mahesh I want to thank you for all the things you gave and showed me.

Friend: that one special person who makes life a bit easier by just being there and listening to your problems and difficulties. Thanks dear, Ubaid for being there for me always.

Friends are like flowers, they give pleasure by just being there. Thank you, Swapna, Manas, Sushmit for those precious moments we spent together.

To have a good friend is one of the highest delights of life. And I am delighted that I have you. Thanks Ruchi for being a good friend.

We need old friends to help us grow old and new friends to help us stay young. Thank you all my old and new classmates for your perfect company.

My dear seniors and juniors, each one you have helped me to shape up my career in some or the other way. Thanks a lot.

The only rock I know that stays steady, the only institution I know that works, is the family. Thank you for always believing in me and encouraging me.

The love of God ought continually to predominate in the mind, and give to every act of duty grace and animation. Thank you for showering blessing in my life.

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Chapter I

INTRODUCTION

Clinical tools for diagnosing vestibular disorders caused by semicircular canal dysfunction are readily available like, Electronystagmography, Caloric test, Stepping test, Romberg test and Rotation test.

Electronystagmography is intended to diagnose central nervous system disorders, such as cerebellar degenerations while assessing lateral semicircular canal and central vestibular system. Caloric test is a test of the lateral semicircular canals alone; it does not assess vertical canal function or otolithic function. Romberg test assesses if there is a loss of coordination due to loss of sensory input into the control of movement. More specifically, it is indicative of a defective position sense, i.e. abnormal (or pathological) proprioception or pathology of the semicircular canals. Thus all the tests assess only the semicircular canals, while tests sensitive to otolith disorders are scarce.

During past few years, there have been studies on vestibular evoked myogenic potentials (VEMP) in animals and humans. Briefly, the VEMP is an inhibitory potential recorded from the sternocleidomastoid (SCM) muscle in response to loud sounds. VEMP testing may provide a useful, noninvasive method for assessment of otolith function and the functional integrity of the inferior vestibular nerve (Al Abdulhadi, Zeitouni, Al-Sebeih & Katsarkas, 2002; Chen, Young & Wu, 2000; Clarke, Schonfeld & Helling, 2003; Colebatch, Halmagyi & Skuse, 1994; Ferber-Viart, Duclaux, Colleaux & Dubreuil, 1998; Li, Houlden & Tomlinson, 1999; McCue & Guinan, 1995; Ochi, Ohashi & Nishino, 2001; Welgampola & Colebatch, 2001). The serial peaks are labeled as P13, N23, N34 and P44 based on their

latencies. Clinically, the test is relatively easy to perform and can be performed with most evoked potentials recording systems.

VEMP are widely used to detect several diseases. They are absent in vestibular neurolabyrinthitis patients due to involvement of the inferior vestibular nerve or structures that it innervates (Murofushi, Halmagyi, Yavor & Colebatch, 1996). Patients with Tullio phenomenon have pathologically reduced threshold to click evoked myogenic potentials (Colbatch et al., 1994). There are absent or decreased VEMPs in 51% of patients with Meniere's disease, 39% with vestibular neuritis, 77% with acoustic neuroma and 25% of multiple sclerosis patients concluding that absent or reduced VEMP are suggestive of lesion in the retro labyrinthine, especially in the inferior vestibular nerve (Murofushi et al., 2001). VEMP can be used to assess the residual function of inferior vestibular nerve in post operative Cerebellopontine angle tumor (Chen et al., 2002). It can be useful in assessing balance functions in deaf or hard of hearing patients (Steven et al., 2004). Subjects with SNHL greater than 40 dB HL showed significantly more saccular deterioration (Sazgar, Akrami & Yazdi, 2006).

In all these studies the focus was solely on investigating waves p l3-n23 which are saccular in origin possibly due to the higher response rate in normals, whereas the N34- P44 which are believed to be cochlear origin were explored scarcely thus ignoring their clinical significance (Huang, Young & Cheng, 2004).

Need for the study

The VEMP later peaks may answer many queries related to the pathology and pathophysiology in sensory neural hearing loss individuals. There are evidences which

suggest that later peaks of VEMP are cochlear origin. Colebatch, Halmagyi, and Skuse (1994) and Robertson and Ireland (1995) reported presence of N34-P44 peaks of VEMP in 60% to 68% of their normal hearing subjects. Rosengren (2006) reported two children with Mondini dysplasia and one child with vestibulocochlear nerve abnormality showed presence of VEMP responses on activation of the cochlear implant device. Ferber-Viart et al., (1998) evaluated Cochleo-vestibular afferent pathways of trapezius muscle responses to clicks in subjects with selective vestibular lesions as well as selective cochlear lesions and found presence of N34 and P44 with normal latencies and reduced amplitude in both the conditions thus suggesting cochlear origin.

It was essential to know anatomical and functional relationship between the cochlear and vestibular system which was making the initial peaks of VEMP to be of vestibular origin and later peaks to be of cochlear origin. The morphological and histopathological studies showed presence of 'vestibulocochlear anastomosis' which was first described by Oort in 1918. It is situated deeply at the bottom of the internal acoustic meatus, spreads from the saccular nerve before its terminal ramifications and to the cochlear nerve before its penetration into the cochlea. Nerve fibers of the cochlear efferent system are believed to pass through it. Burian, Gstoettner & Zundritsch (1989) visualized several primary saccular afferent fibers progress to cochlear nucleus, the axons terminated at cells lying between the dorsal and posterior ventral cochlear nucleus. Bukocuska (2002) explained about the morphological evidence for the secondary vestibular afferent connections to the dorsal cochlear nucleus in mammals.

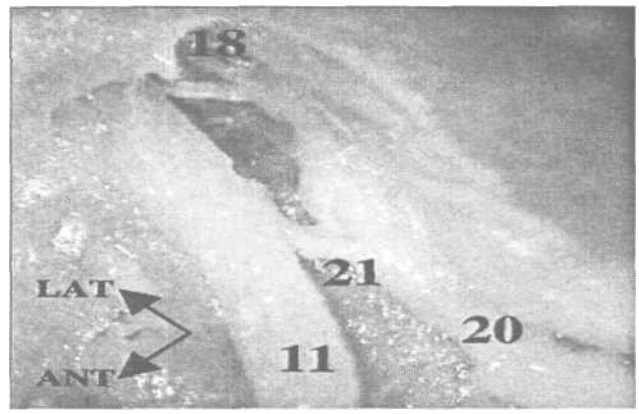


Figure 1: Depicts vestibulocochlear anastomosis- 11, Cochlear nerve; 18, saccular nerve terminal ramifications; 20, saccular nerve and 21, vestibulocochlear anastomosis.

All these above studies suggest that this intimate connection of vestibular and cochlear systems makes them, to a greater degree, interdependent and stimulation of one system can stimulate the other thus functioning of one has a direct impact on the functioning of the other system. Thus the exclusive study on later peaks of VEMP might help us to understand the possible route of the later peaks of VEMP, Hence, adding into the diagnostic importance.

When N34-P44 peaks recorded from the Stemocleidomastoid muscle are thought to be of cochlear in origin this implies that auditory nerve needs to stimulate the vestibular nerve to elicit responses from the Sternocleidomastoid muscle. Thus it indicates that later potentials are likely to be absent or decreased in cases with hearing loss. However, there are a few studies in which n34-p44 potentials are present in profound hearing loss individuals (Ferber-Viart et al., 1999), which raised the question whether these potentials are really of cochlear origin? This could be understood if the study is carried out in normal and in subjects with hearing loss.

The N3 potential is the negative peak at 3 msec in ABR recording which is of vestibular origin. Todd et al., (2001) explained that saccular system is sensitive to

acoustic stimuli. Rosengren et al., (2001), have correlated VEMP and N3 potential in normal individuals and unilateral profound hearing loss individuals and concluded that N3 potential are saccular in origin. Kato et al., (1998) studied the N3 potential in profound hearing loss cases and presence of this negative peak confirms vestibular system especially saccule as a site of origin whereas, N34-P44 peaks of VEMP recorded by stimulating the SCM muscle are thought to be cochlear origin.

Thus it is necessary for us to know is there any relation between these two potentials? If there is a relation then it may help us to understand the physiological process for testing the structural and functional relationship between cochlear and vestibular neural pathways?

The presence and absence of later peaks of VEMP and N3 potential or presence of both might give us some idea about the presence of the auditory nerve which in turn might then be included in the protocol to select the candidacy for cochlear implant.

Aims of the study

Keeping all this in mind the study has been taken up with the following aim.

1. To study the relationship between the severity of hearing loss and N34-P44 potentials of VEMPs.
2. To understand the relationship between N3 potentials and VEMP.
3. To understand the possible route for later potentials of VEMP.
4. To understand possible route for N3 potential.
5. To understand the structural and functional relationship between the Vestibulo-cochlear nerve root.

Chapter II

REVIEW OF LITERATURE

The neurogenic vestibular evoked potentials (VEPs) remain difficult to elicit, and their real origin and clinical application remains controversial. Some authors have begun to focus on the possibility of recording muscular responses, which are secondary to strong acoustic stimulation and likely to originate from the vestibule. These have been named either "click-evoked Vestibulo-Collic responses" or "vestibular evoked myogenic potentials" (VEMP) so that they can be distinguished from the usual evoked potentials of neurogenic origin.

The VEMP procedure is an emerging diagnostic tool for identifying vestibular lesions. The VEMP procedure is noninvasive and causes little or no discomfort to the patient, unlike the caloric irrigation component of the electronystagmography (ENG) or video nystagmography (VNG) procedure. VEMP testing targets the vestibule and neural connections to the sternocleidomastoid muscles (SCM) of the neck. The VNG procedures evaluate semicircular canals and neural input to Pons and Cerebellar structures, while the VEMP procedure stimulates the saccule and connections through the medulla and into the neck. The procedures are complementary in the sense that VEMP testing completes the lower brainstem and upper spinal column assessment component not targeted with VNG procedure. VEMP tests linear acceleration/gravitational orientation balance function. Further, as noted, VEMP testing is tolerated well by the patient making it a useful adjunct procedure to VNG in a single test session.

The VEMP by definition is a short-latency electromyogram recorded from the tonically contracted SCM in response to high-intensity acoustic stimulation (Bickford and Cody, 1964; Cody and Bickford, 1969; Colebatch et al., 1994). With electrodes placed on the SCM muscles, waves occur at approximately 13-15 ms (PI3 or wave I) and 21-24 ms (N23 or wave II) post stimulus delivery to the ear ipsilateral to the contracted SCM. The VEMP neural pathway consists of the saccule, inferior vestibular nerve, and vestibulospinal tract (Colebatch and Halmagyi, 1992; Itoh et al., 2001; Murofushi et al., 1996; Murofushi et al.. 2001).

Hypothesized Pathway for VEMP:

Given that VEMP are assumed to be of vestibular origin, several works have been assigned for the study of changes in responses in cases of specific impairment of the labyrinth or of the vestibular nerve.

1. *Neurosensory deafness:* Bickford et al., (1964) obtained a normal response from both the normal and the deaf ear in a patient with complete unilateral neurosensory deafness but with normal labyrinth. In a patient with unilateral neurosensory deafness and loss of labyrinthine function, however, responses were absent from the affected ear. These results suggest that response to sound-click was initiated via the vestibular system rather than the cochlear one. Colebatch et al., (1994) studied three patients with severe unilateral sensory deafness but normal caloric testing. All of them had P13-N23 responses following stimulation of the affected ear, suggesting that the P13-N23 component of the response was of labyrinthine origin.

2. Vestibular defects: Townsend and Cody (1971) studied patients with bilateral neuronitis but normal hearing: no inion response was obtained from either ear. These observations confirm Cody and Bickford's (1969) hypothesis that inion response depends on the integrity of the vestibule. Furthermore, these authors reported a case of normal hearing but with supposed bilateral labyrinthine defect secondary to streptomycin toxicity. In that case, inion responses were evoked on stimulation of each ear. The Author's hypothesis is that the receptor could be the saccule or utricle rather than the ampullae. Conversely, responses were recorded symmetrically on SM and TRP in the case of vestibular nerve section with preservation of cochlea and cochlear nerve; in contrast, responses are always abolished following total destruction of the cochlea and the vestibule, Ferber-Viart, Dubreuil, Duclaux, & Collet (1998, 1999). It can be suggested from these results that responses could involve both receptors: the cochlea and the vestibule.

3. *Vestibular nerve lesions:* Townsend and Cody (1971) observed an abolishment of the whole response following vestibular neurotomy, but recording anion response and using tone-burst at 1,000 Hz. Recent reports suggest that VEMP recorded on the cervical muscles in man are mediated through the vestibular nerve. Colebatch and Halmagyi (1992) investigated VEMP before and after selective vestibular nerve section. Three months after selective right vestibular nerve section, the first wave was abolished, whereas the later potentials were preserved. Responses from the left SCM were unchanged. On the basis of these results, the authors conclude that only the earlier component is dependent on vestibular nerve integrity.

The proposed pathway for the VEMP is as follows:

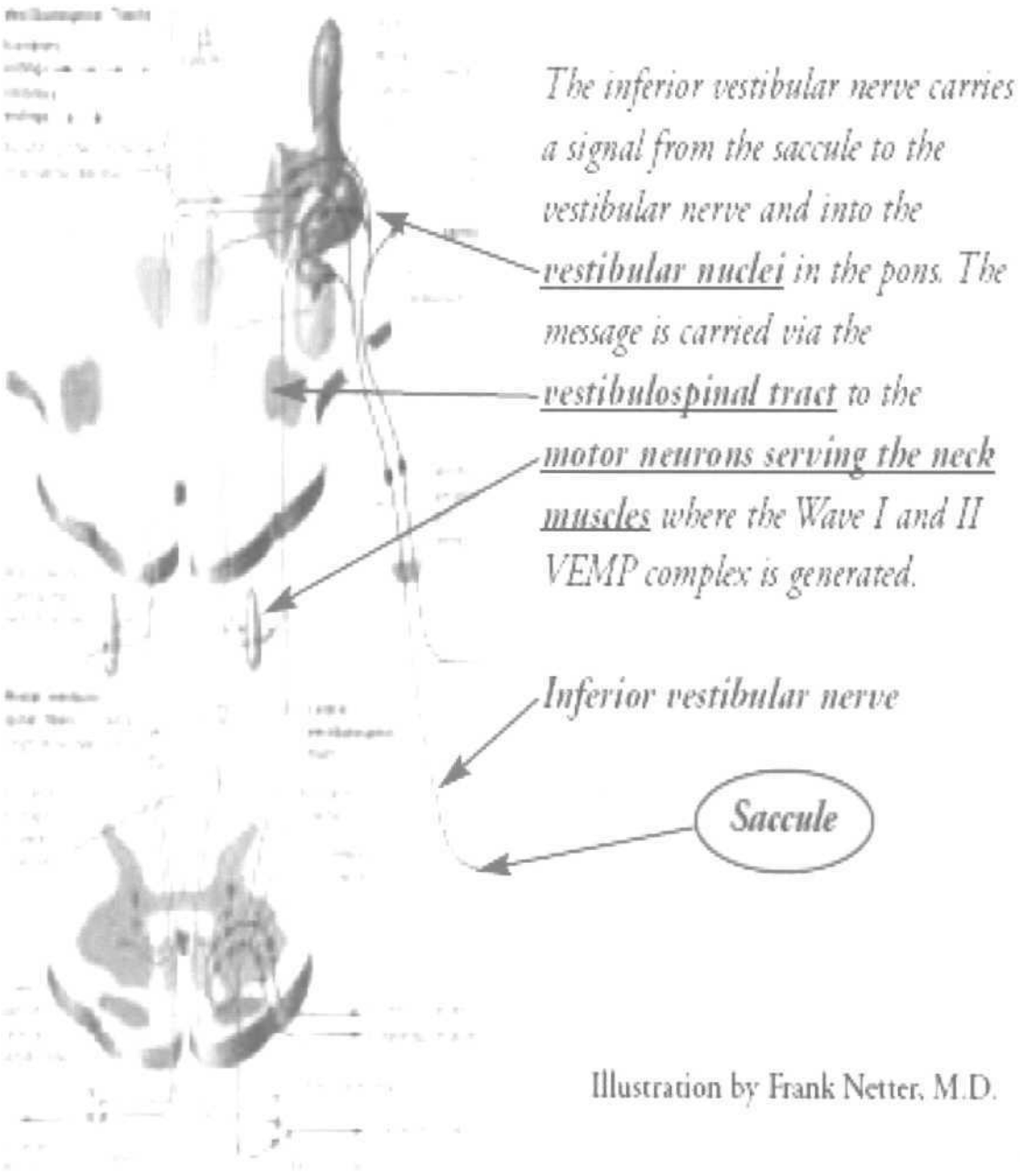


Fig. 2. The neural route for the VEMP response is illustrated here.

Colebatch et al., (1994) successfully applied loud sounds to evoke vestibular-evoked myogenic potentials (VEMP) in the tonically contracted ipsilateral sternocleidomastoid (SCM) muscle, and labeled the serial peaks P13, N23, N34 and P44, based on their latencies. In contrast to the biphasic waves P13- N23, which are supposed to originate from the sacculo-collic reflex, the origin of waves N34- P44 remains undetermined, although a cochlear origin has been proposed as waves N34-P44 could be obtained in ears after selective vestibular nerve section. In the past decade, VEMP have been widely studied in several clinical diseases, such as Meniere's disease, cerebellopontine angle tumor, multiple sclerosis, superior canal dehiscence syndrome, etc. However, researchers have focused almost solely on investigating wave P13 - N23, possibly due to the higher response rate in normal controls. In contrast, wave N34 - P44 could be elicited in only 55 - 60% of healthy subjects, interrupting the investigation of their clinical significance.

Clinical applications of VEMP:

The VEMP gives important information about saccular and inferior vestibular nerve functions, which supplements caloric assessment of lateral semicircular canals, as well as other components of the VNG/ENG procedure that target non-saccular vestibular systems. Recently, a mathematical calculation of VEMP amplitude was proposed (Wu & Young, 2002). Finding the difference in amplitude between the two sides divided by the sum of the amplitudes gives a ratio. When the ratio exceeds 0.36 the result indicates 'distended saccule' or saccular hydrops. This condition of excessive endolymph

traditionally defines Meniere's disease. This calculation is applied in all cases when the VEMP amplitudes between the ears appear to be significant. Recent discovery in the application of VEMP procedure clinically is identification of an inner ear pathology known as 'superior canal dehiscence' (SCD), or thinning or opening of the bony superior semicircular canal of the inner ear (Minor et al., 2000; Streubel, Cremer, Cary, Weg, & Minor, 2001). Other studies report VEMP sensitivity to acoustic nerve tumor (Murofushi et al., 2001), Meniere's disease (Murofushi et al., 2001; Shojaku, Takemori, Kobayashi, & Watanabe. 2001), brainstem stroke (Itoh, Kim, Yoshika, Kanaya, Enomoto, Hiraiwa et al.. 2001), and multiple sclerosis (Versino, Colnaghi. Callieco, Berganaschi, Romani, & Cosi, 2002).

VEMPs so far have been mainly useful in documenting abnormally low thresholds in persons with the "Tullio effect, which largely occurs in persons with Superior Canal Dehisence syndrome.(Brandtberg, Bergenius & Tribukait, 1999). If one does not do thresholds, there nearly always is an asymmetry in this syndrome, as well as a very large VEMP in an ear with air-bone gap. However, they seem likely to be of much wider utility than this because they offer an objective method of assessing the vestibular nerve, including a portion of it for which there is no other available clinical test suggesting that VEMP are sensitive to saccule pathway disease, Ochi and associates (2003) reported use of VEMP to diagnose Vestibular neuritis involving the inferior division of the vestibular nerve. Because the saccule is supplied by the inferior division, VEMP should be absent in this situation. VEMP does not distinguish between the saccule and inferior vestibular nerve, and available techniques seem unlikely to be able to resolve between these two. As

most types of vestibular neuritis spare the inferior vestibular nerve, VEMP would not be expected to generally be normal.

Galvanic VEMP stimulation stimulates the entire vestibular nerve and accordingly would be expected to be normal even if the inferior vestibular nerve were damaged. Thus an absent sound-VEMP and present galvanic-VEMP would not differentiate between a saccule lesion and an inferior vestibular nerve lesion. Prolonged latency of VEMPs has recently been suggested to be a sign of a retrocochlear (vestibular nerve) lesion, such as is found in Vestibular neuritis. Abnormal VEMPs (asymmetrical or long latency) are reported in about 25% of persons diagnosed with vestibular neuritis (Murofushi et al, 1996). Vestibular nerve sections fail to control intractable vertigo due to Miniere's disease in about 5% of patients. When they fail, the question can arise whether the nerve section was incomplete.

VEMPs might, in theory, be useful for detecting residual function in the inferior vestibular nerve, as this branch of the vestibular nerve is sometimes intermingled with cochlear fibers (Lehnen et al., 2004). However, as VEMPs require a very strong stimulus, it seems unlikely that they would be very sensitive. Head impulse tests for the posterior canal reveal residual function more frequently than do VEMPs (Lehnen et al., 2004). It has been reported that low amplitude of VEMPs may be found in the affected ear (DeWaele, Huy, Diard & Vidal, 1999) and a substantial proportion of subjects show no VEMP, or a higher threshold (Rauch, Zhou, Kujawa, Gunian & Herrmann, 2004). VEMP amplitudes can be increased in early Meniere's disease, as well as fluctuate

oppositely to hearing, perhaps due to saccular dilatation (Young, Huang, & Cheng 2003). Absent VEMP in advanced disease may represent collapse of the saccule.

It has recently been proposed that VEMP that increase on glycerol loading or furosemide injections are suggestive of Meniere's disease (Shojaku et al., 2002). Rauch et al (2004) recently reported that threshold differences in VEMP, particularly at 250 Hz, were about 80% accurate in detecting the side of lesion in persons already known to have Meniere's disease from audiometric and clinical data. Lacking a pathological "gold standard" diagnosis, however, it is difficult to know how to interpret this observation.

VEMPs in central disorders:

The difficulty seems to be that the latencies in VEMPs (at least with tone bursts), are so variable that there is inadequate sensitivity to disease. VEMPs are often asymmetrical in spasmodic torticollis (Colebatch, Di Lazzaro et al., 1995).

VEMP, like other evoked potential tests, can also be abnormal in central diseases such as multiple sclerosis (MS). (Shimizu, Murofushi, Sakurai & Halmyagi, 2000; Versino, 2002; Murofuschi et al., 2001) and Brainstem stroke (Chen et al., 2003). VEMPs test mainly lower brainstem function (medulla), while the ABR also tests upper brainstem function (medulla Pons and midbrain). Here, latency measures would seem more logical than amplitude measures.

VEMP and Hearing loss:

Although VEMP can be obtained in people with complete hearing loss, the hearing loss has to be of the sensorineural type. Persons with Conductive hearing loss, even just a small amount such as 10-15 dB, often do not have VEMP, presumably because the sound stimulus, conventionally delivered by earphones, does not get to the saccule. The saccule has a high threshold, and if you are stimulating the ear close to that threshold (i.e. 95 dB); it is easy to drop below it. This means that VEMPs are less useful in older persons, who often have a component of conductive hearing loss due to otosclerosis and related disorders, and also should be interpreted with a recent audiogram, including bone and air conduction testing, in hand.

A way around this may be to do bone-conduction VEMP when the air-conduction VEMP is absent. While this substitutes for the bone conduction audiogram, it requires more testing and potentially may fatigue the patients. The above mentioned clinical applications concentrate on P13 and N23 of VEMP and the later peaks i.e. N34- P44 physiology is ambiguous and hence they are not discussed.

Later peaks of VEMP:

According to Huang, Young and Cheng (2004) the definite origin of wave N34-P44 is still unknown. On the one hand, as wave N34-P44 could be obtained in ears after selective vestibular nerve section, it was proposed that they probably arose from cochlear afferents. Sacculo-collic reflex, which is generated via a disynaptic pathway beginning in the saccular macula and then runs via the inferior vestibular nerve, lateral vestibular nucleus and medial vestibulospinal tract, before finally terminating in the motor neurons

of the SCM muscle i.e. vestibulocollic neurons are monosynaptic ally excited from the ipsilateral saccule and terminate on neck motoneurons. In contrast, the latency of waves N34-P44 was much longer than that of waves P13-N23 but they had similar peak-to-peak intervals, implying that the former might occur via a polysynaptic pathway, also terminating on the motor neuron of SCM muscles (Wilson, Fukushima, Rose, Shinoda et al., 1995; Murofushi et. al., 1996 & Kushiro, Zakir, Sato, Ono, Ogawa, & Meng, 2000).

Colebatch et al., (1994) recorded VEMP in normal hearing individuals and marked the later peaks of VEMP according to their latencies and found that wave P13 - N23 was present in all normal subjects whereas wave N34 - P 44 was present only in 60% of the subjects. Huang, Young and Cheng (2004) tried to elicit steady and prominent wave N34 - P44 in individuals with normal hearing and who were not having any complains of balancing problem. They could elicit these peaks in 89% of the individuals at 105 dB nHL.

Wu and Young (2002) studied VEMP in individuals with unilateral sudden deafness and found that later peaks of VEMP were present in 45% of the individuals showing no difference from contralateral ears and explained that these results might be due to either residual function of cochlea/cochlear nerve or dual origin of the N34 - P44 peak. Taking these results together suggests that wave N34-P44 may have both a cochlear and vestibular origin.

One possible pathway to explain this dual origin, in addition to the cochlear afferent, is the vestibulocochlear projection, which has been proven to arise from saccular afferents to the cochlear nucleus in guinea pigs. Another question is whether wave N34-P44 is related to the startle reflex. The acoustic startle reflex is a relatively simple motor

response characterized by rapid habituation and a latency of: 50 ms, in contrast to the higher rates of repetition and shorter latency of wave N34- P44. Consequently, the startle reflex would not seem to be involved in wave N34-P44.

Anatomical and Physiological studies related to Vestibulocochlear pathway:

The physiological and morphological studies have indicated that either the saccule or the cupula of the lateral canal is a source of an acoustic transmission. Oort (1918) first described the vestibulocochlear anastomosis. There have been very few anatomical studies describing it. It is located at the bottom of the internal auditory meatus and links the saccular nerve to the cochlear nerve. Cazals, Eire and Aurousseau (1987) were able to demonstrate acoustically evoked responses after destruction of the cochlear hair cells by means of ototoxic antibiotics. For these authors the propagation of the acoustic response via the ipsilateral lateral vestibular nucleus up to the superior olives and the auditory cortices bilaterally indicated the existence of a vestibular-cochlear interaction.

.Labrousse, Ouedraogo, Avisse, Chays & Delattre (2005) the micro-anatomical characteristics of this anastomosis were assessed with the help of dissected 10 human temporal bones from five heads. It was found that the vestibulocochlear anastomosis in seven of the specimens, of which six were clearly visible and unable to uncover it in three specimens due to dissection problems. Its length was evaluated to be between 0.5 and 1 mm, with a diameter of 0.5 mm. The vestibulocochlear anastomosis could be the pathway for the nerve fibers of the cochlear efferent system, whose description remains incomplete. From the results of this study, it seems likely that the vestibulocochlear

anastomosis exists. However, no anatomist, histologist or physiologist has demonstrated this function.

Burian, Wutschitz, Gstoettner (1988) after tracing the vestibular nerve of the guinea pig with horseradish peroxidase (HRP), found a conspicuous fiber bundle that passed to the ipsilateral cochlear nucleus. HRP-labeled fibers were seen to leave the descending vestibular nucleus at a level caudal to subgroup "y" in a lateral direction. Traveling close to the restiform body, the axons terminated at cells lying between the dorsal and posteroventral cochlear nucleus. These cells could be distinguished cytoarchitecturally from surrounding cells of the cochlear nuclei. Several electrophysiological investigations have assumed that there is a direct connection between the vestibular and the cochlear system. Compared to these, the fibers under consideration might be the morphological basis for such a "Vestibulo- cochlear anastomosis."

Whether any of the mammalian vestibular organs plays a role in normal hearing is an open question that hinges on two factors- the acoustic sensitivity of the receptors and the central processing of their outputs. The normal acoustic sensitivity of the vestibular receptors has been controversial. Young, Fernandez and Goldberg (1977) sampled primary vestibular afferents from all of the vestibular organs in the squirrel monkey and found that, in response to intense sounds, many fibers fired preferentially during one sound phase. However, increases in mean discharge rates were not observed in most fibers until the sound reached levels associated with rapid cochlear damage (> 120 dB SPL). This study, which demonstrated acoustic responsiveness yet emphasized high

thresholds, has been cited as evidence both for (Cazals et al., 1980) and against (Kevetter and Perachio, 1989) a hearing role for the mammalian vestibular system.

Even if a class of vestibular nerve fibers holds the remote possibility of facilitating treatment for profound sensorineural deafness. An electronic hearing prosthesis interfaced with the saccule ("saccular implant") might produce an interpretable sensation, perhaps comparable to the single-channel cochlear prosthesis (Kiang and Moxon, 1972) for patients lacking cochlear neurons. Much, of course, depends upon the current use and plasticity of central connections, McCue and Guinan (1994).

If the vestibular system is sensitive to low-frequency sound stimulation, then use of the vestibular system would be a serious alternative for the cochlear implant, especially because of the greater dynamic range of the vestibular signal (Bleeker and Wit, 1984). Regardless of the type of inner ear anomaly, VEMP could still be evoked from patients if they had a preserved saccule. Studies in mammals have shown that some of the primary vestibular afferent nerves send projections to the cochlear nucleus and to various auditory fields on the cortex. (Burian and Gstoettner, 1988, 1989)

Cazals, Aran, Erre, Guihaume and Aurousseau (1983b) recorded acoustically evoked neural activity from the brainstem and auditory cortex of guinea pigs after complete destruction of the Organ of Corti by Amikacin. Ribaric and Wit (1984) were able to measure long-latency (up to 50 ms) bioelectric responses, to bone conducted 100 Hz tones from profoundly deaf patients who had otherwise normal vestibular function. These long-latency responses probably, originated in a higher center of the central nervous system. Demonstrated that there is a short-latency acoustic response that

originate from the saccule and which is elicited by sounds of frequency and intensity well within the range of human hearing (Sheykholeslami & Kaga, 2002).

Hardy (1934) demonstrated the presence of some vestibular fibers, including the saccular fibers, within the cochlear part of the nerve in humans. Rasmussen's (1940) histological studies showed that a variable number of vestibular fibers were localized within the cochlear nerve. Additionally, connecting fibers between the inferior vestibular and cochlear nerves were demonstrated via MRI (Kim, Chung, Lee, & Kim, 1998). Arnesen (1984) calculated the connecting branches between the vestibular and cochlear nerves, and found 1360 fibers. Bergstrom (1973a) showed that the fibers of the Vestibulo-facial anastomosis were generally much thinner than those of the vestibular nerve, and that these anastomotic fibers contained approximately 700 fibers (Silverstein, 1984 and Nageris, Kalamanowitz, Segal & Frenkiel. 2000).

Ozdogmus, Kubilay, Saka, Duman, San, & Cavda, (2004) On scanning electro microscopy (SEM) the superior vestibular and the inferior vestibular nerve bundles showed an increase in the number of nerve fibers from the inner ear end towards the brainstem end of the internal auditory canal (IAC), whereas the facial and cochlear nerve bundles showed a reduction in the number of nerve fibers on both sides. Some of the superior vestibular and inferior vestibular nerve bundles may receive fibers from the facial and/or cochlear nerve bundles observations clearly showed superior vestibular-facial and inferior vestibular-cochlear connections there is existence of Vestibulo-cochlear and Vestibulo- facial connections within the IAC.

The human vestibule has preserved an ancestral sound sensitivity and it has been suggested that a reflex could originate from this property underlying cervical muscle

micro-contractions secondary to strong acoustic stimulation. Previous studies have established that an early component of loud sound-evoked myogenic potentials from the sternocleidomastoid muscle originate in the vestibule. This is based on findings that the response can still be obtained from patients with complete loss of cochlear and vestibular (semi-circular canal) function, in a more direct way, a saccular origin of this short-latency acoustic response and verifies that a saccular acoustic response persists in the human ear. There is contribution of this response to the perception of loud sounds. It is concluded that vestibular response to sound might be used to assist in the rehabilitation of deafness.

The retrograde axonal tracer, wheat germ agglutinin-horseradish peroxidase (WGA-HRP) in the rabbit showed that, in addition to its afferents from the brainstem auditory nuclei (they are not described herein), the dorsal cochlear nucleus received few bilateral connections from the caudal three quarters of the vestibular nuclear complex (VNC) especially in the rostral and caudal portions of the medial vestibular nucleus and in the inferior vestibular nucleus suggesting that the certain portions of the vestibular and cochlear systems are functionally interconnected.

The study on guinea pigs medial and lateral olivocochlear system, gives off branches to the medial vestibular nuclei (Winter, Robertson, & Cole, 1989).

The study on mice done with light and electron microscopy studied the central branches of medial olivocochlear neurons that are given off to the inferior vestibular nucleus, results indicated that the inferior vestibular nucleus is an integrating center for vestibular, auditory, and other types of information (Brown, 1993; Benson & Brown, 1987).

N3 potential:

In ABR recording, a large negative deflection with latency of 3 ms (N3) has been recorded in patients with peripheral profound deafness. It has been suggested that N3 might be of vestibular origin. So far, N3 has been recorded only in patients with peripheral profound deafness (Toshihisa, Shinichi, Yoshinari & Hideki, 2005).

Kato et al., (1998) showed that there is large negative deflection with a latency of 3 msec, observed in the ABR and they have reported it to be of vestibular origin. Since it is recorded from the majority of patients with profound deafness who have responses in low frequency range hence they are thought to be of vestibular origin especially saccule. In fact, the waveforms of the farfield recording of ABR were recorded after complete destruction of cochlea in guinea pigs are extremely close to N3 potential. Cazals et al., (1980) hence these potentials are likely to be originating from saccule.

These potentials appear to originate in the brainstem where it most likely arises by two potential mechanisms: a direct potential from the lower brainstem (cochlear nuclei) or superior olive (Cazals and Aurousseau, 1987 & Buriean et al., 1989), And a stationary potential, generated when the propagating saccular nerve potential crosses the conductive boundaries to the lower brainstem, similar to the origin of the human brainstem response wave II Waring (1995).

This potential is present in individuals with profound hearing loss who have the responses at low frequency region. This potential is present in sudden hearing loss individuals who have thresholds above 70 dB HL. The repitation rate and polarity of stimulus have no significant affect on N3 potential until the repitation rate is increased beyond 40/ sec but repitation rate of 83.3/ sec the latency was prolonged by about 0.2

msec, and the amplitude of the N3 potential decreased by around 60%. As per the effect of polarity of clicks on latency and amplitude, there is no difference among each click polarity.

Kato et al., (1995) showed that the N3 potential is widely distributed over the scalp, rather than being limited to the stimulated side. This means that an N3 potential has a far- field nature similar to ABR. The presence of N3 in the patients was in agreement with the presence of the VEMP, which were also recorded. N3 was recorded in healthy subjects and in vestibular disorder patients with preserved hearing. This negative peak is likely to be of vestibular origin. N3 may be measured from subjects who cannot contract neck muscles due to their ages, mental states, or consciousness disorders. In other words, N3 may be measured from subjects from whom VEMP cannot be recorded (Ochi and Ohashi, 2001; Nong, Kyuma, Owa, & Noda, 2002).

The vestibular-evoked myogenic potential (VEMP) has shed new light on vestibular testing. This study investigated the relationship between the VEMP and the N3 potential. The oto-neurological tests, including caloric test, hearing sensitivity test, VEMP, and ABR, were performed and data were analyzed. Both the VEMP and the N3 potential appear to originate from the sacculus, but because the characteristics of these two responses are not identical, additional factors might be involved in the generation of the N3 potential (Ochi & Ohashi, 2001). In combination with VEMP, N3 may be useful for the detection of lesion sites (Murofushi et al., 2005).

Thus the review of the literature clearly indicates that there is some connection between Cochlear and vestibular nerve which can be assessed and clinically utilized for benefits of hearing impaired individuals.

Chapter III

METHOD

The present study was taken up with the aim to understand structural and functional relationship between Vestibulo-Cochlear nerve routes with the help of N3 potential and N34-P44 peaks of VEMP.

Subjects

The present study comprised of two major subject groups, the Control group and the Clinical group. The Control group comprised of 30 (60 ears) normal hearing individuals in the age range of 16 to 45 years. The Clinical group consisted of 35 (70 ears) subjects with sensorineural hearing loss in the age range of 16 to 45 years. This clinical group was further sub divided into three groups based on their severity of hearing loss as:

Group A: comprised of 10 (20 ears) individuals with mild sensorineural hearing loss.

Group B: consisted of 10 (20 ears) individuals with severe sensorineural hearing loss

Group C: included 15 (30 ears) individuals with profound hearing loss.

Subject selection criteria

Control group:

1. All the subjects had normal hearing sensitivity, having puretone thresholds within 15dBHL at frequencies from 250 to 8000 Hz in octaves, in both ears.
2. All of them showed 'A' type tympanogram with normal reflexes in both ears.
3. They did not have any history or presence of any otological problems.
4. They reported no complaints of giddiness, vertigo and balancing problem.

5. Subjects did not report of having high blood pressure and spondilitis.
6. All the subjects had UCL (uncomfortable level) above 105dB HL.

Clinical group:

1. Subjects with pure tone thresholds of varying degrees with sensorineural hearing loss were chosen.
2. Subjects did not report of having high blood pressure and spondilitis.
3. Attempts were made to rule out space occupying lesions based on ABR results or neurological assessment as and when it was required.
4. They had 'A' type tympanogram with presence, elevated or absence of acoustic reflexes in both the ears.
5. Subjects did not have any history of middle ear pathology.
6. All the subjects had UCL (uncomfortable level) above 105 dB HL.

Instrumentation:

1. To evaluate hearing sensitivity a calibrated two channel (GSI-61) diagnostic audiometer was used.
2. Calibrated GSI-Tympstar immittance meter was used for tympanometry and to check acoustic reflexes.
3. The vestibular evoked myogenic potentials and N3 potentials were recorded using IHS smart EP version 2.39 (Intelligent hearing system, Florida, USA) instrument.

Test environment

All the tests were carried out in a sound treated double room situation and noise levels were maintained within permissible limits as per ANSI (1991, cited in Wilber, 1994).

Procedure

Phase I: Routine evaluations for the selection of subjects

1. Detailed case history was taken for all the individuals to rule out any history or presence of any otological problems, general weakness, giddiness, vertigo, high blood pressure and spondilitis.
2. The pure tone audiometric thresholds were obtained using modified version of Hugson and Westlak procedure (Carhart & Jerger, 1959) for air conduction across 250 Hz to 8000 Hz and for bone conduction across 250 Hz to 4000 Hz, in octaves.
3. Tympanometry was observed using 226 Hz probe tone to know middle ear status for all the subjects. Acoustic reflexes, both ipsilateral and contralateral, were checked using 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz. tone. They were made to sit comfortably and were asked not to move or swallow during the testing.
4. ABR was done by cleaning the electrode site with the help of skin preparing gel. Electrodes were placed on the recording site by dipping it in conducting paste and then fixing them with the help of surgical tape. It was recorded using following protocol to rule out space occupying lesions as and when required.

Table 3: Shows the parameters used for the ABR recording

Stimulus parameters	Intensity	90 dBnHL
	Repetition rate	11.1/sec; 90.1/sec
	Polarity	Rarefaction
	Click duration	100 |isec
Acquisition parameter	Analysis time	10 msec
	Filter setting	100 to 3000 Hz
	Electrode placement	Cz - Non-inverting (+ve); Both mastoids - Inverting (-ve); Forehead - Ground
	Notch filter	On
	Artifact rejection	40 uV

Only subjects who fulfilled the selection criteria either for control group and or for clinical group were considered for the study.

Phase II: Experiment

VEMP:

VEMPs were recorded for all the subjects in control and clinical group.

Subjects were instructed:

- To sit straight and turn their head to opposite side of the test ear so as to stretch the Ipsilateral Sternocleidomastoid muscle.
- To close their eyes at the time of recording to avoid interference by occulomotor reflexes.
- To avoid extraneous movements of head, neck and jaw to elude muscle artifacts.

The protocol proposed by Huang, Young and Cheng (2004) was used in the present study to record VEMP which is given below:

Table 1: Depicts the parameters used for VEMP recording

Electrode Montage	
Inverting electrode	Sternoclavicular joint
Non Inverting electrode	Midpoint of SCM.
Ground electrode	Forehead
Acquisition parameters	
Analysis time	100 msec.
Filter setting	20-2000 Hz.
Amplification	50,000
Stimulus parameters	
Type of stimulus	Clicks
Repetition rate	5/sec.
Polarity	Rarefraction
Intensity	105 dBnHL.
Stimulus duration	500 msec.

Before placing the electrodes the sites were cleaned using skin preparation gel to reduce the impedance. The electrodes were placed on respective sites as given in the table above with conducting paste to improve the conduction. VEMP were recorded for all the subjects. It was ensured that impedance was within 5 K ohms at each recording site and inter electrode impedance was within 3 K ohms to obtain good responses.

N3 potential:

N3 potentials were recorded for individuals with profound hearing loss. Instructions given to the subjects were as follows:

1. Subjects were asked to sit in a chair and close their eyes.
2. They were informed not to stretch their neck, instead, were asked to sit quietly.
3. They were instructed to avoid extraneous movements of head, neck and jaw to elude muscle artifacts.
4. Electrodes were placed on respective sites as mentioned above. Prior to placing the electrodes, each site was cleaned with the help of skin preparing gel to reduce the impedance. Electrodes were placed on the recording site with the help of conducting paste to improve the conduction. The Impedance of the electrodes was maintained within 5 K ohms at each recording site and inter electrode impedance was maintained within 3 K ohms.

N3 potential was recorded using the protocol proposed by Toshihisa et al., (2005) as shown in the following table:

Table 2: Depicts the parameters used to record N3 potential

Electrode montage	
Non Inverting electrode	Vertex
Inverting electrode	Ipsilateral mastoid
Ground electrode	Nape of the neck
Acquisition parameters	
Analysis time	10 msec.
Filter setting	100-3000 Hz.
Amplification	10,000
Stimulus parameters	
Type of stimulus	Clicks
Repetition rate	10/sec.
Polarity	Rarefraction
Intensity	95 dBnHL
Total no. of stimuli	500 stimuli.
Stimulus duration	100 msec.

For all the subjects VEMP and N3 potential were recorded for right side first and then for the left side. It was ensured that each recording was repeated to have reproducibility of the responses. For subjects in Group C, N3 potential was recorded after the VEMP recording.

Analysis

N34-P44 peaks of VEMP were recorded for all subjects participated in the study.

1. Presence and absence of later peaks of VEMP was assessed with reference to severity of hearing loss.
2. Amplitude and latencies of later peaks of VEMP were noted down for Control and Clinical group and were compared between the both groups and subgroups of the Clinical group.
3. N3 potential was recorded and tapped only for individuals with profound hearing loss.
4. Later peaks of VEMP and N3 potential were compared for the subjects with profound hearing loss.

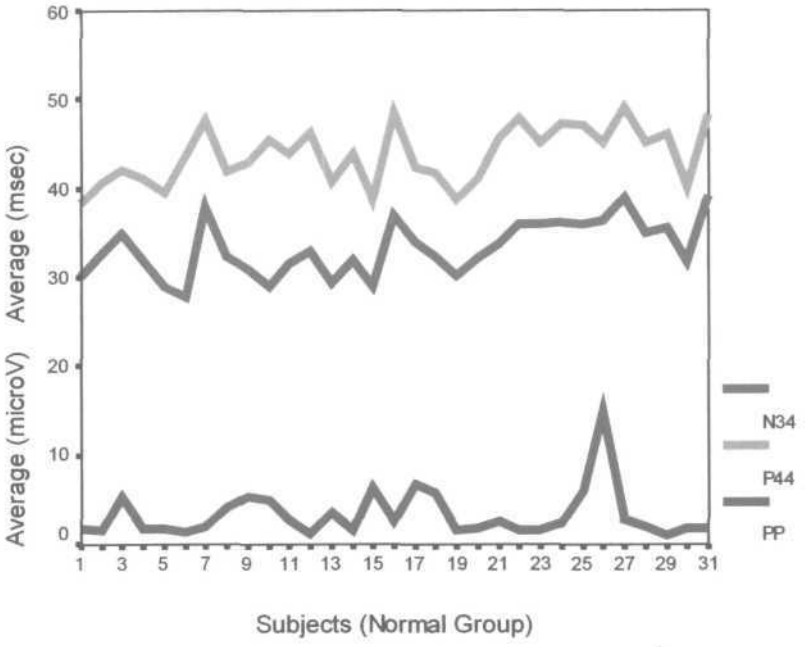
Chapter IV

RESULTS

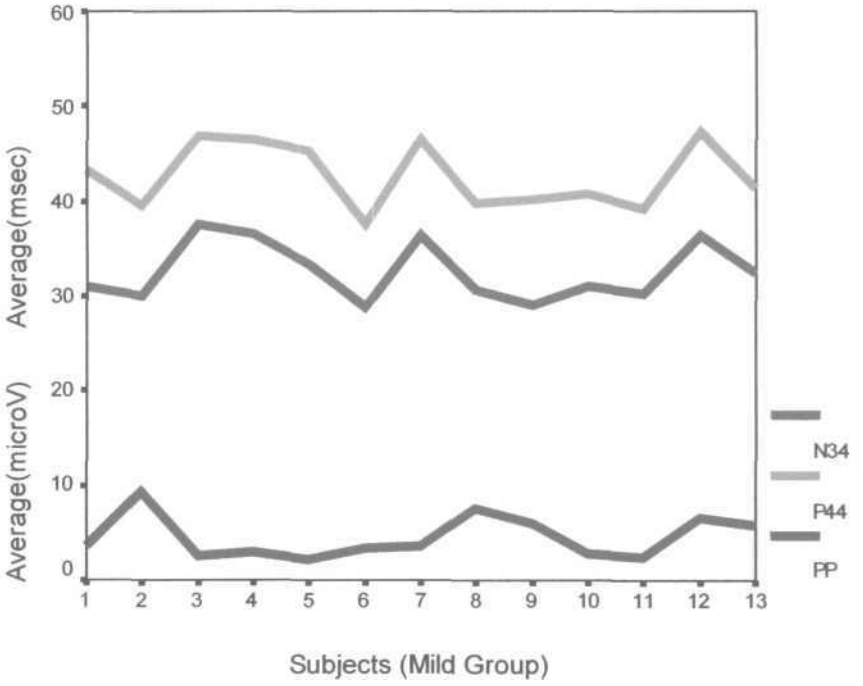
Data from 30 individuals with normal hearing and 35 individuals with sensorineural hearing loss were obtained to understand the structural and functional relationship between the Vestibulo-cochlear nerve roots with the help of N34 - P44 peaks of VEMP and N3 potential.

Data obtained from both Control and Clinical group were subjected to One-way ANOVA to know the effect of hearing loss on later peaks of VEMP and was plotted on a graph to see the homogeneity of the data obtained from the subjects.

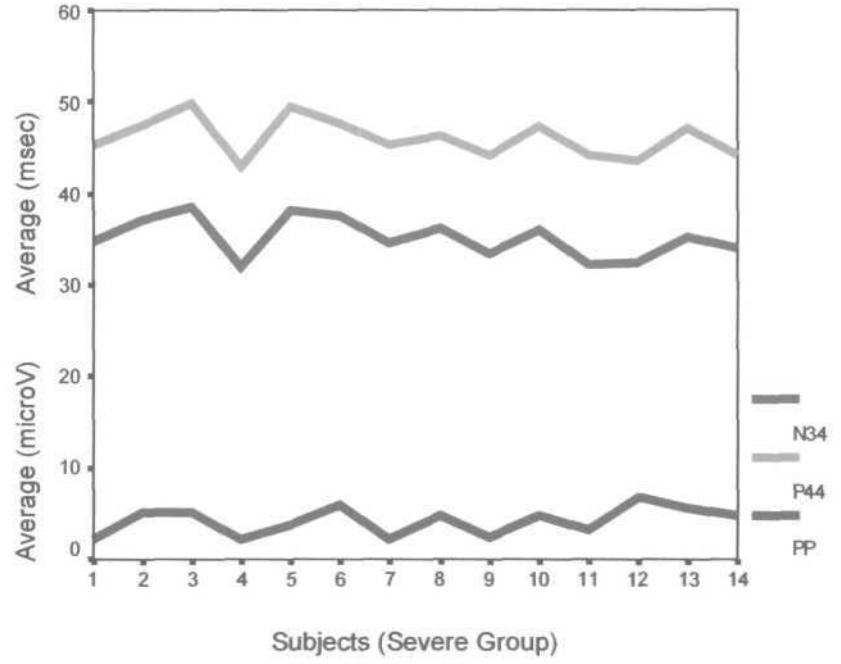
It was observed that initial peaks (P13 - N23) of VEMP were present in all subjects taken for the statistical analysis. Individual data obtained from the subjects from the control group and subgroups of the clinical group were plotted against each subject to visualize the individual data. The graph also highlights the homogeneity of the data obtained from the different subjects with in the group and subgroups. Below are the graphs that clearly depict the homogeneity of each group data.



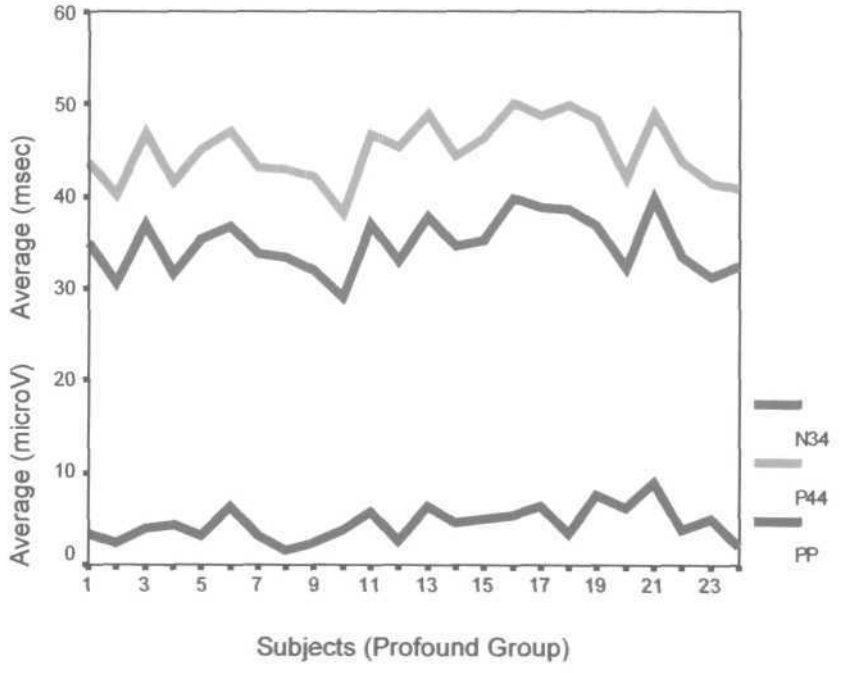
Graph 1: Depicts the homogeneity of the data obtained for N34 - P44 peaks of VEMP from subjects with normal hearing sensitivity.



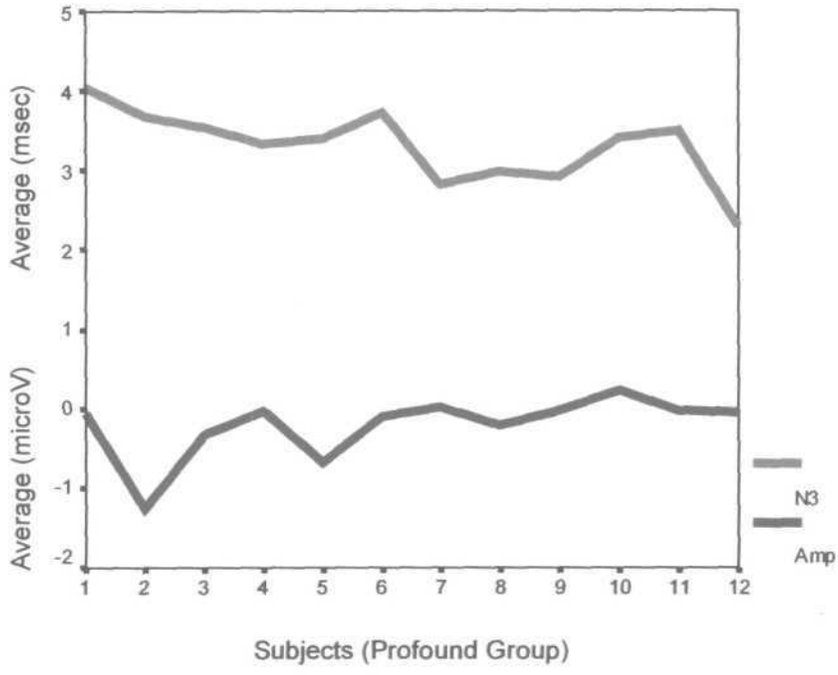
Graph 2: Depicts the homogeneity of the data obtained for N34 - P44 peaks of VEMP from subjects with mild hearing loss



Graph 3: Depicts the homogeneity of the data obtained for the N34 - P44 peaks of VEMP from the subjects with severe hearing loss



Graph 4: Depicts the homogeneity of data obtained for N34 - P44 peaks of VEMP from subjects with profound hearing loss



Graph 5: Depicts the homogeneity of data obtained for N3 potential from the subjects with profound hearing loss

It is evident from the graphs 1, 2, 3, 4 and 5 that the latency and peak to peak amplitude values, obtained from the later peak of VEMP and N3 potential, are homogenous in control and subgroups of clinical group except for the peak to peak amplitude obtained from subject number 26 in the control group. This highlights the reliability of the data obtained form the different groups of subject for later peaks of VEMP and N3 potential.

The data obtained from Control group and all the subgroups of clinical group were homogeneous. The data was further statistically analyzed using One - way ANOVA, Duncan's post — hoc test, Chi — square test and Cramer's V. All the statistical analysis was carried out using SPSS software (Version 10.0).

In the first stage the effect of hearing loss on the N34 - P44 wave latencies in msec and peak to peak amplitude in micro volts were compared with the help of One-way ANOVA and Duncan's post- hoc test was administered to see pair wise differences among the control group and subgroups of clinical group. In the second stage of the analysis, association of the presence or absence of N34 - P 44 peaks of VEMP between the control and subgroups of clinical group was tested with the help of Chi - square test to know whether the degree of hearing loss has an effect on presence or absence of N34 - P44 peaks of VEMP.

Further Cramer's V was administered to see percentage of ears in which N34 - P 44 wave of VEMP was present in control group and subgroups of clinical groups. In the final stage of the analysis data obtained from subjects with profound hearing loss were tested to know if there is any association between the presence or absence of N34 - P44 potentials of VEMP and presence or absence of N3 potential with the help of Chi - square test. Cross tabulation was done to see the distribution of the percentage of presence or absence of later peaks of VEMP versus presence or absence of N3 potential. The results obtained from all the 3 stages of statistical analysis were used to unfold the possible root for both N34 - P44 peak of VEMP and N3 potential. These results were also further utilized to understand the possible anatomical and physiological basis of the Vestibulo-cochlear nerve root.

1. Relationship between the severity of hearing loss and N34 - P44 potentials of VEMP:

The mean and standard deviation values obtained for the latencies of N34 and P44 in msec along with the peak to peak amplitude in micro Volts can be seen in the table below:

Table 4: Depicts the Mean and Standard deviation of latencies and peak to peak amplitude of later peaks of VEMP:

Parameter	No. of Ears	Group	Mean	Std. Deviation
N34	13	Mild	32.5538	3.1532
	14	Severe	35.1714	2.2228
	24	Profound	34.7937	3.0226
	31	Normal	33.3161	3.1136
P44	13	Mild	42.6154	3.4024
	14	Severe	46.0143	2.1260
	24	Profound	44.8138	3.2994
	31	Normal	43.7574	3.1351
PP	13	Mild	4.4885	2.2823
	14	Severe	4.1950	1.5442
	24	Profound	4.4579	1.8855
	31	Normal	3.3110	2.7835

It is evident form the table 4 that, the data did not follow specific trend i.e. the increase or decrease in hearing loss did not lead to increase or decrease in later peaks of VEMP. The latencies for N34 and P44 were shortest for group with mild hearing loss and maximum for individuals with severe hearing loss. Peak to peak amplitude of the wave N34 - P44 showed a specific pattern. There was increase in amplitude of the peaks

as the severity of hearing loss increased except in individuals with mild hearing loss which had maximum amplitude.

Further, the minimum and maximum latencies values along with mean and median for N34, P44 and peak to peak amplitude respectively for all the groups i.e. Control and Clinical groups were as seen in table below:

Table 5: Depicts the mean, median, minimum and maximum latencies of later peaks of VEMP and peak to peak amplitude

Parameter	**Groups**	**Mean**	**Median**	**Minimum**	**Maximum**
N34	Mild	32.5538	31.0000	28.80	37.60
	Severe	35.1714	35.0000	32.00	38.60
	Profound	34.7937	34.8000	29.00	39.80
	Normal	33.3161	32.8000	27.80	39.20
P44	Mild	42.6154	41.4000	37.60	47.20
	Severe	46.0143	45.7000	43.00	49.80
	Profound	44.8138	44.7000	38.20	50.00
	Normal	43.7574	44.0000	38.40	49.00
PP	Mild	4.4885	3.5000	2.18	9.32
	Severe	4.1950	4.7250	2.09	6.78
	Profound	4.4579	4.1600	1.58	8.97
	Normal	3.3110	1.9700	0.90	15.00

From the table it can be understood that the minimum and maximum values range differs for all the groups. The largest range for N34 latency was seen for group with normal hearing individual which was 11.4 msec, where as the smallest range of 6.60 msec was observed for individuals with severe hearing loss. For P44 latency, largest

range was seen for individuals with profound hearing loss as 11.8 msec and least was 6.8 msec in individuals with sever hearing loss. Similarly for peak to peak amplitude individuals having normal hearing showed largest variations. Overall it was observed that variations were more for individuals with normal hearing compared to individuals with hearing loss.

It is seen in the Table 4 and 5 that there is a slight variation in latency and peak to peak amplitude of N34 - P44 peak of VEMP with the varying degree of hearing sensitivity. The One-way ANOVA was administered, to check whether latency and peak to peak amplitude are significantly different or not. The Duncan's post-hoc test was done to see significant differences between the groups of subjects for N34, P44 latency and Peak to peak amplitude separately when One-way ANOVA test results showed significant difference at, ($p<0.05$).

Table 6: Depicts the Duncan's post-hoc test results for N34 peak latency of VEMP

Groups	**No. of ears**	**Subset for alpha = .05**	
		1	2
Mild	13	32.5538	
Normal	31	33.3161	33.3161
Profound	24		34.7937
Severe	14		35.1714
Sig.		0.443	0.079

From the table it is evident that for N34, there was a significant difference between various groups i.e. control group and subgroups of clinical group, ($p<0.05$). The results of Duncan's test revealed that there is significant difference between the data obtained

from individuals with mild hearing loss from individuals with profound hearing loss and severe hearing loss. However, the data obtained from individuals with normal hearing did not differ significantly from individuals with mild hearing loss or severe hearing loss and profound hearing loss, ($p>0.05$) for N34 peak of VEMP.

Table 7: depicts the Duncan's post-hoc test results for P44 peak of VEMP

Groups	**No. of ears**	**Subset for alpha = .05**		
		1	2	3
Mild	13	42.6154		
Normal	31	43.7574	43.7574	
Profound	24		44.8137	44.8137
Severe	14			46.0143
Sig.		.270	.308	.247

As from the above table it is clear that for P44 peak latency of VEMP, One-way ANOVA showed significant differences between 4 groups and Duncan's post hoc test showed significant difference between individuals with mild hearing loss from individuals with sever and profound hearing loss but not from individuals with normal hearing. Whereas individuals with normal hearing differ significantly from individuals with severe hearing loss but not from individuals with mild and profound hearing loss, ($p>0.05$). Similarly, when Peak to Peak amplitude values in micro volts were compared, no significant difference between 4 groups was observed, ($p> 0.05$). Hence Duncan' post hoc test was not administered.

An attempt was made to see if there is any association between the presence or absence of N34- P44 wave and hearing sensitivity based on the data obtained from

control group and subgroups of clinical group. Chi square test was administered and results revealed that there lies a significant association between the presence of N34 - P44 wave of VEMP and increase in hearing sensitivity, x^2 (1) = 0.464, (0.05<p<0.1).

On Cramer's V test it was seen that association is 23% and the response rate to eliciting wave N34 - P44 from group with normal hearing sensitivity to mild to sever group with profound hearing loss were 51.7%, 65%, 70% and 80% respectively, which is shown in the following table:

Table 8: Depicts the no. of ears and percentage of the presence or absence of later peaks of VEMP for all the subject groups

Groups	No. of ears	**Absent**	**Present**	**Total**
Mild	No. of ears	7	13	20
		35.0%	65.0%	100.0%
Severe	No. of ear	6	14	20
		30.0%	70.0%	100.0%
Profound	No. of ears	6	24	30
		20.0%	80.0%	100.0%
Normal	No. of ears	29	31	60
		48.3%	51.7%	100.0%
Total	No. of ears	48	82	130
		36.9%	63.1%	100.0%

From the above table it is clear that as the severity of hearing loss increased the percentage of presence of N34 - P44 wave of VEMP also increased. The group with profound hearing loss showed highest percentage of presence of N34 — P 44 peaks of VEMP followed by group with severe hearing loss and mild hearing loss. The individuals with normal hearing showed the least percentage i.e. 51.7% of presence of later peak of VEMP among all the groups.

2. Relationship between N3 potentials and N34 - P44 peaks of VEMPs:

The later peaks of VEMP and N3 potential were recorded in individuals with profound hearing loss. The mean and the standard deviation along with minimum and maximum values for N3 potential latency and absolute amplitude are given in the table below:

Table 9: Depicts the Mean, median, Standard deviation (SD), minimum and maximum values for N3 potential latency and absolute amplitude in subjects with profound hearing loss

Parameters	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**
N3	3.3033	0.4782	3.40	2.28	4.05
Amplitude	-0.2142	0.3941	-5.50	0.22	-1.25

From the table it is evident that N3 potential was present with a mean latency of 3.33 msec and the mean absolute amplitude around -0.22 micro Volts. It was seen that N3 potential was recorded with a median of 3.40 msec but the range was of 1.77 msec for absolute amplitude the range was 1.05 micro Volts.

The Chi - square test was done to see if there lies any association between the presence and absence of N34 - P44 peak of VEMP and presence or absence of N3 potential. Chi square test showed no significant association between the presence and absence of the two potentials for x^2 (3) = 7.486, ($p>0.05$). On cross tabulation it was evident that N3 potential was present in 4 ears when N34 - P44 peak of VEMP were

absent where as 12 ears had absence of N3 potential with presence of later peaks of VEMP.

Table 10: depicts the distribution of data for presence / absence of later peaks of VEMP and N3 potential in subjects with profound hearing loss

Parameter		**N3**		**Total**
		Absent	Present	
N34 P44	No. of ears	2	4	6
	Absent	6.7%	13.3%	20%
	No. of ears present	12	12	24
		40%	40%	80%
Total	No. of ears	14	16	30
		46.7%	53.3%	100%

Form the table it is evident that only 6.7% of the subjects when VEMP was absent, N3 potential was also absent. And for 40% of the subjects when later peaks of VEMP were present, N3 potentials were also present. Thus 46.7% of the population had similar test results suggesting that there might be some similarity in pathway between later peaks of VEMP and N3 potential. The disagreement between the presence or absence of later peaks of VEMP and N3 potential is 53.33% which might also suggest that there could be two different mechanisms for generation of the N3 potential also.

These results are discussed to understand the possible root of VEMP and the physiological relationship between the Vestibulo-cochlear nerve routes in the following chapter.

Chapter V

Discussion

1. Relationship between the severity of hearing loss and N34 - P44 potentials of VEMP:

The results of the present study have shown that there is association between presence of later peaks of VEMP and severity of hearing loss. Chi square test showed that there is association of 23% between presence of N34- P44 wave of VEMP and severity of hearing loss. Duncan's post-hoc test did not show any specific trend in increase or decrease of latencies and amplitude of later peaks of VEMP in individuals with different hearing sensitivity. On the Cramer's V test it was seen that in individuals with normal hearing sensitivity, only 51% had presence of N34 - P44 peak of VEMP compared to 80% which was seen in individuals with profound hearing loss. The initial findings reported in the literature, Colebatch et al. (1994) could record later peaks of VEMP from 60% of individuals with normal hearing. Whereas Huang et al. (2004) could record from 80% of the individuals with normal hearing sensitivity. In the present study later peaks of VEMP could be recorded from 80% of the individuals with profound hearing loss which is much higher that what has been reported in the literature by Wu and Young in (2002). They could record later peaks of VEMP only from 45% of the individuals with sudden hearing loss. It is also evident from the current study that as the severity of hearing loss increased the percentage of presence of later peaks of VEMP also increased. However there are no

such studies available in the literature which compared the presence of later peaks of VEMP in population with different degrees of hearing loss.

In the current study the findings suggest that probably later peaks of VEMP may not be cochlear origin as wave complex is present in 80% of individuals with profound hearing loss. However, there are reports in literature which support the fact that later peaks of VEMP are cochlear in origin as Colebatch et al., (1994) found presence of later peaks of VEMP in before and after selective vestibular nerve section and concluded that the second component (N34- P44) generated by afferents originating from both ears probably arises from cochlear afferents.

Taking these results together it might suggests that wave n34_ p44 may have both a cochlear and vestibular origin. The possible pathways for generation of N34- P44 peak of VEMP are discussed below:

The first possible pathway:

The study by Colebatch et al. (1994) suggests that later peaks of VEMP are present in individuals with vestibular neurectomy and concluded that they are generated by afferent originating from both ears probably arising from cochlear afferents. Thus, it suggests the possible connections between cochlear and vestibular nerve.

There are histopathological and morphological studies which have proven that, the (saccular nerve) inferior vestibular nerve links to the cochlear nerve in internal acoustic canal and this intimate connection was named as Vestibulocochlear anastomosis (Oort. 1918; Rasmussen, 1940; House, 1961; Kim et al., 1998; Nageris et al., 2000 & Labrousse, Ouedraogo, Avisse, Chays & Delattre, 2005). It was also found that cochlear afferent fibers go to the lateral ipsilateral vestibular nucleus (Cazals et al. 1987) may be

via vestibulocochlear anastomosis. There are reports which suggest that vestibulospinal nerve fibers nerve fibers from the medial and lateral vestibular nucleus descend down to the SCM muscle via MVST and to leg muscle via LVST, Colebatch (1992 & 1994).

Thus the possible pathway to explain cochlear origin can be explained from following figure:

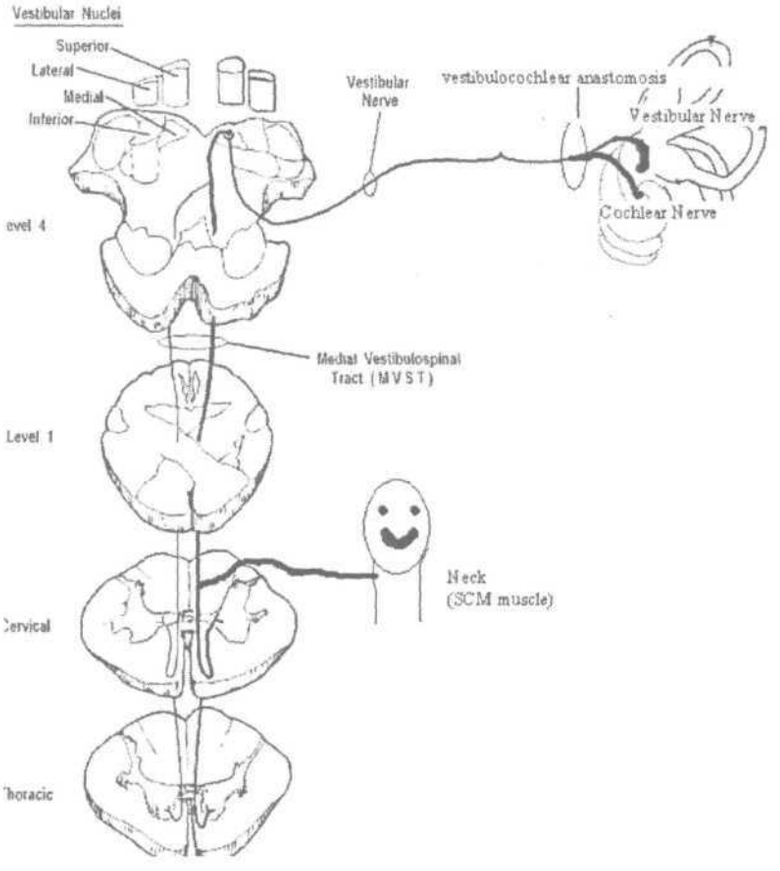


Figure 3: Depicts the possible pathway for generation of later peaks of VEMP via cochlear afferents.

Thus present study hypothesize that this vestibulocochlear anastomosis plays a role in generation of later peaks of VEMP. From the above figure it can be explained that there is a possibility of acoustic stimulation to the cochlea stimulates the cochlear afferents which in turn might be stimulating vestibular nucleus in the brainstem via vestibulocochlear anastomosis. From there, impulses are sent to the neck muscles via the

medial vestibulospinal tract (MVST) and the leg muscles via the lateral vestibulospinal tract (LVST).

Second possible pathway:

On the other hand, current study suggests that the wave n34_ p44 could also be obtained in deaf ears, implying that they were probably not of cochlear afferent origin as WU & Young (2002) observed the presence of later peaks of VEMP in 45% of subjects after sudden hearing loss. This implies that these peaks might occur via a polysynaptic pathway, also terminating on the motor neuron of SCM muscles, Wilson et al. (1969), Murofushi et al. (1996) & Kushiro et al. (2000). So this suggests that there could be another possible pathway for the generation of later peaks of VEMP surpassing the cochlear afferents.

The second possible pathway could be explained as follows:

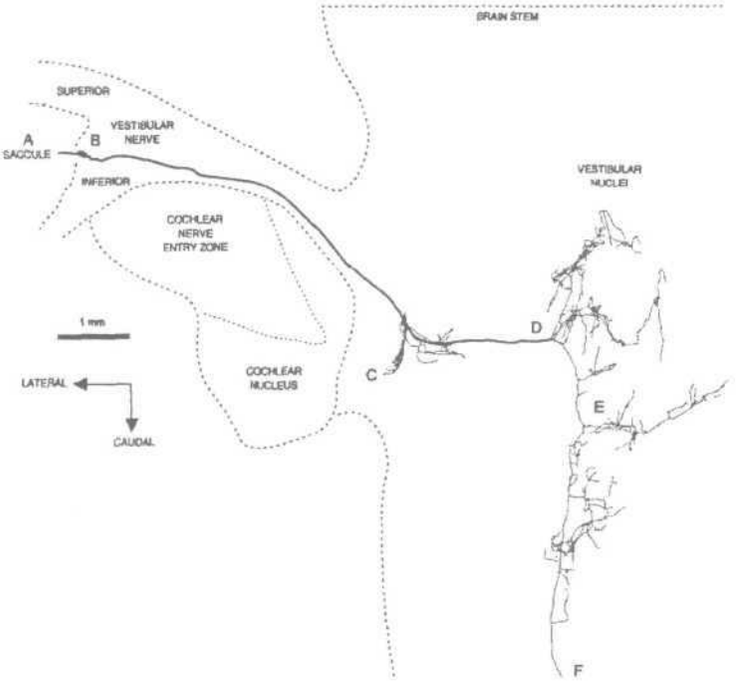


Fig. 4: shows vestibular nerve fibers progressing to vestibular nucleus and few fibers progressing to cochlear nucleus

It can be seen from the above figure that inferior vestibular nerve originates from saccule and utricle and sends a few projections into the dorsal cochlear nucleus. Gstoettner (1988, 1991), Kevetter and Perachio (1989) also reported that the vestibulospinal fibers send projections into the cochlear nucleus. There are studies which prove that Cochlear nucleus especially dorsal cochlear nucleus and medial and lateral vestibular nuclei are anatomically and functionally interconnected (Bukowska, 2002). There is a possibility of passing the impulses from dorsal cochlear nucleus to medial and lateral vestibular nucleus. Hence the possible pathway could be as follow:

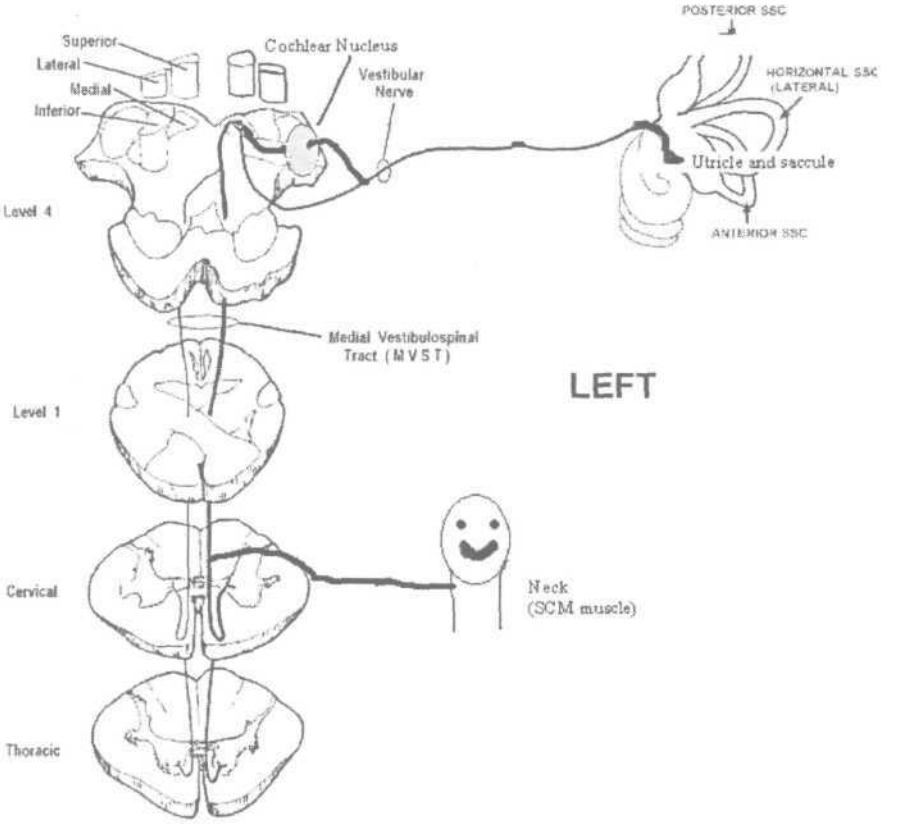


Figure 5: depicts the possible pathway for later peaks of VEMP via dorsal cochlear nucleus

From the above figure it is obvious that from saccule the inferior vestibular nerve fibers progress to the vestibular nuclei which are responsible for generation of early

peaks of VEMP. Where as, few fibers progressed to the cochlear nucleus. These few fibers later via the intimate connection between cochlear and vestibular nucleus terminates in medial and lateral vestibular nuclei. From this vestibular nuclei they innervate the SCM i.e. neck muscle via MVST and to leg muscle via LVST resulting in the generation of later peaks of VEMP.

From the above discussion and information from the literature it may be concluded that the above mentioned route could be the generator of later peaks of VEMP. This could be the possible route as, 80% of individuals with profound hearing loss showed presence of later peaks of VEMP. Thus the longer latencies of later peaks could be due to the longer path traveled by the nerve fibers to stimulate the neck muscle. However there could be another possible pathway which might involve cochlear afferents as it is observed in first possible pathway but it may not follow the first pathway completely.

Third possible pathway:

There could also be a possibility of the third route for generation of later peaks of VEMP via olivocochlear bundle. Brown (1993) and Benson and Brown (1996) and Winter et al. (1989) found that, the medial and lateral olivocochlear fiber systems, give off branches to the inferior vestibular nucleus and the lateral vestibular nucleus, respectively, apart from those given to the cochlear nucleus in the mouse and guinea pig.. This suggests that these few olivocochlear fibers might progress further to vestibulospinal tract to stimulate SCM muscle via MVST. This pathway can be explained from the figure given below:

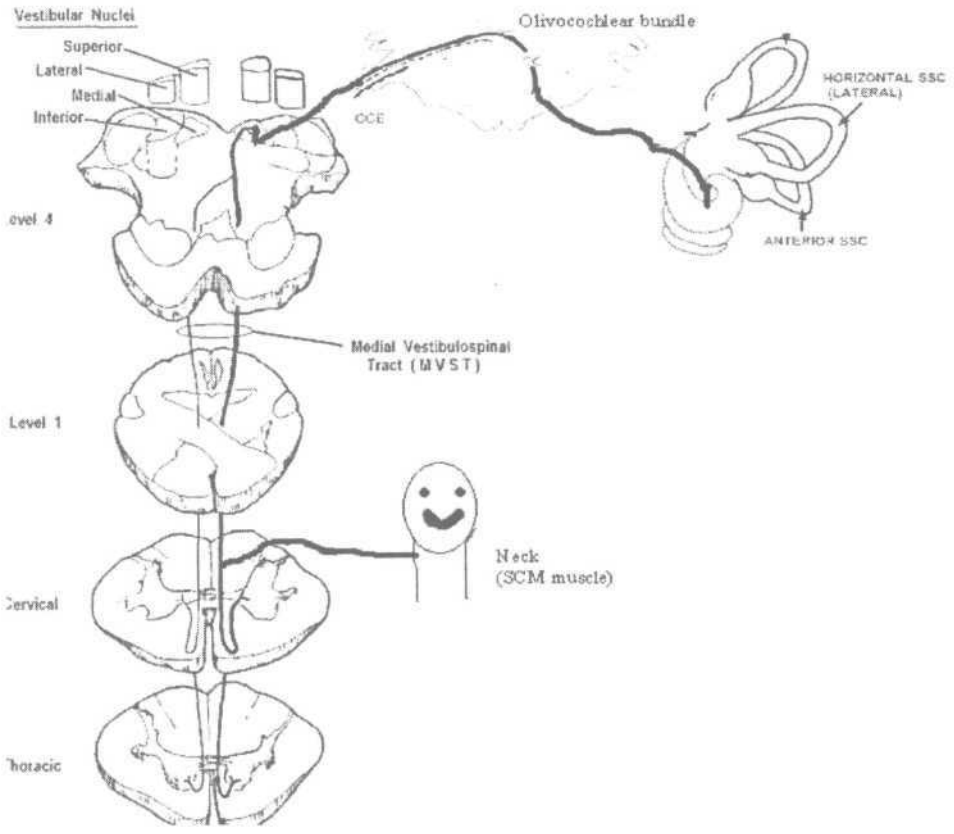


Figure 6: Depicts pathway for generation of later peaks of VEMP via olivocochlear bundle.

The figure 5 shows the possible pathway, first the acoustic stimulations are given to the cochlea. This information gets transmitted to the olivary complex through the cochlear afferents. Form the olivary complex fewer number of efferent fibers project into lateral and medial vestibular nuclei. Form these nuclei fibers descend down to the neck muscle and leg muscle via MVST and LVST respectively and generate later peaks of VEMP. Thus findings indicate that regardless of the type of inner ear anomaly, VEMPs could still be evoked from patients if they have a preserved saccule.

Thus form the above discussion it is evident that there could be three possible pathways which help in eliciting later peaks of VEMP in individuals with normal hearing sensitivity as well as in individuals with profound hearing loss. The possible first and

third pathway are more applicable for generation of later peaks of VEMP in individuals with normal hearing sensitivity where as, second possible pathway might explain the generation of later peaks of VEMP in individuals with profound hearing loss. So these two mechanisms for generation of later peaks of VEMP for two different groups might have resulted in lesser and more percentage of presence of later peaks of VEMP in individuals with normal hearing sensitivity or individuals with profound hearing loss.

The possible multiple pathways could also be the reason for not getting a specific response pattern for the later peaks of VEMP that means there is no specific trend could be observed in the current study as, with increase in hearing sensitivity there is increase or decrease in latency or amplitude of the later peaks of VEMP though significant differences either in latency or amplitude could be observed between the groups. This no significance difference in data between the normal hearing individuals and individuals with profound hearing loss might also suggest that possibility of the two different mechanisms for generation of later peaks of VEMP in both the groups of population.

Thus, this presence of later peaks of VEMP can give some information of integrity of cochlear nerve which in turn might help in selecting candidates for cochlear implants. The proposed possible second pathway might encourage considering acoustic stimulation of the saccule as an alternative to the cochlear implant. However, this alternative is viable only if vestibular acoustic stimulation is perceptible and it does not interfere with normal vestibular physiology. As presence of later peaks of VEMP was evident for 80% of individuals with profound hearing loss this highlights the role of vestibular system in compensatory mechanism. This shows that when auditory nerve looses its function, the vestibular nerve might become sensitive to acoustic stimulation.

The increase in amplitude of later peaks of VEMP in individuals with profound hearing loss compared to normal hearing individuals also suggest the same. Scheurink et al. (1985) demonstrated that deaf pigeons with fenestrated Semicircular canal could learn to respond to sound (up to approximately 2 kHz) and showed no signs of balance disturbances to this sound. Thus it might be possible for a totally deaf person to process acoustic stimulation via a saccular implant and, with training, learn to adapt to and use any vestibular information to further distinguish the acoustic signal.

2. Pathways for N3 potential:

To understand the possible pathway for N3 potential, later peaks of VEMP and N3 potential were recorded from individuals with profound hearing loss. Results revealed 46.7% of the population had similar results suggesting that there could be similar pathway for later peaks of VEMP and N3 potential. Where as, 53% showed the disagreement between the results suggesting that there could be two different sites for generation of N3 potential. Thus there could also be two different sites of origin for N3 potential, one could be vestibular nucleus and other could be the cochlear nucleus.

The possible site for generation of N3 potential suggested in literature is vestibular nucleus. Mason (1996) reported a short latency negative component during ABR recordings in child candidates for cochlear implant suggesting it to be of vestibular origin hence the relation between sound and the vestibular system is undoubtedly believed.

Studies from Elidan et al. (1987) and (Cazals et al., 1987) suggested origin of N3 potential could be the vestibular nerve and vestibular nuclei. Nong et al. (2002) and Ochi and Ohashi (2001) suggested that N3 potential might be of vestibular origin as is VEMP. Thus, the high level of acoustic stimulation to the cochlea stimulates the saccule. This excitation of saccular cells in the saccule then sends the information to the vestibular nucleus via inferior vestibular nerve and resulted in low amplitude negative potential at around 3 msec.

In the process of exploring the possible pathway for later peaks of VEMP it was observed that a few fibers of the vestibulospinal tract progress to the dorsal cochlear nucleus (Bukoswka, 2002). So this suggests that negative peak at 3 msec might be of the cochlear nucleus origin.

Thus the second possible route could be explained from the figure 4. The figure highlights the saccular fibers entering the cochlear nucleus. Also study by Neuro anatomical research on guinea pigs ascertained that the saccular afferents run towards the cochlear nucleus, Kevetter and Perachio (1989).

Thus the intense stimulation to the cochlea stimulates the saccule. Stimulation to the sensory cells of saccule in turn sends the information to the dorsal cochlear nucleus which might result in generation of low amplitude negative peak at around 3 msec.

The above discussion suggests that there could be three different pathways for the generation of the later peaks of VEMP and two possible pathways for generation of N3 potential. It also suggests that Vestibular nerves are likely to become more sensitive in subjects with profound hearing impairment. This might help in transmission of sounds through the saccular system and also to develop compensatory mechanism for balance.

Chapter VI

Summary and Conclusion

The VEMP by definition is a short-latency electromyogram recorded from the tonically contracted SCM in response to high-intensity acoustic stimulation (Bickford et al., 1964; Cody and Bickford, 1969; Colebatch et al., 1994). Colebatch et al., (1994) labeled the serial peaks PI3, N23, N34 and P44, based on their latencies. VEMP have been widely studied in several clinical diseases. These studies almost solely investigated wave P13 - N23 complex. In contrast, wave N34 - P44 complex could be elicited in only 55 - 60% of healthy subjects, interrupting the investigation of their clinical significance.

In ABR recording, a large negative deflection with latency of 3 ms (N3) has been recorded in patients with peripheral profound deafness and they have reported it to be of vestibular origin Kato et al., (1998). The later peaks of VEMP are thought to be of cochlear origin and N3 potentials were thought to be of vestibular origin though both of them are elicited by acoustic stimulation. Hence it was necessary to know, is there any relation between the two potentials? If there is a relation then what could be the possible pathway for both later peaks of VEMP and N3 potential? How these potentials can help in understanding Vestibulo-cochlear nerve pathology?

To answer the above questions present study was taken up:

- To study the relationship between the severity of hearing loss and N34-P44 potentials of VEMP.
- To understand the relationship between N3 potentials and VEMP.

- To understand the possible route for later peaks of VEMP and the possible route for the N3 potential.
- To understand the structural and functional relationship between the Vestibulo-cochlear nerve root.

For this purpose later peaks of VEMP were recorded from 30 individuals with normal hearing and 35 individuals with sensorineural hearing loss. These subjects with hearing loss were further divided into 3 groups with respect to the degree of loss as group A, group B and group C consisting of subjects with mild, severe and profound hearing loss respectively. Further N3 potential was recorded from individuals with profound hearing loss. The data was statistically analyzed using One - way ANOVA, Duncan's post - hoc test, Cramer's V test and Chi - square test.

Results of the study revealed that:

> On One- way ANOVA, control group and subgroups of clinical group were significantly different for latency N34 peak and P44 peak and not for peak to peak amplitude for later peaks of VEMP.

> There was significant difference between the data obtained from individuals with mild hearing loss from individuals with profound hearing loss and severe hearing loss and rest of the groups were not different for N34 peak of VEMP.

> For P44 peak of VEMP, there was significant difference between individuals with mild hearing loss from individuals with severe and profound hearing loss but not from individuals with normal hearing. Where as, individuals with normal hearing

differed significantly from individuals with severe hearing loss and not from individuals with mild and profound hearing loss.

> The percentage of presence of later peaks of VEMP increased with increase in hearing loss i.e. 51.3% obtained from individuals with normal hearing and 80% in individuals with profound hearing loss.

> On comparison between presence of later peaks of VEMP and N3 potential, there were only 6.7% of the subjects when VEMP was absent, N3 potential was also absent. And for 40% of the subjects when later peaks of VEMP were present, N3 potentials were also present.

Thus it can be concluded that, later peaks of VEMP can be recorded at higher percentage in profound hearing loss individuals compared to normals. There lies relationship between later peaks of VEMP and N3 potential as 46.7% of the population showing similar results. Thus, there might be possibility of multiple pathways for later peaks of VEMP as well as N3 potential. For later peaks of VEMP one pathway might be from cochlea to the Vestibulo-cochlear anastomosis further progressing to the vestibular nuclei ending at SCM muscle and second could be via cochlear nucleus to the vestibular nucleus to the SCM muscle. There could also be a third pathway from cochlea to the medial olivocochlear bundle to the vestibular nucleus descending to the SCM muscle.

For N3 potential there could be two possible sites of origins. First as Vestibular nucleus and second might be the cochlear nucleus by stimulating saccule using acoustic stimulation. Thus this communication between the two systems might have lot of implications in field of Audiology.

Thus the present study highlights that there is possibility of increase in percentage of presence of later peaks of VEMP with increase in hearing loss. All this suggest that there is greater sensitivity of vestibular system in individuals with profound hearing loss. This study also suggests the possible three different pathways for later peaks of VEMP and two different sites of origin for N3 potential. Further, it helps to understand the physiological relationship between the vestibular and cochlear system as there exist multiple pathways for later peaks of VEMP and N3 potential.

Implications of the study:

- The study has implication in knowing the pathophysiology of hearing loss in profound hearing loss.
- Non-invasively, condition of the vestibular system (especially the saccule and inferior vestibular nerve and medial and lateral vestibular nuclei) can be assessed as the later peaks of VEMP and N3 potentials can only be obtained when saccule is intact.
- If late peaks of VEMP present in profound hearing loss might suggest about the residual function of cochlea/ cochlear nerve in turn helping to decide on candidacy for cochlear implant.
- The N3 potential and later peaks of VEMP might serve as two different tests to check saccular system.

.— " O n the basis of all possible pathways it is evident that, vestibular acoustic stimulation is perceptible and it does not interfere with normal vestibular

physiology hence, it might be possible for a totally deaf person to process acoustic stimulation via a saccular implant.

Limitations of the study:

- All the possible pathways proposed have been based on the electrophysiological results. It would have been better if the results were correlated with other direct methods like injecting wheat germ agglutinin-horseradish peroxidase (WGA-HRP).
- Multiple pathway for each potential limits to find out exact lesion when they are absent, leading to lack of diagnostic purpose.

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