Assessment of Semicircular canal, Saccule and Utricle function in older adults

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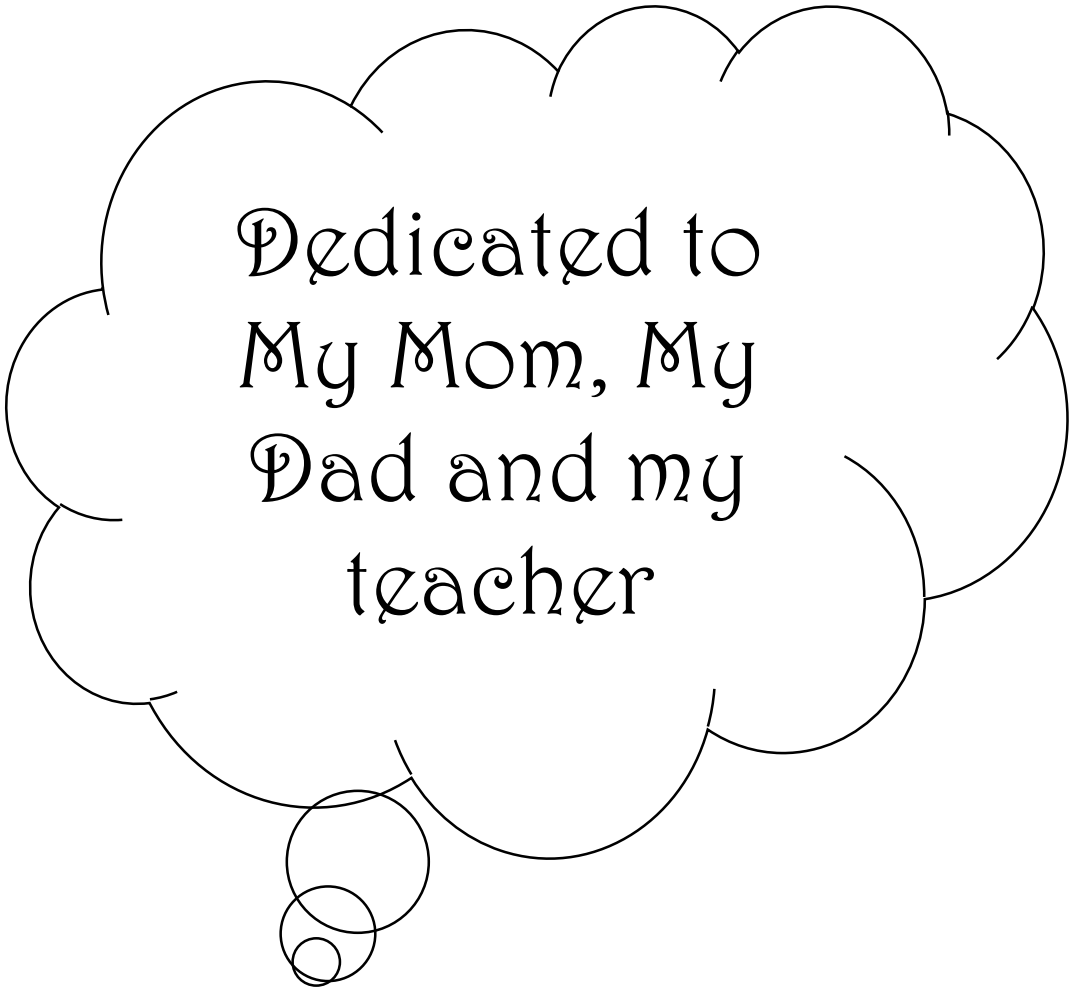
Dedicated to
My Mom, My
Dad and my
teacher

CERTIFICATE

This is to certify that this dissertation entitled "Assessment of Semicircular canal, Saccule and Utricle function in older adults" is the bonafide work submitted in part fulfilment for the Degree of Masters of Science in Audiology of the student with registration number 14AUD007. This has been carried out under the guidance of faculty of this institute and has not been submitted earlier anywhere else for the award of any type.

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This is to certify that this dissertation entitled “Assessment of Semicircular canal, Saccule and Utricle function in older adults” has been prepared under my supervision and guidance. It is also certified that this has not been submitted earlier anywhere else for award of any type.

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DECLARATION

This is to certify that this dissertation entitled "Assessment of Semicircular canal, Saccule and Utricle function in older adults" is the result of my own study under the guidance of Dr. Sujeet Kumar Sinha, Reader in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore. This work has not been submitted earlier anywhere else for any type of award.

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Abstract

Aim: The study aimed at assessing the effect of ageing on peripheral vestibular organs in older adults. Sixty four participants in the age range of 18 – 70 years were selected for the study.

Method: The participants were further divided into four groups (18 – 30, 41 – 50, 51 – 60 and 61 – 70 years). Cervical vestibular evoked myogenic potential, ocular vestibular evoked myogenic potential and video head impulse test was used to assess the sacculo-collic, utriculo ocular pathway and the lateral semicircular canals respectively.

Results: With advancing age there occurred increase in the latency of P1 of cVEMP and in the latency of N1 and P1 of oVEMP. The amplitude of both cVEMP and oVEMP decreased significantly with increase in age. Individuals in 61 – 70 years had significantly poorest cVEMP amplitudes compared to other groups. The individuals in 18 – 30 years had significantly higher oVEMP amplitudes compared to other older groups. There was a marginally significant reduction in the VOR gain seen with increasing age.

Conclusion: There occurred rapid decline in the amplitudes of oVEMP compared to cVEMP suggesting that the utricle and superior vestibular nerve are more susceptible to damage due to ageing compared to other organs. Thus the onset of damage could be predicted to be around 60 years for saccule and at 40 years for utricle. The vHIT test results did not reveal significant deterioration in the functioning of the lateral semicircular canals probably due to its moderate sensitivity. Thus to conclude use of cVEMP, oVEMP can be effectively used to predict the extent of vestibular damage due to ageing. vHIT should be complemented with caloric while assessing the lateral semicircular canals due to its poor sensitivity for moderate problems.

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Chapter 1

Introduction

Increasing age and health of the elderly individuals is one of the major growing concerns world wide. There occurs deterioration in the structure and the function of the human body including the vestibular system. Due to that increased risks of falls from loss of balance are among health concerns and are considered by the WHO as an important burden on both the health care system and health of the population.

Thirty to forty per cent of elderly people living in the community, fall each year (Prudham & Evans, 1981) and falling often results in deaths or fractures reducing the quality of life of an individual, thus associated with high rates of morbidity and mortality (Peterka & Black, 1990). Falls have been one of the major cause of hospital admission and accidental death in older people, (Delbaere, Crombez, Vanderstraeten, Willems, & Cambier, 2004b). Although the 60+ population represents only 9% of the population they account for over 40% of hospitalizations due to injuries and majority of these injuries occur due to accidental falls.

These symptoms in elderly often occur due to degenerative changes in the vestibular organs namely the saccule, utricule, semicircular canals and vestibular nerve. Saccule degeneration are more susceptible to aging compared to utricle. Only moderate amount of changes takes place in the utricle (Schuknecht & McNeill, 2007). Reduction in the sensory epithelia of the cristae ampularis occurs in the semicircular canal (Orleans, 1973). Saccular degeneration is often accompanied by loss of statoconia (Johnsson, 1971). Degeneration of the nerve cells upto 40 % (Bergstrom, 1972), reduction in the cell bodies in the scarpas ganglion (Richter & Richter, 2016) are few of the age related that occur and affect the vestibular system.. It has been reported that degeneration in the innervation of the macula in the sacculi occur in older people (Johnsson, 1971).

Thus the degenerative changes in the vestibular system causes changes in the sensory end organs namely the saccule, utricle and the three semicircular canals and result in adverse consequences, hence for effective treatment and management of elderly individuals effective assessment is required. An effective assessment can occur with the battery of test including C-VEMP, O-VEMP and V-HIT which tests the saccule, utricle and the three semicircular canals effectively.

C-VEMP as tests determines whether the saccule and/or the inferior vestibular nerve are intact and functioning normally or not. C-VEMP has been useful in assessing saccule in individual with menieres disease with the sensitivity of 54% (Taylor et al., 2011a), 34.1% (Shin et al., 2012) with vestibular neuritis with sensitivity of 25% (Adamec, Krbot Skoric, Ozretic, & Habek, 2014) , 34% (Murofushi, Halmagyi, Yavor, & Colebatch, 1996), in BPPV (E.-J. Kim, Oh, Kim, Yang, & Yang, 2015) with superior semicircular canal dihescence syndromes with 85% (Niesten, McKenna, Herrmann, Grolman, & Lee, 2013),

O-VEMP determines the functioning of the utricle and the superior vestibular nerve function. It has been found to be useful in assessing patients with utricular disorder like menieres disease 80% (Weele & Cathrin), vestibular neuritis with the sensitivity of 100% (Shin et al., 2012), in superior semicircular canal dihescence syndrome (Niesten et al., 2013), in vestibular neuritis 85% (T Murofushi, Shimizu, Takegoshi, & Cheng, 2001).

The caloric test detects the function of only the lateral semicircular canals. Measurement techniques involving high-acceleration head rotations and recording the head and eye movement responses in all three planes will present the possibility of reliably detecting individual semicircular canal lesion. (Aw et al., 1999)

Incase of partial or total unilateral loss of semicircular canal function there occurs VOR (the ratio of eye velocity to head velocity) gain deficits in yaw, pitch and roll head

impulses. This can help in assessing the deficiency in the functioning of the semicircular canals; (Walther, Hormann, Bloching & Blodow, 2013).

Video Head Impulse test has been useful in assessing patients with various vestibular pathologieslike vestibular neuritis (Bartolomeo et al., 2014) Menierres disease (Mccaslin, 2014), with good sensitivity and specificity.

Thus using cervical VEMP ,Ocular VEMP and Video Head Impulse Test one can assess all the sensory end organs of vestibular system effectively and can give a complete vestibular profile in an elderly population.

Need of the Study:

1. Need of the study in aging Populations:

Among elderly individuals, injurious falls is among the 6th leading cause of death. Thus there is significant morbidity and mortality due to falls thereby reducing the quality of life. The major consequence of fall is hip fracture and it has been reported there is higher prevalence of hip fracture in elderly population due to falls (Delbaere et al., 2004b). Sustained hip fracture results in death of 20 % of elderly people within a year (Todd, Cody, & Banks, 2000). Similar scenario exists in in the United Kingdom. The mortality rate due to hip fracture is almost 17 % (Prudham & Evans, 1981). More than one tenth of the population die each year due to falls which consists of 75 % of elderly individuals (Delbaere, Crombez, Vanderstraeten, Willems, & Cambier, 2004a). Falls resulting into fracture often results in decreased mobility and increased financial burden on the family of the concerned. The cost of rehabilitation was estimated to be $8–10 billion annually (Tinetti, 2000). Thus falls in the elderly population are associated with s reductions in quality of life, mortality, and, expense to the health-care system.

One of the causes of falls in elderly individuals could be deterioration in the vestibular system due to ageing. It has been reported that vestibular impairments results in falls more often than any other can cause (Thorbahn, Newton, & Chandler, 1996). Vestibular Symptoms like vertigo and dizziness is not uncommon among elderly population. According to (Lawson, Fitzgerald, Birchall, Aldren, & Kenny, 1999) there is higher incidence of vertigo in individuals above 70 years of age and most common complaint in patients over 75 years of age. It is present in 65% of persons aged 65 years and above, in 50% to 60% of the community dwelling elderly and in 81 to 91% of the elderly seen in geriatric outpatient clinics.

Majority of the vestibular related complaints in elderly is an outcome of age related changes occurring in the sensory end organs of the balance system. Krmpotic and Nemanic (1964 and 1969) found that as age increases there occurs piling up of bony deposition in the fundus of foramina of internal auditory canal which results in compression of the auditory and vestibular nerve as the nerve bundles passes through this foramina.

Schuknecht et al, (1965) found that there occurs degeneration in the the saccule of elderly cats and dogs. He also reported that degeneration of saccule is seen in individuals greater than 85 years of age. The saccule is phylogenetically younger and more susceptible to ageing than the utricle. Shuknecht et al, 1965 also found more saccular degeneration compared to utricle and semicircular canals. They found that more than 50 % of haircell of saccule was lost compared to utricle. Similar findings were reported by Johnson, (1971). After exposing the inner ear he found moderate nerve degeneration in utricular hair cells compared to the saccule.

Bergstrom, (1973) reported that there also occurs reduction in the nerve fibres due to the effect of ageing. He found that the vestibula nerve fibre reduces by around 37 % in older individuals beyond 60 years.

Thus the degenerative changes in the vestibular system causes changes in the sensory end organs namely the saccule, utricle and the three semicirular canals and result in adverse consequences like falls consequently reducing the quality of life, hence for effective treatment and management of elderly individuals effective assessment is a must. An effective assessment can occur with the battery of test including C-VEMP, O-VEMP and V-HIT which tests the saccule, utricle and the three semicircular canals effectively.

2. Need for V-HIT

Halmagyi and Curthoys,(1988) found that impulses of the head toward a completely damaged peripheral organ would yield a saccadic movement of the eye. The head impulse test was initialy used in coma patient and those who are unresponsive (Jacobson, McCaslin, Grantham, & Piker, 2008). HIT assess the integrity of the vestibular system by monitoring vestibular ocular reflex. The patient is asked to look at the target while his head is given a jerk in the yaw, roll or pitch plane. If an SCC is damaged the patients VOR is affected and there occurs a compensatory overt saccade to reacquire a stationary target (Jacobson et al., 2008) Post impulse saccades can be detected with naked eye by experienced clinicians while saccades occurring during head thrust are virtually impossible to detect with naked eye (MacDougall, Weber, McGarvie, Halmagyi, & Curthoys, 2009; Black, Halmagyi, Thurtell, Todd, & Curthoys, 2005)

Video Head Impulse Test requires same amplitude, high acceleration head impuse as that required in Head Impulse Test. It only requires the patient to wear a pair of goggles similar to that worn during electronystagmography. The cameras track pupil movement compared to head movement which is monitored by gryoscopes that are fixed to the frames. The goggles are light weighted and can be tightened to the patients head. This minimizes inertial slips when head is thrust in direction. The V-HIT is capable of recording overt and covert saccades.

Caloric test assess lateral semicircular canal function (Parez, Rama & Lopez, 2003). The vestibular system optimally codes for head rotations of 0.1 to 3 Hz (Barin, 2008).Caloric test evokes response to head rotation of 0.003 Hz (Lopez et. al 2003; Barin 2008).The head impulse test measures the response of the VOR to a to a high frequency stimulus. The caloric test is efficient in determining the function of only horizontal semicircular canal but the video head impulse test assess all the semicircular canal.V-HIT can assess various vestibular pathologies like vestibular neuritis (Baromoleo, 2013), Menierres disease (Mccaslin, 2014), with good sensitivity and specificity.

3. Need for CVEMP-

Cervical Vemp tests the integrity of the saccule and the inferior vestibular nerve. It can be effectively used to identify various vestibular pathologies. There is an increasing body of evidence that the VEMP recorded from the SCM muscle (SCM VEMP) can be altered by pathologic processes affecting the vestibular end organ, particularly the saccule (Murofushi et al, 1999; Ito, 2001; Ochi, 2001). For example, abnormal VEMP responses have been recorded in cases of Meniere's disease or Meniere's syndrome (Huang & Young, 2015; Singh, Sinha, Rajeshwari, Apeksha, & Barman, 2015), acute peripheral vestibulopathy (Heide, 1999), vestibular neuronitis (Murofushi et al, 1996; Chen, 2000; Halmagyi et al, 2002), superior canal dehiscence syndrome (Niesten et al., 2013), idiopathic bilateral loss of vestibular function (Matsuzaki & Murofushi, 2001), ototoxicity (Perez et al, 2000), and congenital malformations of the labyrinth. Additionally, several researchers have demonstrated that sound-evoked muscle contractions may persist in the face of considerable sensorineural hearing loss (Colebatch & Halmagyi, 1992). Sensitivity and specificity of cvemp is 65% and 85% respectively.

4. Need for O-VEMP:

O-VEMP can be elcited by stimulating the ear with a loud sounds. It can be recorded from the extra ocular muscles bilaterally, however better amplitudes are obtained from the contra inferior oblique muscleocular muscles. O-VEMP tests the integrity of the utricle and the superior vestibular nerve (Chihara et al., 2009; Neil, 2011). OVEMP can be useful in identifying various vestibular pathologies like vestibular neuritis involving superior vestibular nerve (Shin, 2012;), minnierres (Huang, 2011) disease and superior semicircular canal dihescence (Tailor 2012; Manzari et. al 2012).

Thus C-VEMP, O-VEMP and video head impulse test can be an effective tool in identifying vestibular pathologies in vestibular sensory organs in elderly which would help us to prevent and manage risk of falls which otherwise would result in complicated injuries and lowering the quality of life and increasing the cost of health concerns.

Aim of the Study:

The study aims at assessing the semicircular canal, saccule, and utricle in elderly population.

Objectives:

1. To assess the functioning of semicircular canal in elderly individuals
2. To assess the functioning of saccule in elderly individuals.
3. To assess the functioning of the utricle in elderly individuals.
4. To find out correlation between the functioning of utricle, saccule and semicircular canal in elderly individuals.
5. To find out if there is any correlation between the degree of hearing loss and C-VEMP, O-VEMP and V-HIT findings in elderly.

Chapter 2

Review of Literature

Older people are fastest growing segment of the population. According to 2011 survey, number of individual above 50 years accounted for 15.86% of the total population among which 8% were male and 7.9% were female. As age progresses anatomical and physiological degenerative changes takes place in the body and these changes result in many health problems.

Age related changes in vestibular system

The degenerative changes are also known to occur to in the vestibular system resulting in balance problems in elderly. Many authors have reported that with advancing age, changes in the vestibular system takes place.

Progressive piling up of the bony substance around the foramina has been reported with increasing age. Krmpotić-nemanić, (2009) studied the fundus of the internal auditory meatus and found that as age increases there is piling up of bony substance which compresses the vestibular nerve fibers.

The damage occurring to the vestibular system is more to the newly formed cells in terms of phylogenetical development. The saccule is more susceptible to damage compared to the utricle. Schuknecht, Northrop, & Igarashi, (2009) studied vestibular degeneration in an older cats, an older dogs and one 85-year-old man.. They found a loss of about half the number of hair cells in macula sacculi, while the macula utriculi and the cristae appeared normal.

Rosenhall, (2009) analysed vestibular haircell using specimen technique. They studied 113 inner ear specimen of infants, children, young adults, middle aged individuals and elderly people. They found that as age increases the number of haircells in the maculae of saccule and utricle and the cristae ampullaris decreases. The reduction in the

utricluar hair cell was found to be least. The reduction of haircells of saccule was reported to be 20% whereas that of the semicircular canals were upto 40%.

Ageing also causes reduction in the number of nerve fibres in the vestibular system. Bergström, (1972) examined the vestibular nerve from 11 individuals aged from birth to 85 years. The nerves were cross-sectioned at a pre- ganglionic level and the sections were studied using ocular micrometer disc. In this study it was found that young children had myelinated vestibular nerve fibres between 18,773 and 20,212 and that there was a clear and statistically significant reduction in number of fibres occurring with increasing age. The average reduction of nerve fibres was about 40%. They attributed the reduction in the number of nerve fibres to ageing as in none of the case was there a known history of neuro-degenerative disease, vestibular disorders, treatment with ototoxic antibiotics or irradiation.

Bittner & Johnson, (1974) studied 150 temporal bones of patients ranging in age from newborns upto 97 years obtained at autopsy centres. The author exposed the inner ear and studied the innervation of the maculae and found degeneration of the innervation of nerves in the macula of saccule as well as in the utricule in old individuals. He also found that degeneration of saccule is accompanied by loss of otoconia. These anatomical changes in the vestibular system right from the hair cells of the end organs to the nerve fibres causes balance problems in elderly individuals consequently resulting into falls and further health hazards in them.

Clinical applications cVEMP

Cervical Vestibular Evoked Myogenic Potential is recorded as a inhibitory response of the sternocleidomastoid muscle (Todd et al., 2000) by stimulating vestibular system with a loud sound (Toshihisa Murofushi & Kaga, 2009b). Although the saccule is served by both superior and inferior vestibular nerves, clinical findings in patients with various

pathologies provide evidence that cVEMP is dependent on the integrity of the inferior vestibular portion of the vestibular nerve (Toshihisa Murofushi & Kaga, 2009a). Thus cVEMP evaluates the integrity of the saccule and the inferior vestibular nerve and can be recorded in a short time.

Menieres disease:

Menieres disease is a disorder of inner ear often symptomized with fluctuating hearing loss, tinnitus and recurrent vertigo attacks (Hamann & Arnold, 1998). cVEMP can be an effective tool in assessment of menieres disease.

The cVEMP amplitudes are reduced and frequency tuning is shifted towards high frequency in individuals with menieres disease and this can be used as diagnostic measure. Rauch, Zhou, Kujawa, Guinan, & Herrmann, (2004) did a study on 48 young individual of which 14 were normal and 34 had symptoms like menieres. They used Broad band click and tone burst at 250, 500, 1000, 2000 and 4000 Hz ipsilaterally to obtain cVEMP threshold in the 2 groups. cVEMP thresholds, amplitude P1N1 and latency were recorded. The results revealed presence of cVEMP in all 48 participants. The normal group which included 14 participants had the maximum amplitude at 500 Hz whereas participants with menieres disease had maximum amplitude at higher frequencies. The participants with menieres disease had elevated thresholds compared to control group.

Murofushi, Shimizu, Takegoshi, & Cheng, (2001) had found similar results on cVEMP in patients with Menieres disease. They studied 43 patients diagnosed with menieres disease in the age range from 20-75 years and 18 normals in the age range of 18 – 38 years. cVEMP was recorded using surface electrodes in individuals with Menieres disease and compared it with normal control group. They reported that 22 / 43 showed abnormal amplitudes on the affected side.

As the amplitude of VEMP is reduced in ears affected with menieres disease the asymmetry between the ears also increases and this can be helpful as a diagnostic criteria. Taylor et al., (2011) recorded cVEMP on 112 individuals out of which 77 were patients with menieres disease and 35 were normal subjects. The authors administerd cVEMP from rectified and unrectified sternocleidomastoid muscle using air-conduction as well as bone conduction stimuli. Air-conduction stimuli was delivered through the headphone while the BC stimuli was delivered using bone vibrator on the forehead. The amplitude asymmetry ratio was calculated for both click AC cVEMP and BC cVEMP. The average asymmetry reflex ratio were significantly higher in patients with Menieres diseases than with the control group. Thus amplitude asymmetry ratio can be used to find menieres disease.

The abnormal asymmetry ratio between normal ears and patients with Menieres disease was reported by Yang, et. al (2008) in 29 patients with Menieres disease. They found that 69% of them showed abnormal cVEMPs results and cVEMP amplitude asymmetry between ears was more in this population.

VEMP can also be useful in grading the stage of Menieres disease. As the severity of menieres increases the asymmetry between the ears for the VEMP amplitudes also increases. Thus Inter amplitude difference (IAD) can be useful in grading the stage of menieres disease. Kim et al., (2013) studied 77 individuals out of which 33 were normal and 44 with symptoms of menieres disease to find the clinical value of cervical vestibular evoked myogenic potential (VEMP) in Meniere's disease (MD) and to evaluate whether the VEMP results can be useful in assessing the stage of MD. They administered cVEMP and calculated asymmetry amplitude ratio. In clinically definite unilateral MD (n=41), the prevalence of cervical VEMP abnormality in the Inter aural amplitude difference (IAD) was 23% in stage I of menieres whereas the it was 34.1% in

stage II and greater than 40% in stage III. The authors concluded that as the stage increased, the IAD ratio significantly increased.

Vestibular Neuritis

cVEMP can be useful in diagnosing individuals with vestibular neuritis. Murofushi, Halmagyi, Yavor, & Colebatch, (1996) reported that cVEMP waveforms are affected in vestibular neuritis cases. They reviewed 47 individuals with vestibular neuritis. Out of them 10 had developed benign paroxysmal positional vertigo (BPPV). cVEMP was administered on them using 500 Hz tone burst stimulation. The findings showed absence of cVEMP in 16/37. The authors concluded that absence of cVEMP could be due to involvement of the inferior vestibular nerve and also that BPPV is likely to develop following vestibular neuritis.

cVEMP can also help us to understand whether vestibular neuritis is of superior vestibular nerve or inferior nerve. Absent or presence of cVEMP can be helpful in locating the lesional area. Shin et al., (2012) evaluated cervical (cVEMP) in patients with vestibular neuritis (VN) to find which part of vestibular nerve is more susceptible neuritis. AC tone burst were measured in 60 normals and 41 patients with acute vestibular neuritis. The vestibular neuritis involved selectively superior vestibular nerve in 30 patients, and inferior vestibular nerve only in 3, and damaged both inferior and superior branch in eight subjects. All the findings were confirmed using MRI. In the subject with only inferior vestibular nerve involvement the cVEMPs were abnormal.

As and when the vestibular neuritis recovers the amplitude of cVEMP also increases. Thus cVEMP can be used to evaluate the recovery process of vestibular nerve function post vestibular neuritis. Adamec, Krbot Skoric, Ozretic, & Habek, (2014) included 26 patients with diagnosis of vestibular neuritis. All patients underwent cervical VEMP (cVEMP) and oVEMP recordings, at 6 days and 6 months from the onset

of the symptoms. Of the 26 patients, 14 showed improvement on oVEMP at month 6. There was no change in the amplitudes of the cVEMP on either healthy or affected sides in both groups. The authors concluded that cVEMPs along with oVEMP can be used as a diagnostic tool for identifying the site of lesion in individuals with vestibular neuritis.

Chiarovano, Darlington, Vidal, Lamas, & de Waele, (2014) studied 12 individuals with vestibular neuritis at the acute stage using air conduction cVEMP and oVEMP. 8/12 i.e nearly 67% subject showed abnormal cVEMP whereas 9/12 showed reduced oVEMP responses. There was no difference in terms of latencies between the affected and the intact side. However there was greater than 50% dissociation between cVEMP and oVEMP results. Thus the authors concluded that cVEMP along with oVEMP can be used to find whether vestibular neuritis has affected or spared the inferior vestibular nerve.

Similar finding was reported by Murofushi & Kaga, (2009). The authors administered cVEMPs, oVEMPs and caloric test on 6 participants with vestibular neuritis. All the participants had absence of oVEMP. However only 2/6 individuals had absent cVEMP. Thus author concluded that oVEMP and cVEMP can be used together to identify the site of lesion in vestibular neuritis.

Auditory Neuropathy

There is a high indication of vestibular involvement in auditory neuropathy cases as cVEMPs are reported to be absent in higher percentage in individuals with auditory neuropathy. Kumar, Sinha, Singh, Bharti, & Barman, (2013) described cVEMP in 10 subject with auditory neuropathy. The result showed absent or abnormal cVEMP in 9/10 patients. They found that 80% of the ears with auditory neuropathy has absent cVEMP.

Akdogan, Selcuk, Ozcan, & Dere, (2008)studied vestibular functions in children with auditory neuropathy. Magnetic resonance imaging, Caloric testing and cVEMP were

carried out in 3 children. Results revealed normal cochlear nerve structure, normal caloric responses, but cVEMP was absent in 2/3 children with auditory neuropathy. Thus cVEMP can be useful in children with auditory neuropathy.

Sazgar, Yazdani, Rezazadeh, & Yazdi, (2010) recorded cVEMP on 8 individuals with auditory neuropathy age ranging from 21 – 45 years. The control group consisted of 30 normal healthy individuals with no neurological complaints. Out of 16 ears with auditory neuropathy only 3 had normal responses. There were 4 ears who had unrepeatable waves and 9 ears had absent cVEMPs.

Sujeet, Niraj, Animesh, Rajeshwari, & Sharanya, (2014) studied 26 individuals with bilateral auditory neuropathy spectrum disorder (ANSD) age ranging from 13 – 42 years. They also included 26 individuals as control age ranging from 18 – 28 years and compared the results of cVEMP with the particpants with ANSD. Out of 52 ears 50 had unreapeatable waveforms and 2 ears had reduced amplitudes. Thus 96% of individuals with ANSD had absent cVEMP.

BPPV

cVEMP is a promising method for diagnosing and following BPPV. cVEMP latencies shown to be prolonged and amplitude reduced in cases with benign paroxysmal positional vertigo. In BPPV, cVEMP helps to better define the extent of damage in the sacullocollic pathway.

E.-J. Kim, Oh, Kim, Yang, & Yang, (2015) evaluated utricular and saccular function during the acute and resolved phases of BPPV, cervical vestibular evoked myogenic potentials (cVEMPs) were studied in 112 patients with BPPV and 50 normal controls. cVEMP was induced using air-conducted sound (1000Hz tone burst, 100dB normal hearing level) at the time of initial diagnosis and 2months after successful repositioning in

patients with BPPV, and the results were compared with those of the controls. Abnormalities of cVEMPs in patients with BPPV was prevalent and significantly higher compare to the healthy control group. 17.6% individuals with BPPV had absence of cVEMPs. Post repositioning the amplitude of cVEMP was not improved. There occurs degeneration of saccular maculae following BPPV as even after repositioning or rehabilitative exercises the cVEMPs show no change in amplitude.

Similarly Bremova et al., (2013) included thirty patients with unilateral pc-BPPV in their study. They all underwent liberatory execrcises and cVEMP was recorded before, and after 1 week and 1 month post maneuvers. There was no change in cVEMP amplitudes suggesting degeneration of saccular maculae.

Korres et al., (2011) recorded cVEMP using 500 Hz tone burst in 27 individuals diagnosed with BPPV. The responses in these individuals were compared with 30 healthy individual. cVEMP was recorded from the ipsilateral sternocleidomastoid muscle. Higher number of individuals in the BPPV group showed prolonged latencies and absent VEMP. The authors concluded that higher abnormality in VEMP can be due to the involvement of the saccule in BPPV.

Hong, Yeo, Kim, & Cha, (2008) reported that cVEMP was affected in individuals with BPPV. They included 53 patients with BPPV and 84 normal individuals. Among 53 BPPV patients 13 i.e nearly 25% showed abnormal cVEMP on the affected side. The amplitude was reduced and latency were prolonged.

cVEMPs provides valuable information in diagnosing BPPV. Akkuzu, Akkuzu, & Ozluoglu, (2006) carried out cVEMP on 25 individuals with BPPV and 25 normal control group. 30 ears from the 25 BPPV patients showed prolonged latencies in eight ears and decreased amplitude in one ear. The rate of abnormality was significantly greater than in

the control group. The authors concluded that 30% of individuals with BPPV showed abnormal VEMPs.

Acoustic Neuroma

VEMP is reported to be abnormal in terms of latency and amplitudes or absent in cases with tumours. Murofushi et al., (2001) administered cVEMP in 62 individuals with acoustic neuroma and reported that 39 patients showed absence of cVEMP. 9 showed decreased amplitude and 14 showed normal amplitude. Overall 48/62 patients had abnormal findings concerning the amplitude while out of 23 having present responses four of them had prolonged latencies. The authors concluded that there were prolonged latencies in cVEMP responses in patients with large tumours which were larger than 2 cms.

cVEMPs can be useful test along with ABR, caloric and cVEMP to clicks and tone burst in identifying vestibular schwannoma. G., L.C., Zhou, & Cox, (2004) studied cVEMP responses to click and short tone burst in individual with acoustic neuroma. Subject had vestibular schawanoma in the inferior vestibular nerve as confirmed by magnetic resonance imaging. The subjects had normal ABR, cVEMP to 500 Hz toneburst and normal caloric responses in the affected side. cVEMPs to clicks were absent. Thus cVEMP using clicks can be useful along with other tests in a test battery.

cVEMP can be used as a tool to monitor vestibular functioning pre and post vestibular schwanoma removal using gamma-knife surgery. Lee et al., (2015) studied 14 participants with unilateral Vestibular schwannoma who underwent gamma-knife surgery. All of them received a battery of auditory-vestibular function tests including PTA, caloric, and cVEMP tests before and after GKS at each time point (1, 6, and 12 months). The PTA, caloric, and cVEMP tests showed abnormal results before GKS in

85.7%, 78.6% and 78.6% of VS patients, respectively. The PTA and cVEMP test results remained stable during the 1-year follow-up after GKS.

A test battery of PTA, cVEMP, oVEMP and caloric can be helpful in differentiating between cerebellopontine angle meningioma and schwannoma. Su, Chen, & Young, (2013) included 11 Cerebellopontineangle (CPA) meningioma ,11 CPA schwannoma patients. They administered audiometry, caloric, cVEMP and oVEMP on all 22 participants. The abnormal percentage of caloric test in the meningioma group was 36%, compared to 91% in the schwannoma. Correlation between the caloric and oVEMP test results in a CPA tumor indicates a schwannoma nature, while dissociation between the caloric and oVEMP test results depicts a meningioma character.

Clinical applications of oVEMP

Menieres disease

oVEMP results can give us findings not so evident in cVEMP. oVEMP responses are more frequently absent in meniere's disease than cVEMP. Chiarovano, Zamith, Vidal, & de Waele, (2011),studied oVEMP, caloric and cVEMP in 26 individual with menieres disease. 13 subject showed abnormal results in cVEMP among which 5/13 had reduced amplitude and 8/13 had absent response. in the affected side. Reduced or absent oVEMPs responses were observed in the affected side of the 18 subjects. More number of participants had abnormal results in oVEMPs than in cVEMPs. Thus the two test should be used complementary to one another.

oVEMP can be useful in diagnosing menieres disease. Asymmetry ratio can help us identifying unilateral cases. Egami et al., (2013) studied oVEMP in 37 individuals with Menieres disease. 55 individuals with normal hearing were included in this study to compare the results. The results revealed that amplitude of oVEMP in individuals with

menieres disease were less compared to healthy individuals and asymmetry ratio of more than 30 % was found in unilateral cases.

Taylor et al., (2011) included 112 individuals out of which 77 were patients with Menieres disease and 35 were normal subjects. Theyadministerd oVEMP using air-conduction as well as bone conduction stimuli. Air-conduction stimuli was delivered through the headphone while the BC stimuli was delivered using bone vibrator on the forehead. 50% of the unilateral cases and 40 % of the bilateral cases had abnormal VEMP. The amplitude asymmetry ratio was calculated for both click AC oVEMP and BC oVEMP which was around 33.3% and 26% respectively. The average asymmetry reflex ratio were significantly higher in patients with Menieres diseases than with the control group. Thus amplitude asymmetry ratio can be used to find MD.

oVEMP can be used in grading the stage of menieres disease**.** Huang, Wang, & Young, (2015) used a test battery which included cVEMP, oVEMP, and caloric test to grade the stage of menieres disease. From 2009 to 2012, 100 (20%) of 498 MD patients were diagnosed with bilateral involvement, oVEMP, cVEMP and caloric test was administered on all of them. Of 100 patients with bilateral MD, 54% had the same grade and 46% had different grades in their 2 ears. Thus oVEMP can be used as an important test in the test battery along with PTA, cVEMP and caloric to grade the stage of Menieres disease.

Vestibular neuritis

Vestibular neuritis affects the superior vestibular nerve more often than the inferior vestibular nerve. Thus oVEMPs are more often absent compared to cVEMP in vestibular neuritis individuals. oVEMP is also useful in identifying which nerve is damaged in cases with vestibular neuritis. Presence or absence of oVEMP cues the site of lesion. Presence of oVEMP in individuals with vestibular neuritis indicates damage to the

inferior vestibular nerve however its absence indicates involvement of the superior vestibular nerve. Shin et al., (2012) evaluated ocular VEMPs in patients with vestibular neuritis (VN) to find which part of vestibular nerve is more susceptible neuritis. AC tone burst were measured in 60 normals and 41 patients with acute VN. The VN involved selectively SVN in 30 patients, and IVN only in 3, and damaged both inferior and superior branch in eight subjects. All the findings were confirmed using MRI. oVEMP was absent in all 30 cases with damaged SVN.

Chiarovano et al., (2011) studied 12 individuals with vestibualar neuritis at the acute stage using airconduction cVEMP and oVEMP. 8/12 i.e nearly 67% subject showed abnormal cVEMP whereas 9/12 showed reduced oVEMP responses. There was no difference in terms of latencies between the affected and the intact side. However there was greater than 50% dissociation between cVEMP and oVEMP results. Thus the authors concluded that cVEMP along with oVEMP can be used to find whether vestibular neuritis has affected or spared the inferior vestibular nerve

Murofushi, Monobe, Ochiai, & Ozeki, (2003) studied ocular VEMP and cervical VEMP in individuals with vestibular neuritis. 6 participants with VN were included in the study. All the 6 participants showed absent oVEMP. This finding was attributed to the more susceptibility of superior vestibular nerve being damaged in cases with vestibular neuritis.

BPPV

BPPV is the disease of vestibular apparatus. oVEMP is abnormal or absent in these individuals. Kim et al., (2015) evaluated utricular during the acute and resolved phases of BPPV, Ocular VEMP were studied in 112 patients with BPPV and 50 normal controls. oVEMPs were induced using air-conducted sound (1000Hz tone burst, 100dB normal hearing level) at the time of initial diagnosis and 2months after successful repositioning in

patients with BPPV, and the results were compared with those of the controls. Abnormalities of oVEMP in patients with BPPV were prevalent and significantly higher compare to the healthy control group. 21.6% of individuals had absence of oVEMPs.

oVEMP has been used to assess the effectiveness of the treatment. Successful rehabilitative manoeuvres can lead to repositioning of the otoconia in the utricle. Bremova et al., (2013) study showed a transient increase of ocular vestibular evoked myogenic potential (oVEMP) amplitudes in the affected ear after successful liberatory maneuvers. Thirty patients with unilateral pc-BPPV were included in this study and oVEMP were administered four time points: before, after, 1 week after, and 1 month after the liberatory maneuvers (Semont maneuvers). The oVEMP amplitude increase in 11 of the cases after 1week of liberatory maneuvers.

Acoustic neuroma:

oVEMPs have been reported to be absent or abnormal in individuals with acoustic neuroma. Zhang et al., (2015) administered oVEMP on 45 patients with vestibular schwannoma. Each participant underwent oVEMP to Airconduction stimulation and to bone conduction stimulation. Of 45 patients with acoustic neuroma, 28 had absent oVEMP. The authors concluded that oVEMPs are absent in more than 50% of individuals with acoustic neuroma.

oVEMP along with cVEMP can be useful in differentiating between cerebellar and brainstem lesions. Su & Young, (2011), included 12 patients with cerebellar disorder, 8 with extended cerebellar lesion (involving the brainstem) and 4 localized cerebellar lesion (excluding the brainstem), in their study. All patients underwent oVEMP and cVEMP tests via bone-conducted vibration stimuli. The rate of abnormal oVEMP results significantly differed between the two groups, but cVEMP test results did not

differ. In conclusion, thus ocular VEMP test can differentiate between cerebellar and brainstem lesions.

oVEMP along with other vestibular tests like caloric and cVEMP can be useful in differentiating between cerebellopontine angle and meningioma and schwannoma. Su et al., (2013) included 11 individuals with CPA meningioma ,11 individuals with CPA schwannoma patients in their study. All patients underwent oVEMP, cVEMP caloric and pure tone audiometry. The abnormal percentage of caloric test in the meningioma group was 36%, compared to 91% in the schwannoma. Correlation between the caloric and oVEMP test results in a CPA tumor indicates a schwannoma nature, while dissociation between the caloric and oVEMP test results depicts a meningioma character.

vHIT

Aw et al., (1999) found that when the head is moved with a high velocity toward a completely damaged peripheral it would yield a saccadic eye movement. This method was initially used in coma patient and those who are unable to responsd. The test is called as Head Impulse Test (HIT). HIT is utilises the Vestibulo-ocular reflex path. The patient is asked to look at the target while his head is given a jerk in the yaw, roll or pitch plane. If an SCC is damaged the patients VOR is affected and there occurs a compensatory overt saccade to reacquire a stationary target. Post impulse saccades can be detected with naked eye by experienced clinicians while saccades occurring during head thrust are virtually impossible to detect with naked eye (Black et al., 2005; Weber et al., 2008)

Video Head Impulse Test requires same amplitude, high acceleration head impulse as that required in Head Impulse Test. It only requires the patient to wear a pair of goggles similar to that worn during electronystagmography. The cameras track pupil movement compared to head movement which is monitored by gryoscopes that are fixed

to the frames. The goggles are light weighted and can be tightened to the patients head to minimize inertial slips. The v-HIT is capable of recording overt and covert saccades(which cannot be detected by naked eye).

Clinical applications of vHIT:

vHIT has been found useful in diagnosing the various pathologies of the semicircular canals in children and has advantage over other vestibular tests. Hamilton et al, (2015) recorded vHIT, rotatory chair test and caloric test in 33 participant (age < 20 years) with confirmed vestibular pathologies. The authors reported that VOR gain was lesser in all individuals with vestibular pathologies, however percentage abnormalities on other tests such as caloric and rotatory chair test was less compared to vHIT. Authors concluded that vHIT is valuable tool in diagnosing peripheral vestibular pathologies in children.

Hulse, Hormann, Servais, Hulse, & Wenzel, (2015) evaluated 55 children in the age range of 3- 16 years using video head impulse test. The children were divided into 2 groups depending whether they have vestibular symptoms or not. Group I without any sign of vestibular development disorder and group II with possible signs for a pathological equilibrium development. Children with no balance problems had median gain of 1.02, however children with balance problems had significantly reduced VOR gain. Therefore, the authors concluded that video head impulse test can be easily used as a screening tool to detect vestibular dysfunction in the pediatric population.

Video head impulse test results in elderly individuals

Matino-Soler, Esteller-More, Martin-Sanchez, Martinez-Sanchez, & Perez-Fernandez, (2015) included 212 subjects with no history of vestibular or neurologic impairment and vHIT was administered in yaw plane. Mean gain was 1.06 ± 0.07,

Reflexive saccades were detected in 52 subjects, occurring after impulses to both sides of the head. The number of subjects with RSs was significantly higher after age 71 years, and velocity was correlated, not with age, but with head impulse velocity. As the head head velocity increased the VOR gain reduced. The authors concluded that VOR gain is stable uptill the age of 90years however declines after that.

Mossman, Mossman, Purdie, & Schneider, (2015) tried to establish a normative data using 60 control subjects aged 20 to 80 years. The participants included in the study had no previous complaints of brain disorder or vestibular lesions. vHIT was administered on all of them. The authors found that the mean Horizontal VOR velocity gain of 60 normal subjects was 0.97 but as age advanced the VOR gain reduced.

Vestibular neuritis

vHIT can be a useful tool to assess the semicircular canal functioning and can be helpful in finding site of lesion in in vestibular neuritis cases. Merchant et al., (2015) did a study in patients with vestibular neuritis. They recorded air conduction cVEMP and oVEMP using 500 Hz tone burst and and vHIT in all planes. The authors concluded that using cVEMP, oVEMP, and vHIT helped differentiate 4 types of VN, i.e. entire VN, Superior VN, Inferior VN, and ampullary VN. Partial superior and inferior vestibular nerve fibres involvement results in absence of oVEMP.

Caloric test assesses the low frequency response of the semicircular canal and the vHIT assesses the high frequency response, hence both should be used it complementary to each other. Redondo-Martínez et al., (2015) administered Video head impulse test and Caloric test on the patients with vestibular neuritis on the same day. They calculated gain asymmetry and and compared it with caloric test. There was no correlation between the two test. The authors concluded that the two test can be used to complement each other

and one does not substitute the other as the two test shows different frequencies of vestibule- ocular reflex.

vHIT is a fast, quick and noninvasive tool to assess the functioning of the semicircular canals. It has been found to be useful in identifying patients with confirmed vestibular neuritis along with caloric test. Bartolomeo et al., (2014) evaluated 29 patients with vestibular neuritis and followed them for 1-3 months. At the follow-up visit, complete recovery occurred in 31% of cases according to caloric evaluation, and VHIT normalized in 51.8%. The authors concluded that vHIT is fast and convenient test it is less sensitive compared to caloric test for patients with moderate problems.

vHIT is more affected in vestibular neuritis than vestibular migraine. Song et al., (2015) evaluated 36 patients with vestibular migraine and 23 with vestibular neuritis. Caloric test was used to probe the low-frequency range of lateral canal function and video head impulse test (vHIT) was used to test the high-frequency range of horizontal semi-circular canal function in patients with vestibular disorders. Only 8% of individual with vestibular migraine had abnormal lateral canal function. In vestibular neuritis, caloric and vHIT responses are more frequently affected 56% and 30% respectively, There existed a significant positive correlation between both tests. The authors concluded that Caloric and vHIT probe different frequencies of head movement and provide complementary information regarding the lateral canal function.

VOR gain has been used to differentiate between vestibular neuritis and stroke. Schubert, Mantokoudis, Xie, & Agrawal, (2014) measured VOR gain in 26 patients with acute vestibular symptoms one week post onset. All the patient underwent brain magnetic resonance imaging and were classified as posterior inferior cerebellar artery (PICA) or anterior inferior cerebellar artery (AICA) depending on the lesion. 16/26 had vestibular neuritis, 7/26 had PICA and 3/26 had AICA. Mean VOR gains ipsilesional and

contralesional were as follows: vestibular neuritis (0.52, 0.87); PICA stroke (0.94, 0.93); AICA stroke (0.84, 0.74). VOR gains were asymmetric in neuritis (unilateral vestibulopathy) and symmetric in PICA stroke (bilaterally normal VOR), whereas gains in AICA stroke were heterogeneous. Thus the authors concluded that vHIT can be used in classifying vestibular symptoms as neuritis or stroke using VOR gain.

Zellhuber, Mahringer, & Rambold, (2014) tried to find a correlation between caloric and video head impulse test in individuals with vestibular neuritis. The authors did not find any correlation between canal paresis and reduced horizontal VOR gain. Therefore they concluded that the two tests assesses two different aspect of angular movement.

Meniere's disease

vHIT can be used as an important diagnostic tool to identify involvement of semicircular canals in individuals with vestibular problems. Zulueta-Santos, Lujan, Manrique-Huarte, & Perez-Fernandez, (2014) evaluated 36 individuals with menieres disease and VOR was evoked in all 6 planes. In 12 (33.3%) patients the examination of both ears was normal for all the semicircular canals, in 12 patients the results from the affected ear were abnormal in at least 1 of the semicircular canals, in 11 (30.5%) patients the results were abnormal in at least 1 of the semicircular canals in both the affected and unaffected ears, The most frequent abnormal result was obtained from the posterior canal of the affected ear and from the coupled superior canal of the unaffected ear. There was a correlation between disease duration and abnormal findings. The authors concluded that The distribution of abnormal results is not uniform between different canals in each patient; the most frequent gain reduction is obtained for the posterior canal. Gain reduction reflects the disease duration and amount of hearing loss.

vHIT has been reported to be useful in identifying patients with menieres disease. Chen et al., (2015) admisnistered vHIT on patients with Menieres disease. They included 30 patients suffering from unilateral MD. They classified them on the basis of severity. The VOR gain difference was not significant across normal and mild menierres disease however it was very significant between normal and severe group.

vHIT can also be used in evaluating and estimating prognosis in individuals with Meniere's disease who are treated with gentamycin. It has been reported that the VOR gain is reduced in individuals with post gentamycin injection. Marques, Manrique-Huarte, & Perez-Fernandez, (2015) included 31 participants with unilateral Meniere's disease in his study. The mean age of the participants was 59 years. All the patient underwent intratympanic gentamycin dose. They were followed upto 6 – 7 month. vHIT was administered pre and post treatment. All the participant had reduced VOR gain post treatment in all semicircular canals. The rate of reduction in the VOR gain was 47.9 %, 26 %, and 35.8 % in superior horizontal and posterior planes. The authors concluded that when evaluated with the vHIT, intratympanic gentamicin changes in VOR seem to foresee short-term control of vertigo attacks.

Vestibulopathy

vHIT has been reported to be important in diagnosing vestibular pathologies. Eza-Nunez, Farinas-Alvarez, & Perez-Fernandez, (2014) did a study in 2015 in 30 unilateral vestibulopathy cases to see the responses in vHIT for assessment of vestibule ocular reflex in patients with vertigo and dizziness. The test was administered in horizontal plane. After the rightward and the leftward impulse refixation of saccades was seen in 21/30 and it was seen on the affected side. However the VOR gain was 0.91. The authors concluded that In the assessment of patients with dizziness, finding a normal gain VOR

with refixation saccades can be an indication of the existence of a peripheral vestibulopathy

Superficial siderosis (SS) of the central nervous system is a disorder associated with cerebellar ataxia and sensorineural hearing loss. The condition results from excessive iron depositions on central nervous surfaces. Superficial siderosis can consequently result in bilateral vestibulopathy as the vestibulo-cochlear nerve very vulnerable. Lee et al., (2015) reported 60-year-old man who had progressive bilateral hearing loss, oscillopsia, and a severe gait disturbance. Superficial siderosis was diagnosed with the help of MRI. vHIT was administered and showed impaired VOR gains that were 0.55, 0.59, and 0.45 in the horizontal, anterior, and posterior canals, respectively. The authors concluded that SS may result in chronic bilateral vestibulopathy with SNHL and vHIT can be a useful tool to document vestibular dysfunction.

BPPV

vHIT has been useful in patient with Benign paroxysmal positional vertigo (BPPV). Xu et al., (2015) administered video head impulse test (vHIT) and caloric test on 190 individuals with BPPV. 50% of them had posterior semi-circular canal canalithiasis, 37% cases of horizontal semicircular canal canalithiasis, 13 % cases of horizontal semicircular canal cupulolithiasis. Reduced VOR gain was found in 15 and canal paresis was found on 151 of them. The authors hypothesized that in BPPV the low frequency component of semicircular canal is affected. Thus they concluded that vHIT which assesses the high frequency component of semicircular canal would not be a good tool for screening individuals with BPPV.

Mangabeira Albernaz & Zuma E Maia, (2014) reported a 42 year old man with benign paroxysmal positional vertigo due to otoconia causing plug in the horizontal

semicircular canal. vHIT and cVEMP was administered pre and post liberatory manoeuvres. The VOR gain was reduced and improved immediately 2 days after manoeuvres. VEMP was absent before the exercise and and identifiable VEMP was recorded 30 days after treatment. The authors concluded that vHIT can be useful in identifying the effectiveness of treatment in BPPV.

Other disorders

In individuals with vestibular pathology VOR gain can be useful tool in diagnosing the disorder. Guerra & Perez, (2015) evaluated 363 individuals in 2 years duration. Out of those 363, 57 showed abnormal gains and later they were diagnosed with BBPV, menierres disease, Vestibular neuritis with help of other tests. Thus authors concluded that vHIT can be used to assess and find pathological gains and can be an important diagnostic tool along with other tests.

The usefulness of Vestibular tests in ushers syndrome cases were tried to be found by (Magliulo, Iannella, Gagliardi, & Re, 2015) They included 15 participants. They administered vHIT. 10/15 of the subjects had abnormal VOR gain. However reduced VOR gain was due to poor visual ability or reduced vestibular functioning needs to be answered.

vHIT has also showed to be abnormal in various peripheral and central vestibular pathologies. Zhang et al., (2015) administered Video head impulse test (vHIT) to measure the saccadic movement of eye and VOR gain in 48 patients with central pathology and 47 peripheral pathology. vHIT responses in 23 ears with menieres disease showed to affect 21 of them, whereas 4 patients with schwannoma,2 patients with vestibular neuritis, 5 of them with delayed endolymphatic hydrops, 6 with sudden hearing loss and vertigo and 8 patients with vestibular dysfunction were found to have reduced VOR gain. The abnormal

vHIT results were also found in 35 of 48 patients (72. 9%) with central vertigo, which including posterior cerebral circulation ischemia (7 patients), cerebral infarction/stroke(6 patients), and dizziness with vertigo(17 patients) and others(18 patients). Abnormal rate of vHIT in patients with peripheral vertigo was 95. 7% (45/47), whereas it was (72. 9%) in patients with central vertigo. Thus abnormal vHIT can be a sign of central or peripheral pathology.

Chapter 3

Method

The present study aimed at assessing the functioning of sacculocollic pathway, utirclulo-ocular pathway and semicircular canals in older adults. The functioning of the three system was assessed using cVEMP, oVEMP and video head impulse test respectively.

Participants:

The present study consisted of two groups. Group I consisted 46 participants, 27 male and 19 female in the age range of 40 to 70 years. Further group I was subdivided into 3 sub-groups. Sub group I consisted of 15 participants (mean age = 44.13 yrs, 8 male & 7 female) in the age range of 41 to 50 years. Sub group II consisted 15 participants (mean age = 55.86 yrs, 9 male & 6 female) in the age range of 51-60 years and the sub group III consisted of 16 (mean age = 64.2 yrs, 10 male & 6 female) participants in the age range of 61-70 years. Group II consisted of 18 participant 9 male and 9 female in the age range of 18 to 30 years. Their mean age was 23.1 yrs. A total of 64 participants 36 male and 28 female were included in the study.

Participant selection Criteria:

(Group I)

Subjects included in the group I were of age ranging from 41 to 70 years. All of them fulfilled following criteria.

1. The participants included in the study had absence of air-bone gap or any middle ear problem which was confirmed using conventional air conduction and bone conduction audiometry and tympanometry respectively.
2. Participants included in the study had hearing loss no more than moderate degree.
3. Participants did not have history of any neurological problem.
4. Participants had did not have any history of vestibular dysfunction.

5. No history of spondylitis, No history or present complaints of pain in the neck region.
6. None of the participant included in the study had uncomfortable level less than 100dBSPL.
7. Participants included in the study did not have complaints of diabetes mellitus.

(Group II)

The subjects included in the control group had age ranging from 18 to 30 years. They had fulfilled following criteria.

1. Participants had normal hearing sensitivity in both ears and did not have any conductive pathology.
2. Participants did not have any neurological problem.
3. Participants did not have any vestibular related complaints. No history of any vestibular dysfunction.
4. Participants did not have any complaint or history of spondylitis or any pain in the neck region.
5. None of the participants had uncomfortable level less than 100dBSPL.
6. Participants included in the study did not have complaints of diabetes mellitus.

Instrumentation and test environment

A calibrated two channel clinical audiometer Inventis Piano with TDH-39 headphones, housed in MX-41/AR (Telephonics, Farmingdale, NY, USA) ear cushions was used for finding air-conduction thresholds and doing speech audiometry. Radio ear B-71 bone vibrator (Radio ear, KIMMETRICS, smithsburgh, Maryland, USA along with the same audiometer was used for measuring bone conduction thresholds.

A calibrated middle ear analyser Grason-Stadler Incorporated (GSI) Tympstar (GSI VIASYS Healthcare, WI, USA) was used for obtaining tympanogram type, static compliance, ear canal volume and acoustic reflex threshold. The Otodynamics ILO 292 V-6 (Otodynamics Ltd., Hatfield, Herts, UK) was used for recording Distortion product optoacoustic emissions (DPOAEs).

Cervical and Ocular Vestibular evoked myogenic potential were recorded using Biologic Navigator Pro version 7.2.1 (Natus Medical Incorporated, San Carlos, CA, USA) with SINSER - 012 insert earphones.

V-HIT was carried out using ICS Impulse OTOsuite vestibular software version 1.2 (GN Otometrics, Denmark). The patient had to wear frenzel glasses provided by the manufacturer of the OTO-SUITE software All the test were carried out in acoustically treated air-conditioned rooms with permissible noise level as per the guidelines recommended by the American National Standards Institute (ANSI S3.1-1991).

Procedure:

1. **Case History and Administration of Maryland Dizziness Questionnaire.**

   A Detailed clinical history were obtained regarding any present complaint or previous history of ear related problem. Information were obtained regarding the existence of associated visual, neurological conditions along with pertinent medical history. Additionally, a part of the dizziness questionnaire developed by Maryland hearing and balance centre was administered. The questionnaire consists of 5 sections; only the 2nd section which pertained to the symptoms of dizziness were administered. The participants having any previous history or present complaint of vestibular symptoms were not selected for the study.

2. **Audiometry:**

Air conduction and bone conduction threshold were tracked from 250 Hz to 8000 and 250 Hz to 4000 Hz respectively at octave frequencies using modified ascending version of Hughson & Westlake procedure (Carhart & Jerger, 1959) to assess the hearing sensitivity of the participant. PTA was calculated by averaging air conduction thresholds obtained at 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz. Uncomfortable level was tested to find if any of the participant exhibited any tolerance problem to loud sounds. Individuals exhibiting reduced uncomfortable levels were not included in the study.

3. Impedance audiometry:

Tympanometry was done using 226 Hz probe tone, to rule out any middle ear pathology. Ipsilateral as well as contralateral reflexes were checked at 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz. Acoustic reflex threshold were calculated.

Cervical Vestibular Evoked Myogenic Potentials

For recording cVEMP, the site of electrode placement was prepared using a skin preparation gel. Silver chloride disc electrodes were used for recording. Absolute electrode impedances was maintained below 5000 ohms and inter electrode impedances was below 2000 ohms.

C-VEMP was recorded with the inverting electrode at the ipsilateral sternoclavicular junction,non-inverting at the superior 1/3rd of ipsilateral sternocleidomastoid junction and ground electrode at the forehead. The patient was given stimulation in the ipsilateral ear and he/she was asked to turn neck as to certain tightening of the sternocleidomastoid muscle necessary to elicit a good response. Adequate muscle contraction was assured.

The recording was done using 500Hz tone burst, at an intensity of 125 dBSPL. The first positive component occurring around 13ms was marked as P1, while the second negative

peak occurring around 23ms was marked as N1 (Fransson et. al.2001). C-VEMP amplitude were calculated from peak of P1 to N1. The subjects across groups were compared on the amplitude and latency parameters. Table 3.1 shows the recording parameters for cVEMP

Table 3.1: cVEMP recording parameters

Transducer	Insert ear phones
Type of stimulus	500 Hz tone burst
Intensity	125 dBSPL
Polarity	Alternating
Repetition rate	5.1/sec
Analysis window	57 ms +20 ms prestimulus
Filter settings	30 Hz to 1500 Hz
Sweeps	200
Amplification	5000

Electrode Placement

Inverting	Ipsi-Sterno-clavicular junction
Non-Inverting	Ipsi-Superior 1/3rd of the sternocleido-mastoid muscle
Ground	Forehead

Occular Vestibular Evoked Myogenic potential (oVEMP)

O-VEMP was calculated with non-inverting electrode being at the contra supra inferior oblique muscle and the inverting electrode just below the non-inverting. Ground was placed at the forehead (Rosengren et al., 2005).The participant had to look upwards at a spot placed 30 degree elevation without elevating his neck. The recordings was contralateral to that of the stimulated ear. A negative peak occurs around 10 ms and a positive peak occurs at 15 ms. They were marked as N1 and P1 respectively. Amplitude were calculated from peak of N1 to P1.The participants were compared on amplitude and latency parameters. Table 3.2 shows oVEMP recording parameters

. **Table 3.2: oVEMP recording parameters**

Transducer	Insert ear phones
Type of stimulus	500 Hz tone burst
Intensity	125 dBSPL
Polarity	Alternating
Repetition rate	5.1/sec
Analysis window	57 ms +20 msprestimulus
Filter settings	1 Hz to 1000 Hz
Sweeps	200
Amplification	30000

Electrode Placement

Non-Inverting	1 cm below eye
Inverting	2 cm below the non-inverting electrode
Ground	Forehead

Video Head Impulse Test:

Video Head Impulse test was administered using ICS Impulse OTOsuite vestibular software version 1.2 (GN Otometrics, Denmark. Frenzel glasses were used. Calibration was performed. For calibration participants were instructed to look straight and the red beam was on. The two red beams were spaced by an approximately 40 degree. A target was placed at the distance of 1 metre from the subject bisecting the two red beams. The subject was asked to gaze at the target irrespective of the thrust given to the head. A head thrust was given in lateral planes on both sides. VOR gain was calculated as ratio of eye acceleration to head acceleration in all the planes. 20 accepted recordings from each plane was averaged and mean VOR gain was calculated. Saccades at the time of head thrust i.e covert saccades and after the head thrust i.e overt saccades was looked for. Responses from the lateral planes were thus obtained.

Analysis:

The recorded cVEMP, oVEMP and vHIT responses were analysed and peaks (cVEMP: P1, N1, P1N1; oVEMP: N1, P1, N1P1) were identified for all the participants in the each of the groups. The following latency and amplitude measures of these identified VEMP responses were measured and tabulated.

In cVEMP responses

a) The absolute latency of P1 and N1
b) The amplitude of P1-N1 complex
c) The amplitude asymmetry ratio for P1-N1 complex using the formula.
d) Amplitude asymmetry ratio =

$$\frac{\text{Amp P1-N1in better ear} - \text{Amp P1-N1 in poorer ear}}{\text{Amp P1-N1 in better ear} + \text{Amp P1-N1 in poorer ear}} * 100$$

In oVEMP responses

a) The absolute latency of N1 and P1

b) The amplitude of N1-P1. complex

c) The amplitude asymmetry ratio for N1-P1 complex using the formula.

d) Amplitude asymmetry ratio =

$$\frac{\text{Amp N1-P1 in better ear} - \text{Amp N1-P1 in poorer ear}}{\text{Amp N1-P1 in better ear} + \text{Amp N1-P1 in poorer ear}} * 100$$

Video Head Impulse test:

1) The VOR gain obtained were analysed across all the groups for lateral planes

2) If the responses were saccadic, they were considered pathological.

Statistical Analyses:

Shapiro Wilk test for normality was done to see whether the data follows the normal distribution or not. Since the data was not following the normal distribution Wilcoxon sign ranked test was done to find difference between ears within subject. There was no significant effect of ear for the subjects. Hence the right and the left ear data were grouped and studied together. Kruskal Wallis test was done to find the effect of ageing on outcomes of cervical vestibular evoked myogenic potential (cVEMP), ocular vestibular evoked myogenic potential (oVEMP) and video head impulse test (vHIT) in the lateral planes. If there existed a significant difference between the outcomes of tests as the function of ageing, Mann Whitney U test along with Bonferroni correction was used to find difference between two groups. Spearman's correlation was done to see if there existed any correlation between the vestibular tests and ageing and also between cVEMP and oVEMP, cVEMP and vHIT and oVEMP and vHIT. The equality of test for proportions was done to find the differences if any existed in the response rates of subjective and objective vestibular tests.

Chapter 4

Results

Present study was conducted with an aim of studying the effect of ageing on saccule, utricle and semicircular canals. To achieve the aim three measures: cervical vestibular evoked myogenic potentials, ocular vestibular evoked myogenic potentials and the video head impulse test was administered for younger and the older participants. For cervical vestibular evoked myogenic potentials the latency of P1, N1 and amplitude of P1-N1 complex was measured. For ocular vestibular evoked myogenic potentials, the latency of N1, P1 and amplitude of N1-P1 complex was measured for both the groups. The VOR gain function was measured for lateral canal using video head impulse test for both the groups.

4. 1. Cervical vestibular evoked myogenic potentials

Out of 128 ears included in the study on which cVEMP was administered, 100% of the participants in the subgroup I of group I had presence of cVEMP. However in the subgroup II and subgroup III of group I the response rates were 96.67% and 78.12% respectively. All the participants in the group II had present cVEMP. The results of equality of test for proportion revealed that significantly higher proportion of participants in the subgroup III had absent cVEMP responses compared to group II ($Z = 2.96$ $p = 0.00$), subgroup I ($Z = 2.72$ $p = 0.00$) and subgroup II ($Z = 2.18$ $p = 0.02$).

The representative waveform of present and absent cVEMP recorded from different age groups is given below. X axis represents latency in milliseconds and on Y axis represents amplitude in microvolts.

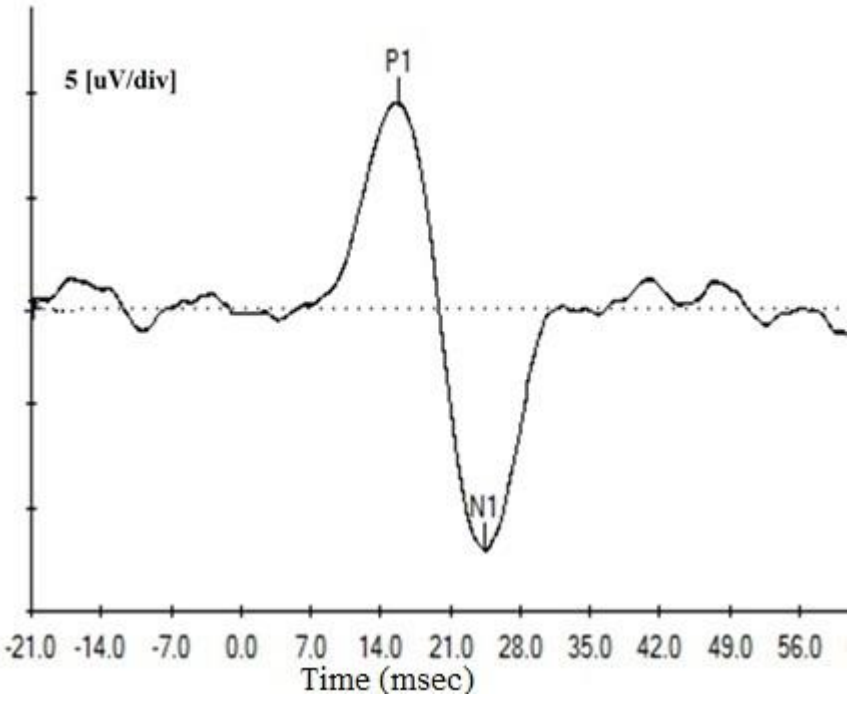

Fig. 4.1.1: Representative waveform for presence of cVEMP recorded from group II (18 – 30 years.)

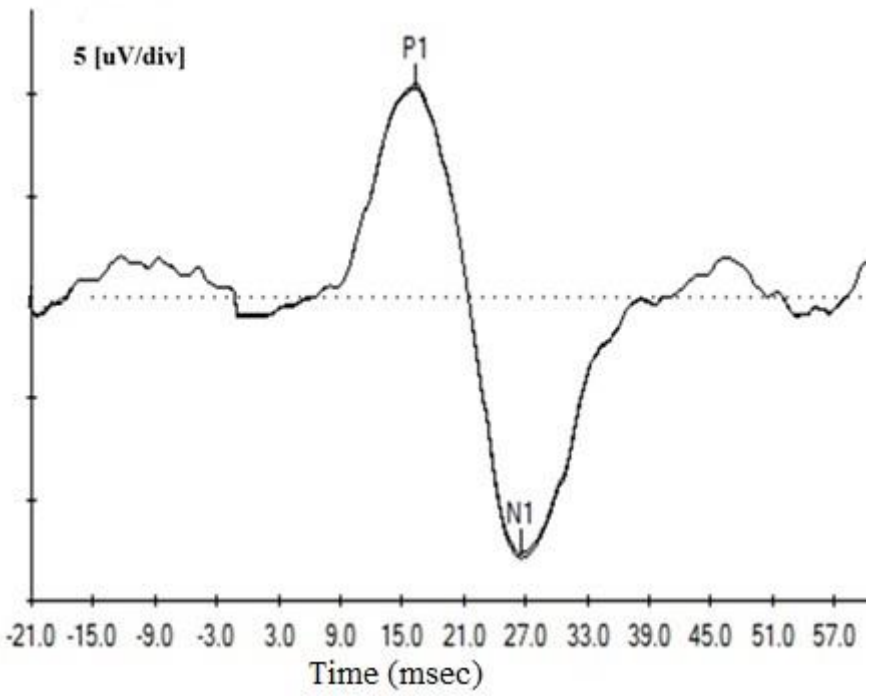

Fig 4.1.2: Representative waveform for presence of cVEMP recorded from subgroup I (41 – 50 years)

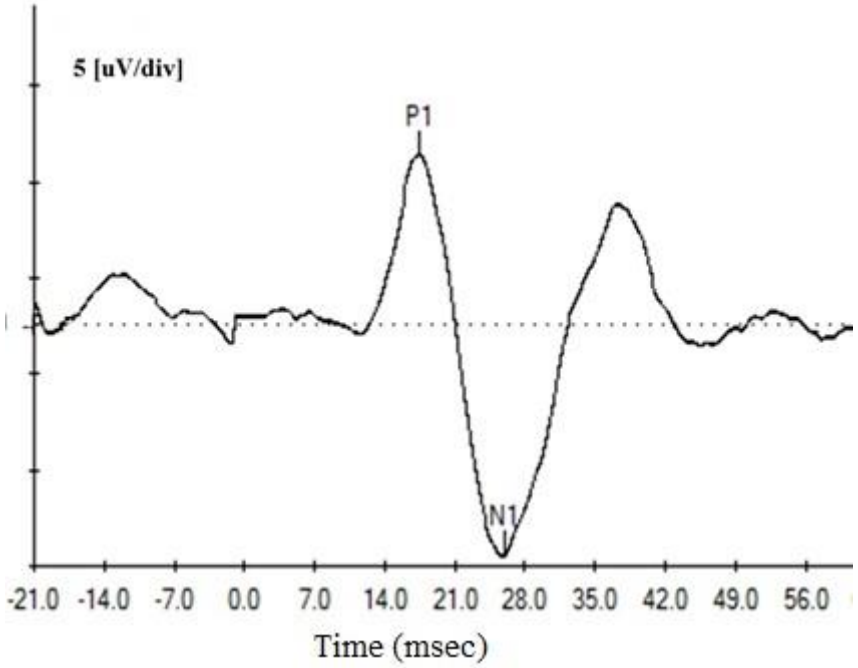

Fig 4.1.3: Representative waveform for presence of cVEMP recorded from subgroup II (51 – 60 years)

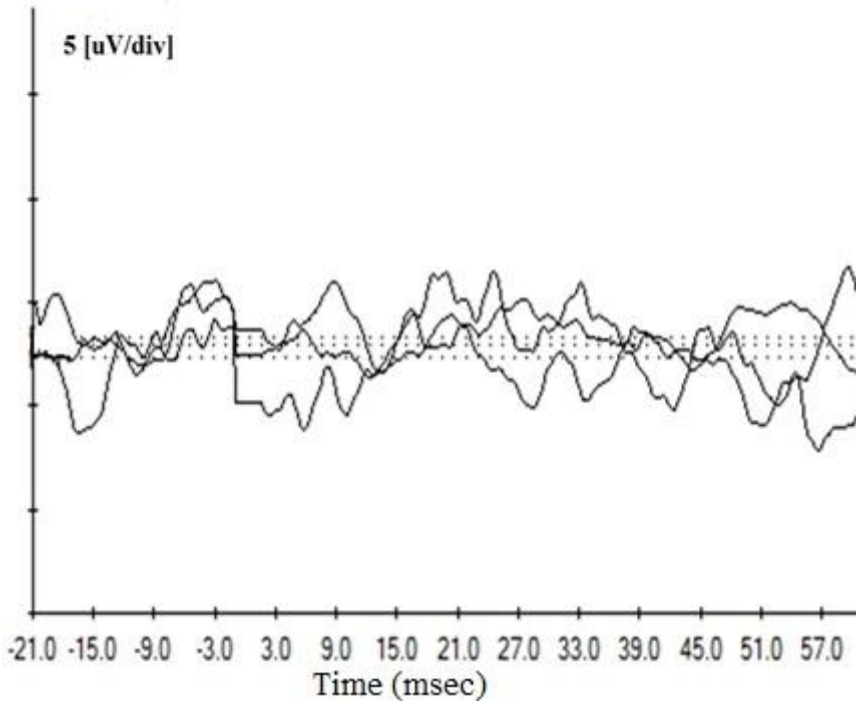

Fig 4.1.4 : Representative waveform for absence of cVEMP recorded from subgroup II (51 – 60 years)

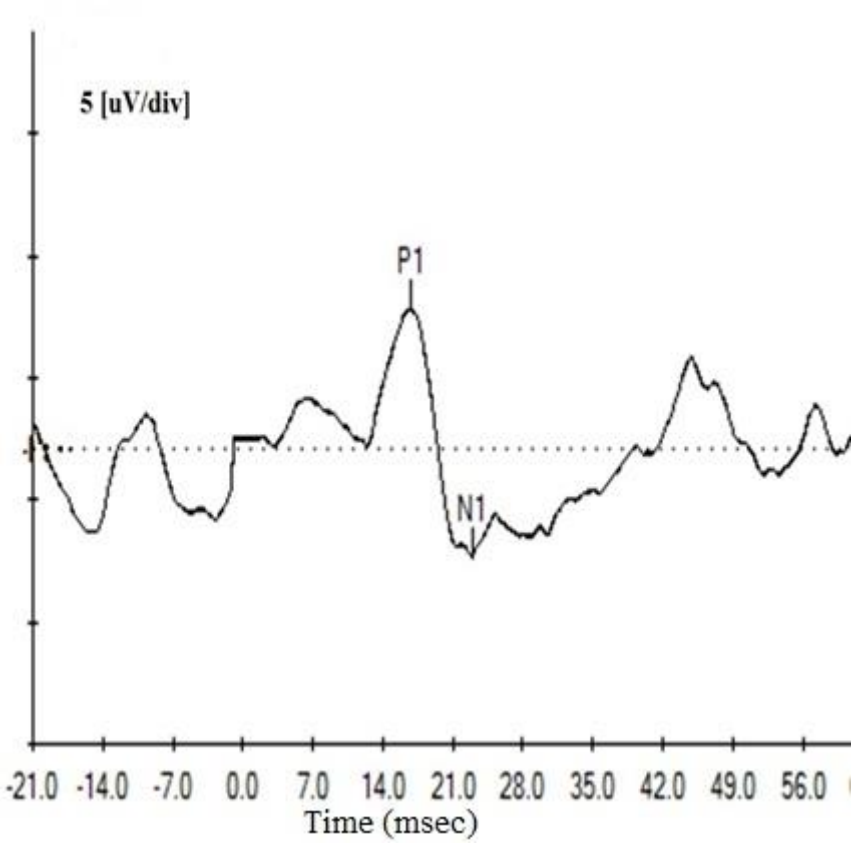

Fig 4.1.5 : Representative waveform for presence of cVEMP recorded from subgroup III (61 – 70 years)

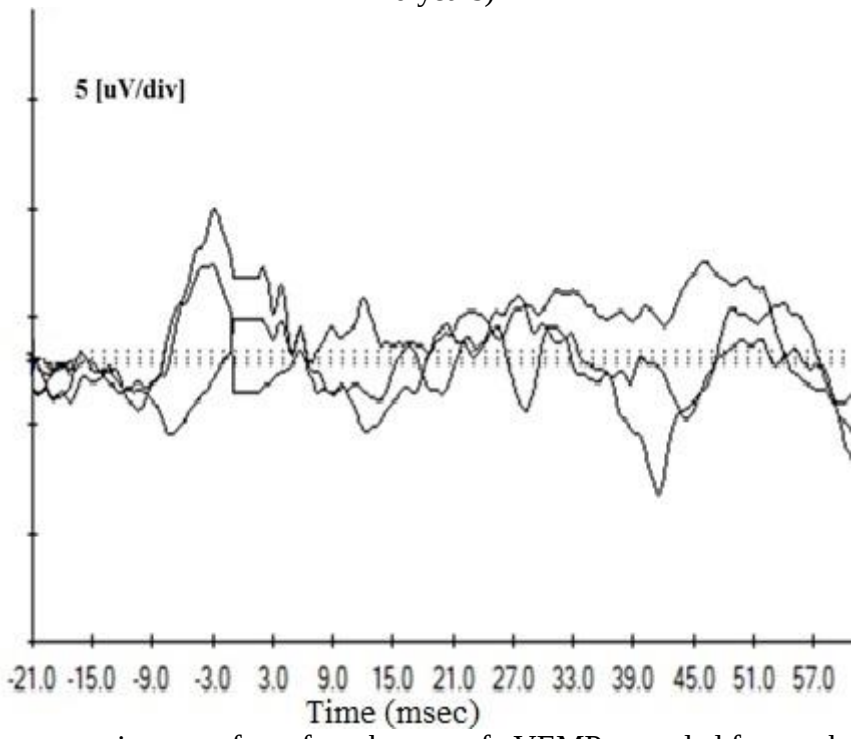

Fig 4.1.6 : Representative waveform for absence of cVEMP recorded from subgroup II (61 – 70 years)

Descriptive statistics was done to find out the mean and the satandard deviations of different cVEMP parameters for the young and the older groups. The mean, median and the standard deviation for the two groups are given in Table 4.1.1

Table 4.1.1: cVEMP responses for Left and Right ear for different age groups

cVEMP		P1 latency			N1 latency			P1N1 amplitude		
		$\bar{x}$	*M*	SD	$\bar{x}$	*M*	SD	$\bar{x}$	*M*	SD
Group II	R	15.67	15.43	1.7	24.88	24.34	1.84	15.64	15.81	4.94
N = 36	18									
18 -30 years	L	15.67	15.43	1.14	24.98	24.9	1.6	15.95	15.42	3.89
N =	18									
Subgroup I	R	16.30	15.94	1.64	24.48	23.76	2.17	16.47	16.11	6.43
N = 30	15									
41 – 50 years	L	16.23	16.26	1.31	24.45	23.96	1.5	16.22	13.66	9.01
N =	15									
Subgroup II	R	16.16	16.05	0.68	24.34	23.9	1.46	15.88	16.11	11.0
N = 29	15									
51 – 60 years	L	16.71	16.57	1.17	24.41	24.6	1.78	16.46	16.83	10.94
N =	14									
Subgroup II	R	16.01	16.06	1.7	24.13	24.11	2.70	7.73	7.70	5.03
N = 25	13									
61 – 70 years	L	16.11	16.57	1.7	23.78	24.07	3.8	7.67	8.31	6.91
N =	12									

Note : N = number of participants with present responses, P1 = latency of P1 peak in milliseconds; N1 = latency of N1peak in milliseconds; P1N1 = peak-to-peak amplitude of cVEMP in microvolts.

From the table 4.1.1 it can be seen that mean latency of P1 was more for older groups compared to younger groups. The mean latency of N1 was more for group II compared to subgroups in group I. The amplitude for the subgroup III was reduced for older groups compared to the younger groups. The mean values for the parameters of cVEMP did not differ much across ears.

Shapiro Wilk test was administered to check whether the data follows the normal distribution or not. Since Shapiro Wilk test for normality did not show a normal distribution for the most of the parameters ($p<0.05$), non-parametric test was administered.

Wilcoxon sign ranked test was administered to check effect of ear as a subject within factor. Table 4.1.2 shows the results obtained from Wilcoxon sign ranked test.

Table 4.1.2.Wilcoxon sign ranked test results for parameters of cVEMP across groups

	Group II (18- 30 Years)		**Group I (41 – 70 years)**					
cVEMP	**Group II** (N = 36) (18 – 30 years)		**Subgroup I** (N = 30) (41 – 50 years)		**Subgroup II** (N = 29) (51 – 60 years)		**Subgroup III** (N = 25) (61 – 70 years)	
	Z	**p**	**Z**	**p**	**Z**	**p**	**Z**	**p**
P1	1.37	0.17	0.71	0.48	1.91	0.06	1.18	0.24
N1	0.52	0.6	0.2	0.84	0.56	0.57	0.98	0.33
P1N1	1.37	0.17	0.51	0.61	0.45	0.65	0.79	0.43

Note: Z = Wilcoxon ranked test, p = α confidence level, P1 = latency of P1 peak, N1 = Latency of N1 peak, P1N1 = amplitude of P1N1

Since Wilcoxon signed rank test did not reveal any significant differences for the cVEMP parameters for the two ears, the data was combined from the two ears. Table 4.1.3 shows the mean, median and standard deviation of the parameters of cVEMP taken together for both ears.

Table 4.1.3: Mean, median and standard deviation of latencies of P1, N1 and peak-to-peak amplitude of P1N1 for 500Hz in cVEMP recordings of the four groups.

		Group II	**Group I**		
cVEMP		18-30 years (group II) (N = 36)	41-50 years (sub group I) (N = 30)	51-60 years (sub group II) (N = 29)	61-70 years (sub group III) (N = 25)
P1	Mean	15.64	16.27	16.43	16.01
	Median	15.43	16.05	16.26	16.36
	SD	1.42	1.46	0.98	4.10
N1	Mean	24.93	24.46	24.37	23.67
	Median	24.59	23.86	24.17	24.7
	SD	1.69	1.83	1.60	6.29
P1N1	Mean	15.79	16.13	16.30	7.69
	Median	15.74	15.15	14.67	6.14
	SD	4.46	7.51	11.0	7.0

Note : N = number of participants with present responses, P1 = latency of P1 peak in milliseconds; N1 = latency of N1peak in milliseconds; P1N1 = peak-to-peak amplitude of cVEMP in microvolts.

It can be seen from Table 4.1.3 that the mean latency of P1 was more for all the subgroups in group 1 compared to the group II. Within group I the latency of subgroup II was more compared to I and III. The mean latency of N1 peak was more for group II compared to all the subgroups of group I. Further it can be seen that amplitude of P1-N1 complex was least for subgroup III compared to subgroup I and II of group I and also it was lesser compared to the group II amplitude.

To understand the overall group differences for the various cVEMP parameters, Kruskal Wallis H test was administered. Kruskal Wallis H test revealed overall group difference between groups for the latency of P1 peak ($\chi^2(3) = 8.8$, $p = 0.03$) , but revealed no difference between groups for the latency of N1 peak ($\chi^2(3) = 2.75$, $p = 0.45$). However, there was significant difference for the amplitude of cVEMP between the groups ($\chi^2(3) = 27.93$, $p = 0.00$).

Further, to understand the significant differences between different groups for different cVEMP parameters, Mann Whitney U test was done. Mann Whitney U test revealed no significant difference for latency of P1 between, group II and subgroup I of group I (Z = 1.38, p = 0.17), group II and subgroup III of group I (Z = 1.6, p = 0.11), but revealed a significant difference for the latency of p1 between group II and subgroup II of group I (Z = 2.1, p = 0.04).

Again for P1 latency of cVEMP within group I, Mann Whitney U test revealed no significant differences between subgroup I and subgroup II (Z = 1.4, p = 0.17), no significant differences between subgroup I and subgroup III (Z = 0.81, p = 0.47) and no significant differences between subgroup II and subgroup III (Z = 1.41, p = 0.15).

There was a significant difference between the peak to peak amplitude of P1N1 of subgroup III of group I and group II (Z = 5.0, $p = 0.00$), subgroup III and subgroup I (Z =4.16, $p = 0.00$), and subgroup III and subgroup II (Z = 3.50, $p = 0.00$). However no

significant difference for amplitude of N1-P1 complex was observed between subgroup I and subgroup II (Z = 0.50 p = 0.61), between group II and subgroup I (Z = 0.064 p = 0.949), between group II and subgroup II (Z = 0.44, p = 0.66).

To summarize the results, a significant difference was observed for p1 latency across groups overall. There was no significant difference between any two groups for latency of P1. Latency of N1 latency did not differ across the group. The amplitude of P1-N1 was least for 60-70 years old individuals compared to 18 – 30 years, 41 – 50 years and 51 – 60 years.

4.2. Ocular vestibular evoked myogenic potentials

The percentage of ears having presence of oVEMP in subgroup I was 93.3%, in subgroup II, it was 83%, in subgroup III, it was 68.75% and group II which consisted of individuals in the age range of 18 – 30 years had present oVEMP in all the participants in both the ears. The test of equality for proportion revealed that older age group participants had higher proportion of individuals in whom there was absence of oVEMPs in either ear compared to the lower age group participants. There was a significant difference in terms of response rates for oVEMP between subgroup III and group II (Z = 3.63 p = 0.000), between subgroup II and group II (Z = 2.54 p = 0.01), and between subgroup I and subgroup III (Z = 2.44 p = 0.01).

The representative waveforms of present and absent oVEMP recorded from different age groups is given below. X axis represents latency in milliseconds and Y axis represents amplitude in microvolts. Each division on Y axis represents 2 microvolts.

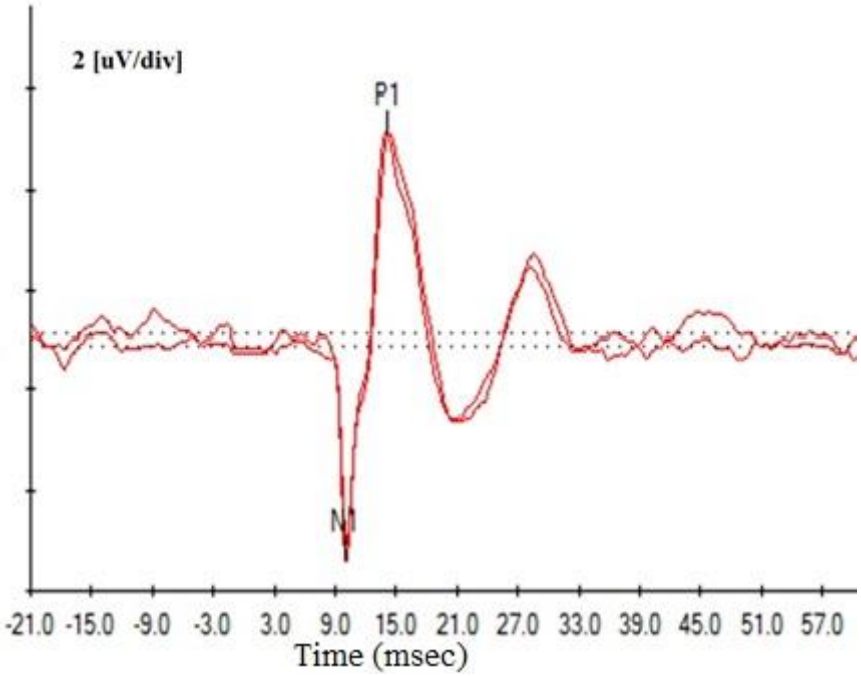

Fig 4.2.1 : Representative waveform for presence of oVEMP recorded from Group II (18 - 30 years)

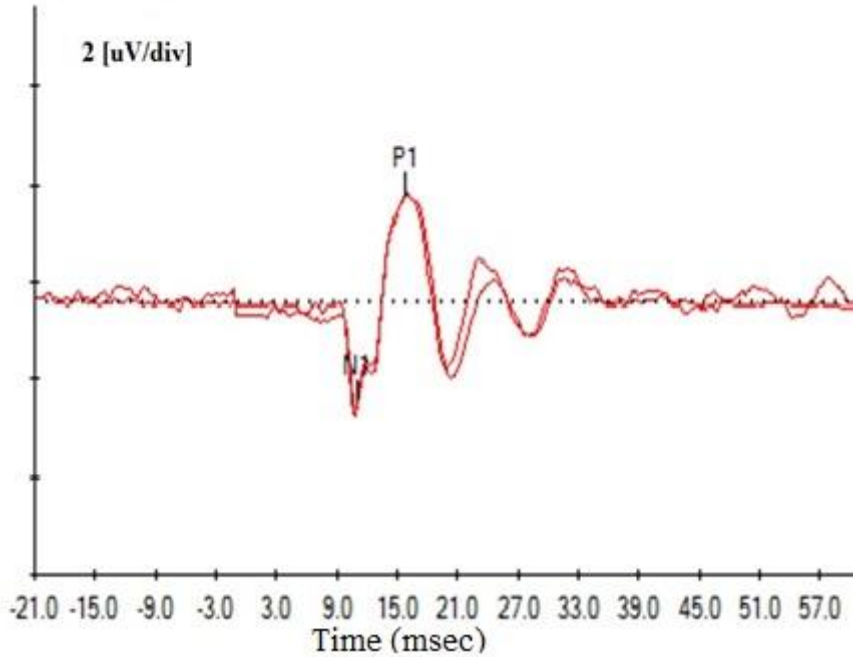

Fig 4.2.2 : Representative waveform for presence of oVEMP recorded from subgroup I (41 – 50 years)

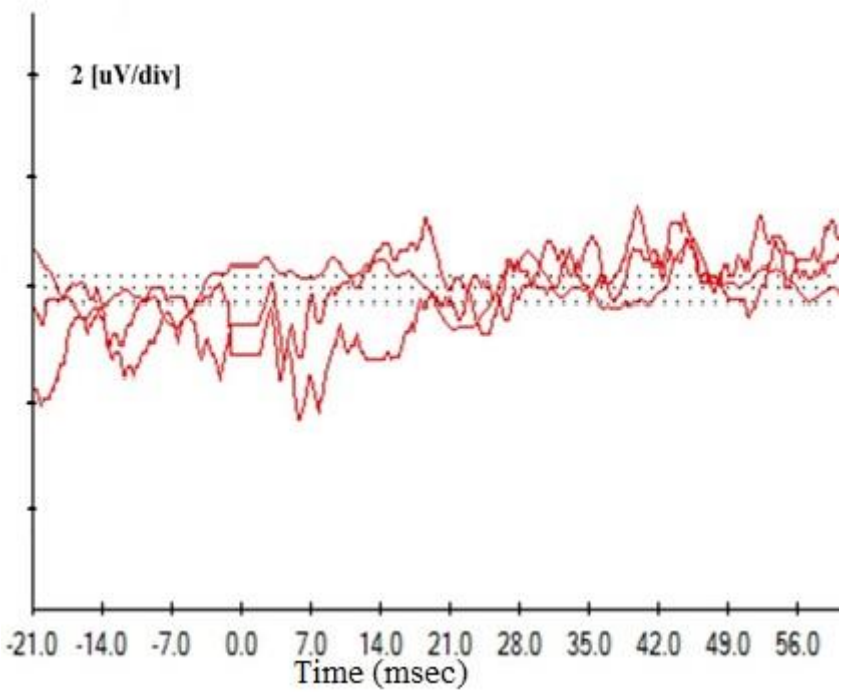

Fig 4.2.3 : Representative waveform for absence of VEMP recorded from subgroup I (41 – 50 years)

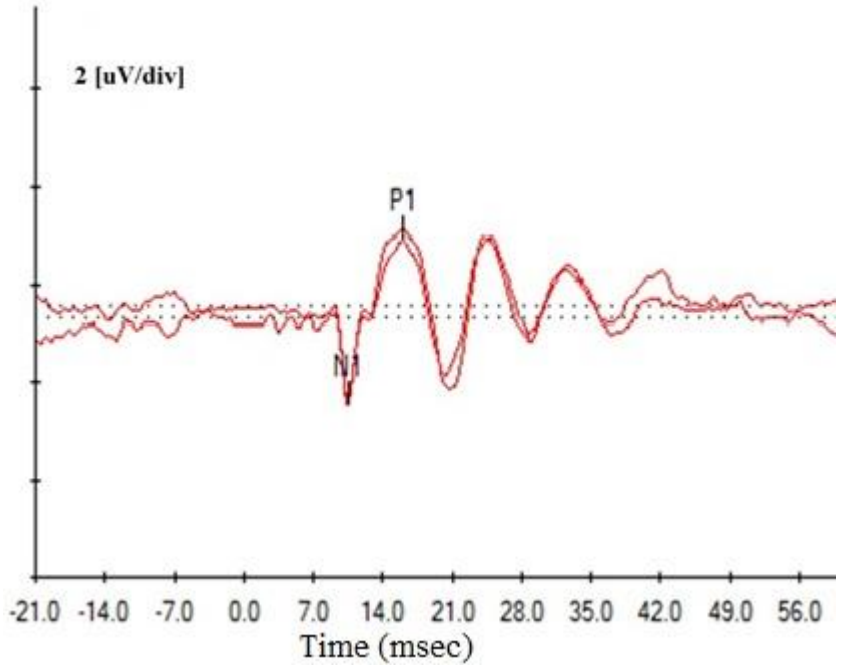

Fig 4.2.4 : Representative waveform for presence of oVEMP recorded from subgroup II (51 – 60 years)

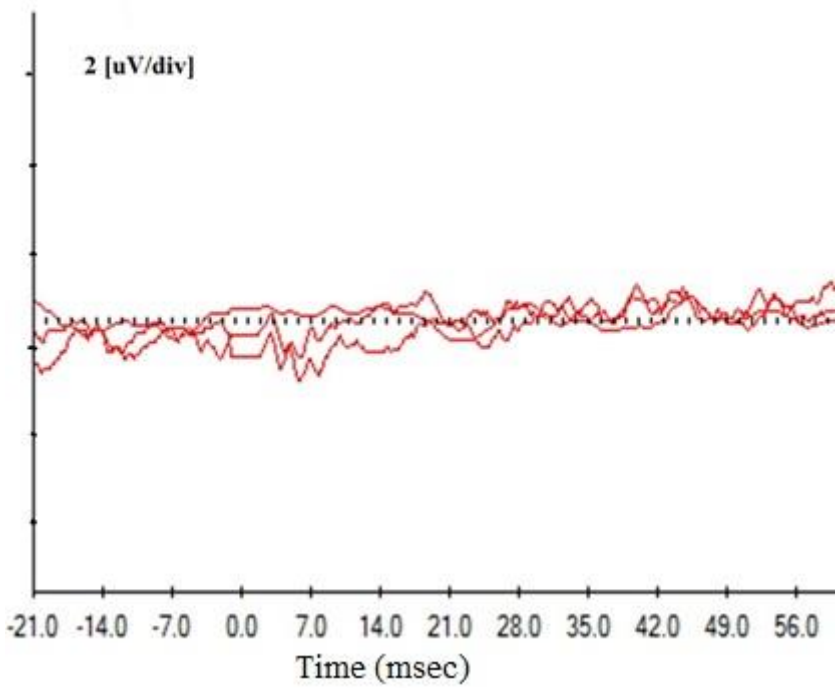

Fig 4.2.5 : Representative waveform for absence of oVEMP recorded from subgroup II (51 – 60 years)

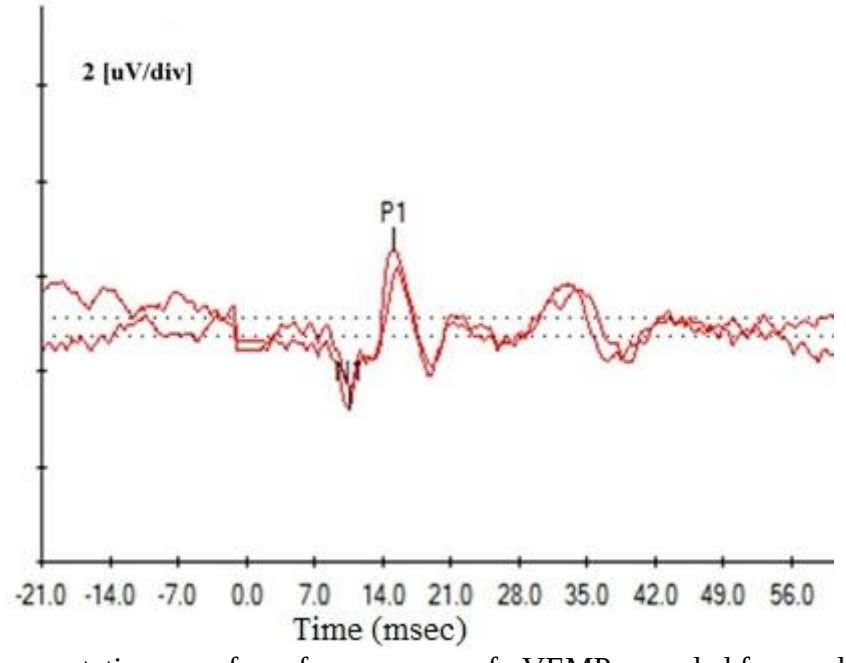

Fig 4.2.6 : Representative waveform for presence of oVEMP recorded from subgroup III (61 – 70 years)

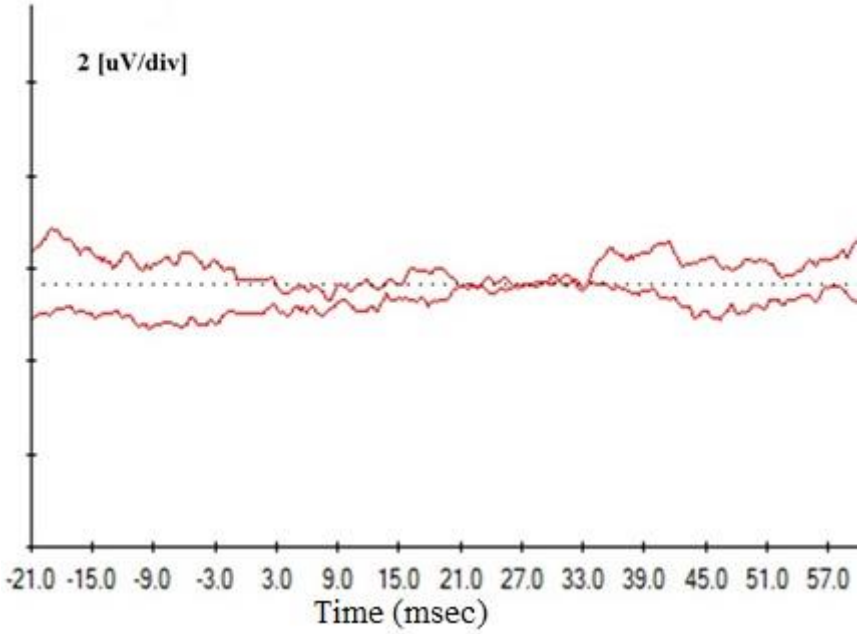

Fig 4.2.7 : Representative waveform for absence of cVEMP recorded from subgroup III (61 – 70 years)

Descriptive statistics was done to find out the mean and the standard deviations of different cVEMP parameters for the young and the older groups. The mean, median and the standard deviation for the two groups are given in **Table 4.2.1**

Table 4.2.1: oVEMP responses for Left and Right ear for different age groups

		Latency N1			Latency P1			Amplitude N1P1		
		x̄	*M*	SD	x̄	*M*	SD	x̄	*M*	SD
Group II	R	11.19	11.13	0.93	16.53	16.7	1.56	5.45	4.20	4.03
N = 36	18									
18 -30 years	L	11.37	11.94	1.06	16.57	16.54	2.35	5.38	4.01	4.10
N =	18									
Subgroup I	R	11.82	11.93	1.65	16.64	16.53	1.34	2.76	2.49	1.38
N = 28	14									
41 - 50 years	L	11.84	12.06	1.16	16.65	16.88	0.55	2.7	2.17	1.58
N =	14									
Subgroup II	R	11.71	12.2	1.12	16.99	16.99	0.86	2.78	2.91	1.22
N = 25	12									
51 - 60 years	L	11.73	11.16	1.39	17.40	17.37	1.13	2.60	1.98	1.75
N =	13									
Subgroup II	R	12.63	12.82	1.14	12.87	13.34	1.62	2.06	2.15	1.31
N = 22	11									
61 -70 years	L	12.87	13.34	1.62	18.26	17.72	2.45	1.91	1.64	2.35
N =	11									

Note : N1 = latency of N1 peak in milliseconds; P1 = latency of N1peak in milliseconds; N1P1= peak-to-peak amplitude of oVEMP in microvolts.

From **Table 4.2.1** we can see that the mean latency of N1 was more for subgroup III compared to the younger groups. For P1 the mean latency was seen to be increasing with increase in age groups. The amplitude of N1P1 complex was lower for the older groups compared to group II. The left ear for all the groups had increased latency compared to right ear for both N1 and P1 latency. However the amplitude was seen to be more in right ear than in the left ear for all the groups.

Shapiro Wilk test was administered to check whether the data follows the normal distribution or not. Shapiro Wilk test for normality did not show a normal distribution for the entire data ($p<0.05$) and hence a non-parametric test was administered.

Wilcoxon sign ranked test was administered to check effect of ear as a subject within factor. **Table 4.2.2** shows the results obtained from Wilcoxon sign ranked test.

Table 4.2.2 Wilcoxon sign ranked test results for parameters of oVEMP across groups

	Group II (18- 30 Years)		**Group I (41 – 70 years)**					
oVEMP	Group II (N = 36) (18 – 30 years)		Subgroup I (N = 28) (41 – 50 years)		Subgroup II (N = 25) (41 – 50 years)		Subgroup III (N = 22) (41 – 50 years)	
	Z	**p**	**Z**	**p**	**Z**	**p**	**Z**	**p**
N1	0.88	0.38	0.41	0.69	0.89	0.93	1.17	0.24
P1	0.24	0.81	0.63	0.95	1.45	0.15	0.3	0.77
N1P1	0.78	0.43	0.22	0.83	1.72	0.08	0.73	0.46

Note: Z = Wilcoxon ranked test, p = α confidence level, P1 = latency of P1 peak, N1 = Latency of N1 peak, P1N1 = amplitude of P1N1

Wilcoxon sign ranked test did not show significant difference between ears for any of the groups. Hence the data for the two ears was combined. Table 4.2.3 shows the mean, median and standard deviation for parameters of oVEMP for the groups with combined data for two ears.

Table 4.2.3: Mean, median and standard deviation of latencies of N1, P1 and peak-to-peak amplitude of N1P1 for 500Hz in oVEMP recordings of the four groups.

oVEMP		Group II	Group I		
		18-30 years (group II) (N = 36)	40-50 years (sub group I) (N = 28)	50-60 years (sub group II) (N = 25)	60-70 years (sub group III) (N = 22)
N1	Mean	11.28	11.80	11.73	12.7
	Median	11.13	12.03	11.47	12.82
	SD	0.99	1.40	1.24	1.44
P1	Mean	16.30	16.65	17.08	18.19
	Median	16.64	16.74	17.09	18.03
	SD	2.0	1.0	1.03	1.88
N1P1	Mean	5.43	2.78	2.59	1.94
	Median	4.15	2.17	1.88	0.96
	SD	4.0	2.74	2.26	3.29

Note : N1 = latency of N1 peak in milliseconds; P1 = latency of N1peak in milliseconds; N1P1 = peak-to-peak amplitude of oVEMP in microvolts.

From the Table 4.2.3 we can see that the mean latency of N1 as well as mean latency of P1 was more in the older groups compared to the group II consisting of the youngest group. There was a decreasing trend seen for the amplitude of N1P1 with increasing age.

To understand the overall group difference between groups for different parameters of oVEMP, Kruskal Wallis H test was administered. The test findings revealed there was a significant difference in latency of N1 across groups ($\chi^2(3) = 16.61$, $p = 0.01$) and latency of P1 across groups ($\chi^2(3) = 20.74$, $p = 0.00$). There was also a significant difference for the amplitudes of oVEMP across group (χ^2 (3) = 33.98, p = 0. 00).

Further to understand the significant differences between different groups and subgroups Mann Whitney U test was used. The test findings revealed that there was significant difference for latency of N1 between group II and subgroup III of group I (Z = 3.91 p = 0.00). There was no significant difference between group II and subgroup I of group I (Z = 1.76 p = 0.08), between group II and subgroup II of group I (Z = 1.6, p = 0.11), subgroup I and subgroup II (Z = 0.05, p = 0.96), however it showed a significant difference between subgroup I and subgroup III (Z = 2.5 p = 0.01) and between subgroup II and subgroup III (Z = 2.4, p = 0.01).

There was significant difference for latency of P1 for oVEMP between group II and subgroup III of group I (Z = 3.83, p = 0.00) and for group I, between subgroup I and subgroup III (Z = 3.6, p = 0.00). There was no significant difference between group II and subgroup I of group I (Z = 1.19, p = 0.23), and subgroup II and subgroup III (Z = 0.04, p = 0.97), however it showed a significant difference between group II and subgroup II of group I (Z = 2.28, p = 0.02), subgroup II and subgroup I (Z = 1.95, p = 0.05).

The test findings revealed that there existed significant difference for amplitude N1P1 between group II and subgroup I of group I (Z = 3.9, p = 0.00), between group II and subgroup II of group I (Z = -3.6, p = 0.00), between group II and subgroup III of group I (Z =

5.14, p = 0.00). For group I there existed significant difference between subgroup I and subgroup III (Z = 3.1, p = 0.003), and between subgroup II and subgroup III (Z = 2.61, p = 0.00). There was no significant difference between subgroup I and subgroup II (Z = 0.192, p = 0.847).

Finally to summarise there was significant difference for the latency of N1 between group II and subgroup III, for latency of P1 there existed difference between group II and subgroup III and in group I between subgroup I and subgroup III. The amplitude in the participants for the age between 18 – 30 years was significantly more compared to the older groups. In group I, the 41 – 50 years individuals had significantly higher amplitude than the individuals between 61 – 70 years. Thus the findings suggest that the amplitude as well the latency parameters were significantly affected as the process of aging among the participants in the subgroup III (age 60 – 70 years). Also the group II (age 18 – 30 years) had significantly higher amplitude and early latency compared to all the other older grouped participants.

4.3. Video Head Impulse test

The test was administered in lateral planes. The VOR gain that is the ratio of eye velocity and the head velocity was calculated. The VOR gain lesser than 0.8 was considered to be abnormal. As age increased the number of participants having abnormal VOR gain also increased. The % of individuals having reduced VOR gain in group II was 2.7%, in subgroup I, it was 16.7%, in subgroup II, it was 13.3% and in subgroup III it was 25%. The proportion of individuals having VOR gain less than 0.8 was significantly higher in age group 60 – 70 years compared to age group 18 – 30 years (Z = 2.7 p = 0.007).

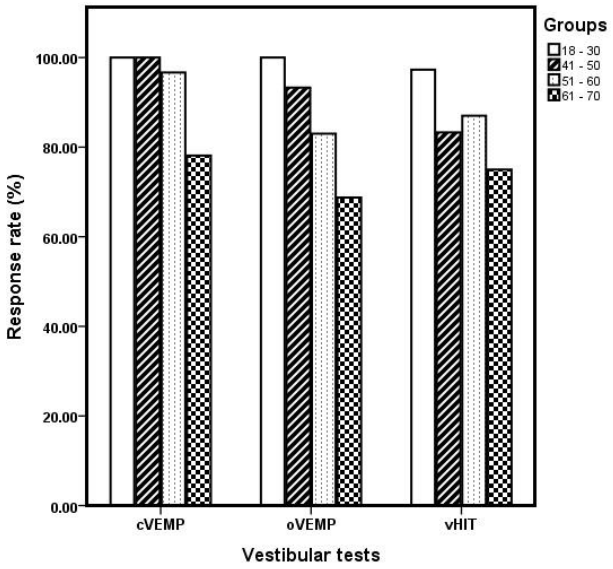

Fig 4.3.1. The response rates of vestibular tests in different groups. The groups are divided on the basis of age in years. 18 – 30 years (group II), 41 – 50 years (subgroup I), 51 – 60 (subgroup II), 61-70 (subgroup III).

Following below is given the representative outcome of normal and abnormal vHIT test results from the all groups in lateral planes.

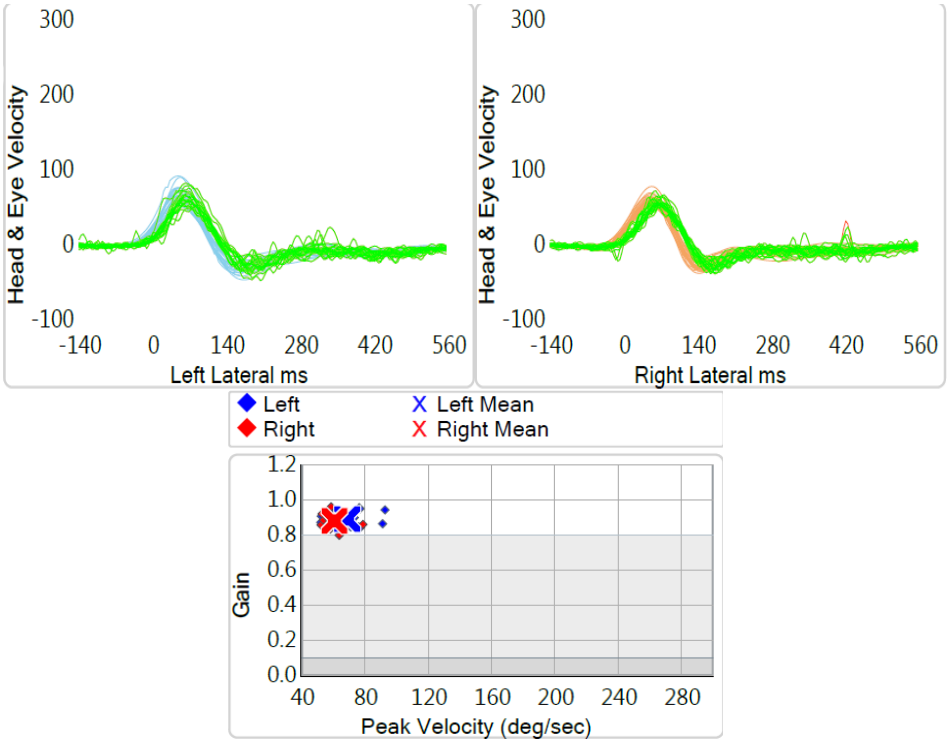

Fig 4.3.2 : Normal VOR gain from age group II (18 – 30 years)

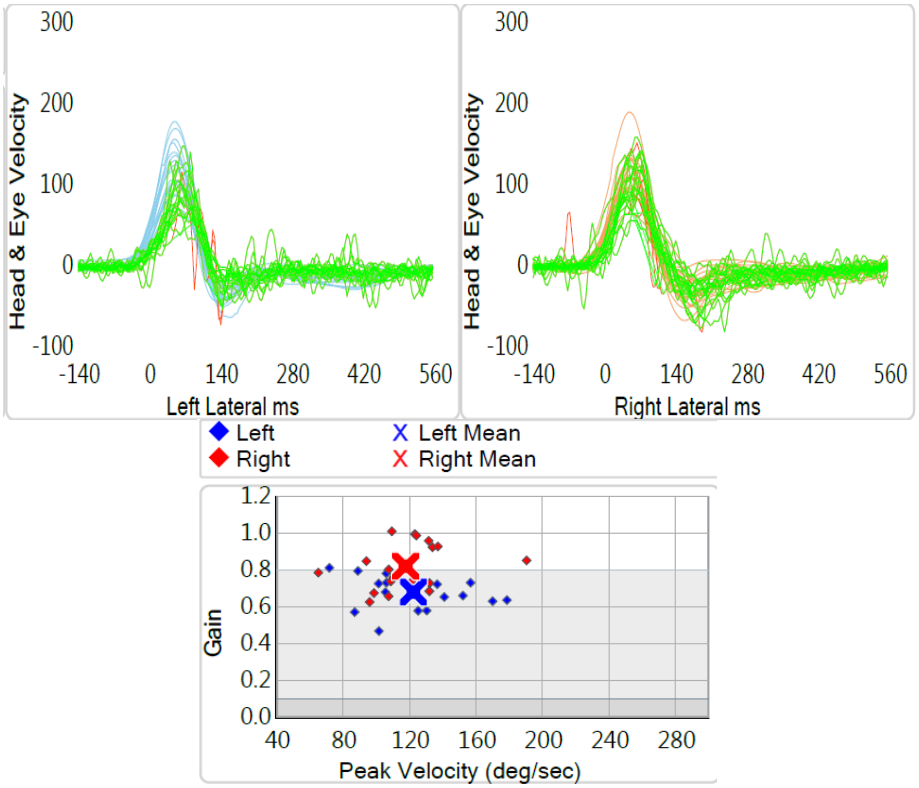

Fig 4.3.3 : Reduced VOR gain from age group II (18 – 30 years)

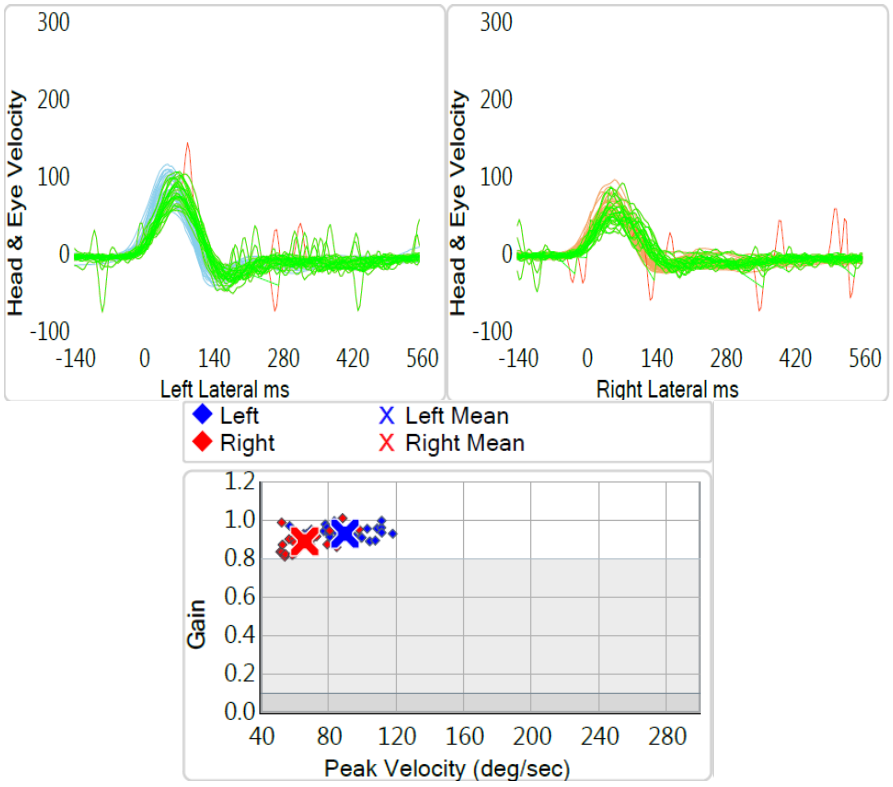

Fig 4.3.4 : Normal VOR gain from Subgroup II (41 – 50 years)

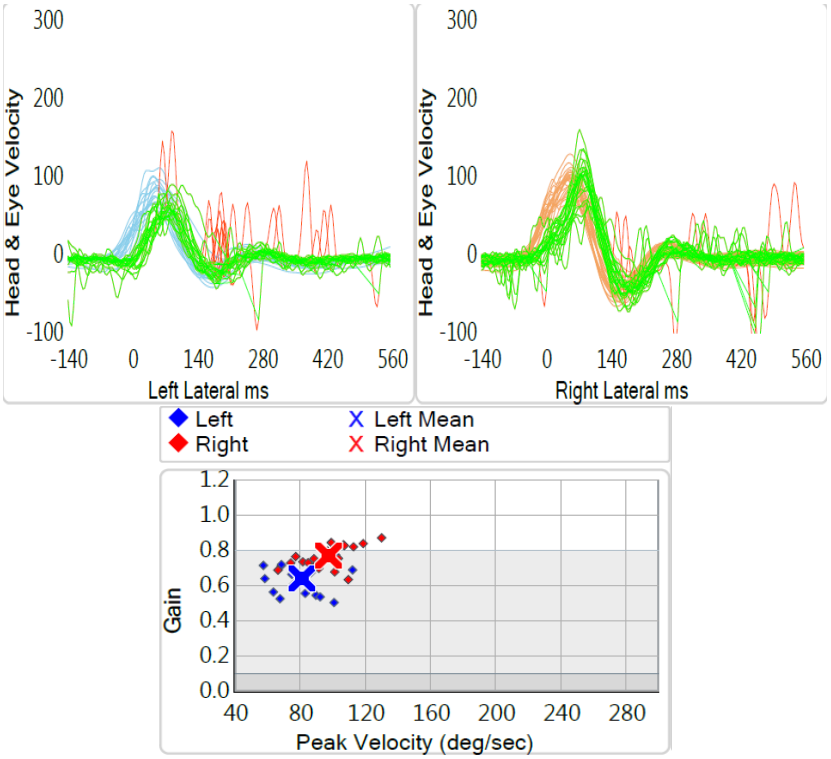

Fig 4.3.5 : Reduced VOR gain from Subgroup I (41 – 50 years)

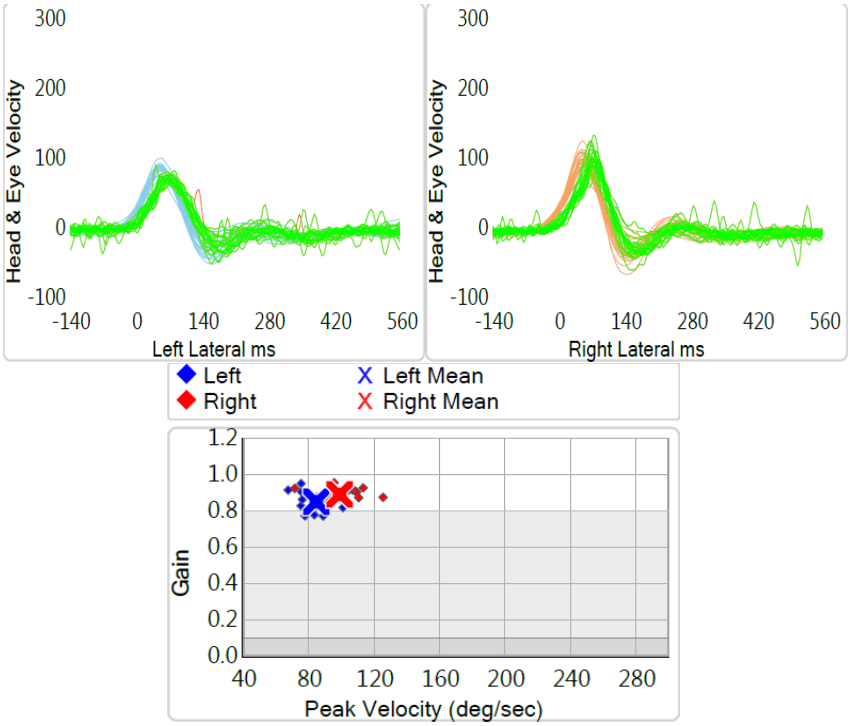

Fig 4.3.6 : Normal VOR gain from Subgroup II (51 – 60 years)

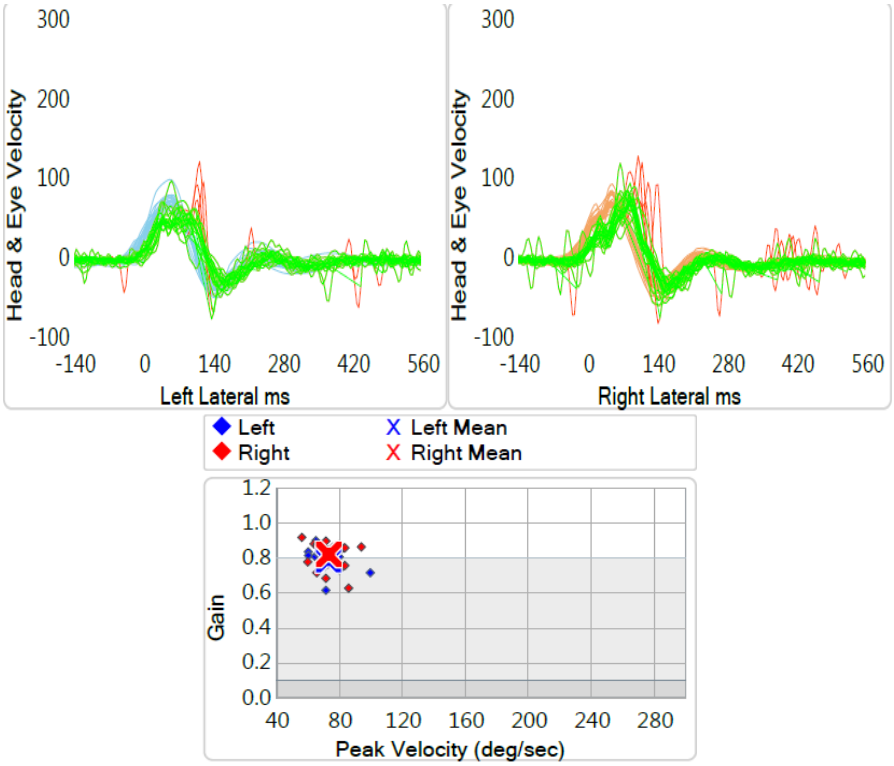

Fig 4.3.7 : Reduced VOR gain from Subgroup II (51 – 60 years)

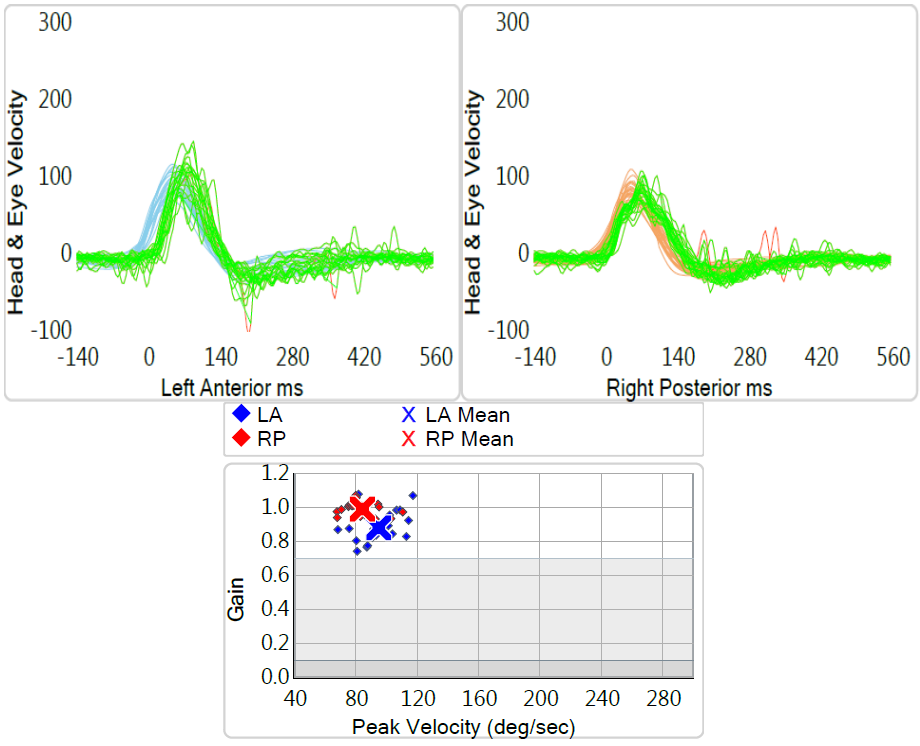

Fig 4.3.8 : Normal VOR gain from Subgroup III (61 – 70 years)

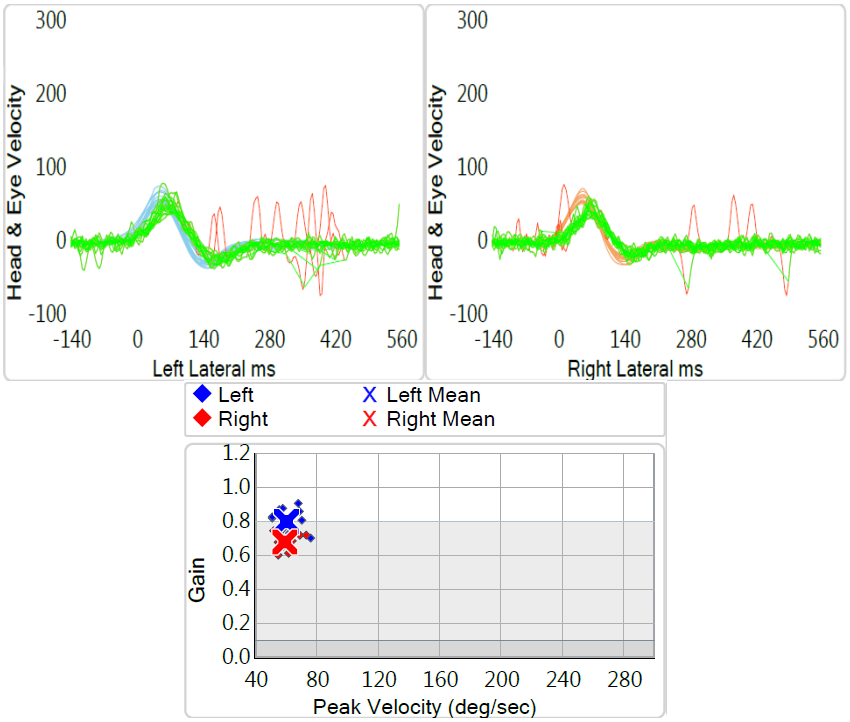

Fig 4.3.9 : Reduced VOR gain from Subgroup I (41 – 50 years)

Descriptive statistics was done to find out the mean, median and standard deviation of individuals in lateral planes. Table 4.3.1 gives the descriptive statistics for VOR gain for right as well as left lateral planes.

Table 4.3.1: Mean, median and standard deviation of VOR gain for right and left lateral planes

	Group II		**Subgroup I**		**Subgroup II**		**Subgroup III**	
vHIT	RL	LL	RL	LL	RL	LL	RL	LL
x̄	0.94	0.95	0.95	0.98	1.0	0.97	0.90	0.88
M	0.92	0.91	0.94	0.91	0.98	0.99	0.88	0.86
SD	0.12	0.15	0.16	0.11	0.17	0.85	0.14	0.27

Note: x̄ = mean; *M* = median; SD = standard deviation; RL = right lateral, LL = left lateral

From the Table 4.3.1 we can see that the mean VOR gain value is more in the subgroup II compared to subgroup III and subgroup I in group I. The gain is less in group II compared to subgroup I and subgroup II of group I. The lateral planes from the two ears do not show much difference.

To find out if there exists a significant difference between two lateral planes in the individual Wilcoxon sign ranked test was administered. The table 4.3.2 shows the Wilcoxon sign ranked test statistics.

Table 4.3.2 Wilcoxon sign ranked test results for parameters of VOR gain across groups

	Group II (18- 30 Years)		**Group I (41 – 70 years)**					
vHIT	Group II (N = 36) (18 – 30 years)		Subgroup I (N = 28) (41 – 50 years)		Subgroup II (N = 25) (41 – 50 years)		Subgroup III (N = 22) (41 – 50 years)	
	Z	**p**	**Z**	**p**	**Z**	**P**	**Z**	**p**
VOR gain	1.39	0.16	0.77	0.44	0.89	0.93	0.97	0.33

Note: Z = Wilcoxon ranked test, p = α confidence level, VOR = Vestibulo-ocular reflex

Since Wilcoxon sign ranked test did not show significant difference between right and the left lateral planes the data of the two planes were taken together. Table 4.3.3 shows the combined mean values of the two planes.

Table 4.3.3: Mean, median and standard deviation of VOR gain for lateral planes

vHIT (Lateral plane)		Group II	Group I		
		18-30 years (group II) (N = 36)	41-50 years (sub group I) (N = 30)	51-60 years (sub group II) (N = 30)	61-70 years (sub group III) (N = 32)
VOR	Mean	0.95	0.95	1.00	0.89
	Median	0.92	0.92	0.98	0.88
	SD	0.121	0.16	0.17	0.14

Note :VOR = Vestibulo ocular reflex gain, SD = standard deviation.

From the Table 4.3.3 we can see that the mean VOR gain value is least in the age range of 61 – 70 years. The mean VOR gain value was more in the subgroup II of group I compared to group II and also subgroup I and III of group I.

To find the difference between the groups for VOR gain Kruskal Wallis H test was used. The test revealed there was existed marginally significance difference between the VOR gain values across groups ($\chi^2(3) = 7.78$, $p = 0.05$). Mann Whitney U test was used to find if there existed any difference between 2 groups. There was no significant difference for VOR gain values between group II and subgroup I (Z = 0.28, p = 0.77), group II and subgroup II (Z = 1.8, p = 0.07), group II and subgroup III(Z = 1.56, p = 0.12), subgroup I and subgroup II (Z = 1.53, p = 0.13), subgroup I and subgroup III (Z = 1.06, p = 0.28), however it showed a significant difference between subgroup II and subgroup III (Z = 2.55, p = 0.01) .

4.4. Correlation results

To find out if there existed any significant correlation between the variables of the study Spearman's correlation was administered. There was no significant correlation between latency of peak P1 of cVEMP and age (p >0.05) Peak N1 of cVEMP and age (p >0.05). There was significant increase in oVEMP latency of peak N1 and peak P1 with advancing age. The correlation was highly significant for latency of N1 (r_s = 0.348, $p < 0.01$) and P1 (r_s = 0.36, $p < 0.01$) with age. Fig. 2 shows the correlation between the latency of oVEMP peaks P1 and N1 and age. For vHIT there was no significant correlation for VOR gain values and age (r_s = 0.26 p >0.5).

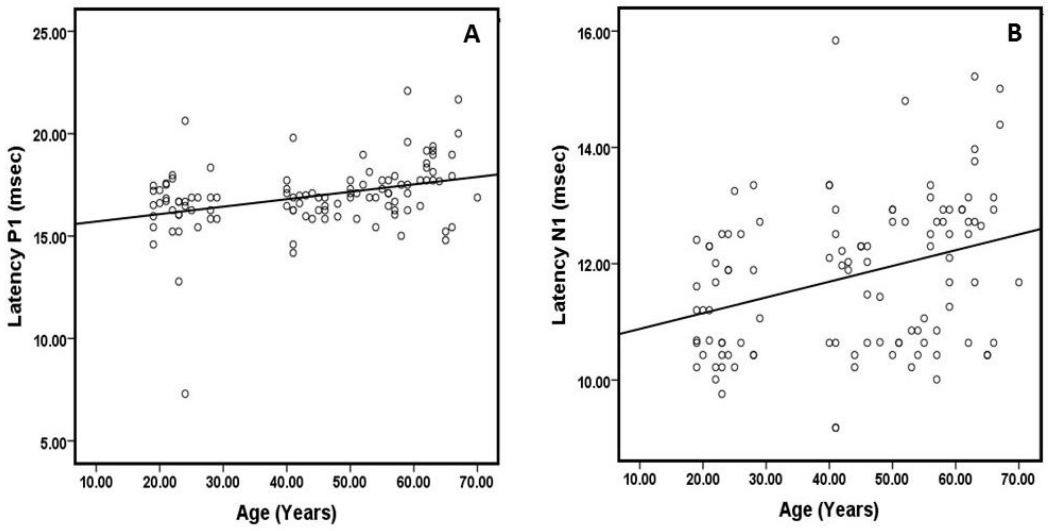

Fig. 4.4.1 Scatter plot showing relation between age and N1 & P1 latency of oVEMP.

As the age increased both cVEMP and oVEMP amplitude was seen to be reduced significantly i.e there was a significant negative correlation between age and cVEMP amplitude (r_s = 0.427, $p < 0.01$) and age and oVEMP amplitude (r_s = 0.497, $p < 0.01$). Thus significant effect of aging was seen on the latency as well as the amplitude of oVEMP and only significant reduction in the amplitude of cVEMP was seen as a function of aging. *Fig.* 3 shows the correlation between age and cVEMP and oVEMP amplitude. There was no correlation between the VOR gain values and age (r_s = 0.019, $p > 0.05$).

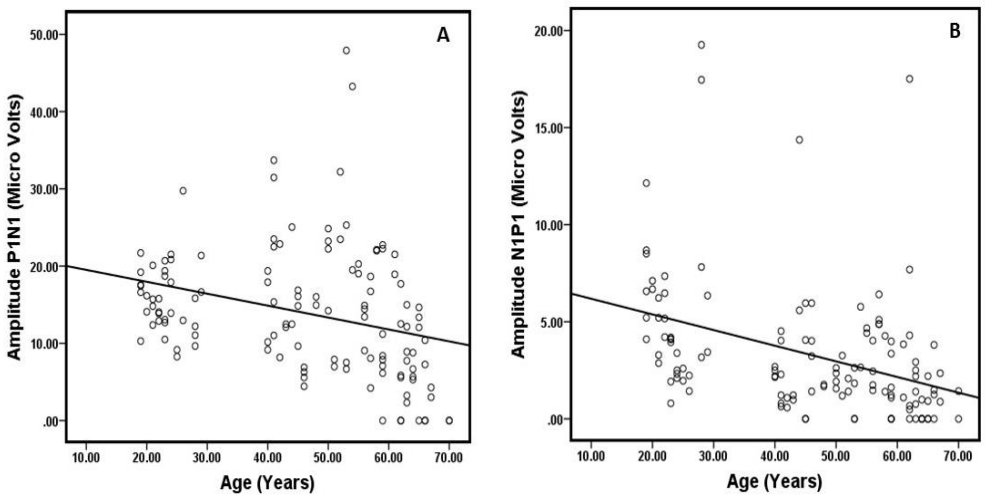

Fig. 4.4.2. Scatter plot showing relation between age and P1N1 of cVEMP (A) and N1-P1 amplitude complex of oVEMP(B)

There was a positive correlation between cVEMP and oVEMP amplitudes i.e as the the cVEMP amplitude decreased the oVEMP amplitude also decreased significantly (r_s = -0.331, $p < 0.05$). *Fig*. 4 shows the correlation between cVEMP and oVEMP amplitudes. There was no correlation between VOR gain for lateral planes and amplitude of cVEMP (r_s = -0.297, $p > 0.05$) and oVEMP (r_s = - .33, $p > 0.05$).

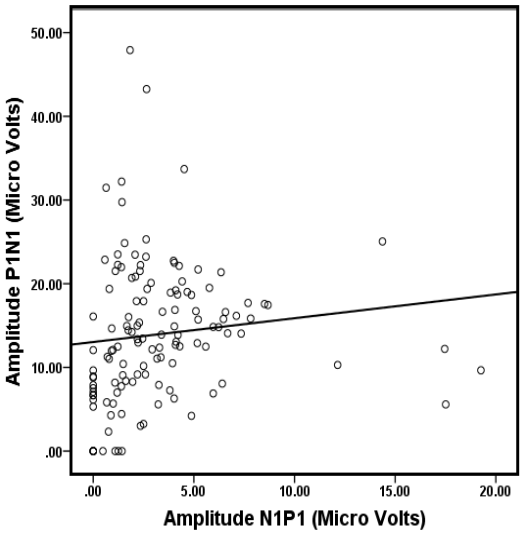

Fig. 4.4.3 correlation between cVEMP amplitude and oVEMP amplitude (r_s = -0.331, $p < 0.05$).

Chapter 5

Discussion

5.1. Cervical vestibular evoked Myogenic Potentials:

There existed a significant difference between participants of subgroup II (51 – 60 years) and group II (18 – 30 years) for latency of P1 peak. Latency of N1 latency did not differ across the group. A significant effect of ageing was seen on the amplitudes of cVEMP. The group in age range of 61- 70 years had higher proportion of participants who had absent cVEMP compared to the younger groups. Also the cVEMP amplitude was found to be significantly reduced in this group than the other groups.

Previously reported studies have found similar results on the parameters of latency of P1 and N1 i. e increase in the latency of P1 (Maleki, Jafari, Zarrinkoob, & Akbarzadeh Baghban, 2014; Singh, Kashyap, Supreetha, & Sahana, 2014) and decrease in the latency of N1 with advancing age. However few studies have shown to have no significant effect aging on the latency of P1 and N1 as the effect of aging (Layman et al., 2015; Nguyen, Welgampola, & Carey, 2010). There was an increasing trend seen for latency of P1 as well as N1 in the study by Nguyen et al, 2010 which was similar to our findings however their results did not differ significantly between age groups.

In the present study there was no significant difference in latency between different groups, however only latency of P1 was prolonged for 51-60 years age group only. Thus prolongation of P1 peak did not show any kind of definite pattern of aging effect. The equivocal findings in literature could be due to the different population tested. For example, study by Layman et al (2015) showed significant effect of aging on latency parameters in males and not in females. Also the different age groups taken for the different studies are different.

The cVEMP amplitude decreases as age increases (Agrawal et al., 2012; Layman et al., 2015; Maes et al., 2010; Maleki et al., 2014; Singh et al., 2014) It has been reported in literature that there occurs decline in the amplitude of the cVEMP by 0.14 microV after every decade (Li, Layman, Carey, & Agrawal, 2015) irrespective of the stimulus used (Nguyen et al., 2010). It has also been reported that the response rate for presence of cVEMP is less for people above 65 years of age. (Maes et al., 2010). Similar results were found in our study. The participants above 60 years of age had significantly reduced amplitude compared to younger groups. However a (Singh et al., 2014) have reported that the amplitude of cVEMP remains steady upto the age of 50 years however the rate of decline after 50 years is more rapid. The study by singh et al, 2014 was done as a cross sectional study on large sample of 280 participants. The difference in the result could be due to their large sample size.

Reduction in the amplitude of cVEMP could be attributed to age related deterioration in the vestibular apparatus in the human body with increasing age. There occur structural changes from the vestibular hair cells up to the vestibular nerve fibres. The reduction in the nerve fibres occurs by around 2000 nerve fibres per decade and reaches up to 40 % reduction by the age of by the age of 60 years (Bergström, 1972). The loss of nerve fibres start to occur at 40 years of age (Park, Tang, Lopez, & Ishiyama, 2001) hence with this loss of nerve fibres with increasing age there decline in the carrying capacity of the vestibular nerve which could have resulted in increase in latency with aging. The effect of aging is also results in loss of haircells (Bergström, 1972; Rosenhall, 2009) and decrease in the density of otoconia in the maculae of saccule (Johnsson, 1971). Thus loss of hair cell and reduction in otoconia density could have resulted in reduced stimulation of the saccule and hence reduced amplitude in the individuals with 61 – 70 years.

5.2. Ocular vestibular evoked Myogenic Potentials:

The amplitude as well the latency parameters were significantly affected as the process of aging among the participants in the subgroup III (age 60 – 70 years). The response rate for presence of cVEMP and the latency of N1 and P1 showed significant difference between two groups that were 20 decades apart. Also the group II that is the youngest group (age 18 – 30 years) had significantly higher amplitude and early latency compared to all the other older grouped participants. The eldest group of participants between 61 – 70 years had significantly reduced amplitudes compared to other younger groups.

The structural changes in the vestibular system the due to the effect of ageing i.e reduction in the otoconia density (Johnsson, 1971) in the uticle, reduction in the nerve fibres and reduction in the number of cell bodies in the scarpas ganglion (Richter & Richter, 2016) could have resulted in prolonged latency and reduced amplitude as a function of ageing.

Many previously reported studies have shown similar results that as age increases there occurs increase in the latency of N1 and latency of P1 (Layman et al., 2015; Li et al., 2015) and this effect on latency due to ageing is more significant in males compared to females (Nguyen et al., 2010). There was significant difference in the amplitude of oVEMP seen among participants of the groups which had difference of 20 years. Studies have reported that there occurs reduction in the amplitude of oVEMP by by 2.14 microvolt for every decade beyond 40 years (Chang, Young, & Cheng, 2012; Maheu, Houde, Landry, & Champoux, 2015). This rapid reduction could have resulted obvious change in the amplitude of oVEMP as a function of ageing.

5.3. Video head impulse test:

VOR gain was significantly reduced in individuals in the age range of 61-70 years compared to the other age groups.

The normal VOR gain is considered to be normal between 0.8 to 1.2 (Patterson, Bassett, Mollak, & Honaker, 2015), individuals having VOR gain below 0.8 was considered to be abnormal. Agrawal et al. (2012) reported that there is not much change seen in the VOR gain up to the age of 50 years, however the mean reduction in the VOR gain beyond 60 years. One of the earlier studies utilising the VHIT to calculate the VOR gain values, has reported significant reduction in VOR gain with advancing age beyond 60 years. (Mossman, Mossman, Purdie, & Schneider, 2015b). In the present study also the VOR gain was reduced for 61-70 years age group.

Histopathological studies have shown that there occurs degeneration in the semicircular canals due to ageing. There occurs hair cell loss and reduction in significant reduction in the hair cell density in individual beyond 70 years of age. The sensitivity of vHIT to assess the functioning of the semicircular canals is less for individuals up to moderate problems (Bartolomeo et al., 2014; Chen et al., 2015).

5.4. Correlation between tests

The latency of oVEMP increased with age. A significant negative correlation between age and the amplitude of cVEMP and oVEMP was also observed in the present study.

The findings of the present study could be attributed to the fact that the superior vestibular nerve that innervates the utricle and form an important part of the utriculo-ocular pathway is more susceptible to damage compared to the inferior vestibular nerve that innervates the saccule (Chiarvano et al., 2011; Shin et al., 2012). The deterioration of the vestibular structures would have resulted in decreased synchronous firing of the more susceptible vestibular nerve resulting in delayed latency as a function of aging. As age

increased the amplitude of both cVEMP and oVEMP decreased suggesting generalized deterioration of the vestibular structure and function as the effect of ageing. Video Head Impulse Test showed results showed no significant correlation probably because of its poor sensitivity in moderate vestibular problems (Bartolomeo et al., 2014; Chen et al., 2015).

Chapter 6

Summary and Conclusion

Elderly individuals are the fastest growing sector of our community. Health of these individuals today is of major concern world wide. As age increases the body starts to degenerate. The process of degeneration affects the entire body including the vestibular system. Damage to the vestibular system due to ageing often results in symptoms like vertigo and dizziness. The elderly individuals are thus at higher risk of falls which can result in fracture or accidental death consequently reducing their quality of life, putting financial burden on the health sector and emotional trauma to the family members. Thus to avoid such consequences an effective management evolved from effective assessment should be done.

Effective assessment of the vestibular system can be done by studying the saccule using cervical vestibular evoked myogenic potential, utricle using ocular vestibular evoked myogenic potential and semicircular canals using video head impulse test. Caloric test has been a known and clinically used tool for assessing the horizontal semicircular canal however a novel video head impulse test can assess the semicircular canals in all planes for high frequency movements. Thus the present study aimed at assessing the saccule using cVEMP, utricle using oVEMP and semicircular canals using vHIT in older adults.

The study consisted of 64 participants age ranging from 19 years to 70 years. The participants were divided into two groups. The group I consisted of 46 participants age between 41 years to 70 years. The group I was further divided into subgroup I, subgroup II and subgroup III with their age range being 41 – 50 years, 51 – 60 years and 61 – 70 years respectively. Subgroup I and subgroup II had 15 participants each and the subgroup III had 16 participants. The group II consisted of 18 participants with their age being from 19 – 30 years.

Routine audiological evaluations were done. The individuals having hearing sensitivity within normal limits were taken for the study. None of the participants had history or presence of any vestibular complaints. cVEPM, oVEMP and Video head impulse test in lateral planes was administered. In cVEMP the absolute latency of P1, N1 and amplitude of P1N1 complex was calculated. In oVEMP absolute latency of N1, P1 and amplitude of N1P1 complex was calculated. In Video head impulse test, Vestibular ocular gain was calculated for lateral planes.

To analyse the data following statistics was done.

- Shapiro Wilk test for normality was done to see whether the data followed normal distribution or not.
- Descriptive statistics was done to find out the mean, median and standard deviation of
  - ✓ cVEMP absolute latency of P1, absolute latency of N1 and amplitude of P1N1 and interaural asymmetry ratio I all the groups.
  - ✓ In oVEMP absolute latency of N1, absolute latency of P1 and amplitude of N1P1 and interaural asymmetry ratio in all the groups.
  - ✓ VOR gain in lateral planes for all the groups.
- Wilcoxon signed rank test was done to find the difference between ears for the subjects in all the groups.
- Kruskal Wallis test was done to find the difference between groups for the parameters
- Mann Whitney U test was done to find the difference between any two group for the parameters.

- ❖ Spearman's correlation was done to see the effect of ageing on cVEMP, oVEMP and vHIT. Also to see if there existed any correlation between cVEMP and oVEMP , cVEMP and vHIT, oVEMP and VHIT.

Results of the study revealed the following

- ✓ There was no difference between ears for any group for cVEMP, oVEMP and VHIT

Cervical vestibular evoked myogenic potentials

- ✓ Significantly higher proportion of participants in age group of 61 – 70 years had absent cVEMP compared to all other younger groups.
- ✓ There was significant difference for latency P1 between group II (18 – 30 years) and subgroup II (51 – 60 years)
- ✓ There was no significant difference for latency N1 across groups.
- ✓ There was a significant difference between the peak to peak amplitude of P1N1 of subgroup III and group II, subgroup III and subgroup I, and subgroup III and subgroup II.
- ✓ There was a significantly negative correlation between age and cVEMP amplitudes.

Ocular vestibular evoked myogenic potentials

- ✓ There was a significant difference in terms of response rates for oVEMP between subgroup III and group II, between subgroup II and group II, and between subgroup I and subgroup III.
- ✓ There was significant difference for the latency of N1 between group II and subgroup III.

- ✓ There existed difference between group II and subgroup III and between subgroup I and subgroup III for P1.
- ✓ There was significant difference for amplitude N1P1 between group II and subgroup I, between group II and subgroup II, between group II and subgroup III, between subgroup I and subgroup III and between subgroup II and subgroup III.
- ✓ There was a significant positive correlation between age and latency N1 and between age and latency P1.
- ✓ There was a significantly negative correlation between amplitude of N1P1 and age.
- ✓ There was a positive correlation between amplitude of P1N1 of cVEMP and amplitude of N1P1 of oVEMP.

Video Head Impulse test

- ✓ Higher proportion of individuals in the subgroup III of group had abnormal VOR in the lateral planes.
- ✓ There existed a significant difference for VOR gain across groups.
- ✓ There was a significant difference for VOR gain between subgroup II and subgroup III.
- ✓ The VOR did not show any correlation with age, cVEMP and oVEMP.

Conclusions

As age increases there occurs increase in the latency of P1 of cVEMP and increase in the latency of both N1 and P1 of oVEMP and decrease in the amplitude of both cVEMP and oVEMP. The VOR gain reduces as age increases but a significant effect of ageing is seen in individuals beyond 60 years of age on the vestibular test results. There also exists comparative difference for vestibular test results between young group and individuals beyond 40 years. To conclude that the three tests administered were able to detect the vestibular deficits in different structures of the vestibular system. The degeneration pattern revealed for the vestibular system in this study indicates that there is an overall degeneration in the vestibular system. Thus, to understand the different mechanisms underlying the vestibular degeneration one must administer different tests. Also, along with the audiological tests the tests for the vestibular system should be administered for these individuals.

Implication of the study:

- ✓ The study helps us to understand the various mechanisms undergoing degenerative changes due to aging.
- ✓ This study provides us with the information of the exact age where degeneration various vestibular end organ begins. Thus, it can be used as a guideline to understand the latency and amplitude changes occurring in various tests due to aging.

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