OPTIMIZING THE cVEMP PROTOCOL FOR THE DIAGNOSIS OF MENIERE'S DISEASE

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AMMA, PAPPA, APPU

&

MY GUIDE

CERTIFICATE

This is to certify that this dissertation entitled "**OPTIMIZING THE cVEMP PROTOCOL FOR THE DIAGNOSIS OF MENIERE'S DISEASE**" is the bonafide work submitted in part fulfillment for the degree of Master of Science (Audiology) of the student with Registration No. 11AUD018). This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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CERTIFICATE

This is to certify that this dissertation entitled "**OPTIMIZING THE cVEMP PROTOCOL FOR THE DIAGNOSIS OF MENIERE'S DISEASE**" has been prepared under my supervision and guidance. It is also certified that this has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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DECLARATION

This dissertation entitled "**OPTIMIZING THE cVEMP PROTOCOL FOR THE DIAGNOSIS OF MENIERE'S DISEASE**" is the result of my own study under the guidance of Mr. Sujeet Kumar Sinha, Lecturer in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted earlier in any other University for the award of any Diploma or Degree.

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CHAPTER – 1

INTRODUCTION

Meniere's disease is a complex, multifactorial disorder of the inner ear which is the most common cause of the episodic vertigo along with fluctuating hearing loss (Gates, 2006). In spite of several investigations, the etiology and pathophysiology of Meniere's disease remain controversial and incompletely understood (Gates, 2006). In majority of the individuals with Meniere's disease is linked to idiopathic endolymphatic hydrops, which is an abnormal increase in the volume of endolymph in the inner ear (Papparella, 1991; Merchant, Adams & Nadol, 2005). The excessive accumulation of endolymph may be due to altered resorption by the endolymphatic duct and sac (Arenberg et al., 1970) or due to increased secretion of the endolymph (Hallpike & Cairns, 1938). The eventually developed high pressure results in distention and rupture of reissner's membrane and intoxication due to mixture of fluids (Lawrence & McCabe, 1959).

The incidence and prevalence of Meniere's disease are estimated to be 15-50 and 21.4 - 220 respectively in 100,000 populations (Lynn, Newton & Rae-grad, 2004; Wladislavosky-Waseman, Facer, Mokri & Kurland, 1984; Shojaku et al, 1995). Even though Meneiere's disease is considered to be occurring unilaterally in most of the cases, the percentage of bilateral involvement is highly variable ranging from 2 – 78% across studies (Castellano, 1951; Jonkees, 1971; Greven, 1975). The large variability in the prevalence and incidence could be due to the difference in target populations selected in each study as well as complex nature of the disorder. The mean age of

onset of Meniere's disease is found to be in middle age that is from 40 – 55 years across studies (Havia & Kentala, 2004; Thomas & Harrison, 1971).

The major auditory symptoms in individuals with Meniere's disease include fluctuating hearing loss (Enander & Stahle, 1967; Thomas & Harrison, 1971; Eliachar, Keels & Wolfson, 1973; Meyerhoff, Paparella & Gudbrandsson, 1981) unilateral in majority especially in the initial stages of the disease, tinnitus and aural fullness (Haid, Watermeier, Wolf & Berg, 1995). A few individuals with Meniere's disease also have complaints of reduced tolerance to loud sounds (Buki, Junger & Avan, 2012).

The foremost vestibular symptoms in Meniere's disease are reported to be episodic vertigo (Haid, Watermeier, Wolf & Berg, 1995) with duration of each episode ranging from 20 minutes to hours and rarely to two days (Paparella, 1984, 1991; Friberg, Stahle & Svedberg, 1984) associated with vegetative symptoms like nausea and vomiting. Drop attacks are also being reported in a few individuals with Meniere's disease (Odkvist & Bergenius, 1988).

The different physiological/electrophysiological tests used to diagnose Meniere's disease includes Electrocohleography (EcochG), Glycerol test, CHAMP (Cochlear Hydrops Analysis by Masking Paradigm), Caloric tests and Cervical Vestibular Evoked Myogenic Potential (cVEMP). In EcochG test, the SP (summating potential)/AP (Action potential) amplitude as well as area ratio are found to be higher in individuals with Meniere's disease (Yen, Lin & Huang, 1995; Ferraro & Durrant, 2006; Baba, Takasaki, Tanaka, Tsukasaki, Kumagami & Takahashi, 2009; Iseli & Gibson, 2010). An improvement in hearing threshold was found to be associated with glycerol administration in individuals with Meniere's disease (Yen, Lin & Huang, 1995; Fukuoka et al, 2012; Cen, Zeng, Wang, Li, Zhang & Liu, 2010; Mom, Gilain &

Avan, 2009; Zhao, Zhu & Liu, 2005; Jablonka, Pospiech & Orendorz-Fraczkowska, 2003). The latency shift of wave V of auditory brainstem response (ABR) for click alone and click plus high pass masking noise is reported to be significantly reduced in individuals with Meniere's disease when compared to non-Meniere's normal hearing individuals (Don et al, 2005).

However there are some inherent problems with the above mentioned tests. In EcochG, it has been reported that the summating potential (SP) is present in 60% of the total normal hearing individuals (Selmani, Pyykko, Ashammakhi & Ishizaki, 2002). Hence, making a diagnosis based on SP/AP (Action potential) ratio becomes difficult. Also, in glycerol test the glycerol cannot be administered to individuals with diabetes and also it produces a side effect of nausea and headache. In CHAMP test, the intensity used to record the responses is 60dB nHL (Don et al, 2005) and hence an individual with hearing loss more than mild degree cannot be evaluated using this technique.

The cervical Vestibular Evoked Myogenic Potential (cVEMP) is another electrophysiology test which has been utilized to assess the integrity of vestibulospinal reflex (Murofushi, Shimizu, Takegoshi & Cheng, 2001; Lin et al, 2006; Rauch et al, 2006). Pathway of cVEMP includes the saccular macula, inferior vestibular nerve, the lateral vestibular nucleus, the medial vestibulospinal tract, and the motor neurons of ipsilateral SCM muscle (Halmagyi & Curthoys, 1999). Cervical VEMP has been used as a part of the test battery for Meniere's disease (Colebatch, Halmagyi & Skuse, 1994; Bath, Harris, McEwan & Yardley, 1999; Rauch et al, 2004) and there is sufficient amount of evidence accumulated on its sensitivity in identifying individuals with Meniere's disease which ranges from 50% to 67% (Ribeiro, de

Almeida, Caovilla & Gananga, 2006; de Waele, Huy & Diard, 1999; Kuo, Yang & Young, 2005).

The major changes seen on cVEMP in Meniere's disease are on the amplitude primarily interaural amplitude difference ratio (Rauch et al., 2004; Rauch et al., 2004; Murofushi et al., 2001; Chen & Young, 2006) and threshold (Lin, et al., 2006; Rauch et al., 2004). The cVEMP amplitude was found to be either absent or reduced in 51% of individuals with MD whereas latency shift was not observed (Murofushi, Shimizu, Takegoshi, Cheng, 2001). Interestingly recent researchers have found that the cVEMP frequency tuning is shifted to 1000Hz in affected ears compared to the unaffected ear (Timmer, Zhou, Guinan, Kujawa, Herrmann, Rauch, 2006). There is a dearth of information regarding relation among these parameters of cVEMP and disease condition that gradient of threshold elevation and altered tuning corresponded to the gradient of worsening of the disease. There are also equivocal findings on amplitude, latency as well as frequency tuning parameters in individuals with Meniere's disease (Osei-Lah, Ceranic & Luxon, 2008).

1. Need for the study

1. The cVEMP majorly assess the saccular function as an end organ when the central vestibule spinal reflex pathway is intact (Baloh, 1990). The vast histopathological studies on Meniere's disease have reported that increased tension of the saccular structure is a key pathological condition in this due to abnormally increased level of enolymph in the membraneous labrynth (Paparella, 1984; Antoli-Candela, 1976). Hence the possibility of cVEMP providing relevant information regarding saccular function in Meniere's disease is quite high.

The major histopathological changes seen in Meniere's disease are saccular hydrops (most of the cases), utricular hydrops (in a few cases), bulging of the endolymphatic space in the helicotrema, saccule bulging into the semicircular canal, bulging of the saccule to the stapes footplate (in 60%), collapsed membrane and rupturing of the saccular membrane in the later stages of Meniere's disease (Hallpike & Carins, 1938; Paparella, 1984; Antoli-Candela, 1976; Fraysse, Alonso & House, 1980).

Kristensen (1961) have reported pronounced degeneration of the stria vascularis and absence of nuclei in the limbus spiralis at some locations. He also reported that the degeneration of sensory cells of urticle and semicircular canals are much compare to saccular maculae. The distended saccular membrane results in complete obliteration of the perilymphatic space. However degeneration of vestibular ganglion cells is reported to be minimal in individuals with meniere's disease.

The above histopathological studies on Meniere's disease reveal that increased osmotic pressure in the inner ear due to endolymphatic hydrops mainly damages the saccular structure first in comparison to the utricular and semicircular structures. Therefore, assessing the function of saccule will give a picture about the extent of this damage in Meniere's disease. Thus cVEMP will be useful in the evaluation of the saccular dysfunction in individuals with Meniere's disease.

2. The sensitivity of cVEMP amplitude parameters in identifying Meniere's disease alone has been reported to be 51% (Timmer et al., 2006), whereas, the sensitivity of threshold measures of cVEMP in Meniere's disease has been reported to be 35% (Osei-Laha et al., 2008). Also, the latency and interaural amplitude difference ratio of cVEMP had a sensitivity of 30% among individuals with Meniere's disease (Young, Wu & Wu, 2002), while, the shift in frequency tuning had a

sensitivity of 45% (Lin et al, 2006). Thus, there is a need to combine all the parameters of the cVEMP in order to increase the diagnostic significance of cVEMP for the diagnosis of Meniere's disease.

3. Vestibular findings in the contralateral ear have also found to be significant in individuals with Meniere's disease (Murofushi, Nakahara, Yoshimura & Tsuda, 2011; Saravanan, 2012). Thus there is a need to administer the different vestibular tests in contralateral ear of the individuals with Meniere's disease.

2. Aim of the study

The present study was undertaken with an aim to find out the most sensitive combination of cVEMP analysis parameters to aid in diagnosis of Meniere's disease.

3. Objectives of the study

The following were the objectives of the study

1. To estimate threshold of cVEMP across frequencies in individuals with Meniere's disease and normal hearing individuals.
2. To estimate the frequency tuning of cVEMP in individuals with Meniere's disease and normal hearing individuals.
3. To analyze the aforementioned parameters of cVEMP in conjunction to detect the most sensitive combination.
4. To find out the association between duration of Meniere's disease with cVEMP findings.
5. To find out the association between degree of hearing loss in Meniere's disease with cVEMP findings.

CHAPTER - 2

REVIEW OF LITERATURE

Meniere's disease has gained sufficient attention among the researchers since its very first description by Prosper Meniere (1981) (Baloh, 1990). It stands as the third most common inner ear disorder after presbycusis and noise-induced hearing loss. Meniere's disease is characterized by hearing loss, tinnitus, aural fullness and recurrent attack of vertigo. The pathophysiological studies reveal that Meniere's disease is related to the oversecretion or underabsorption of endolymph which in turn leads to change in the volume and composition of endolymph (Jerger & Jerger, 1981).

The mean age of onset of Meniere's disease is estimated to be between 38-50 years (stahle et al., 1991; Tokumasu et al., 1996). Wladislavosky-Waserman et al (1998) estimated the incidence of Meniere's disease is peaked in the age group of 45-59 years. The incidence of Meniere's disease in children is noted to be 3% (Meyerhoff et al., 1978; Akagi et al., 2001). The disease is described to be equally affected in both genders (Oosterveld, 1979; Katsarkas, 1996). Nevertheless some authors also reported that the incidence of the disease is slightly more in females compared to males but there is no consensus among studies (Stahle et al., 1991; Lee et al., 1995).

Bickford and Jacobson (1964) reported that in Meneires disease apart from the cochlea, the saccule is the second most frequently affected site. The specific probe into the vestibular symptoms in Meniere's disease has led paparella (1984, 1991) to conclude that episodic vertigo is associated with vegetative symptoms such as nausea and vomiting (96.2%) with defined spells of vertigo ranging from 20 minutes (in 25%) to hours (in 50%) and rarely to days (in 25%). The vertiginous spell may be

preceded by an aura, which would be tinnitus (91.1%) and/or aural fullness (74.1%). The author also reported that vertigo may be associated with pallor, diaphoresis, and prostration and with no neurologic deficit but completely oriented to the surroundings. Positional vertigo and drop attacks are also described quite often in the literature as diagnostically important (Tumarkin, 1936).

The histopathological studies were also conducted right from 1930's to peep into the basics behind the incapacitating symptoms presented by individuals with Meniere's disease. The major observations done by researchers on the histopathology of Meniere's disease are saccular hydrops (most of the cases), utricular hydrops (in a few cases), bulging of the endolymphatic space in the helicotrema, saccule bulging into the semicircular canal, bulging of the saccule to the stapes footplate (in 60%), collapsed membrane and rupturing of the saccular membrane in the later stages of Meniere's disease (Hallpike & Carins, 1938; Paparella, 1984; Fraysse et al, 1980).These changes at the end organ level should also be reflected in those electrophysiological tests meant to assess the functioning of saccule and utricle.

2.1 Clinical Symptoms of Meniere's disease

2.1.1 Type, degree and configuration of hearing loss

The audiological features of Meniere's disease are characterized by sensorineural hearing loss which is progressive as well as fluctuating in most of the cases. The other related symptoms include intolerance to loud sounds, feeling of aural pressure and diplacusis (Lee ta al, 1995). A study done by Stahle (1976) on 356 patients with advanced Meniere's disease have shown that the disease progress over time but reaches to an asymptotic level with mean pure tone average (PTA), speech recognition threshold (SRT) and speech discrimination scores (SDS) to 56 dBHL, 60

dBHL and 54% respectively. Retrospective investigations conducted by Frieberg et al. (1984) on 161 patients with Meniere's disease over 9 years have reported that the mean PTA was less than 30 dBHL. However caution to be taken while interpreting such data that beyond the age of 50 years, aging would be play as a confounding variable (Kotimaki et al, 2001). However data across studies have revealed that the prevalence of patients ended up having profound hearing loss solely due to Meniere's disease is much lesser ranging from 1 – 6% (Stahle, 1976; Shojaku et al., 1995).

The hearing loss in the early stages of idiopathic endolymphatic hydrops is characterized by rising pattern (Goodman, 1965; Eliachar et al., 1973) and eventually transforming into flat (Enander & Stahle 1967; Hedgecook, 1968; Thomas & Harrison, 1971; Eliachar et al., 1973; Meyerhoff, Paparella & Gudbrandsson, 1981) and rarely to sloping (Friberg et al., 1984) configurations over the period of time. The configuration of hearing loss would depend upon the duration of disease to a greater extent. It could be of rising (in 27%) or flat (55%) in the early Meniere's disease and becomes progresses to sloping in a few cases (Antoni-Candela, 1976). The most common pattern of audiogram is peak type (seen in 50%), then falling type (seen in 26%) and least common is a dip type (seen in 9%) as reported by Lee et al., 1995. However, a study done on 111 patients with Meniere's disease have shown that pattern of audiogram is not solely depends upon the duration of disease (Mateijsen et al, 2001).

A longitudinal investigation performed on 34 patients with Meniere's disease over 20 years have reported that the 47% of patients showed bilateral involvement by then (Frieberg, Stahle and Svedberg, 1984). Salvinelli et al (1999) followed up 49 patients with Meniere's disease and reported that with a mean of 7 years (5 to 12 years) after the onset of Meniere's disease 23 patients did show

bilateral symptoms, however the diagnostic criteria classified only 7 (14.3%) out of them as having true bilateral involvement. Hence it should be noted that the diagnostic criterion used across studies restricts the exact prediction of bilateral involvement in patients with Meniere's disease.

2.1.2 Tinnitus

Tinnitus in patients with Meniere's disease is predominantly of low frequency, but some of them have also reported high pitch tinnitus (Vernon et al., 1980; Kolbe et al., 2000). In general it is continuous during and just after the attack in most of the patients and they describe tinnitus as roaring, buzzing, ringing, or popping sound (Stouffer and Tyler 1990). Tinnitus is the most bothersome symptom at least in the early stages of Meniere's disease (Hagnebo et al., 1997). Generally tinnitus is found to be severe in patients with Meniere's disease and the loudness would increase overtime with the disease (Kolbe et al., 2000). Along with reduction in symptoms in some patients tinnitus is reported to be vanishing gradually (Vernon et al., 1980).

Kentala (1996) studied the prevalence of tinnitus in six major diseases resulting in vertigo and reported that tinnitus is predominant among patients with Meniere's disease than the other 5 conditions. An investigation on 564 individuals suffering from tinnitus due to a diversity of conditions revealed that the severity of tinnitus was more in individuals with Meniere's disease compared to other conditions (Stouffer & Tyler, 1990).

2.1.3 Vertigo

Vertigo in Meniere's disease tends to be episodic as well as true spinning and which is accompanied by nausea or vomiting in some of the cases (Alford, 1972). A

single vertigo attack last for 20 minutes to 24 hours (Alford, 1972; AAO-HNS, 1995). The course of vertigo during attack is described as the feeling of spinning sensation would reach to its peak within some minutes, persists as severe for a few hours and then gradually comes down to normal state over a few hours (Baloh, 1995). Even though vertigo remains mild and not bothersome between attacks, it becomes the most dangerous symptom among the three during attacks (Meyerhoff et al., 1981). In the early stages of Meniere's disease the number of vertigo spells is more, which can go beyond 30/year in 1/3 of the patient suffering from Meniere's disease (Haye & Quist-Hanssen, 1976).

Hagnebo et al (1997) investigated tinnitus aspects in 514 patients with Meniere's disease and reported the following: the duration of vertigo attack was less than 10 minutes in 20% individuals, 10-59 minutes in 36%, 1-4 hours in another 36%, more than 4 hours in 28%. Most of this patients reported that occurrence of vertigo is irregular (in 65%), however a few of them reported of occurring mostly in day time (23%), in the evenings (7%) and rarely at night time (5%). Friberg et al (1984) reported that the mean number of attacks per year remained 6-11/year up to 20 years from the onset of the disease and comes down to 3-4/year thereafter. Nevertheless a few researchers reported that vertigo will not be troublesome in 3 or more years after onset in nearly 71% of patients (Silvestein et al, 1989).

2.1.4 Drop attacks

Tumarkin (1936) have reported that patients with Meniere's disease often complaints of abrupt falling without losing consciousness. In general this symptom is seen in those who have Meniere's disease at its advanced stage or long-lasting conditions but rarely occurs inits early stage too (Baloh et al., 1990). Drop attacks

lasts for some seconds to one minute which is associated with hearing loss, aural pressure as well as tinnitus (Tumarkin, 1936). Even though not understood completely, the mechanism behind drop attacks is assumed to be related to the mechanical deformation of the otolithic organs which in turn stimulates vestibular nerves and initiates VOR (Vestibular Ocular reflex).

Black et al (1982) reported that the incidence of drop attacks in Meniere's disease is around 6-7%. However, Ballester et al (2002) studied Meniere's disease in 498 patients and revealed that incidence and severity of drop attack in patients aged greater than 65 depends upon the duration of Meniere's disease. The incidence was 11% among those with longstanding Meniere's disease and aged less than 65 years, however in those patients with greater than 65 years of age the incidence went up to 26%.

2.2 Audiological and Vestibular Test findings

2.2.1 Electrocochleography (ECochG)

One among the common application of ECochG involves comparing the amplitude of AP (Action Potential) to that of SP (Summating Potential) in patients suspected of having Meniere's disease/Endolymphatic hydrops (ELH). Enlarged SP/AP magnitude ratio to click stimulus is a positive finding for ELH (Eggermont, 1976). The sensitivity and specificity of SP/AP ratio was 62% and 95% respectively using transtympanic electrocochleography (Selmani, Pyykko, Ishizaki, & Ashammakhi, 2002). The incidence of abnormal increase in SP amplitude in Meneires disease has been estimated to be between 60-65% (Coats, 1987). Sensitivity and specificity of extra tympanic electrocochleography in the diagnosis of Meneires disease was found to be 71% and 96% respectively (Chung et al, 2004). Both

transtympanic approach and extra tympanic approach has lesser sensitivity with transtympanic approach being invasive in nature. The average summating potential to action potential (SP/AP) ratio was reported to be high in patients with significant endolymphatic hydrops in the cochlea. Yamamoto et al (2009) reported that the SP/AP ratio was not enlarged in some patients with a relatively short period from the onset of clinical symptoms to the electrocochleography examination in spite of significant endolymphatic hydrops in the cochlea. Considering these entire one may conclude that ECochG may not be a good tool to predict Meneires disease.

2.2.2 Otoacoustic Emissions (OAEs)

Equivocal findings in OAEs have been reported in individuals with Meniere's disease. In general OAEs are found to be absent in most of the cochlear pathologies exceeding 30-50 dBHL. Since Meniere's disease results in damage to the cochlea directly, OAEs is found to be abnormal / absent when the hearing loss exceeds 25 to 30 dB. However in contrast to this some studies have also reported that Transient Evoked Otoacoustic Emissions (TEOAEs) as well as Distortion Product Otoacoustic Emissions (DPOAEs) amplitudes are found to be either present like in normal or exceeding that of normal (Harris & Probst, 1991). Since there are equivocal results with respect to OAEs in Meniere's disease the diagnostic significance of OAEs is hampered.

2.2.3 Cochlear Hydrops Analysis Masking Procedure (CHAMP)

Cochlear Hydrops Analysis Masking Procedure (CHAMP) is a diagnostic tool to detect the presence of excessive tension on basilar membrane based on the principles of travelling wave movement. In this procedure clicks are presented alone as well as along with masking noise high-pass filtered at 8, 4, 2, 1 and 0.5 kHz. With

this masking noise the peak latency of wave V increases as the high-pass filter frequency moves from 8 KHz to 0.5 KHz. Nevertheless, due to increased mass and tension on the basilar membrane especially at the apex resulting in similar wave V latency for click alone and click with different masking procedures. The sensivity and specificity of CHAMP has been questioned and reported to 31% and 28% respectively (De Valck, Claes, Wuyts, Vande Heying, 2007). However the disadvantage of CHAMP responses is that it is affected by post auricular muscle response as well as with greater degree of hearing loss (severe- profound). Thus, the role played by does not become very useful in the diagnosis either.

2.2.4 Glycerol test

Osmotic diuretics have the capability to absorb endolymph and thereby reducing the pressure in the inner ear. This would result in an improved peripheral auditory and vestibular function. Hence such principle is used generally to confirm endolymphatic hydrops by administering osmotic diuretic agents like glycerol or urea after baseline audiometric testing.

The general clinical protocol recommended for glycerol test is administration of oral dosage of 1.2 ml of glycerol per kg of body weight with the addition of equal amount of physiologic saline (Lee, Paparella, Margolis and Le, 1995). A 10 dB improvement in two or more adjacent pure tone thresholds and a 12% improvement of speech recognition ability are considered to be positive glycerol test.

Positive findings in glycerol test are commonly seen in ears with Meniere's disease. Snyder (1974) administered glycerol test in patients suspecting endolymphatic hydrops and found that fifty percent of patients was found to have endolymphatic hydrops with positive test results. Akioka et al (1990) reported 47 %

of patients with Meniere's disease to have a positive glycerol dehydration test. Stahle and Klockhoff (1966) reported 60 % of patients with Meniere's disease were found to have positive tests, and that positive tests were only found in ears with Meniere's disease.

The findings of glycerol test may also depend upon the stage of Meniere's disease. Klockhoff and Lindblom (1986) stated that single doses of glycerol, 1.5 g/kg body weight orally, produced significant hearing threshold shifts in cases of Meniere's disease with fluctuating hearing loss. No effect was seen in more advanced Meneires cases with non-fluctuating flat loss or in cases of perceptive deafness of less specific types. The observations indicate that endolymphatic hypertension is of direct importance for the fluctuating hearing loss in Meniere's disease. A glycerol test may be adopted as a simple and rapid method for separation of reversible Meneires cases from irreversible cases of the disease and from other cases of perceptive deafness where endolymphatic hydrops is not involved.

2.2.5 Electronystagmography (ENG)

Electronystagmography (ENG) is a battery of test which is based on the principle of evoking nystagmus through various non harmful stimuli. The nystagmic movements of eyes are recorded by placing electrodes around the eyes. The ENG test battery consists of tests that are meant to assess the peripheral vestibular system (like Caloric test, Dix-Hallpike maneuver, and Positional test) and the central balance system (like Gaze test, Saccade test, Pursuit test, Optokinetic test, and failure of fixation suppression test) which assess the central and peripheral components of the balance system. The most frequently reported ENG findings in Meniere's disease were unilateral caloric weakness (49%), directional preponderance (36%), and

spontaneous and/or positional nystagmus (32%) whereas bilateral caloric weakness (BW) was reported in 36% of patients with bilateral hearing loss (Dobie, Snyder & Donaldson 1982). Desmond (2004) reported normal or strong caloric response in early stage of Meniere's disease, and attributed this finding to inflammation of the labyrinth. In individuals with long history of episodic vertigo, caloric test showed hypofunction on the affected side.

The reduced caloric response is a common finding among Meniere's disease cases with various percentage of occurrences across studies ranging from 59% (Stahle, 1975), 80% (Thomas & Harrison, 1971), and to 83% (Cawthorne & Hewlett, 1954) of unilateral Meniere's disease cases. However, directional preponderance (DP) was not taken into consideration in Stahle & Bergman (1967) investigation. The caloric test revealed unilateral weakness (UW) in 42.1% (Park, Migiaccio, Santina, Minor & Carey, 2005) and 50-90% of individuals with Meniere's disease (Black, 1980). They also reported of reduced caloric responses on the diseased side in 28% of the cases and completely abolished in 4%. A directional preponderance was seen in 13% and hyperreflexia on the diseased side in 5%. The spontaneous nystagmus was observed in 25% of the patients suffering from Meniere's disease (Haid, Watermeier, Wolf and Berg, 1995) and is usually direction-fixed, towards better hearing ear (Dix, 1969; Babin, 1979).

2.3 Vestibular Evoked Myogenic Potentials (VEMP)

The Cervical Vestibular Evoked Myogenic Potentials (cVEMP) is an inhibitory potential which can be recorded from the tonically contracted ipsilateral sternocleidomastoid muscle (SCM) in response to a loud monaural click or tone-burst. VEMP is characterized by a biphasic response with a positive peak namely p13 (latency at about 13 ms) and a negative peak namely n23 (latency at about 23ms) (Colebatch, Halmagyi and Skuse, 1994). Robertson & Ireland (1995) reported that the VEMP p13–n13 originates from the saccule and may travel along the inferior vestibular nerve to the vestibular nuclei. The anatomical pathway of cVEMP is illustrated in figure 2.1 (Uchino et al., 1997).

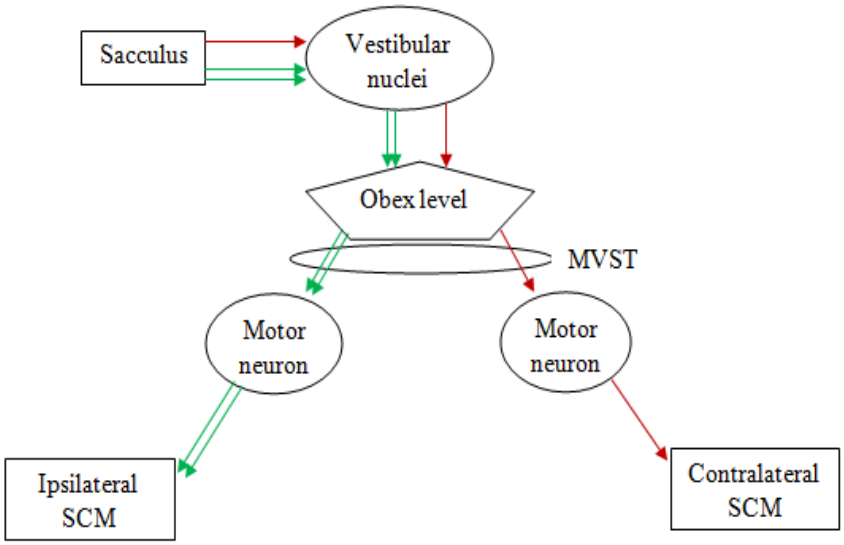

Figure 2.1. Anatomical pathway of cVEMP

It has been reported that anatomical pathway of cVEMP consists of saccular maccula, afferent inferior vestibular nerve, brainstem vestibular nuclei, descending medial vestibulo spinal tract and the motor neurons of sternocleidomastoid muscle. Acoustic stimulation of the vestibular system results in stimulation of sensory tissue in the saccule. These impulses then travel down the inferior vestibular nerve and reach

the vestibular nucleus in the brainstem. Impulses are then sent to the sternocleidomastoid muscle via the medial vestibulospinal tract (Colebatch, Halmagyi, Skuse (1994). Akin et al (2004) reported that the tonic state of SCM muscle is a vital factor in the recording method of the cVEMP, as the p13-n23 amplitude of cVEMP is proportional to the level of SCM muscle activity.

The diagnostic utility of Cervical Vestibular Evoked Myogenic Potentials (cVEMP) has been examined for the assessment of various vestibular disorders (Welgampola & Colebatch, 2003). The VEMP response has been clinically investigated in several pathological conditions, including acoustic neuromas, vestibular neuronitis, Meneires disease, sensorineural hearing loss, multiple sclerosis, and superior canal dehiscence syndrome.

The cVEMP has been promoted as a means of assessing integrity of saccular function. Vestibular evoked myogenic potential (VEMP) testing is currently being utilized in the assessment of a variety of vestibular etiologies. Many studies have shown the value of cVEMP in the assessment of saccular functions. The cVEMP is reported to be non-invasive, objective procedure, easy to perform and interpret, and does not result in patients' discomfort.

The neural pathway mediating the cVEMP differs from that of standard electronystagmographic evaluation being cVEMP to be sensitive to disorders affecting the inferior vestibular branch, which is the site of many vestibular schwannomas (Matsuzaki et al, 1997; Chen et al, 2002). Shimizu et al, 2000 reported that cVEMP is sensitive to lesions involving the saccule, inferior vestibular nerve, and descending vestibulospinal pathway.

The cVEMP abnormalities was found to vary across pathologies, however, in general, abnormal interaural amplitude differences and absent responses are most common findings in vestibular disorders. But abnormally low VEMP threshold is a common finding that has been reported in superior canal dehiscence syndrome and in Tullio phenomenon (Welgampola & Colebatch, 2005).

According to de Waele, Huy, Diard, Freyss and Vidal (1999) patients with Meniere's disease could have a saccular dysfunction. This saccular impairment correlated with low frequency hearing loss but not with canal paresis. VEMP testing is useful for detecting patients at risk, in patients with saccular lesion.

Various parameters which are considered for the assessment of VEMP include amplitude, latency, interpeak latency, asymmetry ratio and frequency tuning. In order to quantify the right/left amplitude difference and to normalize person-to-person variations, degree of asymmetry in amplitude can be calculated. However, there is a limitation to apply the value directly on clinical decisions because interaural amplitude difference ratio shows large variations even among normal subjects.

2.3.1 The Amplitude of cVEMP in Meniere's disease

There is a direct correlation between muscle tension and VEMP amplitude. More tonic the muscle tension, larger the cVEMP amplitude response. Amplitude-related parameters change according to the degree of tonic contraction of ipsilateral SCM, therefore latency is a more reliable parameter.

Numerous studies have examined the effects of Meniere's disease or endolymphatic hydrops on VEMP and the findings was found to vary across studies. The cVEMP may be reduced in amplitude or abolished in patients with endolymphatic hydrops in the vestibule (Lin et al, 2006). However, Young et al.

(2002) reported that augmentation of VEMP may be recognized in cases with extremely large endolymphatic hydrops in which the endolymphatic space contacts the stapes footplate.

Hassan (2011) conducted a study on 28 individuals with definite unilateral Meniere's disease and reported that the absolute amplitude of cVEMP is reduced in the affected ear of individuals with Meniere's disease when compared to their unaffected ear as well as ears of control groups. There was significant inter subject variability reported among individuals with Meniere's disease in the affected ear whereas homogenous amplitude was found among control group as well as in the unaffected ears of individuals with Meniere's disease. Hence the average data for individuals with Meniere's disase shown in this study may not be an actual representative of the group. More over the statistical tools used in this study lik t-test, Pearson's correlation coefficient may not be appropriate when considering the large standard deviation in the data.

Murofushi et al (2001) studied the impact of Mnieres diaese on cVEMP responses on 43 patients and found that cVEMP was absent in 15 of them (affected ear) and significantly reduced responses in 7 of them, hence accounting for a 51% amplitude related abnormality in this population of Meniere's disease.

Young, Haung and Cheng (2003) studied cVEMP responses in 40 patients with Meniere's disease and reported that the amplitude of cVEMP depends upon the stages of the disease. The stage of Meniere's disease was determined base on the four frequency pure tone average (0.5, 1K, 2K, 3K Hz) starting from less than 26 dB HL (Stage I), 26 – 40 dB HL (Stage II), 41 – 70 (Stage III) up to more than 70 dB HL (Stage IV). Among the six ears classified as stage 1, one showed augmented cVEMP indicating initial stages of the disease wherein which the stapes foot plate proximity

augments vibration of saccular structure. Among the 12 ears of stage II 2 were augmented, one was depressed and in 2 cVEMP was absent. Among the 17 ears of stage III 4 were depressed and in 3 it was absent. Among the 5 ears in stage IV responses were absent in 2 and depressed in one. Hence this study provides a crude conclusion that cVEMP responses may be associated with stages of the disease.

Rauch et al (2004) performed cVEMP testing on 34 patients with Meniere's disease and found that cVEMPs were present in 82% - 94% of affected ears and 97 % of the unaffected ears. The amplitude of cVEMP was significantly reduced in general when compared to the unaffected ear. This difference was more evident when 500 Hz was used as the stimuli when compared to 250 as well as 2k Hz stimuli.

2.3.2 The cVEMP Threshold in Meniere's disease

The cVEMP response in humans has been found to be present at high presentation levels. The cVEMP thresholds have been reported between 120–135 dB SPL (Welgampola & Colebatch 2001) and 75-105 dBnHL (Ochi & Ohashi, 2003) in response to click stimuli, 105–120 dB SPL in response to 1000 Hz tone burst stimuli (Welgampola and Colebatch, 2001) and 60 to 75 dBnHL in response to 250 Hz tone burst stimuli (Zapala & Brey, 2004).

The cVEMP threshold is elevated in ears with Meniere's disease. Rauch et al (2004) performed cVEMP testing on 34 patients with Meniere's disease and reported that cVEMP threshold is significantly shifted in patients with Meniere's disease in the affected ears. The elevation of threshold was more prominent when 500 Hz was used as stimuli. Sandhu et al (2011) conducted a detailed study on the cVEMP response indices in patients with Meniere's disease. Their study included 12 patients with unilateral Meniere's disease (8 definite & 4 probable Meniere's disease) and 8 normal individuals. The result of the study showed that amplitude of cVEMP was

significantly reduced in the affected ear irrespective of stimulus frequency. The maximum amplitude in definite Meniere's disease group was found for 750 Hz (54.1 μV), however including both the subgroup maximum amplitude of p13-n23 complex was found for 1000 Hz (0.8 μV) stimuli. The response rate across frequencies in the affect ear was 100% (500 Hz), 80% (250 Hz), 88% (750 Hz), 88 % (1000 Hz), 75% (1.5 KHz), 25% (2 KHz). However the maximum amplitude in the unaffected ear was found to be at 500 Hz (0.86 μV) as like in the control group. Hence in conclusion the threshold for cVEMP across frequency moved higher in dB HL and the significance of this is shown more at 500 Hz stimuli.

2.3.3 The cVEMP Latency in Meniere's disease

Equivocal findings in cVEMP latencies have been reported in individuals with Meniere's disease. It has been found that in patients with Ménière's disease the latency of the initial positive and negative peaks is unlikely to change as saccular hydrops does not affect electrical or acoustic transmission (Rauch et al. 2004). The authors de Waele, Huy, Diard, Freyss, and Vidal (1999) and Osei-Lah et al. (2008) conducted cVEMP assessment in individuals with Meniere's disease and found that p13 as well as n23 latency is not deviated from that of control group. Another study by Akkuzu, Akkuzu, and Ozluoglu (2006) pointed out that the significant prolongation of p13 peak is occurring in only 10% of the total Meniere's disease population under their study.

However in contradiction to the above studies, Hassan (2011) reported prolonged latency of both p13 and n23 peaks of cVEMP in the affected ears of individuals with Meniere's disease. The latency difference between unaffected ears of individuals with Meniere's disease and ears of control group was found to be non-significant. Murofushi et al (2011) studied cVEMP responses in 11 individuals with

Meniere's disease and reported prolonged P13 latencies in 2 subjects where response itself was absent in another 9 subjects. However latencies on the unaffected side were not deviated in 9 subjects in whom responses were present. Murofushi et al (2001) evaluated cVEMP responses in 43 individuals with Meniere's disease and reported that one among the 43 showed prolonged p13 latency where 15 had absent responses.

2.3.4 The cVEMP Amplitude Asymmetry Ratio in Meniere's disease

Murofushi and Kaga (2009) defined asymmetry ratio as 100 X (Au − Aa)/(Au + Aa), in which Au and Aa are the amplitudes measured at the unaffected and affected side, respectively . The cVEMP amplitude asymmetry should exceed 34% to be pathological. . Welgampola and Colebatch (2001) gave values for the asymmetry range for click stimulation in normal subjects which was about 30% for subjects between 20 and 40 years of age, 45% for 40–60 years and even larger for subjects older than 60 years.

Hansson (2011) reported that the interaural amplitude ration (IAR) of individuals with Meneire's disease discloses a significant difference when compared to the of control group that IAR was lesser in the latter group. However large individual variability in IAR is foun among individuals with Meneire's disease.

2.3.5 The cVEMP frequency tuning in Meniere's disease

The cVEMP demonstrate frequency tuning to air conduction tone bursts. Akin et al (2003) reported that frequency tuning can be done by obtaining response characteristics and thresholds of tone burst-evoked cVEMPs. The sensitivity of the p13-n23 biphasic waves of VEMP is found to be at a low frequency, as the frequency dynamics between VEMP and the saccular nerve is similar. The frequency dynamics of acoustically responsive vestibular afferents, thought to be saccular afferents, were

identified between 500 and 1,000 Hz in cats (McCue & Guinan, 1995) and between 200 and 400 Hz in squirrel monkeys (Young, Fernandez & Goldberg, 1977).

The cVEMP responses in humans have been found to show optimal frequency sensitivity. Optimal stimulus frequencies have been reported at 300–350 Hz (Todd et al, 2000), 500 Hz (Rauch et al, 2004) and 700 Hz in normal subjects (Welgampola & Colebatch, 2001). Because the cVEMP responds optimally at specific frequencies, VEMP threshold response curves can be generated. These threshold response curves are showing promise in the identification of Meniere's disease and discrimination between the symptomatic and asymptomatic ear (Rauch et al, 2004; Lin et al, 2006). Welgampola & Colebatch (2001) obtained cVEMP responses using tone bursts at 100 Hz increments between 200 Hz and 1000 Hz and obtained largest cVEMP amplitude in response to tone bursts between 600 Hz and 1000 Hz, with a mean of 700 Hz.

The cVEMP frequency tuning has been reported to be maintained in some peripheral vestibular pathology. Taylor, Bradshaw, Halmagyi and Welgampola (2012) investigated frequency tuning for cVEMP in individuals with semi circular canal dehiscence and reported that, cVEMPs were tuned to lower frequencies with greatest amplitude at 500 Hz.

Altered frequency tuning of cVEMP response has been reported in ears with Meniere's disease. Rauch , Zhou, Kujawa, Guinan and Herrmann (2004) examined vestibular evoked myogenic potential testing using ipsilateral broadband click and short tone-burst stimuli at 250, 500, 1,000, 2,000, and 4,000 Hz on normals and in unilateral Meniere's disease patients. Results revealed that normal subjects showed a frequency-dependent vestibular evoked myogenic potential threshold, with best response (frequency tuning) at 500 Hz. Affected Meniere's ears showed significantly

increased vestibular evoked myogenic potential thresholds with less tuning apparent at 500 Hz. Node, Seo, Miyamoto, Adachi, Hashimoto and Sakagami (2005) also reported that frequency tuning of cVEMP were noted at 500 Hz for control group (consisted of normal hearing and balance function) and at 1000 Hz in the group consisted of individuals with endolymphatic hydrops.

Altered frequency tuning in individuals with Meniere's disease is also found to be associated with type of Meniere's disease. Sandhu et al. (2012) investigated on the frequency dynamics of cVEMP in 12 individuals with Meniere's disease. Out of 12, 8 were diagnosed as having definite Meniere's disease whereas remaining 4 had probable Meniere's disease. The cVEMP were recorded with 250, 500, 750, 1000, 1500, 2000, 3000 and 4000 Hz tone bursts from all participants. The results of their study showed that the frequency tuning was shifted significantly to 750 Hz only in individuals with definite Meniere's disease where at this stimulation frequency the mean amplitude of cVEMP was largest. However, in individuals with probable Meniere's disease the frequency tuning was towards 500 Hz. The frequency tuning of cVEMP in the ear contralateral ear to ears with Meniere's disease showed frequency tuning similar to that observed in control group.

The vestibular evoked myogenic potentials can indicate abnormalities in the affected and asymptomatic ears in patients with diagnosis of unilaterally defined Ménière's disease (Ribeiro et al, 2006). Despite the fact that various other tests are available for the assessment of Meniere's disease, frequency tuning of vestibular evoked myogenic potentials can provide more reliable information as the frequency dynamics of VEMP depend on the resonance frequency of the saccular membrane (Node et al, 2005) which in turn depends upon the integrity of saccule. VEMP testing may be more specific in locating lesions by revealing abnormal function of the

saccule and/or the inferior vestibular nerve. Hence, VEMP testing could be sensitive and able to detect minor changes in the function of the vestibular system.

The combination of different parameters in cVEMP may better aid in diagnosis of Meniere's disease.

CHAPTER - 3

METHOD

The purpose of the present study was to find out the best combination of Cervical Vestibular Evoked Myogenic Potential (cVEMP) parameters to assist in diagnosis of Meniere's disease.

3.1 Participants

Participants in the study were divided into two groups

1. **Experimental group:** The experimental group consisted of 18 participants (11 males & 7 females) between the age ranges of 21 – 61 years with a mean age of 42.56 years.
2. **Control group:** The control group consisted of 18 participants (11 males & 7 females) aged between 21 – 61 years with the mean age range of 41.25 years

3.2 Participant's selection criterion for experimental group

1. All participants were diagnosed as having unilateral minimal to moderately severe rising/flat sensorineural hearing loss based on pure tone audiometry.
2. The diagnosis of definite Meniere's disease was made based on the guidelines given by American Association of Otolaryngology - Head and neck surgery (1995) and report from the otorhinolaryngologist.
3. All the participants had the classical triads of Meniere's disease (hearing loss, episodic vertigo and tinnitus).
4. All participants had "A" type tympanogram with present or elevated acoustic reflexes in both ears.

5. All participants had an Uncomfortable level (UCL) for speech greater than 100 dBHL in both ears.
6. The Participants did not have any evidence of space occupying lesion (based upon the results obtained by the auditory brainstem response and neurologist report).
7. The Participants did not have a history of presence of ear pain, ear discharge, and exposure to loud levels of noise.
8. The Participants did not have had a history or presence of any neurological problems.
9. The Participants did not have any other neuromuscular problems

3.3 Participant's selection criterion for control group

1. All the participants had their pure tone hearing thresholds within 15 dBHL for frequencies between 250 Hz to 8000 Hz.
2. All participants had "A" type tympanogram with present or elevated acoustic reflexes in both ears.
3. All participants had an Uncomfortable level (UCL) for speech greater than 100 dBHL in both ears.
4. The Participants did not have any evidence of space occupying lesion (based upon the results obtained by the auditory brainstem response and neurologist report).
5. The Participants did not have a history of presence of ear pain, ear discharge, and exposure to loud levels of noise.
6. The Participants did not have a history or presence of any other otological or neurological problems
7. The Participants did not have any other neuromuscular problems.

8. The Participants did not have any complaint or history of dizziness, vertigo, tinnitus or headache.

3.4 Instrumentation

1. A calibrated two channel GSI-61diagnostic audiometer with TDH – 39 headphones and B-71 bone vibrator was used for threshold estimation and for finding out Uncomfortable level (UCL) level for all the participants.
2. Calibrated GSI TYMPSTAR Immittance meter was used for conducting tympanometry and reflexometry.
3. An Intelligent Hearing Systems (IHS version 4.3.02) was used for recording air conducted auditory brainstem responses (Click evoked) and cervical VEMP (Tone burst evoked). Eartone 3 – An insert earphone was used to deliver the air conduction click stimuli.

3.5 Test Environment

All the audiological tests were conducted in the acoustically treated rooms and noise levels during the testing were within permissible limits (ANSI, 1991).

3.6 Procedure

Case history: A thorough case history was taken for each client before testing. The participants were asked about the sign and symptoms related to vestibular disorders.

Pure tone thresholds: Pure tone thresholds were obtained using modified version of Hughson and Westlak procedure (Carhart&Jerger, 1959) at octave frequencies between 250 Hz to 8000 Hz for air conduction and between 250 Hz to 4000 Hz for bone conduction.

Tympanometry: Immittance audiometry was performed in both ears using a probe tone frequency of 226 Hz. Tympanometry was carried out initially and

then acoustic reflex thresholds were measured for 500, 1000, 2000 and 4000 Hz stimuli ipsilaterally as well as contralaterally.

Uncomfortable level: The Uncomfortable level (UCL) was obtained in both ears for air conducted speech stimuli using ascending method.

Auditory brainstem evoked responses: Two channel ABR recording was done for a click of 100µsec stimuli at 90 dB nHL with the rarefaction polarity. Total number of sweeps used for recording was kept as 2000 with repetition rates of 11.1/sec and 90.1/sec. The gain settings of the ABR recording were kept as 100,000 with a filter setting of 100 – 30000 Hz and by keeping 50 Hz notch filter on.

Cervical Vestibular Evoked Myogenic Potential (cVEMP): The electrode sites were cleaned with abrasive gel prior to the VEMP recording. The silver chloride disc type electrodes were used along with appropriate conduction gel. The non-inverting (Positive) electrode was placed in the midpoint of the sternocleidomastoid muscle of the side being stimulated whereas the inverting (Negative) electrode was placed on the sternoclavicular junction. The ground electrode was placed on the lower forehead. Surgical tape was used to keep the electrodes on respective sites to avoid any kind of movement during acquisition. The recording protocol for cVEMP is given below in table 3.1

Table 3.1

Recording protocol for Cervical Vestibular Evoked Myogenic Potential (cVEMP)

Parameters	**Specifications**
Type of stimuli	Tone burst (2-0-2 cycles)
Intensity	At 95 dBnHL initially and decreasing the intensity in case of response till the threshold. The intensity is reduced in 5dB steps until the threshold is reached at each frequency.
Repetition rate	5.1/sec
Polarity	Rarefaction
Transducer	Insert ear phone (ER-3A)
Total number of stimuli	200
Analysis time	60 msec including 10 msec pre stimulus recording
Filter setting	High pass: 30Hz Low pass: 1500Hz
Notch filter	Off
Amplification	5,000
Number of channels	Single channel
Electrode montage	Non-inverting electrode (+): midpoint of the sternocleidomastoid muscle of the side being stimulated. Inverting electrode (-): sternoclavicular junction. Ground electrode: forehead

The instruction given to the participants during test was to sit straight and turn their head to the opposite side of the ear in which stimulus was presented, so as to activate ipsilateral sternocleidomastoid (SCM) muscle to obtain reliable and greater amplitude. They were also instructed to maintain the same posture throughout the test run. In order to assist them in maintaining the tonicity of the sternocleidomastoid muscle during test run, a visual feedback was provided using the EMG (Electromyograph) facility of the Intelligent Hearing Systems (IHS) instrument. This visual feedback would indicate adequate muscle tension (Between 50 µv to 100 µv) with a green light and under/over muscle tension with a red light. This monitoring system ensures that the responses recorded are neural responses and not the muscle responses.

The cVEMP recording for all the participants were started with a stimulus of 250 Hz tone burst and threshold estimation was done. Then the same procedure was continued for 500 Hz, 1000 Hz and 2000 Hz stimuli. Whenever there was an absent cVEMP responses at any of these frequencies, the recordings were not terminated but completed it with all the four target frequencies and estimated threshold at those frequencies where it was present.

3.7 Analysis

Analysis of vestibular evoked myogenic potentials

- Absolute latency and peak-to-peak amplitude of p13 and n23 was noted for each participant for each frequency and intensity in both the ears. The typical cVEMP response is shown in figure 3.1.

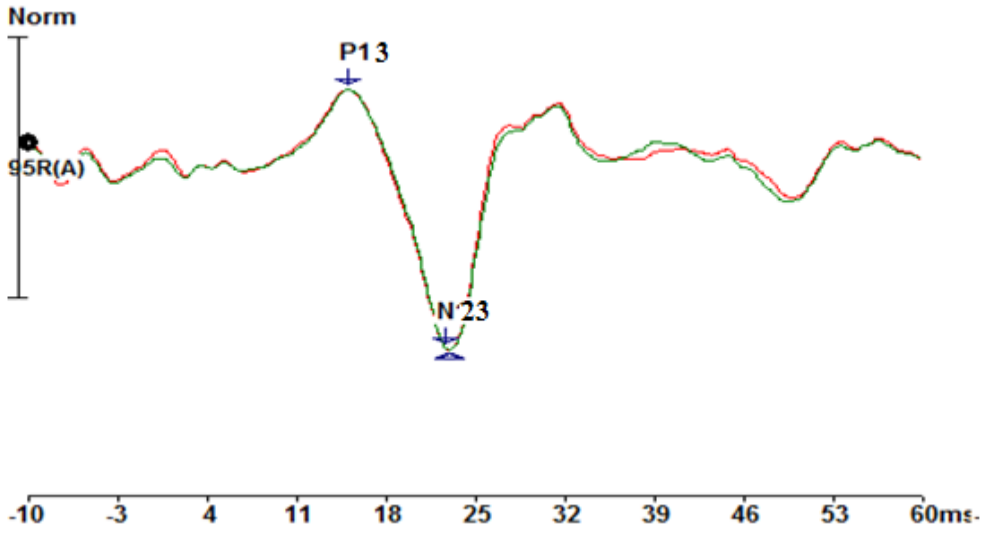

Figure 3.1. Typical cVEMP response from a normal hearing participant at 500 Hz 95 dB nHL

- The threshold of cVEMP across all frequencies was documented for all participants in both the ears.
- The frequency tuning of cVEMP across all participants was determined based on the presence of cVEMP or amplitude of cVEMP in both the ears.

CHAPTER - 4

RESULTS

The present study was conducted with the aim of identifying the most sensitive combination of cVEMP parameters to aid in the diagnosis of Meniere's disease. In specific the objectives were to determine the best combination parameter among the threshold, latency and frequency tuning of the cervical VEMP.

4.1 Vestibular evoked myogenic potentials findings in Control group

4.1a. cVEMP test results

The cVEMP was recorded from all the participants at different frequencies. There was a differential effect of presence/absence of cVEMP responses at different frequencies.

The cVEMP response obtained from right as well as left ears of one participant in the control group at intensity of 95 dB nHL across frequencies 250, 500, 1000 and 2000 Hz are shown in figure 4.1.

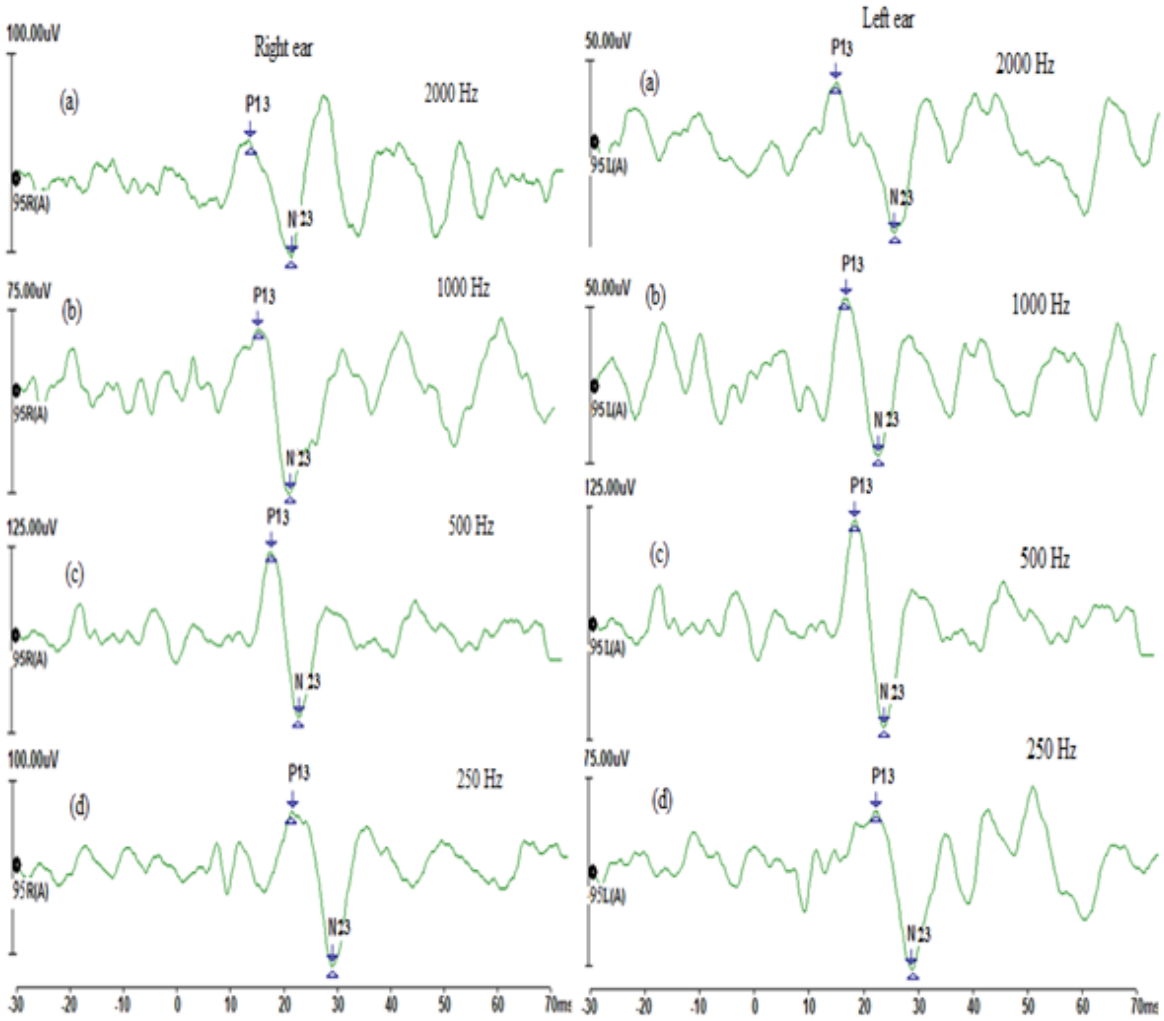

Figure 4.1. The cVEMP response from right and left ear of one of the participant in the control group at an intensity of 95 dB nHL across frequencies. The left most figure shows cVEMP responses from right ear and right most figure shows cVEMP responses from left ear. (a) cVEMP responses at 2000 Hz, (b) cVEMP responses at 1000 Hz, (c) cVEMP responses at 500 Hz, (d) cVEMP responses at 250 Hz.

The latency of p13 peak, n23 peak and amplitude of p13-n23 complex were measured at 250 Hz, 500 Hz, 1000Hz and 2000 Hz. The cVEMP responses were present in all ears (N= 36) at 500 Hz and 1000 Hz tone burst stimulation (response rate of 100%) whereas with 250 Hz stimulation the response rate was 88.89% (N=32) and at 2000 Hz the response rate was 33.33% (N= 12). The figure 4.2 illustrates the

response rate of cVEMP response in the control group across experimental frequencies.

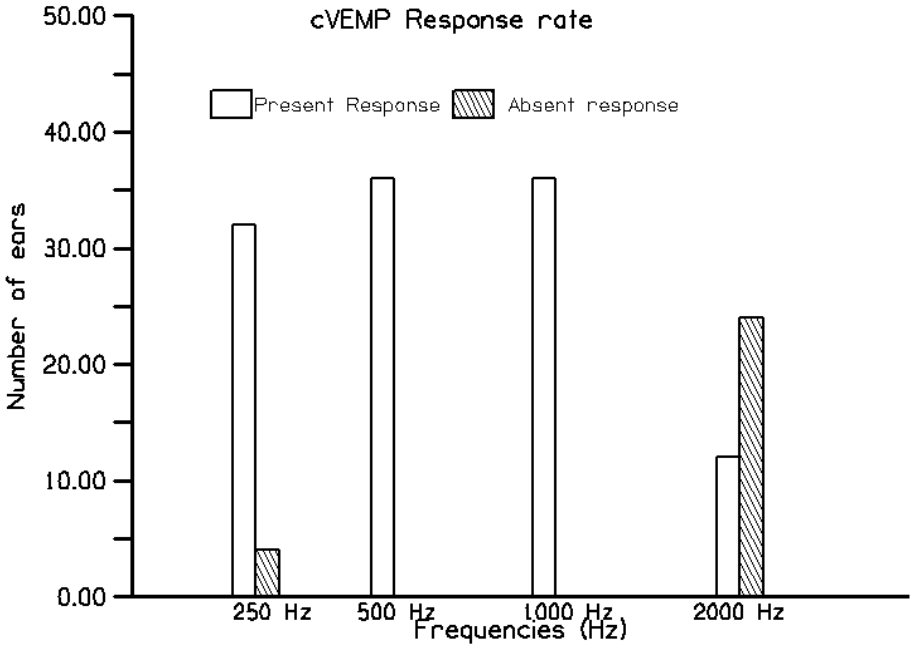

Figure 4.2. Response rate of cVEMP response in the control group across experimental frequencies.

Descriptive statistics was done to find out mean and standard deviation for p13 and n23 latencies and amplitude of p13-n23 complex for p13-n23 complex at 250 Hz, 500 Hz, 1000 Hz and 2000 Hz stimulus frequencies. The mean and standard deviation of the latency of p13 & n23 peaks and amplitude of p13-n23 complex are shown in table 4.1.

Table 4.1.

Mean and standard deviation of latency of p13, n23 peaks and amplitude of p13-n23 complex of control group combined for right and left ears

Parameters	*250 Hz*		*500 Hz*		*1000 Hz*		*2000 Hz*	
	Mean (N=32)	SD	Mean (N=36)	SD	Mean (N=36)	SD	Mean (N=12)	SD
p13 latency (msec)	18.91	1.69	15.83	1.42	14.41	1.52	13.57	1.48
n23 latency (msec)	27.57	1.55	23.63	1.75	21.92	1.56	22.76	1.63
Amplitude of p13-n23 complex (µv)	39.14	18.44	57.61	28.97	41.81	23.78	23.14	4.03

Note: 'N': Total number of ears where the particular response is present; 'SD': Standard deviation'.

It can be seen from the table 4.1 that the p13-n23 complex amplitude was largest at 500 Hz stimulation frequency followed by 1000 Hz and 250 Hz. The least amplitude of p13-n23 complex was observed with 2000 Hz stimulation frequency.

4.1b. Threshold of cVEMP in normal subjects

Threshold of cVEMP was estimated across 250 Hz, 500 Hz, 1000 Hz and 2000 Hz in 5 dB steps starting from 95 dB HL. Threshold was considered as the lowest intensity in dB HL at which p13 and n23 peaks are identifiable. The figure 4.3 represents the mean and standard deviation of cVEMP threshold across four stimulus frequencies combined for right and left ears.

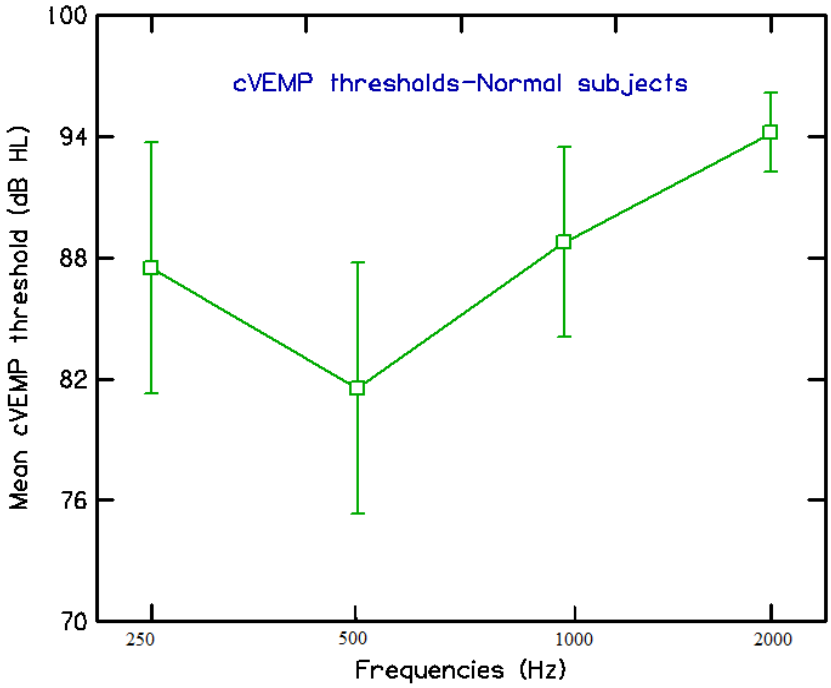

Figure 4.3. Representing the mean and standard deviation of cVEMP threshold across four stimulus frequencies combined for right and left ears

It can be observed from the figure 4.3 that the mean lowest threshold of cVEMP is for 500 Hz frequency when compared to the other test frequencies used in this study. The second lowest threshold of cVEMP is elicited by using 250 Hz followed by 1000 Hz and highest cVEMP threshold is obtained at 2000 Hz.

The statistical significance of the difference in cVEMP threshold across stimulation frequency within group was evaluated using Wilcoxon signed rank test. This test was selected due to the unequal number of ears in each group. Since multiple number of Wilcoxon signed rank tests were done between cVEMP parameters Bonferroni's correction was applied. After Bonferroni correction the adjusted p value was 0.01. After applying Bonferroni's correction it was found that cVEMP thresholds at 500 Hz is significantly different from cVEMP thresholds at 250, 1000 and 2000 Hz (the p values are provided in table 4.2). Hence it can be concluded that cVEMP threshold at 500 Hz is significantly lower when compared to other frequencies.

Table 4.2

The p values for Wilcoxon signed rank test performed on cVEMP thresholds across frequencies within control group

Sl no	Parameters compared		P value
	Parameter 1	Parameter 2	
1	cVEMP threshold at 250 Hz	cVEMP threshold at 500 Hz	0.001
2	cVEMP threshold at 250 Hz	cVEMP threshold at 1000 Hz	0.284
3	cVEMP threshold at 250 Hz	cVEMP threshold at 2000 Hz	0.019
4	cVEMP threshold at 500 Hz	cVEMP threshold at 1000 Hz	0.000
5	cVEMP threshold at 500 Hz	cVEMP threshold at 2000 Hz	0.002
6	cVEMP threshold at 1000 Hz	cVEMP threshold at 2000 Hz	0.010

Note: 'cVEMP': Cervical Vestibular Evoked Myogenic Potential

4.1c. Frequency Tuning of cVEMP in normal subjects

Frequency tuning of cVEMP refers to the stimulation frequency at which largest amplitude of p13-n23 complex is obtained at 95 dB nHL. The figure 4.4 represents the mean and standard deviation of amplitude of p13-n23 complex across stimulation frequency at 95 dB HL.

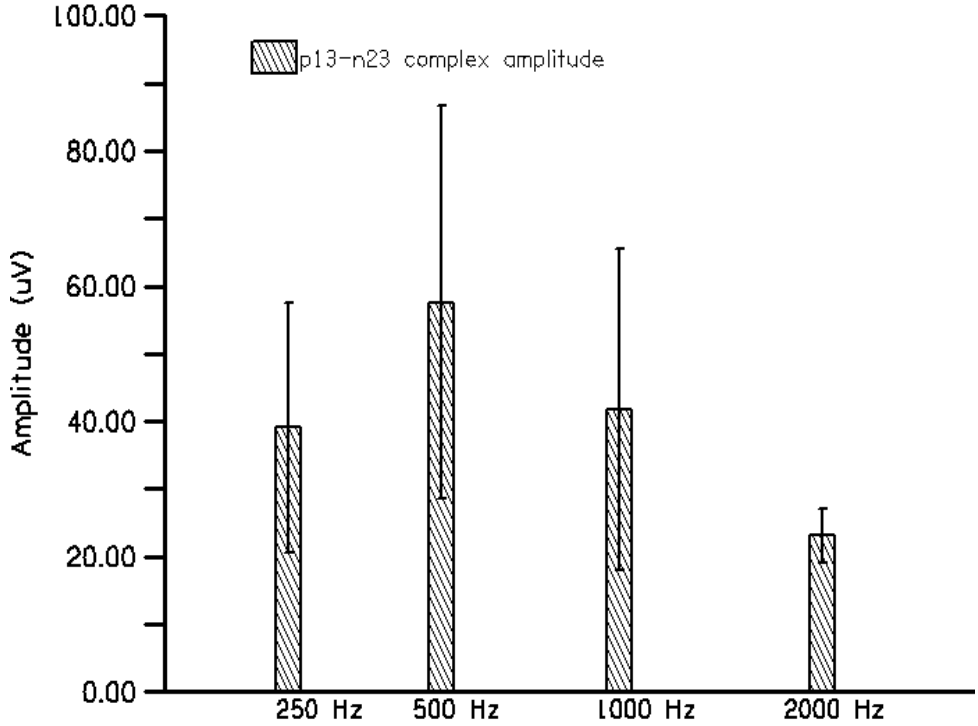

Figure 4.4. Mean and standard deviation of p13-n23 complex amplitude of control group combined for right and left ears.

It is evident from the figure 4.4 that the amplitude of p13-n23 complex at 95 dB HL is largest at 500 Hz stimulation frequency which was followed by 1000 Hz and 250 Hz. The p13-n23 complex amplitude is least at 2000 Hz. To document the statistical significance of the difference in amplitude across stimulation frequencies within group Wilcoxon signed rank test was performed. Since multiple number of Wilcoxon signed rank test was done a Bonferroni correction was applied. After Bonferroni correction the adjusted p value was 0.01. After applying B onferroni's correction it was found that amplitude of p13-n23 complex at 500 Hz is significantly different from the amplitude of p13-n23 complex at 250, 1000 and 2000 Hz (the p values are provided in table 4.3). It is evident from the table 4.3 and subsequent

statistical tests that amplitude of p13-n23 complex is significantly larger than other stimulation frequencies used in this study.

Table 4.3

The p values for Wilcoxon signed rank test performed on cVEMP thresholds across frequencies within control group

Sl no.	Parameters compared		P value
	Parameter 1	Parameter 1	
1	Amplitude of p13-n23 complex at 250 Hz	Amplitude of p13-n23 complex at 500 Hz	0.009
2	Amplitude of p13-n23 complex at 250 Hz	Amplitude of p13-n23 complex at 1000 Hz	0.537
3	Amplitude of p13-n23 complex at 250 Hz	Amplitude of p13-n23 complex at 2000 Hz	0.010
4	Amplitude of p13-n23 complex at 500 Hz	Amplitude of p13-n23 complex at 1000 Hz	0.000
5	Amplitude of p13-n23 complex at 500 Hz	Amplitude of p13-n23 complex at 2000 Hz	0.002
6	Amplitude of p13-n23 complex at 1000 Hz	Amplitude of p13-n23 complex at 2000 Hz	0.060

4.1 Vestibular findings in individuals with Meniere's disease

The 18 subjects with unilateral Meniere's disease participated in the present study. The details of the participants with respect to their age, gender, pattern of hearing loss in the affected ear are given in table 4.4.

Table 4.4

Demographic details pattern of hearing sensitivity in the affected ear of the individuals with unilateral Meniere's diseas

S. No	Age (years)	Sex	Affected Ear	Air conduction thresholds (dB HL)						ABR
				250 Hz	500 Hz	1kHz	2kHz	4kHz	8kHz	
1	56	M	Left	55	45	40	30	30	35	N
2	32	M	Right	35	30	30	20	15	20	N
3	61	F	Left	60	50	55	45	35	45	N
4	38	F	Right	40	45	40	35	40	55	N
5	51	M	Left	65	50	50	35	40	45	N
6	21	M	Right	30	25	20	15	20	15	N
7	46	M	Right	50	40	40	30	30	35	N
8	35	F	Left	65	65	55	50	65	55	N
9	44	M	Left	35	30	25	25	15	25	N
10	47	M	Left	65	50	45	40	35	45	N
11	42	M	Right	70	60	50	55	60	65	N
12	39	F	Right	40	50	35	30	20	25	N
13	45	F	Left	65	60	50	55	50	65	N
14	42	M	Left	45	35	20	15	20	20	N
15	31	M	Right	30	30	25	15	10	15	N
16	50	F	Right	50	35	25	30	30	25	N
17	35	F	Right	40	40	35	20	25	20	N
18	51	M	Left	55	60	55	60	65	60	N

Note: 'F': Female; 'M': Male; 'N': Normal; 'ABR': Auditory Brainstem Response.

From the table 4.4 it is clear that individuals with Meniere's disease had a hearing loss ranging from minimal to moderately severe sensorineural hearing loss and all the participants had presence of ABR.

4.2a. cVEMP test results

The cVEMP response waveforms from two participants in the experimental group representing presence and absence of cVEMP are depicted in figure 4.5.

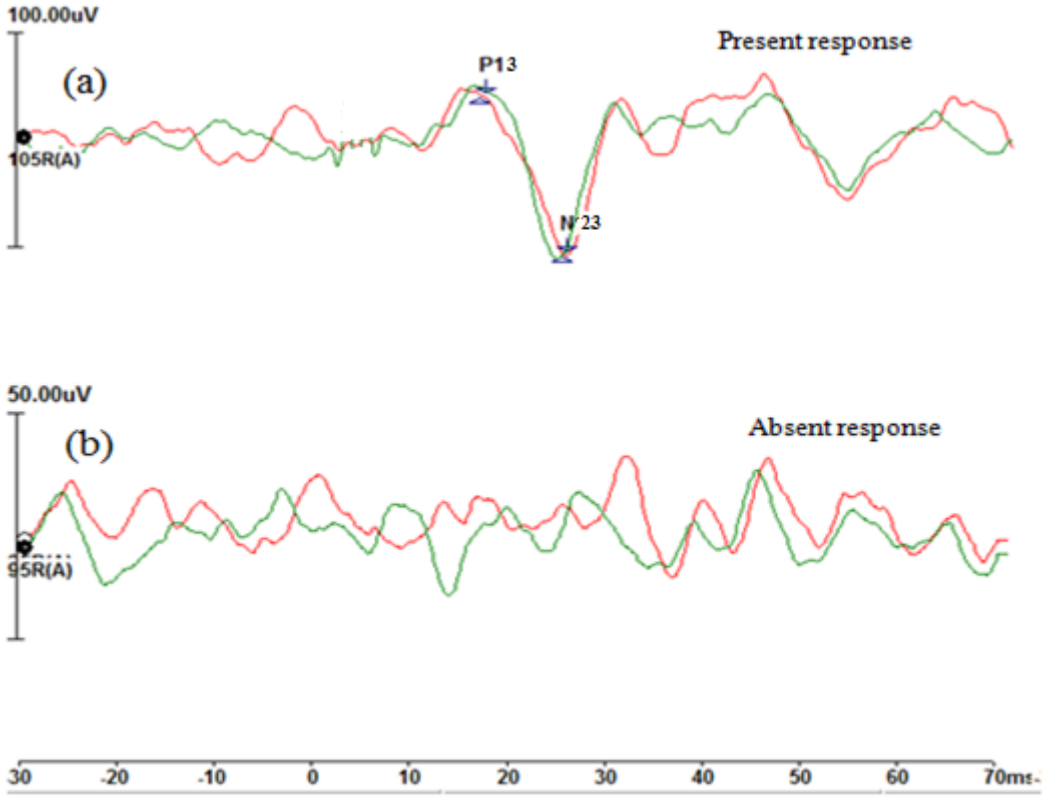

Figure 4.5. The cVEMP response with stimulation frequency of 500 Hz tone burst at 95 dB nHL from the two different affected ears of individuals with Meniere's disease (a) Presence of cVEMP response and (b) Absence of cVEMP response.

Among the total 18 ears with Meniere's disease, in 11 ears the cVEMP was absent at all the frequencies. Rest of the ears cVEMP was present at one or more

frequencies. Among the total 18 ears, 2 (11.11%) of them had cVEMP present at 250 Hz, 4 (22.22 %) of them had cVEMP present at 500 Hz and 5 (27.78 %) of them had cVEMP present at 1000 Hz. The cVEMP could not be elicited with 2000 Hz stimulation frequency in ears with Meniere's disease. Three ears (16.67%) with Meniere's disease had absent cVEMP responses at 500 Hz but present at other frequencies (two of them had at 1000 Hz and one had at 250 Hz).

The latencies of p13 and n23 peaks, amplitude of p13-n23 complex were calculated in ears with Meneiere's disease (experimental group). Table 4.5 represents the mean and standard deviation of latencies of p13, n23 peaks and amplitude of p13-n23 complex in ears with Meneiere's disease (experimental group).

Table 4.5

Mean and standard deviation of latency of p13 & n23 peaks, amplitude of p13-n23 complex in ears with Meneiere's disease

Parameters	*250 Hz*		*500 Hz*		*1000 Hz*		*2000 Hz*	
	Mean (N=2)	SD	Mean (N=4)	SD	Mean (N=5)	SD	Mean (N=0)	SD
p13 latency (msec)	17.25	1.34	15.25	1.72	15.17	1.49	NR	NR
n23 latency (msec)	26.00	0.85	23.18	3.04	21.60	1.67	NR	NR
Amplitude of p13-n23 complex (µv)	24.34	5.47	21.90	7.65	25.87	11.35	NR	NR

Note: 'N': Total number of ears where the particular response is present; 'SD': Standard deviation'; 'NR': No Response.

The table 4.5 reveals that the p13-n23 complex amplitude is slightly better with 1000 Hz stimulation frequency when compared to other stimulation frequencies experimented in this study. It also reveals a trend of decreasing p13 and n23 peak latency with increasing stimulation frequency as seen in control group. This trend can be better observed at 250 Hz versus other stimulation frequencies where the mean p13 peak latency is more compared to other frequencies. Unlike control group the cVEMP responses could not be elicited at 2000 Hz in any of the ears with Meniere's disease. The same can be visualized in figure 4.6.

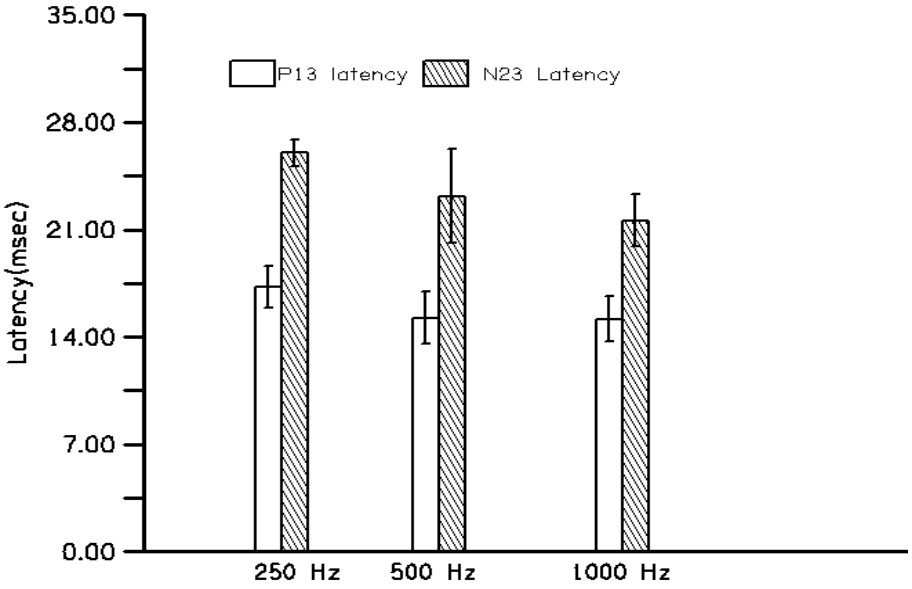

Figure 4.6. Mean and standard deviation of p13 latency and n23 latency ears with Meneiere's disease across experimental frequencies.

To know whether the latency of cVEMP obtained in individuals with Meniere's disease were significantly different from control group, Kruskal-Wallis test was done. The details of Kruskal-Wallis test is given in table 4.6.

Table 4.6

The p values for Kruskal-Walllis test performed on p13 and n23 peak latencies across frequencies in ears with Meniere's disease

Sl no.	Frequency	Parameters compared	P value
1	250 Hz	P13 latency	0.14
2		N23 latency	0.15
3	500 Hz	P13 latency	0.39
4		N23 latency	0.91
5	1000 Hz	P13 latency	0.18
6		N23 latency	0.57

It can be seen from table 4.6 that p13, n23 peak latency for 250 Hz, 500 Hz and 1000 Hz between the control and experimental group were significantly not diffrernt from each other.

4.2b1. The cVEMP threshold in ears with Meneiere's disease

The cVEMP threshold was also estimated across stimulation frequencies in 5 dB steps starting from an intensity of 95 dB HL. The figure 4.7 represents the mean and standard deviation of the cVEMP thresholds across stimulus frequencies.

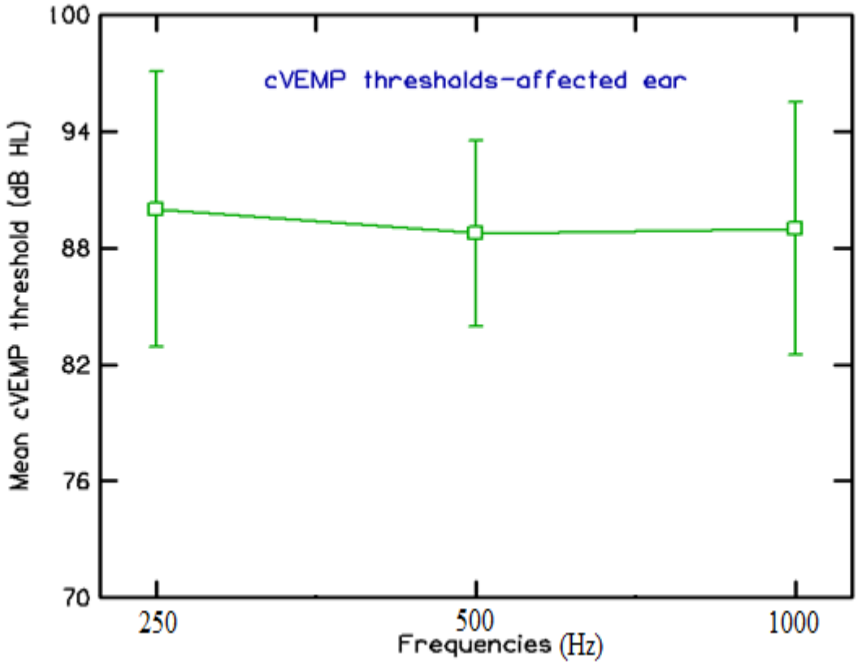

Figure 4.7. Mean and standard deviation of cVEMP thresholds across stimulation frequencies in ears with Meneiere's disease

It can be seen from the figure 4.7 that the cVEMP thresholds in ears with Meneiere's disease are grossly similar across stimulation frequencies. To know the statistical significance of the difference in mean cVEMP threshold across stimulation frequency within group Friedman's test was performed. The Friedman's test revealed

that there is no significant difference within the group in terms of cVEMP threshold across stimulation frequencies (p=0.358).

To know whether the cVEMP threshold at different frequencies were different in the control group and ears with Meneiere's disease Kruskal-Wallis test was done. The details of the Kruskal-Wallis test is given in table 4.7.

Table 4.7

The p values for Kruskal-Walllis test performed on cVEMP threshold across frequencies in ears with Meniere's disease

Sl no.	Frequency	Parameters compared	P value
1	250 Hz	cVEMP threshold	0.83
2	500 Hz	cVEMP threshold	0.02
3	1000 Hz	cVEMP threshold	0.59

It can be seen from the table 4.7 that the cVEMP threshold at 500 Hz for individuals with Meniere's disease is significantly different compared to the control group. However the cVEMP thresholds at 250 Hz and 1000 Hz between control group and ears with Meniere's disease were not significantly different from each other.

4.2b2. Frequency tuning of cVEMP in ears with Meneiere's disease

Similar to the analysis done on cVEMP response of the control group, the frequency tuning of cVEMP in ears with Meneiere's disease (experimental group) was estimated based on the stimulation frequency with which largest amplitude at 95 dB HL across stimulus frequency is obtained. The figure 4.8 represents the mean and standard deviation of p13-n23 complex amplitude across stimulation frequencies in ears with Meneiere's disease (experimental group).

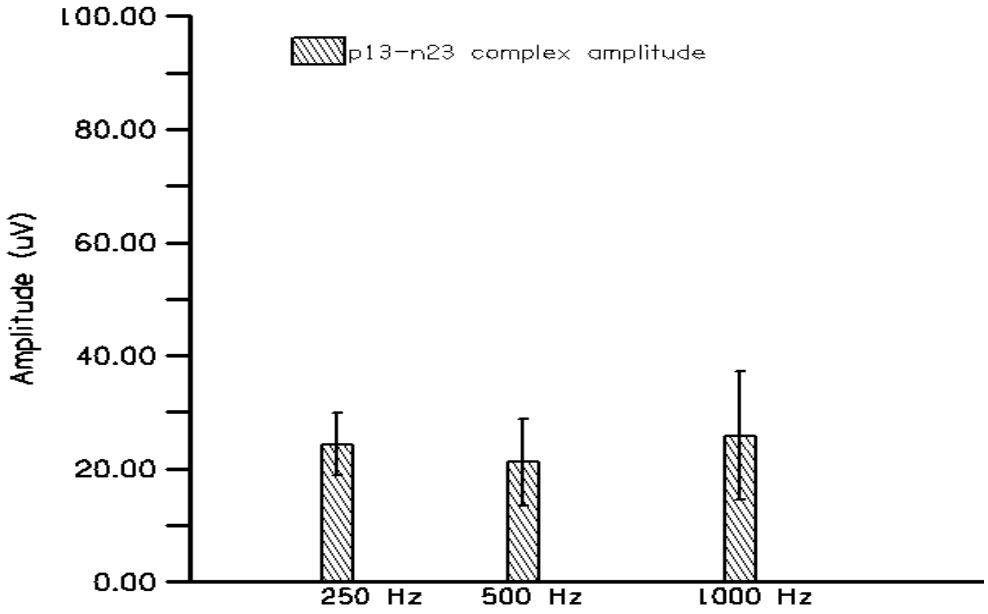

Figure 4.8. Mean and standard deviation of of p13-n23 complex amplitude in ears with Meneiere's disease across experimental frequencies.

From the figure 4.8 it is evident that the p13-n23 complex amplitude is slightly larger at stimulation frequency of 1000 Hz tone burst when compared to the other experimental stimulation frequencies. Three ears (16.67%) with Meniere's disease had absent cVEMP responses at 500 Hz but present at other frequencies (two of them had at 1000 Hz and one had at 250 Hz). To know the statistical significance of the difference in amplitude across stimulation frequency within group Friedman's test was performed. Test Friedman's test revealed that there is no significant difference within the group in terms of p13-n23 amplitude at 95 dB HL across stimulation frequencies (p=0.607).

The p13-n23 complex amplitude across stimulation frequency was compared between control group and ears with Meniere's disease. Due to the unequal number of subjects in both the groups a non-parametric kruskal-wallis test was performed to compare the means. The details of the Kruskal-Wallis test is given in table 4.8.

Table 4.8

The p values for Kruskal-Walllis test performed on amplitude of p13-n23 complex across frequencies in ears with Meniere's disease

Sl no.	Frequency	Parameters compared	P value
1	250 Hz	Amplitude of p13-n23 complex	0.17
2	500 Hz	Amplitude of p13-n23 complex	0.00
3	1000 Hz	Amplitude of p13-n23 complex	0.11

The table 4.8 test reveals a significant difference in amplitude of p13-n23 complex at 500 Hz between control group and ears with Meniere's disease. However the amplitude of p13-n23 complex at 250 Hz and 1000 Hz in ears with Meniere's disease was significantly not different from that of control group. Hence it suggests that amplitude of p13-n23 complex was significantly reduced in ears with Meniere's disease.

4.2c Vestibular findings in the ears contralateral to the ears with Meniere's disease

Similar to ears with Meniere's disease there were 18 ears contralateral to the ears with Meniere's disease investigated in this study. The details of the participants with respect to their age, gender, pattern of hearing sensitivity in the unaffected ear are given in table 4.9

Table 4.9

Demographic details and pattern of hearing sensitivity in the contralateral ear of the individuals with unilateral Meniere's disease

S. No	Age (years)	Sex	Affected Ear	Air conduction thresholds (dB HL)						ABR
				250 Hz	500 Hz	1kHz	2kHz	4kHz	8kHz	
1	56	M	Left	10	10	15	10	10	15	N
2	32	M	Right	5	10	10	5	10	10	N
3	59	F	Left	15	10	5	10	5	20	N
4	38	F	Right	25	15	10	10	5	5	N
5	51	M	Left	5	5	10	10	10	20	N
6	23	M	Right	20	15	5	5	10	15	N
7	46	M	Right	20	10	5	5	10	10	N
8	35	F	Left	15	15	10	10	10	20	N
9	44	M	Left	10	5	5	5	5	10	N
10	47	M	Left	10	10	5	10	10	15	N
11	42	M	Right	15	10	10	5	5	10	N
12	39	F	Right	25	1 5	5	10	5	10	N
13	45	F	Left	10	5	5	5	10	15	N
14	42	M	Left	15	10	15	15	10	15	N
15	31	M	Right	30	30	25	15	10	15	N
16	50	F	Right	10	10	5	10	5	15	N
17	35	F	Right	25	20	10	5	5	10	N
18	51	M	Left	20	10	10	5	10	20	N

Note: 'F': Female; 'M': Male; 'N': Normal; 'ABR': Auditory Brainstem Response.

From the table 4.9 it is clear that the contralateral ear of individuals with Meniere's disease had a clinically normal hearing sensitivity and all the participants had presence of ABR. However a close look into the data reveals that some participants had thresholds greater than 15 dB HL especially at lower frequencies. Out of the 18 ears (contralateral) cVEMP responses were absent in 7 ears at all the frequencies. Out of the 7 ears, the cVEMP response was absent in 5 ears where pure tone threshold at 250 Hz was higher than 15 dB HL.

The cVEMP responses at 250 Hz were present in 5 ears (27.78%), at 500 Hz in 7 ears (38.89%) and at 1000 Hz in 7 ears (38.89%). As like in ears with Meniere's disease responses were totally absent at 2000 Hz in the contralateral ear.

The latency of p13 peak, n23 peak and p13-n23 complex amplitude are measured in ears contralateral to the ears with Meniere's disease. The descriptive analysis of the cVEMP data in terms of mean and standard deviation from the ears contralateral to the ears with Meniere's disease (experimental group) is given in the table 4.10.

Table 4.10

Mean and standard deviation of latency of p13, n23, amplitude p13-n23 complex and cVEMP threshold in ears contralateral to the ears with Meniere's disease

Parameters	*250 Hz*		*500 Hz*		*1000 Hz*		*2000 Hz*	
	Mean (N=4)	SD	Mean (N=6)	SD	Mean (N=5)	SD	Mean (N=0)	SD
p13 latency (msec)	17.74	0.60	15.41	1.17	15.04	0.87	-	-
n23 latency (msec)	25.84	0.41	22.59	2.02	22.17	1.18	-	-
Amplitude of p13-n23 complex (µv)	31.94	9.91	39.91	17.77	29.67	13.30	-	-

Note: 'N': Total number of ears where the particular response is present; 'SD': Standard deviation'

It can be seen from the table 4.10 that unlike control group the cVEMP responses could not be elicited at 2000 Hz in any of the ears with Meniere's disease. It is also evident in the table that the p13-n23 complex amplitude is largest with 500 Hz stimulation frequency followed by 250 Hz and least amplitude at 1000 Hz. The mean and standard deviation of the p13 and n23 latency across stimulation frequencies are depicted in figure 4.10.

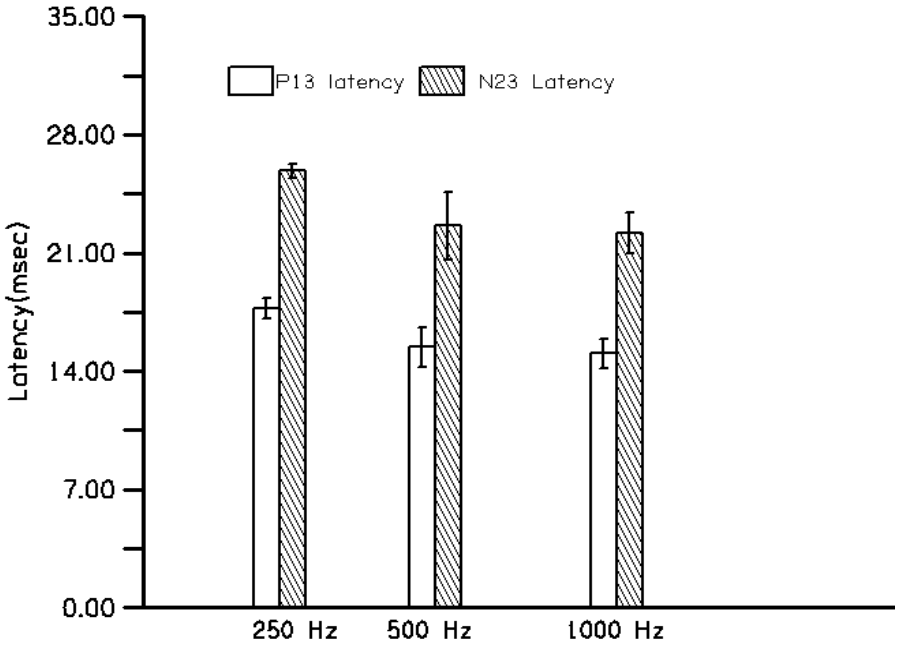

Figure 4.9. Mean and standard deviation of p13 and n23 latency in ears contralateral to the ears with Meniere's disease

In order to estimate the significance of difference in the latency and amplitude of the cVEMP between control group and ears contralateral to the ears with Meniere's disease, Kruskal-Wallis test was performed. The details of Kruskal-Wallis test is given in table 4.11.

Table 4.11

The p values for Kruskal-Walllis test performed on p13 and n23 peak latencies across frequencies in ears contralaterl to the ears with Meniere's disease

Sl no.	Frequency	Parameters compared	P value
1	250 Hz	P13 latency	0.20
2		N23 latency	0.06
3	500 Hz	P13 latency	0.43
4		N23 latency	0.14
5	1000 Hz	P13 latency	0.30
6		N23 latency	0.88

It can be seen from the table 4.11 that the p13 and n23 latencies between control group and ears contralateral to the ears with Meniere's disease were not significantly different from each other across any of the frequencies used in this study.

4.2c1. The cVEMP threshold in ears contralateral to the ears with Meniere's disease

Parallel to the cVEMP threshold estimation procedure described under control group, it was estimated in ears contralateral to the ears with Meniere's disease also in 5 dB steps across stimulation frequencies. The figure 4.10 depicts the mean and standard deviation of cVEMP thresholds across stimulation frequencies in ears contralateral to the ears with Meniere's disease.

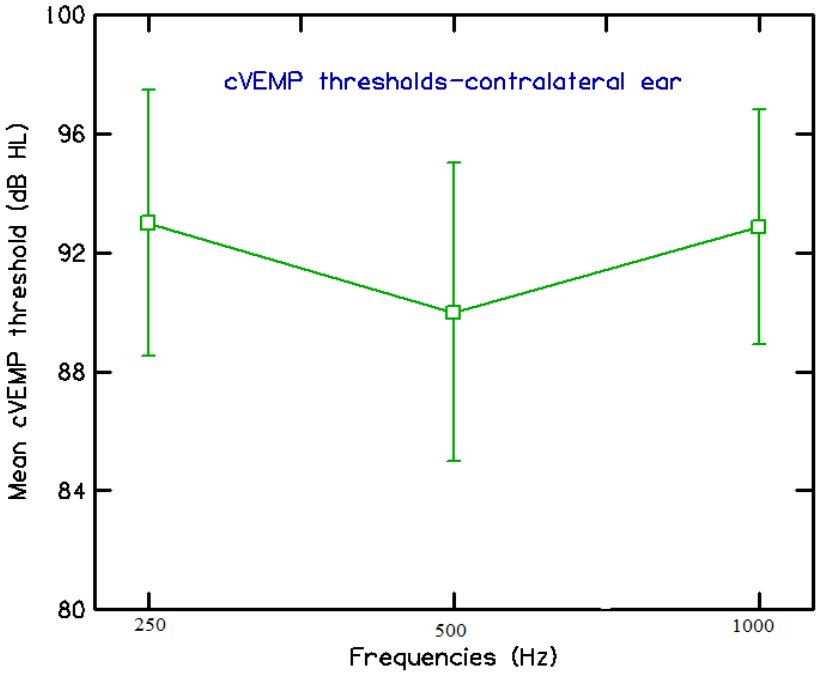

Figure 4.10. Depicting the mean and standard deviation of cVEMP thresholds across stimulation frequencies in ears contralateral to the ears with Meniere's disease

The figure 4.10 reveals that cVEMP threshold obtained using a 500 Hz stimulation frequency is relatively lower when compared to other stimulation

frequencies. It can also be seen from figure 4.10 that cVEMP thresholds at 250 Hz and 1000 Hz are similar.

To check the statistical significance for the cVEMP threshold across stimulus frequencies within group, Friedman's test was performed. Friedman's test revealed no significant difference within the group in terms of cVEMP thresholds across stimulation frequencies (p=0.607).

To estimate the significance of difference on cVEMP thresholds between the control group and ears contralateral to the ears with Meniere's disease across experimental frequencies Kruskal-Wallis test was done. The details of the Kruskal-Wallis test is given in table 4.12.

Table 4.12

The p values for Kruskal-Walllis test performed on cVEMP thresholds across frequencies in ears contralaterl to the ears with Meniere's disease

Sl no.	Frequency	Parameters compared	P value
1	250 Hz	cVEMP threshold	0.14
2	500 Hz	cVEMP threshold	0.00
3	1000 Hz	cVEMP threshold	0.82

It can be seen from the table 4.12 that the cVEMP threshold at 500 Hz is significantly higher in ears contralateral to the ears with Meniere's disease compared to the control group. The cVEMP thresholds at 250 and 1000 Hz are no significantly different between control group and ears contralateral to the ears with Meniere's disease.

4.2c2. Frequency tuning of cVEMP in ears contralateral to the ears with Meniere's disease

The frequency tuning analysis of the cVEMP responses from ears contralateral to the ears with Meniere's disease was performed based on the same criteria mentioned earlier for ears with Meniere's disease. The figure 4.11 represents the mean and standard deviation of amplitude of p13-n23 complex in ears contralateral to the ears with Meniere's disease.

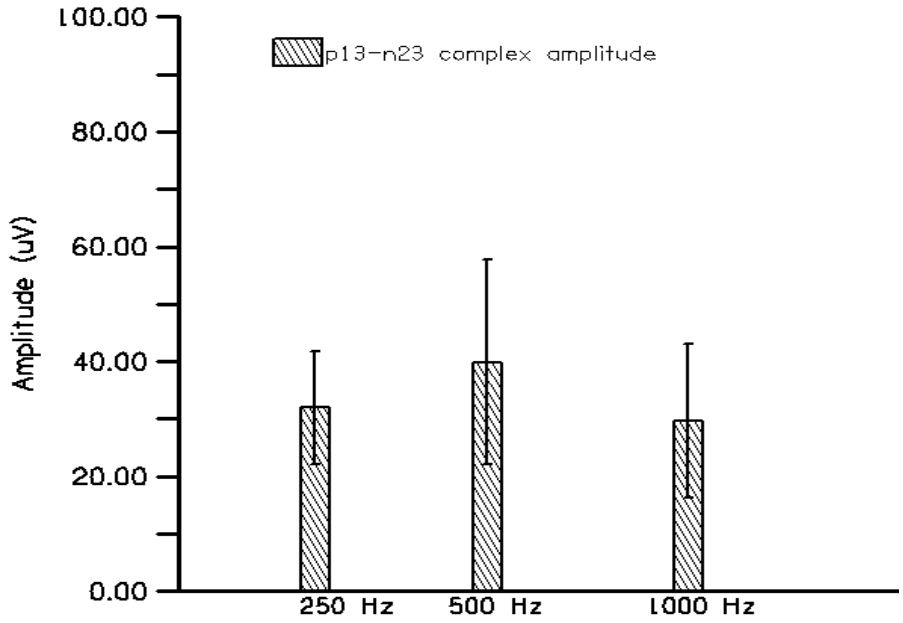

Figure 4.11. Mean and standard deviation of p13-n23 complex amplitude in in ears contralateral to the ears with Meniere's disease.

It is clear from the figure 4.11 that the amplitude of p13-n23 complex is slight larger with 500 Hz stimulation frequency followed by 1000 Hz and the least amplitude was found to be at 250 Hz. There were 4 ears (22.22%) in which the cVEMP response was absent at 500 Hz but present at other frequencies (two of them had cVEMP at 250 Hz and another two had cVEMP at 1000 Hz).

To check the statistical significance for the amplitude across stimulation frequency within group Friedman's test was performed. Friedman's test revealed no

significant difference within the group in terms of p13-n23 amplitude at 95 dB nHL across stimulation frequencies (p=0.449).

The amplitude of p13-n23 complex across stimulation frequencies was compared between control group and ears contralateral to the ears with Meniere's disease using Kruskal-Wallis test. The details of the Kruskal-Wallis test are provided in the table 4.13.

Table 4.13

The p values for Kruskal-Walllis test performed on amplitude of p13-n23 complex across frequencies in ears contralateral to the ears with Meniere's disease

Sl no.	Frequency	Parameters compared	P value
1	250 Hz	Amplitude of p13-n23 complex	0.82
2	500 Hz	Amplitude of p13-n23 complex	0.16
3	1000 Hz	Amplitude of p13-n23 complex	0.57

The table 4.13 reveals that the amplitude of p13-n23 complex was not significantly different between control group and ears contralateral to the ears with Meniere's disease across any of the experimental frequencies.

4.3. Best combination parameters to aid in diagnosing Meniere's disease

The different cVEMP indices considered in this study to aid in diagnosis of Meniere's disease include presence/absence of cVEMP responses at one or more frequency, latency of p13 and n23 peaks, cVEMP thresholds across frequencies and frequency tuning (based on the p13-n23 complex amplitude at 95 dB nHL). The cVEMP responses were totally absent in 11 (61.11%) of the 18 ears with Meniere's disease. The absent cVEMP response in the affected ear at all experimental frequency

itself is considered as sacculocollic pathway dysfunction in individuals with Meniere's disease.

In general 500 Hz is considered as the most sensitive frequency at which cVEMP is elicited with largest amplitude in normals. Hence the data from ears with Meniere's disease was analysed and found that 4 ears (22.22%) with Meneire's disease had cVEMP present at 500 Hz whereas 3 ears (16.67%) did not had a response at 500 Hz but had it at other frequencies (two ears had cVEMP at 1000 Hz & one had cVEMP at 250 Hz). The ears with Meniere's disease where there was a shift in the frequency tuning is also considered as an indicator of pathology in individuals with Meniere's disease.

The ears with Meniere's disease where cVEMP was present at 500 Hz, frequency tuning was analysed in terms of largest amplitude at 95 dB nHL across test frequencies. Out of the four ears with Meniere's disease, two of them had a higher amplitude of p13-n23 complex at 500 Hz and another two had a higher amplitude of p13-n23 complex at 1000 Hz. This indicate shift of frequency tuning in two participants.

In those ears with Meniere's disease where the frequency tuning was not altered (N=2) from 500 Hz, cVEMP thresholds at 500 and 1000 Hz were considered to separate it from the normal ear response. One ear with Meniere's disease had abnormally higher cVEMP threshold (Greater than mean+1 SD when compared to the control group) at 500 Hz and another had abnormally higher cVEMP threshold at 1000 Hz.

Table 4.14 gives the details of the results of all the cVEMP parameters. Since some of the participants with Meniere's disease showed abnormalities in more than one cVEMP parameters. This resulted in a mismatch between the percentage of

identification of Meneire's disease while using combination of cVEMP parameters and percentage of identification by considering parameters independently.

Table 4.14

Illustrating the best combination of cVEMP indices in detecting Meniere's disease using cVEMP response from the ear with Meniere's disease

Sl no.	Independent/Combined cVEMP indices	Number of ears detected as having Meniere's disease (N=18)	Sensitivity in percentages (%)
1	Absence of cVEMP across all frequencies	11	61.11
2	Frequency tuning alone	5	27.78
3	cVEMP threshold at 500 Hz alone (Absent/elevated0	16	88.89
4	cVEMP threshold at 1000 Hz alone (Absent/elevated0	16	88.89
5	Frequency tuning and cVEMP threshold at 500 Hz	7	100
6	Frequency tuning and cVEMP threshold at 1000 Hz	7	100

Note:'N': Total number of ears with Menieres disease where cVEMP was present at 500 Hz.

Table 4.14 reveals that combining all the analysis parameters together the percentage of identification of Meniere's disease reaches to 100%.

Similar analysis of the data was done for ears contralateral to the ears with Meniere's disease to identify the best combination cVEMP indices to aid in the

diagnosis of Menieres disease. Eleven out of 18 ears (61.11%) had absent cVEMP responses in the contralateral ear and hence this absent response itself is considered as an indicator of Meniere's disease. There were 4 ears contralateral to the ears with Meniere's disease where the cVEMP response was present only in the contralateral ear. The absence of ipsilateral cVEMP response itself is an indicator of Meniere's disease in these participants. Out of the 11 cVEMP responses in the contralateral ear, three showed altered frequency tuning.

Among the 8 ears contralateral to the ears with Meniere's disease where the cVEMP response was present at 500 Hz, 4 of them showed frequency tuning at 500 Hz itself whereas one had frequency tuning at 250 Hz and another two had it at 1000 Hz. In those ears contralateral to ears with Meniere's disease where the frequency tuning was not altered (N=4) from 500 Hz, cVEMP thresholds at 500 and 1000 Hz were considered to separate it from the normal ear response. It was found that in one ear contralateral to ear with Meniere's disease, the cVEMP threshold was higher (Greater than mean+1 SD when compared to the control group) at 500 Hz and in another two ears cVEMP threshold was higher at 1000 Hz. One ear had both frequency tuning and cVEMP threshold at 500 Hz similar to control group. However this ear had absent response at other frequencies which may aid in the diagnosis of Meniere's disease.

The table 4.15 illustrates the percentage of ears with Meniere's disease which can be identified using some of the independent and combined essential cVEMP indices of the ear contralateral to the ear with Meniere's disease.

Table 4.15

Illustrating the best combination of cVEMP indices in detecting Meniere's disease using cVEMP response from the ear contralateral to the ear with Meniere's disease

Sl no.	Independent/Combined cVEMP indices	Number of ears detected as having Meniere's disease (N=18)	Sensitivity in percentages (%)
1	Absence of cVEMP across all frequencies	7	38.89
2	Frequency tuning alone	6	33.33
3	cVEMP threshold at 500 Hz alone (Absent/elevated)	14	77.78
4	cVEMP threshold at 1000 Hz alone (Absent/elevated)	14	77.78
5	Frequency tuning and cVEMP threshold at 500 Hz	15	83.33
6	Frequency tuning and cVEMP threshold at 1000 Hz	16	88.89
7	Frequency tuning and cVEMP threshold at 500 Hz and 1000 Hz	17	94.44

Note: 'N': Total number of participants with Meniere's disease

Hence it can be seen from the table 4.15 that frequency tuning and cVEMP thresholds at 500 Hz and 1000 Hz of the ear contralateral to the ear with Meniere's disease can be used to detect abnormal cVEMP responses in individuals with Meniere's disease. However care should be taken while interpreting this data since majority of the cVEMP responses were absent in this data pool and hence the result

may be applicable to the heterogeneous groups similar to the one used in this study. Duration of the disease and symptoms shold also be considered while interpreting this results.

4.4 Association between duration of disease and cVEMP findings in Meniere's disease

An association between duration of Meniere's disease and cVEMP findings in Meniere's disease was carried out. The table 4.16 documents the duration of Meniere's disease and presence or absence of cVEMP at 500 Hz stimulation frequency. The association of duration of Menieres disease was done with 500 Hz as the cVEMP is mostly administered at 500 Hz only.

Table 4.16

Representing the duration of Meniere's disease and cVEMP status in affected and contralateral ear at 500 Hz

Subject no.	Duration of Meniere's disease	cVEMP status of affected ear at 500 Hz	cVEMP status of contralateral ear at 500 Hz
1	15 years	A	A
2	13 years	A	A
3	6 months	A	A
4	20 years	A	A
5	18 years	A	A
6	3year 8 months	A	A
7	21 years	A	A
8	5 years 4 months	A	A
9	11 years	A	P
10	1 year 10 months	A	A
11	6 years 6 months	A	A
12	6 years 2 months	A	P
13	1 year 8 months	P	P
14	9 months	A	P
15	3 months	P	P
16	1 year 1 month	P	P
17	3 months	P	P
18	3 years 5 months	A	A

Note: 'A': Absent cVEMP respone; 'P': Presence of cVEMP response

The detailed analysis of the table 4.16 leads a conclusion that longer duration of Meniere's disease resulting in absence of cVEMP response in many individuals with unilateral Meniere's disease. To check the association between duration of Meniere's disease and presence/absence of cVEMP response a Chi-square test was administered. The Chi-square test revealed a significant association between duration of Meniere's disease and presence/absence of cVEMP response in the affected ear ($p=0.023$). Such an association was marginally significant with respect to presence/absence of cVEMP response in the contralateral ear ($p=0.05$). Table 4.17 illustrates the relation between presence/absence of cVEMP response at one or more test frequency and duration of Meniere's disease.

Table 4.17

Representing the relation between duration of Meniere's disease and presence/absence of cVEMP at one or more test frequency

Duration of the disease (in years)	> 10 years	2 -10 years	< 2 years
Subjects with cVEMP absent in both ears	5	1	1
Subjects with cVEMP present only in unaffected ear	1	2	1
Subjects with cVEMP present in both ears	0	2	5

Note: 'Duration': Duration of Meniere's disease

It can be seen from the table 4.17 that the chance of occurrence of cVEMP in the affected ear is reduced when the duration of the disease is greater than 2 years. Similarly when the duration of the disease exceeds 10 years then the chances of occurrence of cVEMP response in the contralateral ear also reduces to a greater extent.

4.5 Association between degree of hearing loss and cVEMP findings in Meniere's disease

In a similar way association between degree of hearing loss and presence/absence of cVEMP response in the affected as well as contralateral ear was evaluated using a Chi-square test. The association was obtained with reference to cVEMP response at 500 Hz. The result of the Chi-square revealed that there is no significant association between degree of hearing loss and presence/absence of cVEMP response in the affected ear ($p= 0.20$) as well as in the contralateral ear ($p= 0.35$). Thus there is no association between degree of hearing loss and cVEMP findings.

To summarise the present study cVEMP responses were recorded in control and experimental group across test frequencies from both ears. The cVEMP was present in all the participants at 500 Hz in the control group whereas, the cVEMP was absent in 11 out of 18 participants with Meniere's disease. The amplitude of p13-n23 complex was higher at 500 Hz compared to 250 Hz, 1000 Hz and 2000 Hz in the control group.

The cVEMP threshold at 500 Hz was significantly lesser in control group compared to the individuals with Meniere's disease. The mean latencies of p13 and n23 peaks in individuals with Meniere's disease were significantly not different from the control group across all the frequencies.

There was an association between duration of disease and presence or absence of cVEMP responses, at 500 Hz in both affected and unaffected ears. There was no association between degree of hearing loss and presence or absence of cVEMP responses at 500 Hz in both affected and unaffected ears.

Chapter-5

DISCUSSION

The present study was undertaken with an aim to finding out the most sensitive combination of cVEMP parameters to detect Meniere's disease. In order to fulfil this purpose cVEMP recordings were done on control as well as in experimental group at different frequencies and different intensities from both the ears. A detailed case history was also taken to support the objective cVEMP measures with subjective characteristics. Appropriate statistics were performed on the group data on each of the possible indices of cVEMP response to reveal the significance of difference and association. The results from control group and experimental group are explained and discussed in detail with more emphasis given to the experimental group with respect to ears with Meniere's disease and contralateral ear.

5.1. Presence/Absence of cVEMP responses

In the present study in all the 36 ears of the control group cVEMP responses were present at 500 Hz and 1000 Hz stimulation frequencies. However, at 250 Hz and 2000 Hz the responses were present in 88.89% and 33.33% ears respectively. In individuals with Meniere's disease, in the affected ear cVEMP was absent in 11 out of 18 participants (11 out of 18 ears) in all the frequencies. For rest of the ears, cVEMP was present in 22.22% ears at 500 Hz, 27.78% at 1000 Hz and 11.11% for 250 Hz whereas, no responses could be observed at 2000 Hz.

The response rate of cVEMP at different frequencies in the control group is similar to the previous findings (Zapala & Brey, 2004; Janky &Shepard, 2009; Sandhu et al., 2012). It has been reported that the response rate of cVEMP is higher at 500, 750 and 1000 Hz (Zapala & Brey, 2004; Janky &Shepard, 2009; Sandhu et al.,

2012). As the frequency increases beyond 1000 Hz the response rate drastically reduces and reaches to nearly 0% with 4000 Hz (Janky &Shepard, 2009).

In the present study cVEMPs responses were absent in 61.11% of the participants with Meniere's disease. Other studies have reported absence of cVEMP in 46% of the participants (de Waele et al.1999), absence of cVEMP in 35% of the participants (Murofushi et al.2001), absence of cVEMP 12 % of the participants (Young, Hung & Cheng 2003), whereas Rauch et al (2004) reported an absence of cVEMP responses in 18% of the subjects. In the present study the absence of cVEMPs is higher in individuals with Meniere's disease compared to the previous studies. The equivocal findings in the literature could be due the different population of Meniere's disease tested in different studies. Presence or absence of cVEMPs depends upon the stage of Meniere's disease. In the early Meniere's disease the cVEMP might be present but might disappear at a later stage (Young et al. 2003).

The absent cVEMP responses in ears with Meniere's disease may be related to the progressive degeneration of the saccular structure. Rosenhall, Engstrom and Stahle (1977) reported vacuolation of sensory cell and cystic degeneration. The vacuolation results in unspecific damage to the vestibular system whereas cystic formation is specific and affects sensory cells of the macula and the crista ampularis (Rosenhall et al. 1977). The damage to the macula hair cells of the saccular system will lead to an absence of cVEMP responses (Rosenhall et al. 1977). Because of the degeneration of the cysts large cystic spaces will be developed between the sensory cells and the nerve chalice (Rosnhall et al. 1977). This makes the otolithic sensory structure incapable of traducing fluid movement to electrical pulses and an eventual absence of cVEMP which is dependent upon the otolithic hair cell transduction.

5.2 Amplitude of cVEMP responses

The amplitude of p13-n23 complex was higher at 500 Hz compared to 250 Hz, 1000 Hz and 2000 Hz in the control group. This amplitude difference was statistically significant. However, in individuals with Meniere's disease (in affected ear), in three participants the cVEMP was absent at 500 Hz but was present at other frequencies, for rest of the ears this effect was not seen. However, when the group data was compared the amplitude of cVEMP was equal at all the frequencies in ears with presence of cVEMP responses. When the amplitude of the cVEMP was compared between the control group and experimental group, no significant difference could be observed across the two groups for any of the frequencies except for 500 Hz.

In the present study the amplitude of the cVEMP were higher at 500 Hz compared to the other frequency for the participants in the control group i.e the frequency tuning of cVEMP responses were towards 500 Hz. Previous studies have also reported a higher amplitude of cVEMP recorded with 500 Hz stimulating frequency ie. frequency tuning at 500 Hz in normal subjects (Todd et al, 2000; Rauch et al, 2004; Sandhu et al., 2012; Milojcic, Guinan, Rauch & Herrmann, 2013).

The possible explanation for the frequency tuning of the saccule is related to the mass and stiffness characteristics of the otolithic end organs, mechanical resonant properties of each steriocilia and/ or hair cells inherent electrical tuning (Fernandez & Goldberg, 1976; Ashmore, 1983; Todd et al, 2000; Welgampoka & Colebatch, 2001). The mass component of the saccule is mainly contributed by the otoconia and the stiffness component is contributed by the gelatine layer on top of the otoconia as well as its attachments to the temporal bone (Young et al, 1977; Fettiplace & Fuchs, 1999; Todd et al, 2000). Since the saccule has more mass (Baloh & Kerber, 2011), the

chance of the resonant frequency of the saccule gets shifted to a lower frequency (Todd, Cody & Banks, 2000). Hence, if the resonant frequency is lower,

Similar to the otolithic end organ as a whole, stereocilia also possess resonant properties Since the saccular steriocilia are relatively longer and less stiff leading to a possible relative lowering of resonant frequency (Fettiplace & Fuchs, 1999). The inherent electrical tuning of hair cells are related to the number of potassium channels (K^+) available for transduction (Fettiplace & Fuchs, 1999). However, there are equivocal findings related to the resonant frequency related to the number of potassium channels in the otolithic end organ (Welgampoka & Colebatch, 2001; Horner & Rydmarker, 1991; Node et al., 2005).

In the participants with Meniere's disease, the tuning was absent, and also when the amplitude was compared to the normal subjects the amplitude was same except for 500 Hz. This particular finding could be related to the stage of Meniere's disease. The participants in whom the responses were absent at 500 Hz but were present at other frequencies indicates a shift of frequency tuning in these subjects, which could be related to the damage of the saccule macula hair cells. Due to a smaller sample size probably the statistics failed to show any significant difference within the Minere's disease group. Also, the participants for whom the cVEMP responses were present, most of them had Meniere's disease for less than 2 years. Since at 500 Hz frequency the cVEMP responses were absent or were reduced in amplitude the differences between the Minere's and the control group could be observed only at 500 Hz.

5.3 Threshold of the cVEMP

The cVEMP threshold at 500 Hz was lesser compared to other frequencies in the control group. This threshold was statistically significant in control group.

However, in individuals with Meniere's disease the thresholds at all the frequencies were same. When the thresholds were compared across two groups the threshold at 500 Hz was significantly lesser in control group compared to the individuals with Meniere's disease. For rest of the frequencies there was no difference in threshold between the two groups.

The findings of the present study are similar to the previous studies (Bath et al, 1998; Lee, Shin, Lee & Park, 2010; Rauch et al., 2004). However, the absolute threshold values varies across studies and this can be attributed to the stimulus characteristics (rise/fall time and plateau) and reporting of thresholds in dB SPL versus dB nHL. The lowest threshold of cVEMP at 500 Hz is invariably related to the largest amplitude at 500 Hz. Because of higher amplitude at 500 Hz the threshold becomes lower for cVEMP.

The findings of the present study revealed that the cVEMP thresholds in ears with Meniere's disease were found to be significantly higher than the control group at 500 Hz stimulation frequency. Previous studies have reported a significant alteration of the threshold and amplitude in Individuals with Meniere's disease (Rauch et al. 2004; Ohki, Matsuzaki, Sugasawa & Murofushi, 2002). In subjects with Meniere's disease there is a reduction in amplitude and hence the thresholds shift to a higher side. In the present study the amplitude of cVEMP was significantly higher at 500 Hz in the control group compared to the Minere's disease hence the threshold was higher at 500 Hz in individuals with Minere's disease.

5.4 Latency of cVEMP

The mean latencies of p13 and n23 peaks in individuals with Meniere's disease were significantly not different from the control group across all the frequencies.

None of the subject with Meniere's disease showed prolonged latency of either cVEMPs. It is expected that latency is not affected by saccular hydrops or utricular hydrops as a result of Meniere's disease as changes in latency are thought to arise from changes in the conducting pathways of the sacculo-collic reflex pathway for the cervical VEMP (Rauch et al. 2004) or utricular ocular pathway for oVEMPs (Chiarovano et al. 2011). However, a neural delay at the level of the receptor organ may contribute to changes in response latency. Studies by Young et al. (2003), Murofushi et al. (2001) and Ochi et al. (2001) have confirmed this and determined that VEMP latency measures are stable in Meniere's disease. Evidence from the cVEMP data in this study supports this theory.

5.5 cVEMP findings in contralateral ear

1. *In contralateral ears of Meniere's disease, 38.89% had total absence of cVEMP response across test frequencies. Altered frequency tuning was observed in few participants whereas other few participants it was not observed.*
2. *The amplitude of p13-n23 complex cVEMP in contralateral ears of Meniere's disease participants was significantly lower from the control group at 500 Hz.*
3. *The cVEMP threshold in contralateral ears of Meniere's disease participants was significantly higher from the control group at 500 Hz.*

Studies in the literature have reported second ear involvement in individuals with unilateral Meniere's disease was seen in 31% to 37% of cases (Thomas & Harrison, 1971; Green, Blum & Harner, 1991). Study by Lin et al, (2006) found that 27% of participants with unilateral Meniere's disease had abnormal cVEMPs responses in the contralateral ear. Histopathological studies of temporal bones of individuals with Meniere's disease showed hydrops were more common in saccule

and utricle compare to the semicircular canal (Okuno & Sando, 1987) so it can be concluded that, abnormal cVEMPs responses may precede the symptoms in the contralateral ear, so cVEMPs responses can be used to predict the involvement of contralateral ear.

The abnormal findings of cVEMP in contralateral ears may reflect central binaural interaction (because of the bilateral gain of the VOR pathway). Because of this gain of VOR, hypofunction of the affected ear would cause a decreased response on the contralateral side (Rauch et al. 2004). Thus, the abnormal findings in the contralateral ear may indicate a possible involvement of the contralateral ear or a central binaural interaction.

5.6 Association between different variables

a. *There was an association between duration of disease and presence or absence of cVEMP responses, at 500 Hz in both affected and unaffected ears.*
b. *There was no association between degree of hearing loss and presence or absence of cVEMP responses at 500 Hz in both affected and unaffected ears.*

Friberg et al. (1984) reported that there is a progression in the Minere's disease till 5-10 years after the onset after that the progression of the disease relatively slows down. In the present study also it was found that the cVEMP responses were present in individuals with Meniere's disease for whom the onset was lesser than 2 years. Participants for whom the duration of Meniere's disease was more than 2 years chances of cVEMP being present was very less. Hence the present study indicates that cVEMP can be utilised to know the stages of Meniere's disease.

However there was no correlation between the degree of hearing loss and the presence/absence of cVEMP. IT is hypothesised that there might be differential damage in the cochlear and the vestibular system due to the presence of

endolymphatic hydrops. Hence, the threshold shift seen in the puretone audiometry might not correlate with the vestibular findings.

5.7 Best combination analysis parameters to aid in diagnosis of Meniere's disaese

By combining all the analysis parameters, the cVEMP can detect the pathology in 100% of the cases with Meniere's disease.

It is recommended that the cVEMP should be carried out the 500 Hz stimulating frequency and at 95dB nHL. If the responses are absent, then the test can be terminated as the absence of cVEMP will indicate a possible lesion in the sacculocollic pathway in Meniere's disease. If still one is interested to know whether some amount of macula hair cells are intact or not, one can record the cVEMP at 1000 Hz stimulating frequency. If the responses are present at 500 Hz, then one can record the cVEMP responses at 1000 Hz and compare the amplitude with 500 Hz stimulating frequency. If the amplitude of cVEMP is larger at 1000 Hz compared to 500 Hz, the Meniere's disease can be suspected. If there is no difference in amplitude between 500 Hz and 1000 Hz or the amplitude is higher at 500 Hz compare to 1000 Hz, then the threshold at 500 Hz should be obtained and should be compared to the threshold of normal subjects.

Chapter-5

Summary and Conclusions

Meniere's disease was first described by Prosper Meniere's in 1861. The classical triad symptoms of Meniere's disease are fluctuating sensorineural hearing loss, episodic vertigo and tinnitus/aural fullness. The pathophysiology of the Meniere's disease is confined to the membranous inner ear caused due to excessive endolymph in the inner ear (Gelfand, 2001). Various clinical tests which have been utilised to diagnose the Meniere's disease are Electrocochleography (EcochG), CHAMP (Cochlear Hydrops Analysis by Masking Procedure), Glycerol test, and Caloric test.

The Cervical Vestibular Evoked myogenic potential (cVEMP) is another electrophysiological test which has been recently utilised to diagnose various vestibular disorders including Meniere's disease (Ferdinand et al. 2006; Castelein, Deggouj, Wuyts & Gersdorff, 2008; Young, 2012). Basically the cVEMP is utilised to diagnose the integrity of sacullocollic pathway in individuals with Meniere's disease. The sensitivity of the cVEMP in diagnosing the Meniere's disease varies from 50% to 67% (Ribeiro et al., 2006; de Waele et al., 1999; Kuo, Yang & Young, 2005).

Present study was conducted with an aim to find out the most sensitive combination of cVEMP analysis parameters to aid in the diagnosis of Meniere's disease. To achieve the aim two groups of participants were undertaken for the study. First group included 18 individuals with Meniere's disease in the age range of 21 years to 61 years. These participants were diagnosed as Meniere's disease based on the report of an Otorhinolaryngologist and the guidelines given by American Association of Otolaryngology - Head and neck surgery (1995). Second group of

participants included 18 individuals (age range: 21 to 61 years) with normal hearing and no vestibular disorders.

All the participants underwent routine audiological tests such as puretone audiometry, Immittance evaluation, uncomfortable loudness level and auditory brainstem response testing. Prior to the routine audiological test administration a detailed case history was collected from all the participants. After the case history and routine audiological evaluations, rectified cervical vestibular evoked myogenic potentials (cVEMP) were recorded from both the groups. To record the cVEMP the non-inverting electrode was placed on the sternocleidomastoid muscle, the inverting electrode was placed on the sternoclavicular joint and the ground electrode was placed on the forehead. cVEMP was obtained from both the ears in control and clinical group at 250, 500, 1000 and 2000 Hz stimulation frequencies. The responses were filtered from 30 Hz to 1500 Hz. The responses were recorded at 95 dB nHL first and then to estimate the threshold of the cVEMP the intensity was varied in 5 dB steps.

Analysis of vestibular evoked myogenic potentials

- Absolute latency and peak-to-peak amplitude of p13 and n23 was noted for each participant for each frequency and intensity in both the ears.
- The threshold of cVEMP across all frequencies was documented for all participants in both the ears.
- The frequency tuning of cVEMP across all participants was determined based on the presence of cVEMP or amplitude of cVEMP in both the ears.

The main results of the study are as follows:

1. The cVEMP was present in all the participants at 500 Hz in the control group whereas, the cVEMP was absent in 11 out of 18 participants with Meniere's disease.

2. The amplitude of p13-n23 complex was higher at 500 Hz compared to 250 Hz, 1000 Hz and 2000 Hz in the control group. This amplitude difference was statistically significant. However, in individuals with Meniere's disease (in affected ear), in three participants the cVEMP was absent at 500 Hz but was present at other frequencies, for rest of the ears this effect was not seen. However, when the group data was compared the amplitude of cVEMP was equal at all the frequencies in ears with presence of cVEMP responses. When the amplitude of the cVEMP was compared between the control group and experimental group, no significant difference could be observed across the two groups for any of the frequencies except for 500 Hz.

3. The cVEMP threshold at 500 Hz was lesser compared to other frequencies in the control group. This threshold was statistically significant in control group. However, in individuals with Meniere's disease the thresholds at all the frequencies were same. When the thresholds were compared across two groups the threshold at 500 Hz was significantly lesser in control group compared to the individuals with Meniere's disease. For rest of the frequencies there was no difference in threshold between the two groups.

4. The mean latencies of p13 and n23 peaks in individuals with Meniere's disease were significantly not different from the control group across all the frequencies.

5. In contralateral ears of Meniere's disease, 38.89% had total absence of cVEMP response across test frequencies. Altered frequency tuning was observed in few participants whereas other few participants it was not observed.
6. The amplitude of p13-n23 complex cVEMP in contralateral ears of Meniere's disease participants was significantly lower from the control group at 500 Hz.
7. The cVEMP threshold in contralateral ears of Meniere's disease participants was significantly higher from the control group at 500 Hz.
8. In contralateral ears of Meniere's disease participants, 38.89% had total absence of cVEMP response across test frequencies. Altered frequency tuning was observed in 16.67% and reduced amplitude at 500 Hz in 16.67% and reduced amplitude at 1000 Hz in 16.67%. But by combining cVEMP frequency tuning and thresholds at 500 Hz and 1000 Hz resulted in a sensitivity of 94.44% in ears contralateral to ears with Meniere's disease.
9. There was an association between duration of disease and presence or absence of cVEMP responses, at 500 Hz in both affected and unaffected ears.
10. There was no association between degree of hearing loss and presence or absence of cVEMP responses at 500 Hz in both affected and unaffected ears.

Conclusions

It can be concluded that cVEMP can be a useful tool in the diagnosis of the Meniere's disease. By combining all the analysis parameters, the cVEMP can detect the pathology in 100% of the cases with Meniere's disease. Not only the ipsilateral ears should be evaluated but also, the contralateral ears of the individuals with Meniere's disease should be evaluated. Based on the findings in the present study a

plausible flow chart for performing cVEMP test evaluation in suspected Meniere's disease ccan be proposed. This proposed protocol is illustrated in the flow chart given below (figure 5.1)

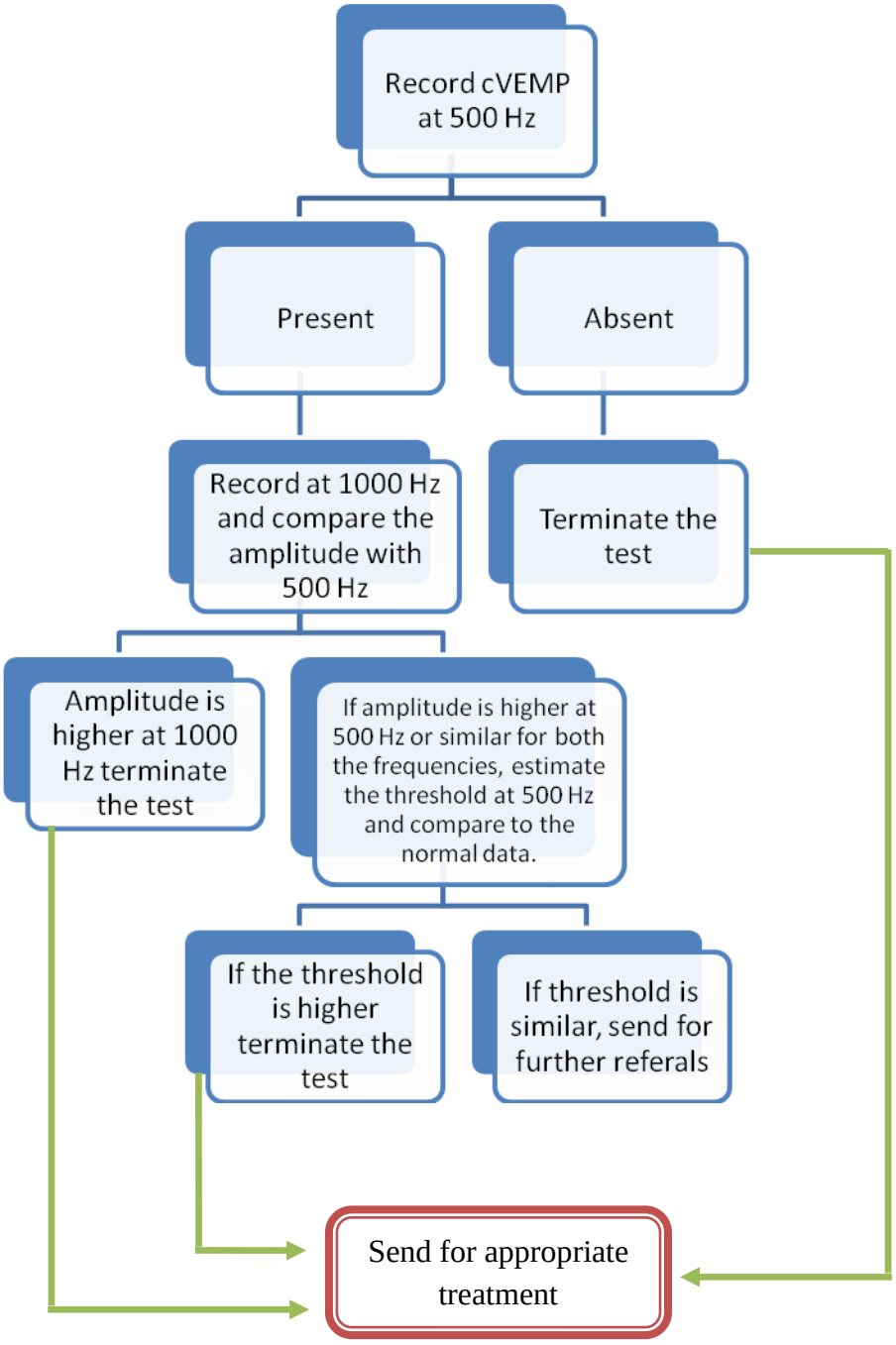

Figure 5.1 The recommended cVEMP protocol to evaluate individuals with suspected Meniere's disease.

Implications of the study

1. The results of the present study will be help in the diagnosis of Meniere's disease.
2. The study will help the clinicians to understand the underlying pathophysiology in individuals with Meniere's disease.
3. Based on the results rehabilitation techniques for the individuals with Meniere's disease can be designed.

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