FEASIBILITY OF BINAURAL RECORDINGS OF oVEMP AND ITS EFFICACY IN DIAGNOSIS OF SOME VESTIBULAR PATHOLOGIES

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CERTIFICATE

This is to certify that the dissertation entitled "**Feasibility of binaural recordings ofoVEMP and its efficacy in diagnosis of some vestibular pathologies"** is a bonafide work submitted in part fulfillment for the Degree of Master of Science (Audiology) of the student (Registration no. 12AUD028). This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any Universities for the award of any Degree or Diploma.

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CERTIFICATE

This is to certify that the dissertation entitled "**Feasibility of binaural recordings of oVEMP and its efficacy in diagnosis of some vestibular pathologies"** has been prepared under my supervision and guidance. It is also certified that this has not been submitted earlier in other University for the award of any Degree or Diploma.

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DECLARATION

This is to certify that this dissertation entitled "**Feasibility of binaural recordings of oVEMP and its efficacy in diagnosis of some vestibular pathologies"** is the result of my own study under the guidance of Mr. Niraj Kumar Singh, Lecturer, Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted earlier in other University for the award of any Degree or Diploma.

Mysore **Register no:** 12AUD028

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Chapter 1

Introduction

Balance of the body in the three-dimensional space is maintained by normal structures and co-ordinated functioning of the vestibular system, visual system and the proprioceptive system. Hence, assessment of balance related disorders should consist of tests to evaluate the functioning of all these systems. Until recently, the testing methods to assess the vestibular system primarily evaluated the integrity of the semicircular canals and no tests were available to assess the otolith organs. Efforts by Colebatch and colleagues lead to the development of vestibular evoked myogenic potentials (VEMP) having wide spread application in evaluation of the saccule and inferior vestibular nerve (Colebatch, & Halmagyi, 1992; Colebatch, Halmagyi, & Skuse, 1994; Halmagyi, Yavor, & Colebatch, 1995; Watson & Colebatch, 1998; Welgampola & Colebatch, 2005). Since then the research on VEMP has advanced markedly.

VEMPs are widely used clinical tool for the assessment of various vestibular pathologies. These potentials are muscle reflexes to loud acoustic stimuli and hence termed as sonomotor reflexes. The structures and connections in generation of VEMP have been reported to consist of receptor end organs (otoliths), afferent pathways (inferior and superior vestibular nerves), central connections (to vestibular nuclei and cerebellum), efferent pathway (vestibulocerebellar, commissural, vestibulospinal, vestibulo-ocular & vestibuloreticular pathways), and end muscles (gastronemius, triceps, trapezius, infra-orbital and sternocleido mastoid). VEMPs are short latency modulations in the electromyograms (EMG) that are evoked by loud acoustic stimuli and which can be recorded from surface electrodes over several muscles of the body.

When recorded from the tonically contracted sternocleidomastoid (SCM) muscle, it is termed as cervical VEMP (cVEMP) and when recorded from the extra ocular muscles, it is termed as ocular VEMP (oVEMP).

Cervical VEMP has been proposed as a reliable non-invasive clinical tool for the assessment of saccular and inferior vestibular nerve function (Colebatch, Halmagyi, & Skuse, 1994; Robertson & Ireland, 1995). The normal cVEMP waveform is established as an ipsilateral inhibitory response characterized by a positive peak at about 13 ms and a negative peak at about 23 ms post stimulus onset (Colebatch, Halmagyi, & Skuse, 1994). It is understood to be recorded as a change in the activity within the sternocleidomastoid muscle (SCM) secondary to the acoustic stimulation of the vestibular system by the acoustic stimuli usually exceeding 90 dB SPL. They have been shown to be evoked by air-conducted (Colebatch, Halmagyi, & Skuse, 1994), bone-conducted (Sheykholeslami et al., 2000; Welgampola et al., 2001; Sheykholeslami et al., 2001) or galvanic (Watson & Colebatch, 1998) stimulation. The pathway reported to be involved in cVEMP production includes saccular macula, inferior vestibular nerve, lateral vestibular nucleus, medial vestibulospinal tract, and the motor neurons of the SCM muscle (Halmagyi & Curthoys, 1999). cVEMPs have also been recorded using binaural acoustic stimulation which yielded similar responses to that of monaural recordings (Wang & Young, 2003).

Ocular VEMP is established as a crossed excitatory biphasic response arising from the vestibulo-ocular reflex and is dominated by response from Inferior oblique and Inferior rectus activity (Iwasaki et al., 2007; Chihara et al., 2009; Rosengren et al., 2005; Todd et al., 2007;Welgampola, Migliaccio, Myrie, Minor, & Carey, 2009). The oVEMP recordings are reported to be best obtained when the electrodes are

placed under the eye and the gaze is elevated while recording (Rosengren et al, 2005; Iwasaki et al,2007; Todd et al, 2007; Cheng et al, 2009; Rosengren et al, 2009). As observed in studies, the elevation of gaze brings the belly of the inferior oblique muscle closer to the recording site, and thus, oVEMP amplitude becomes larger with upward gazing (Chihara et al., 2007; Govender et al., 2009; Welgampola et al., 2009). Upward gazing leads to contraction of muscles and subsequent synchronous activation of the motor units leading to larger amplitude of the compound action potentials. Studies report presence of oVEMP in patients with profound hearing loss, but intact auditory system and either absent or reduced in amplitude in individuals with vestibular pathologies.

Need for the study

Owing to the close proximity of the auditory and the vestibular systems, audiological and the vestibular symptoms may co-exist in an individual with vestibular dysfunction. Hence, a vestibular test battery generally consists of behavioural, electrophysiological and questionnaire based tests, both for auditory as well as vestibular system. The audiological tests which are administered to assess the vestibular dysfunction are detailed history, pure-tone audiometry, speech audiometry, immittance evaluation and auditory brainstem responses. The vestibular battery generally involves vestibular evoked myogenic potentials and electronystagmography (ENG). In addition to these, dynamic posturography, head impulse testing and subjective visual vertical test could be administered. Further, several questionnaires related to the pathology and quality of life assessment could be utilised. ENG is a diagnostic test used to record the corneo-retinal potential. ENG battery assesses only the lateral and superior semicircular canals along with the superior vestibular nerve,

and is not sensitive to pathologies affecting the otoliths organs (Bakr &Saleh, 2000). Vestibular evoked myogenic potential augments in the assessment of vestibular disorders by increasing specificity when investigating the site of lesion. cVEMP is employed in the test battery to assess the functioning of saccule and the inferior vestibular nerve whereas oVEMP assesses the utricle and the utriculo-ocular pathways. This shows that each of these tests hold their own when it comes to the relative importance, and hence, cannot be neglected or omitted from the test battery.

The clinical tests commonly used to assess the functioning of utricle are oVEMP and subjective visual vertical (SVV) testing. SVV is generally performed in complete darkness and requires the patient to adjust a vertical line (usually via remote control) so the line is perceived to be straight up and down. Individuals with normal peripheral vestibular function can generally set this line within 2 to 3 degrees off the true vertical (Bohmer & Mast, 1999; Zwergal et al., 2009). Offsets of the SVV line greater than 3° to either side are considered abnormal, and are generally associated with peripheral vestibular system dysfunction (specifically the utricle) or unilateral brainstem lesions (Bohmer & Mast, 1999; Zwergal et al., 2009). However, SVV has its own limitations. The SVV offsets are more likely to be detected only in the acute stages of the disorder and normal SVVs are frequently encountered in individuals with compensated peripheral vestibular lesion (Vibert, Hausler, & Safran, 1998) which is likely to reduce the sensitivity of the test. Additionally, SVV cannot be administered if the ENG equipment is not equipped with luminous line and remote control. Including this to the battery could add considerably to the overall cost of the set-up. These limitations have acted against the popular use of SVV in the clinics.

As mentioned earlier, oVEMP is recorded as a crossed vestibule-ocular reflex from the belly of the inferior oblique muscle. oVEMPs assess the integrity of the utricle and the superior vestibular nerve. oVEMP has been utilised for the diagnosis of vestibulopathies like inferior vestibular neuriris (Gabelic et al, 2011; Manzari, Burthess & Curthoys, 2012), multiple sclerosis (Gazioglu & Boz, 2012), vestibular schwannoma (Murofoshi & Takehisa, 2010), and other various peripheral vestibular disorders (Chiarovano, Vidal, Zamith & deWaele, 2011). Hence, in addition to the data from ENG and cVEMP recordings, oVEMP aids complementary and reliable information for the diagnosis of vestibulopathies. Unlike SVV, oVEMP has not been reported to alter its responses with central compensation, and this proves its superiority over SVV. Further, no additional special instrumentation is required for recording oVEMP, as it can be recorded from any auditory evoked potential equipment with certain basic requirements. However, adding oVEMP to an already cumbersome battery strains a clinician for time. Hence, recording of oVEMPs with simultaneous binaural acoustic stimulation, if feasible, could reduce the testing time compared to separate monaural recordings.

Few recent studies have reported that the binaural acoustic oVEMP test yields the same information as the monaural oVEMP test in normal hearing healthy individuals (Wang et al., 2008; Kim & Ban, 2012; Iwasaki, 2013). Furthermore, studies have also shown shorter testing time coupled with good test re-test reliability of binaural oVEMPs (Wang et al., 2008; Kim & Ban, 2012; Iwasaki, 2013). However, the number of participants used in these studies were 14 and 20, which is a small number considering the normative study. The statistical validity of the study is likely to be diminished with such a small population. Therefore, additional research is needed to further explore the feasibility of recording binaural oVEMPs in various

vestibular diseases. The study should seek to clarify the potential limitations of the procedure in the disease population, if any.

Aim of the study

The study was aimed to compare the oVEMP findings between monaural and simultaneous binaural acoustic stimulations in healthy individuals. The study further aimed to examine the feasibility and accuracy of binaural oVEMP in evaluation of some unilateral vestibular pathologies.

Objectives of the study

1. To compare the parameters of monaural oVEMP with simultaneous binaural oVEMP in healthy individuals.
2. To compare the parameters of monaural oVEMP with simultaneous binaural oVEMP in individuals with vestibulopathies.
3. To compare the findings of simultaneous binaural acoustic stimulations in healthy individuals to those obtained in a group of vestibular pathologies.

Hypothesis

The following null hypothesis was made for the study:

1. There is statistically no significant difference in oVEMP parameters obtained through monaural and simultaneous binaural acoustic stimulations in normal hearing healthy individuals

2. There is statistically no significant difference in oVEMP parameters obtained through monaural or simultaneous binaural acoustic stimulations in vestibulopathies.

3. There is statistically no significant difference in oVEMP parameters obtained through simultaneous binaural acoustic stimulations between group of healthy individuals and group with vestibular pathologies.

Chapter 2

Review of Literature

Vestibular system's sensitivity to sound has been postulated since the 20th century. Pietro Tullio's (1929) hypothesis that loud sounds generate vestibular symptoms in patients, eventually lead to the concept of "Tullio phenomenon". Technological advancements in electrophysiology and further inquiries about the tullio phenomenon supported initial physiologic studies in animals and humans evolving into VEMP testing. In 1964, Bickford and Cody were the first to record myogenic potentials in response to acoustic stimulations when electrodes were placed over the different muscles of neck and concluded the responses were of vestibular origin. However, the clinical utility of these potentials were not known until the 1990s. Colebatch and colleagues' inquiries lead to Vestibular Evoked Myogenic Potentials (VEMP), which are used clinically for the assessment of saccular and inferior vestibular nerve function (Colebatch, Halmagyi, & Skuse, 1994; Robertson & Ireland, 1995).

VEMPs have reported to be recorded from various muscles in the body such as the triceps (Cherchi et al., 2009), gastronemius muscles (Rudisill & Hain, 2008), trapezius muscle (Viart, Duclaux, Colleaux. & Dubreuil, 1997; Ghorab & Attar, 2004), sternocleidomastoid muscle (SCM) (Halmagyi, & Skuse, 1994; Robertson & Ireland, 1995) and the infra-orbital muscles (Rosengren et al., 2005; Todd et al., 2007; Cheng et al., 2009). When VEMPs are recorded with electrodes placed over the tonically contracted sternocleidomastoid muscle (SCM), they are termed as the cervical vestibular evoked myogenic potential (cVEMP). The system found to be concerned with the stimulation of the cVEMP is the vestibulo-collic reflex (VCR)

pathway (Colebatch, Halmagyi & Skuse, 1994). When the responses are recorded from inferior oblique muscle, they are termed ocular VEMP (oVEMP).

Ocular Vestibular Evoked Myogenic Potential (oVEMP)

VEMPs that are recorded from the extraocular muscles (maximum contribution from inferior oblique) in response to air-conducted sound, bone-conducted sound or galvanic stimulation (Rosengren et al., 2005; Iwasaki et al., 2007; Todd et al., 2007; Cheng et al., 2009; Curthoys, 2010) have been termed ocular VEMP (oVEMP). oVEMP is an excitatory response and comprises of the initial negative-positive biphasic peaks with first negative peak n1 at about 10ms and first positive peak p1 at about 15 ms after the stimulus onset (Todd et al.,2007; Rosengren et al., 2005). The neuronal pathways reported for the generation of oVEMPs include activation of superior vestibular nerve and the vestibular nucleus, which travels across medial longitudinal fasciculus, to the contralateral occulomotor nuclei, ocular nerves and to extra ocular muscles (Chihara et al., 2007).

Unlike cVEMP, the oVEMP is used for the assessment of utricle and functioning of the ascending vestibular pathway as crossed vestibulo-ocular reflex (Chihara et al., 2007; Wang et al., 2009; Govender et al., 2009). Because the inferior oblique muscle is the most superficial extra ocular muscle that transverses to the electrode recording site, oVEMP is reported to be obtained easily from the skin surface beneath the eye, contralateral to the acoustically stimulated ear. Additionally, the studies report that detection of muscular potential requires upward gazing because belly of the inferior oblique muscle is brought close to the recording electrode and relatively synchronous motor unit activation caused by the inferior oblique muscle contraction can be recorded (Chihara et al., 2007; Govender et al., 2009; Welgampola

et al., 2009). Thus, the amplitude of oVEMP has been observed to increase when subject gazes upward (Chihara et al., 2007; Govender et al., 2009; Welgampola et al., 2009). Studies in literature have documented the effects of various subject and stimulus related parameters in normals as well as diseased populations.

Clinical applications of oVEMP

The clinical utility of oVEMP has been evaluated in several studies. In affected ears of patients suffering from MD, oVEMPs were found to be abnormal in 65% when evoked by air conducted stimulation (Huang, Wang & Young, 2011). Abnormalities of oVEMPs in Meniere's disease affected ears were reported to be characterized by declined response prevalence, decreased amplitudes and increased thresholds (Winters, Berg, Grolman, & Klis, 2012). Furthermore, MD has been shown to result in altered frequency tuning characteristics of VEMPs. When eliciting oVEMPs in MD-affected ears, maximal amplitudes and lowest thresholds were achieved using 1000 Hz tone bursts, whereas healthy controls and unaffected MD ears showed optimal oVEMP results upon 500 Hz tone bursts (Winters, Berg, Grolman, & Klis, 2012; Sandhu et al., 2012). It is not only the affected ears in MD patients which have shown VEMP abnormalities, but also unaffected ears. Abnormal oVEMPs and cVEMPs were found in 40% and 15% of unaffected ears, respectively (Huang, Wang & Young, 2011). Thus, VEMP characteristics may enable separation from other disorders and thus facilitate diagnosis of MD.

The prevalence of abnormalities in cVEMP or oVEMP in patients with BPPV was found to be 20.5% (Talaat et al., 2013). The forms of VEMP abnormalities observed were absence of responses, delayed latencies and asymmetrical asymmetry between the two ear responses. Studies have revealed that there was a tendency for

posterior canal BPPV patients to show higher rates of abnormal responses of oVEMP bilaterally as well as unilaterally compared with those of cVEMP and caloric tests (Nakahara, Yoshimura, Tsuda & Murofushi, 2013; Singh, Sinha, Rajeshwari & Barman, 2014).

Since, oVEMPs assess the integrity of the utricle and the superior vestibular nerve, it has been utilised for the diagnosis of vestibulopathies like inferior vestibular neuriris (Gabelic et al, 2011; Manzari, Burthess & Curthoys, 2012), multiple sclerosis (Gazioglu & Boz, 2012), vestibular schwannoma (Murofoshi & Takehisa, 2010), and other various peripheral vestibular disorders (Chiarovano, Vidal, Zamith, & deWaele, 2011). Hence, in addition to the data from ENG and cVEMP recordings, oVEMP aids complementary and reliable information for the diagnosis of vestibulopathies. However, this comes with an additional time burden for an already cumbersome vestibular evaluation battery. This has resulted in exploration of the feasibility for simultaneous multiple recordings.

oVEMP recorded from simultaneous binaural acoustic stimulation

Binaural acoustic stimulation can be used when recording oVEMPs as a more time efficient and comfortable means of acquiring such data. In a study by Wang et al. (2008), the authors obtained monaural oVEMP recordings and binaural oVEMP recordings from 20 healthy normal hearing individuals. Thresholds, peak-to-peak amplitudes, latencies and amplitude asymmetry ratio were compared between monaural and binaural oVEMP recordings. The results revealed significant positive correlations between monaural oVEMP and binaural oVEMP with respect to threshold, latencies and amplitude. However, in this study, the oVEMP recordings

were not done on actual clinical population and therefore validation was not achieved. The study also did not check for the test-retest reliability of binaural recordings.

Kim and Ban (2012) conducted a study to evaluate the test-retest reliability of simultaneous binaural acoustic evoked oVEMP and to identify the convenience of binaural oVEMP in normal population. Their results of recordings for 13 healthy individuals revealed a lack of difference between the stimulation conditions. They concluded that Bin-oVEMP provided almost the same information as the Mon-oVEMP, and additionally, the testing time was shorter. Futhermore, Bin-oVEMP was found to have excellent test-retest reliability. However, this study as with the previous one, also was not validated on actual clinical population.

Iwasaki et al. (2013), recorded oVEMPs to monaural and binaural acoustic stimulations in patients with unilateral vestibular dysfunction as well as healthy subjects. The aim of their study was to investigate the feasibility of recording oVEMPs to binaural acoustic stimulations in patients with vestibular dysfunction as well as healthy subjects. The recordings were obtained from 24 healthy individuals, 9 patients with unilateral vestibular schwannoma and 5 patients with unilateral vestibular neuritis. Their results revealed no significant difference binaural acoustic and monaural acoustic stimulations in terms of response prevalence, amplitude, and latencies, although they showed significantly smaller asymmetry ratios relative to monaural acoustic stimulations. In patients with unilateral vestibular dysfunction, oVEMPs to binaural acoustic stimulation could detect vestibular dysfunction with the same abnormality ratios as oVEMPs to monaural acoustic stimulations, suggesting that oVEMPs to binaural acoustic stimulations were applicable in patients with vestibular dysfunction as well as normal healthy subjects.

The statistical validity of studies by Wang et al (2008) and Kim & Ban (2012) are questionable since the number of participants used in these studies were 14 and 20, which is a small number considering the normative study. The number of clinical subjects of each disorder is small (9 & 5) which is likely to diminish the statistical validity of the study. Therefore, further research regarding the feasibility of binaural oVEMP recordings in clinical population is necessary.

Chapter 3

Method

Participants

The study consisted of two groups of participants; a group of healthy individuals and a clinical group. The group of healthy individuals consisted of 30 participants in the age range of 15-50 years with normal audio-vestibular system. Normal auditory system was ensured through a lack of history of hearing related symptoms and hearing sensitivity within normal limits (≤15 dB HL) at octave frequencies from 250 Hz through 8000 Hz for air conduction and 500 Hz through 4000 Hz for bone conduction. Existence of normal auditory system was further reinforced by normal results on ABR, which was determined by presence of waves I, III and V within normal ranges for absolute latency (2, 4 and 6 msec), inter-peak latency (2.0 ± 0.4 ms,1.8 ± 0.4 ms and, 0.9 ± 0.4 ms), interaural latency difference of wave V not exceeding 0.4ms and, amplitude ratio of V/I not exceeding 1 (Musiek, Kibbe, Rackliffe & Weider, 1984; Glemis & Mitchell, 1977; Rosenhamer, Lindstrom & Lundborg, 1981; Selters & Brackmann, 1977). Normalcy of the vestibular system was ascertained through a lack of positive history for vertigo or imbalance along with normal results on behavioural balance function assessment which included Romberg test (absence of any noticeable sway), Fukuda stepping test (< 45˚ deviation on either side), Tandem gait test (absence of sway or imbalance) and Past pointing test (lack of tremors and undershooting or overshooting of target).

The clinical group consisted of 30 participants diagnosed with either definite Meniere's disease (N=15) or Benign Paroxysmal Positional Vertigo (N=15) in the age range of 15-50 years. The diagnosis of definite MD was reached using the criteria put

forward by the Committee on hearing and equilibrium guidelines for the diagnosis and evaluation of therapy in Meniere's disease of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS, 1995). As per this guideline, 'definite MD' is to be diagnosed if the subject has two or more definitive spontaneous episodes of vertigo lasting for not less than 20 minutes each; existence of hearing loss that has been audiometrically documented on atleast one occasion; and presence of tinnitus or aural fullness with other causes of such precipitations eliminated. The diagnosis of Benign Paroxysmal Positional Vertigo (BPPV) was based on the guidelines set forth by the AAO-HNS (Bhattacharyya et al., 2008). According to this, the diagnosis of BPPV is arrived in case there is history of positional vertigo along with positive results on Dix-Hallpike manoeuvre or Supine roll test. The other causes of similar manifestations as the clinical group was ruled out through a battery of evaluations which was inclusive of otolaryngological evaluations and audiological evaluations. These included pure-tone audiometry, speech audiometry, immittance evaluation, auditory brainstem responses, electronystagmography test battery for peripheral as well as central lesions and a series of laboratory tests that were felt necessary by the otolaryngologist to arrive at the diagnosis. Additionally, all the participants had 'A' type tympanogram and presence of acoustic reflex thresholds within normal limits. Irrespective of the groups, the participants were also required to demonstrate uncomfortable level (UCL) in excess of 105 dBHL. A written consent was obtained from all the participants before their recruitment for the study and their participation in the study was on a non-payment basis.

Instrumentation

A calibrated 2 channel Grason Stadler Incorporated (GSI) -61 clinical audiometer, with TDH-50-P supra-aural earphones encased in MX-41/AR ear cushions, was used to obtain air-conduction thresholds, speech recognition thresholds, speech identification scores and UCL. Radioear B-71 bone vibrator, along with the same audiometer, was used to obtain bone-conduction thresholds. Tympanograms along with ipsilateral and contralateral acoustic reflex thresholds were obtained using GSI- Tympstar middle ear analyzer (Version 2.0.0). A Biologic Navigator Pro auditory evoked potential unit (version 7.0.0) was used to record click evoked auditory brainstem responses and air-conducted tone-burst evoked ocular VEMP. Stimulus was presented through impedance matched Etymotic ER-3A insert earphones for oVEMP as well as auditory brainstem response recording. Recorders and Medicare Systems Pvt. Ltd. (RMS) ENG instrument was used to record Electronystagmography.

Test Environment

All the tests, except ENG, were conducted in well illuminated sound treated rooms with noise levels within permissible limits (ANSI S 3.1, 1999). ENG was recorded in a dark room. Evaluations using the audiometer were carried out in a double room set-up whereas immittance evaluation, ABR, oVEMP and ENG recordings were carried out in single room set-ups.

Procedure

The test procedures were divided into two phases. Phase 1 consisted of tests to fulfill the subject selection criteria and Phase 2 consisted of monaural and binaural oVEMP recordings.

Phase 1: Tests for Subject selection

All the participants underwent a detailed case history using questionnaire developed by Maryland Hearing and Balance Centre (2004). This questionnaire contains five sections and consists of questions regarding nature, duration, frequency and triggering mechanisms of vertiginous attacks, if any. Information regarding any associated neurological problems, visual deficits and prior medical history was also obtained.

Otoscopy was performed for each subject to rule out occlusion of external ear canal prior to the commencement of audiological evaluations. Pure-tone thresholds were obtained for all the participants using Carhart and Jerger (1959) modified Hughson and Westlake procedure at octave frequencies from 250 through 8000 Hz for air-conduction and 250 through 4000 Hz for bone-conduction. Speech recognition threshold (SRTs) for bisyllabic word lists were obtained using bracketing method and word recognition scores (WRS) were obtained using phonetically balanced word lists in participants' native language at the prescribed level for each list. UCL for speech was obtained for both the ears using ascending method. Immittance evaluation was carried out for all the participants using a probe-tone frequency of 226 Hz at 85 dB SPL by varying pressure from -400 to +200 daPa at a 50 daPa/s. Ipsilateral and contralateral acoustic reflex thresholds were obtained using the same probe-tone for stimulus frequencies of 500 Hz, 1 KHz, 2 KHz and 4 KHz. Using rarefaction polarity and Blackmann gated clicks (2 ms rise/fall time and no plateau) two channel ABRs were recorded for 11.1 Hz and 90.1 Hz stimulation rate in order to rule out retro-cochlear pathology.

The vestibular system assessment consisted of both the behavioural tests and ENG tests. These were administered before oVEMP recordings for the fulfilment of the subject selection criteria. The participants were asked to refrain from taking anti-vertigo medications and consumption of alcohol atleast 48 hours before the testing. The behavioural procedures for vestibular assessment were carried out before the participants underwent ENG testing.

Romberg test was carried out by instructing the participant to keep his/her feet firmly together, arms stretched out and parallel to the ground with eyes open at first. The balance of the subject was noted. The same procedure was repeated with eyes closed for 1 minute and balance (any sway) was noted (Goebel, 2008, Black, 1982; Johnson et. al, 2005). To carry out the Fukuda stepping test the participant was made to stand inside a circle of 0.5 m radius divided into angles of 30˚ and instructed to march at the same place at the pace of a brisk walk (approximately 60 steps/second) with eyes closed and both the hands stretched out in front similar to Romberg test. Angle and direction of rotation was noted (Fukuda, 1959) and any deviation of > 45˚ to either side was considered abnormal (Harit & Singh, 2012). In Tandem gait testing the participants were asked to walk in a straight line heel-to-toe with the head held straight and eyes open. Deviation to any side or loss of balance was noted (DeMyer, 1974).

The ENG battery consisted of tests to evaluate both the peripheral and central vestibular system using single channel recording of retino corneal potential. This was started with calibration of ENG equipment for each participant. The input sensitivity of the instrument was adjusted such that every 10˚ of eye movement corresponded to 10mm of markings in the recording paper. The responses were band pass filtered

between 0.01 and 30Hz. The peripheral tests consisted of bithermal caloric tests, positional tests and the Dix-hallpike manuever. The central test consisted of saccade test, gaze test and optokinetic test.

Saccade test required the participants to follow the lights on the light bar without movement of their heads. The lights were randomly generated at the angle of 10˚ either to the right or left. The saccadic testing was interpreted base on the number of hypermetric (eyes overshoot the target) saccades or hypometric (eyes undershoot the target) saccades. Results were considered to be abnormal if atleast 50% of the calibration excursions had overshoot or undershoot (Alpert, Coats & Perusquia, 1975; Haring & Simmons, 1973). The instruction given for optokinetic testing was to track the moving visual target (right to left or left to right) on the calibration light bar without moving the head. The eye movements were recorded for 30 seconds in each direction. Optokinetic nystagmus was assessed in terms of the symmetry of the pattern for the two directions. Asymmetry was considered to be present, if there was difference in slow phase velocity (SPV) of two directions of at least 10-30˚/s (Barber & Stockwell,1980). Gaze testing involved participants to look constantly at a static visual target located on the calibration light bar at centre, 30˚ to the right and 30˚ to the left. The recordings of eye movements were carried out for 1 minute in each position. The results were interpreted based on presence or absence of nystagmus on each position and calculation of the slow phase velocity (SPV) in eyes closed and eyes open condition. Generally, if the average SPV exceeds 8˚/s, it is considered abnormal.

To record the positional nystagmus, the positions used were; Sitting erect, Supine, supine with head turned to right, head and body to lateral right, supine with

head turned left lateral, head and body to lateral left and supine with head hanging for central pathology. The nystagmus was recorded for 30 seconds with eyes closed in each position. The presence of nystagmus in 3 or more positions was considered as abnormal. The presence of direction changing or direction fixed nystagmus was also noted. Dix Hallpike manuever was adopted as a criteria for the diagnosis of posterior canal posterior canal BPPV. The nystagmus was first recorded for 30 seconds in sitting position followed by rapidly bringing the subject from sitting to supine head hanging position with head turned to right and recording for another 30 seconds. The procedure was repeated with head hanging position with head turned to left. All the recordings were carried out with eyes closed. The test was considered positive for BPPV based on the criteria given by Bhattacharya et al. (2008). According to the criteria, BPPV was diagnosed if Vertigo associated with nystagmus was provoked by the Dix-Hallpike test, vertigo and nystagmus appeared a few seconds after administering the test and, the provoked vertigo and nystagmus increase and then resolves within a time period of 60 seconds from onset of nystagmus.

For conducting the caloric testing, the patients were made to lie in supine position with head elevated by 30˚ in order to achieve the vertical orientation of lateral semi circular canal. Open loop water irrigation with warm water at 44˚ C and cold water at 33˚ C was carried out for 30 seconds per temperature per ear. The order of irrigation used were right 44˚ C, left 44˚ C, right 30˚ C and left 30˚ C with a rest period of 8 minutes between two successive irrigations. The recording was done for 3 minutes at the end of each irrigation. Arithmetic problems like addition of 6 in serial fashion (3.9,15 so on) was given to maintain the participants alertness. The cumulative frequency for each irrigation condition was calculated based on the number of beats in 3 adjacent 10 sec intervals which had the highest number of beats.

The obtained culmination frequency for all four irrigation conditions was plotted in Claussen's butterfly chart for interpretation. Table 1 shows the test protocol used for recording ENG.

Phase 2: oVEMP recordings

Bio-Logic Navigator Pro auditory evoked potential unit was used to acquire oVEMP from all the participants. For this, the participant was seated in a reclining chair in a sound treated room. The recording sites were cleaned with commercially available abrasive gel to obtain acceptable electrode impedances. The stimulus and acquisition parameters described by previous studies were replicated for the study (Chihara et al., 2007, Rosengren et al., 2009, Wang et al., 2009; Singh & Barman; 2013). Surface electrodes were placed 1 cm (non-inverting electrode) and 3 cm (inverting electrode) below the centre of each lower eyelid, and the ground electrode was placed at the forehead. Using adequate amount of conductive paste, gold plated disc-type electrodes were placed on the electrode sites described above and secured in place using surgical plaster. Absolute and inter electrode impedance was maintained below 5 kΩ and 2 kΩ respectively. The participants were instructed to elevate their gaze at 30^{o}-35^{o} during recording in order to achieve proximity of the inferior oblique muscle to skin surface. Alternating polarity 500 Hz tone-burst (1 ms rise/fall time with 2 ms plateau time) were presented at a stimulation rate of 5.1 Hz via the standard foam insert earphones ER-3A of the Biologic Navigator Pro evoked potential system. Two hundred sweeps of electromyogenic (EMG) activity was recorded from the side contralateral to the acoustic stimulation using an epoch of 64 ms which was inclusive of 10.5 ms pre-stimulus recording. The responses were band-pass filtered between 1 and 1000 Hz and multiplied by a factor of 30,000. The artifact rejection system was

switched off in order to avoid rejection of inherently large myogenic responses. The initial stimulus intensity used was 125 dB SPL which was subsequently decreased in 10-dB steps until the waveform was absent. The stimulus intensity was then increased in steps of 5 dB until the oVEMP response reappeared. The lowest level in dB SPL that produced replicable and reliable responses was considered as threshold. The recordings for monaural testing of right ear, monaural testing of left ear and binaural presentation of stimuli were carried out in a single session. Adequate rest period between recordings was given in order to avoid muscle strain and involuntary eye blinks. The order of testing between the monaural and binaural modes was counter balanced to avoid the order effect.

The data for monaural recordings was obtained from the contralateral waveforms. The data for binaural presentation of stimuli was obtained simultaneously from electrodes under each eye. At least two waveforms were consecutively obtained for every recording. The two waveforms were then added to obtain the weighted average waveform. These weighted average waveforms were analysed by two independent experienced judges. The above mentioned procedure for oVEMP recording was repeated on randomly selected 10 of the 30 healthy individuals within span of 15 days to measure the test- retest reliability. Prior to the second recording, the questionnaire was re-administered in order to prevent adulteration of responses through recent episodes of vestibular pathologies, if any.

Analysis of oVEMP

Peak-to-peak amplitude and absolute latencies of n1 and p1 peaks were recorded for analysis. Peak-to-peak amplitudes (n1-p1) and absolute latencies (n1 & p1) were calculated from the weighted average waveforms for each condition. The

inter-aural difference ratio (IAD), also called asymmetry ratio (AR) or inter-aural amplitude ratio (IAAR), was calculated using the Jonkee's formula (Li, Howlden and Tomlinson, 1999), mentioned in equation 1.

$$IAD=\left|\frac{\text{Left peak}-\text{to}-\text{peak amplitude}-\text{Right peak}-\text{to}-\text{peak amplitude}}{\text{Left peak}-\text{to}-\text{peak amplitude}+\text{Right peak}-\text{to}-\text{peak amplitude}}\right|*100 \qquad \text{Eqn 1}$$

Where, IAD is inter-aural amplitude ratio.

Statistical analysis

Chronbach's alpha tests and Karl Pearson's correlation coefficient was administered to determine the inter-judge reliability for peak markings. Upon finding of $\alpha > 0.9$, the markings of only one judge were used for further statistical analysis. Descriptive Statistics was done to obtain the mean and standard deviation of n1 latency, p1 latency, peak-to-peak amplitude, threshold and asymmetry ratio for the three groups across.

A one way repeated measures analysis of variance (one way repeated measures ANOVA) was administered to find out the differences, if any, that existed between the presentation modes (monaural vs binaural). This was done separately for each peak latency, peak-to-peak amplitude and threshold of oVEMP. The comparison of IAD between the conditions was achieved using one-way ANOVA. Comparison between the groups for binaural recordings only was done using Multivariate analysis of variance (MANOVA). Chronbach's alpha test was carried out to check for the test retest reliability of the binaural oVEMP responses. Post hoc analysis was carried out using Bonferroni adjusted multiple comparisons wherever required.

Chapter 4

Results

In quest for a time effective method to record oVEMP, the present study was aimed at comparing the findings of oVEMP obtained from monaural acoustic stimulation and simultaneous binaural acoustic stimulations. The study was carried out on two groups of participants; Group 1 consisted of 36 healthy individuals, whereas Group 2 consisted of individuals diagnosed with Meniere's disease (N=15) or BPPV (N=15). The absolute latencies, peak-to-peak amplitudes, thresholds and asymmetry ratio were calculated for both monaural and binaural stimulation condition and the data obtained was subjected to statistical analysis.

Comparison of oVEMP responses in healthy individuals

Among the healthy individuals, all 36 had bilateral presence of oVEMP, thereby showing 100% response rate. This was true for both monaural as well as binaural recording of oVEMP. Figure 1 shows the individual and grand averaged waveforms recorded from each of the ear of healthy subjects in both the recording conditions.

Figure 1

Individual and grand averaged oVEMP waveforms in healthy individuals.

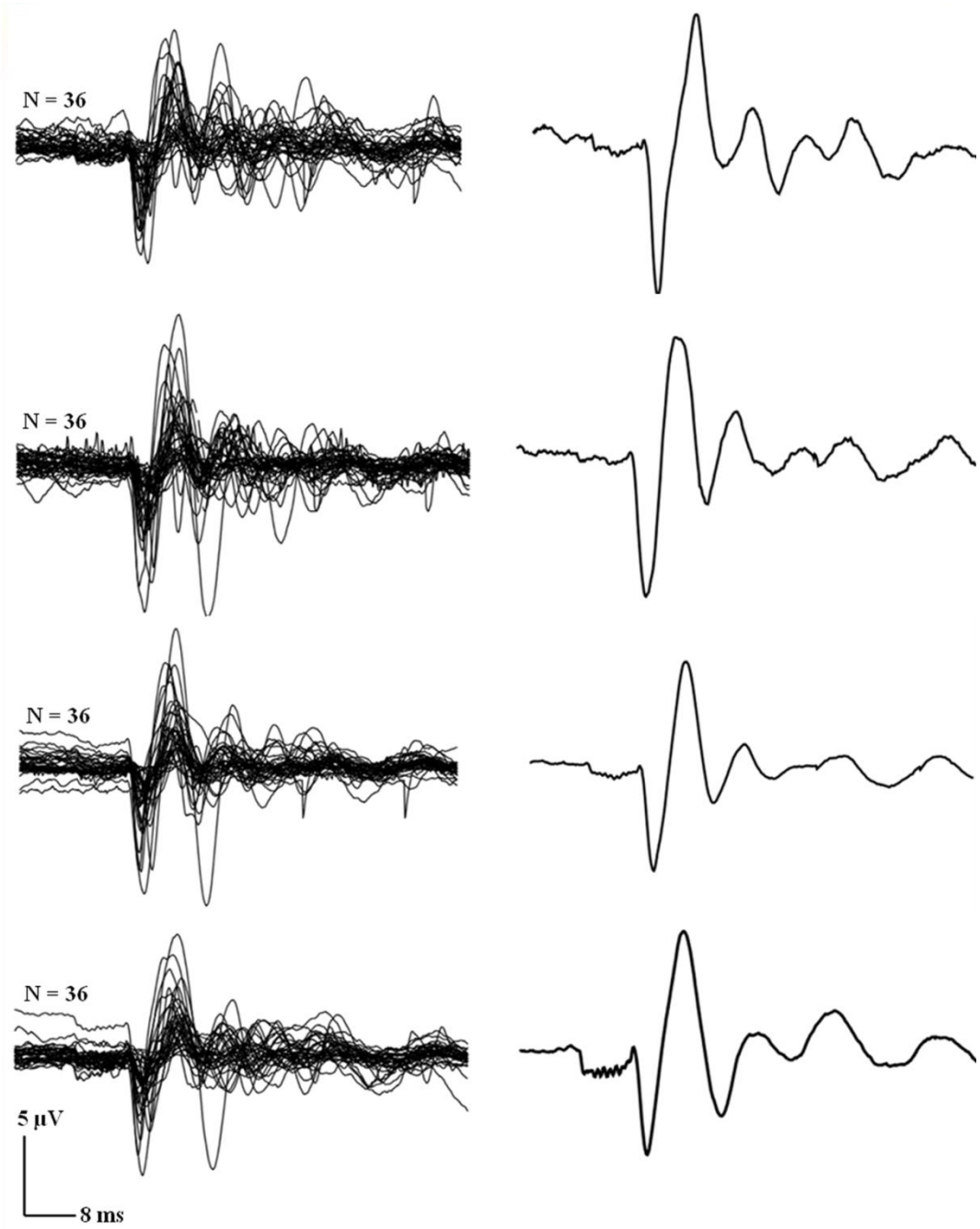

Figure1: The individual and grand averaged responses of healthy individuals for monaural recordings in right ear (panel 1), binaural recordings in right ear (panel 2), monaural recordings in left ear (panel 3) and binaural recordings in left ear (panel 4). 'N' indicates number of individuals in present responses.

Descriptive statistics was administered in order to obtain the mean and standard deviation values for all the oVEMP parameters. For monaural as well as binaural stimulation conditions in healthy individuals, the mean values of each of these parameters did not appear to vary between the two recording conditions. The mean and standard deviation of all the parameters for the two recording conditions are shown in Table 1.

Table 1.

Mean and standard deviation (S.D) values of latency, amplitude, threshold, and asymmetry ratio in healthy individuals group across the two stimulation conditions.

Parameter	Monaural condition		Binaural condition	
Ear	Right	Left	Right	Left
n1 latency (in ms)	10.50 (0.82)	10.38(0.72)	10.70(0.90)	10.53(0.80)
p1 latency (in ms)	16.02(1.19)	15.88 (1.06)	16.13(1.09)	16.06(1.10)
Peak-to-peak amplitude (in μV)	5.85 (4.54)	8.65 (6.00)	5.40 (3.89)	7.85 (5.62)
Threshold (in dB SPL)	112.59 (5.28)	109.31 (5.30)	111.90 (5.73)	108.45 (4.65)
Asymmetry Ratio (in %)	30.09 (20.68)		25.26 (19.40)	

Note: The values in brackets represent standard deviation; 'ms': milli seconds; 'μV': micro volts

In order to examine the statistical significance of the above mentioned observations for absolute peak latencies, peak-to-peak amplitude, threshold and asymmetry ratio, separate one way repeated measures AVOVA for each parameter

and ear. The results revealed no significant main effect of the stimulation condition (monaural and binaural stimulation) on the absolute latencies of N1 in right [F (1,35)=3.588, p >0.05] as well as left ear [F(1,35)=3.059, p >0.05] and P1 in right [F (1,35)=0.462, p >0.05] as well as left ears [F(1,35)=3.710, p >0.05].

Further, the results of one-way repeated measures ANOVA also showed there was no significant main effect of stimulation condition on peak –to-peak amplitude in right [F (1,35)=2.932, p >0.05] or left ears [F (1,35)=3.866, p >0.05]. Similarly, no significant main effect of stimulation condition was seen on asymmetry ratios [F(1,35)=3.013, p >0.05].The lowest intensity at which replicable oVEMP responses were obtained was considered as the threshold. The threshold was compared between the two stimulation conditions using one-way repeated measures ANOVA. The revealed no significant main effect of the stimulation condition on threshold in both right [F(1,35)=2.074, p >0.05] and left ears[F(1,35)=2.381, p >0.05]. Figure 2 represents mean and standard deviation parameters for latency, peak-to-peak amplitude, threshold and asymmetry ration across the two stimulation conditions.

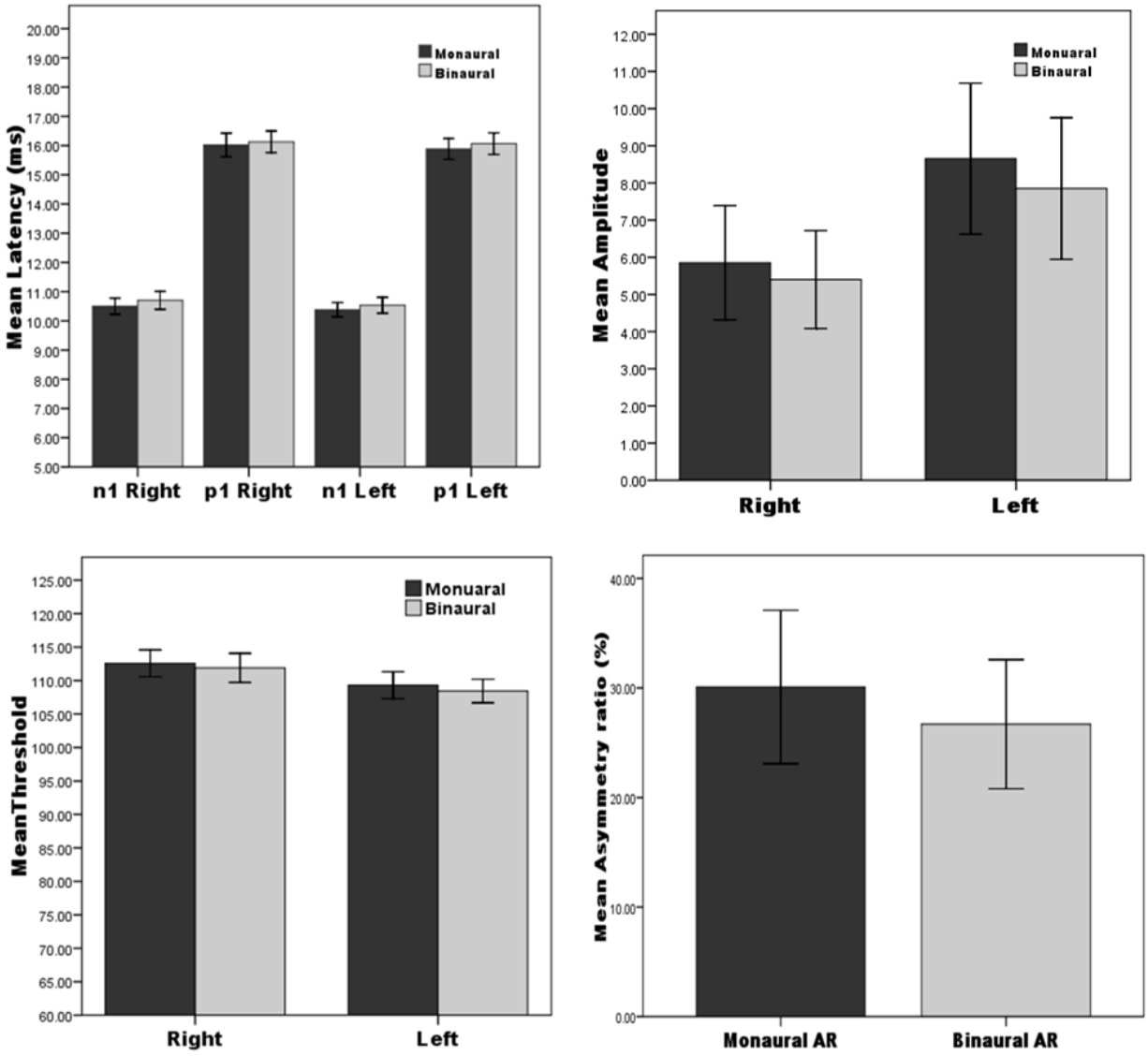

Figure 2: The mean and 95% confidence intervals of n1 and p1 latencies (upper left panel), peak-to-peak amplitude (upper right panel), thresholds (lower left panel) and inter aural amplitude ratio (lower right panel) for monaural and binaural recordings. 'AR': Asymmetry ratio

Based on these findings it can be inferred that, there was no significant difference between the monaural and binaural recording conditions for any of the parameters considered.

Comparison of oVEMP responses in pathologic group

Pathologic group consisted of individuals diagnosed with definite Meniere's disease (N=15) and Benign paroxysmal Positional Vertigo (N=15). The presence/absence of oVEMP responses followed similar trends between monaural and binaural recording conditions. Bilateral absence of oVEMP responses for monaural stimulation showed absence of responses for binaural stimulations as well. Similarly, unilateral absence of oVEMP responses in monaural recordings showed unilateral absence in binaural recordings in the corresponding ear. Thereby, implying 100% agreement between the two stimulation conditions. Table 2 shows the demographic details and oVEMP response presence/absence.

Table 2.

Demographic details of the pathologic group

SL. No	Pathology	Age/ gender	Duration (in months)	Right ear		Left ear	
				Monaural	Binaural	Monaural	Binaural
1	MD	25/F	6	_	_	_	_
2	MD	34/M	5	+	+	+	+
3	MD	39/F	0.66	+	+	+	+
4	MD	51/M	18	_	_	_	_
5	MD	35/M	5	+	+	_	_
6	MD	36/M	1	+	+	+	+
7	MD	33/M	1	+	+	+	+
8	MD	39/F	3	_	_	_	_
9	MD	43/M	2	_	_	_	_

10	MD	47/M	5	+	+	+	+
11	MD	45/F	0.66	+	+	+	+
12	MD	40/M	9	_	_	_	_
13	MD	51/F	2	_	_	+	+
14	MD	30/M	5	_	_	+	+
15	MD	49/F	0.66	_	_	_	_
16	BPPV	40/F	18	+	+	_	_
17	BPPV	50/F	3	_	_	_	_
18	BPPV	64/M	4	+	+	_	_
19	BPPV	36/M	24	_	_	_	_
20	BPPV	58/M	12	+	+	+	+
21	BPPV	60/F	12	_	_	_	_
22	BPPV	57/F	8	_	_	_	_
23	BPPV	50/M	4	_	_	_	_
24	BPPV	37/F	12	+	+	+	+
25	BPPV	45/M	0.42	+	+	+	+
26	BPPV	57/F	0.33	+	+	+	+
27	BPPV	40/F	24	_	_	_	_
28	BPPV	42/M	0.75	+	+	_	_
29	BPPV	52/M	6	+	+	+	+
30	BPPV	65/F	12	_	_	+	+

The oVEMP responses with Monaural acoustic stimulations were absent bilaterally in 40% (N=12) of the participants and unilateral presence of oVEMP

responses were seen in 20% (N=6) of the individuals. The remaining 40% (N=12) of individuals had bilateral presence of oVEMP responses. Exactly same proportions for presence/absence of responses were obtained with simultaneous binaural stimulations. The individual and grand averaged waveforms of the pathologic group are depicted in Figure 3.

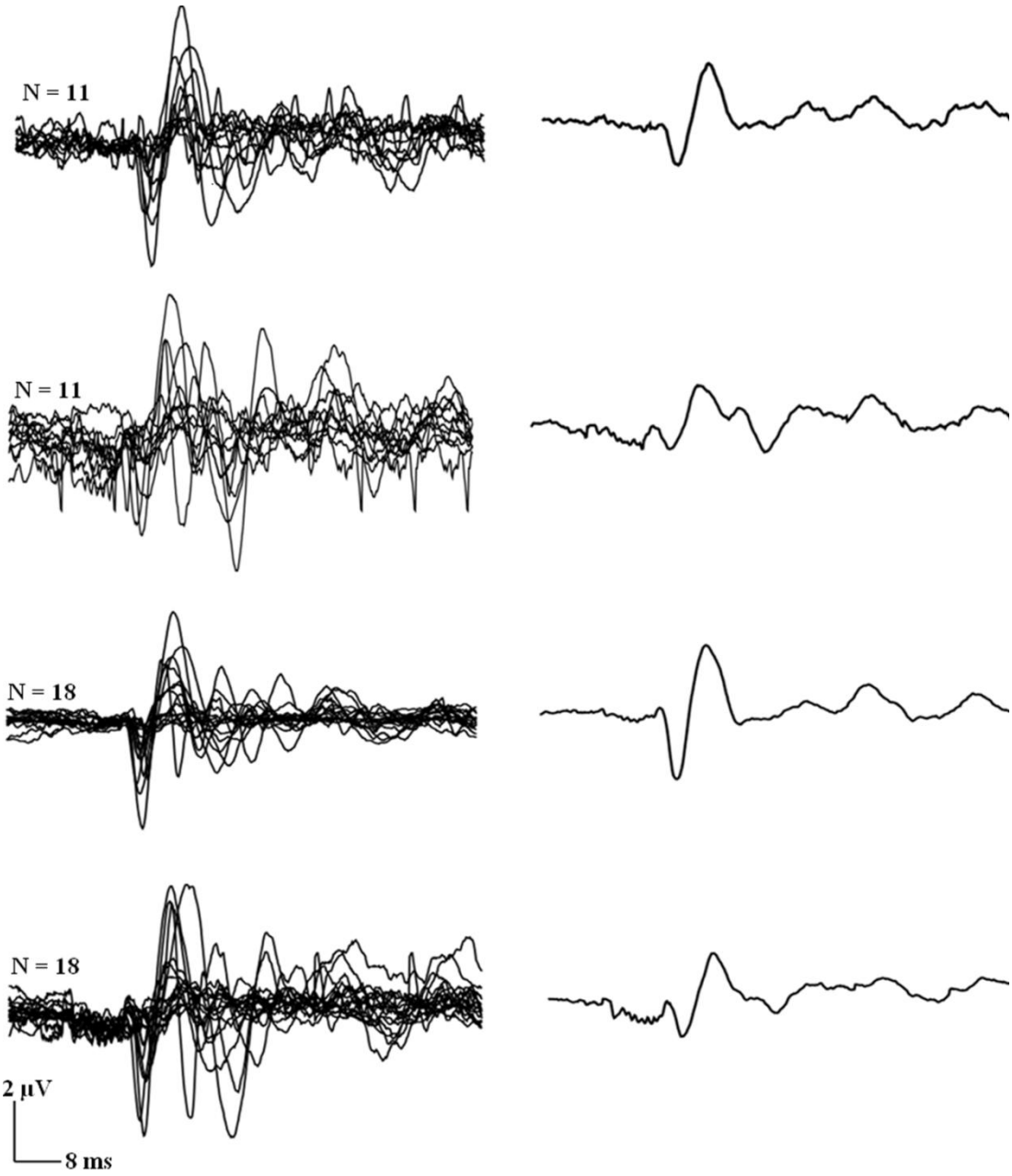

Figure 3: The individual (left panels) and grand averaged (right panels) ocular vestibular evoked myogenic potential responses from pathologic group for monaural

recordings and binaural recordings in right ear (top two panels) and monaural and binaural recordings in left ear (bottom two panels). 'N' indicates number of individuals in present responses.

Descriptive statistics was administered in order to obtain the mean and standard deviation (SD) values for the measures of absolute latencies, peak-to-peak amplitude and threshold. The mean and standard deviation of all these parameters for monaural and binaural stimulation conditions are shown in Table 3.

Table 3.

Mean and Standard deviation (S.D) values of latency, amplitude and threshold measures in pathologic group across the two stimulation conditions.

Parameter	Monaural condition		Binaural condition	
Ear	Unaffected	Affected	Unaffected	Affected
n1 latency(in ms)	10.60(0.97)	11.04 (1.28)	10.71(0.90)	10.93(1.51)
p1 latency (in ms)	16.06(1.28)	16.29(1.05)	16.03(1.39)	16.36(2.15)
Peak-to-peak amplitude (in μV)	4.12(3.86)	2.83 (2.24)	3.75(3.44)	2.52(2.10)
Threshold (in dB SPL)	115 (7.28)	116.25(7.11)	115(7.28)	108.45(4.64)
Asymmetry Ratio (%)	51.25(37.83)		52.1632 (36.73)	

Note: The values in brackets represent standard deviation; 'ms': milli seconds; 'μV': micro volts

In order to examine the statistical significance of the above mentioned observations for absolute peak latencies, peak-to-peak amplitude, threshold and asymmetry ratio, separate one way repeated measures AVOVA for each parameter and ear. The results revealed no significant main effect of the stimulation condition on the absolute latency of n1 in right [F (1,17)=2.2856, p >0.05] as well as left ear [F(1,11)=1.686, p >0.05] and p1 in right [F (1, 17) = 0.057, p >0.05] as well as left ear [F(1,11)=0.246, p >0.05].

The results revealed for amplitude measures revealed no significant main effect of the stimulation condition in both right [F (1,35)=2.932, p >0.05] and left ear [F (1,35)=3.866, p >0.05]. Also, no significant difference existed between the monaural and binaural asymmetry ratios [F(1,35)=3.013, p >0.05] .One-way repeated measures ANOVA revealed no significant main effect of stimulation condition on thresholds in both right [F(1,35)=0, p >0.05] and left ears [F(1,35)=1, p >0.05]. Figure 2 represents mean and standard deviation parameters for latency, peak-to-peak amplitude, threshold and asymmetry ration across the two stimulation conditions. Figure 4 represents mean and standard deviation parameters for latency, peak-to-peak amplitude, threshold and asymmetry ration across the two stimulation conditions.

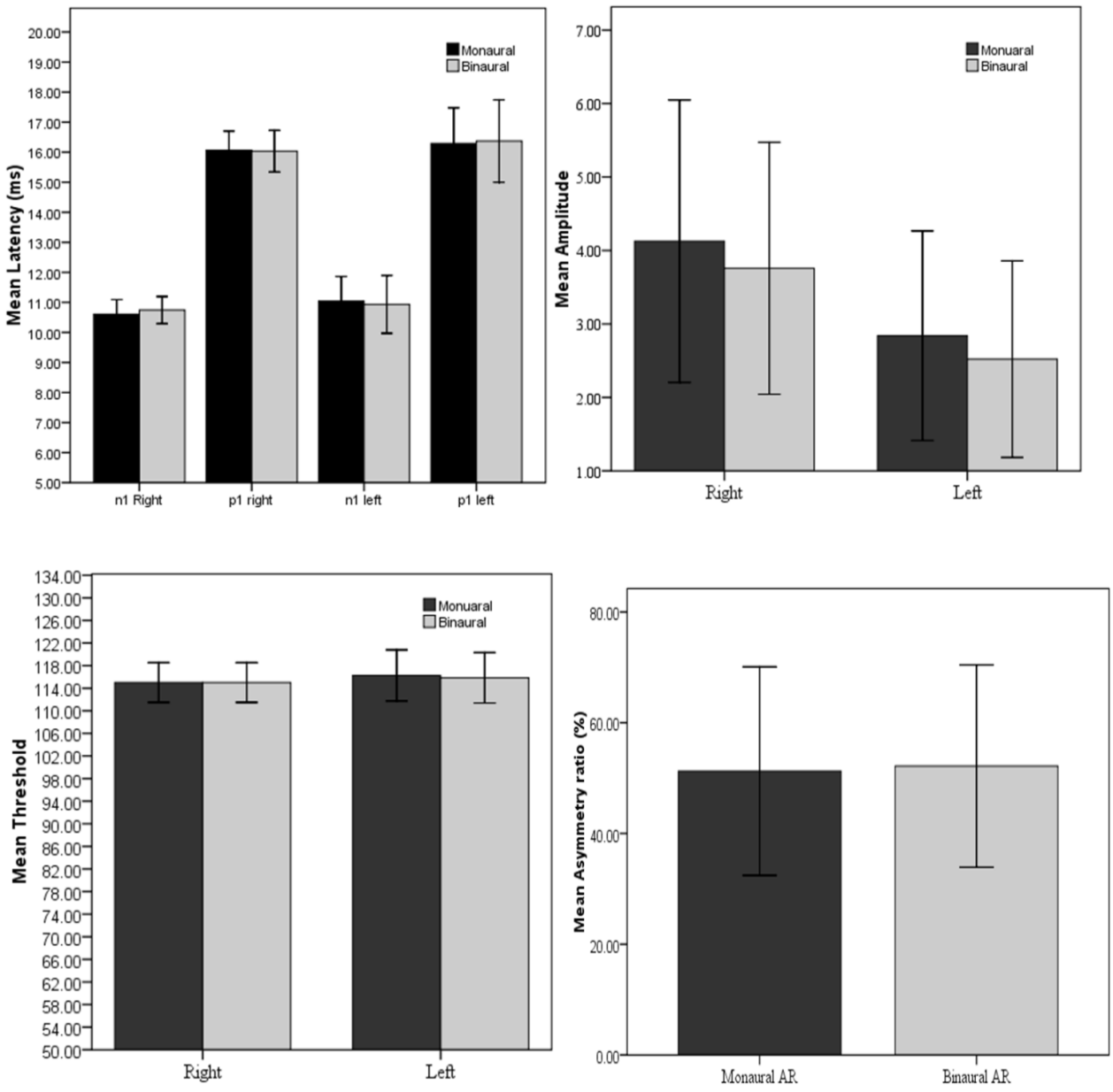

Figure 4: The mean and 95% confidence intervals of n1 and p1 latencies (upper left panel), peak-to-peak amplitude (upper right panel), thresholds (lower left panel) and inter aural amplitude ratio (lower right panel) for monaural and binaural recordings. 'AR': Asymmetry ratio

In agreement with the healthy group, statistical analysis failed to show any significant difference between monaural and binaural stimulations in pathologic group as well.

Comparison between healthy individual and pathologic group for Binaural Recordings

The oVEMP data obtained from the healthy group for simultaneous binaural acoustic stimulation were compared with that of the data obtained from the individuals in the pathologic group to understand if differences existed in the two groups for binaural recordings. The response rate obtained for binaural recordings in normals (100%) was greater than the pathologic group (48.33%). The responses were present unilaterally in 23.3% and bilaterally in 36.67% of the individuals in pathologic group. The responses from the affected ears of the pathologic group were considered for analysis.

The response parameters for binaural recording in both the groups were compared using Multiple analysis of variance (MANOVA). The results showed no significant main effect of groups (normal and pathologic) for N1 absolute latency [$F(1,83)=1.410$, $p > 0.05$] and P1 absolute latency [$F(1,83)=0.731$, $p > 0.05$]. However, MANOVA revealed significant main effect of group when affected ears of pathologic group were compared to ears of the healthy individuals group for n1-p1 peak-to-peak amplitude [$F(1,83)=6.853$, $p < 0.05$] and absolute threshold [$F(1,83)=8.576$, $p < 0.05$]. The differences in asymmetry ratio between the two groups were statistically significant with pathologic group having greater (52.16%) asymmetry ratio compared to the normal group (25.26%). Figure 5 represents the comparison of binaural recordings between normal and pathologic group.

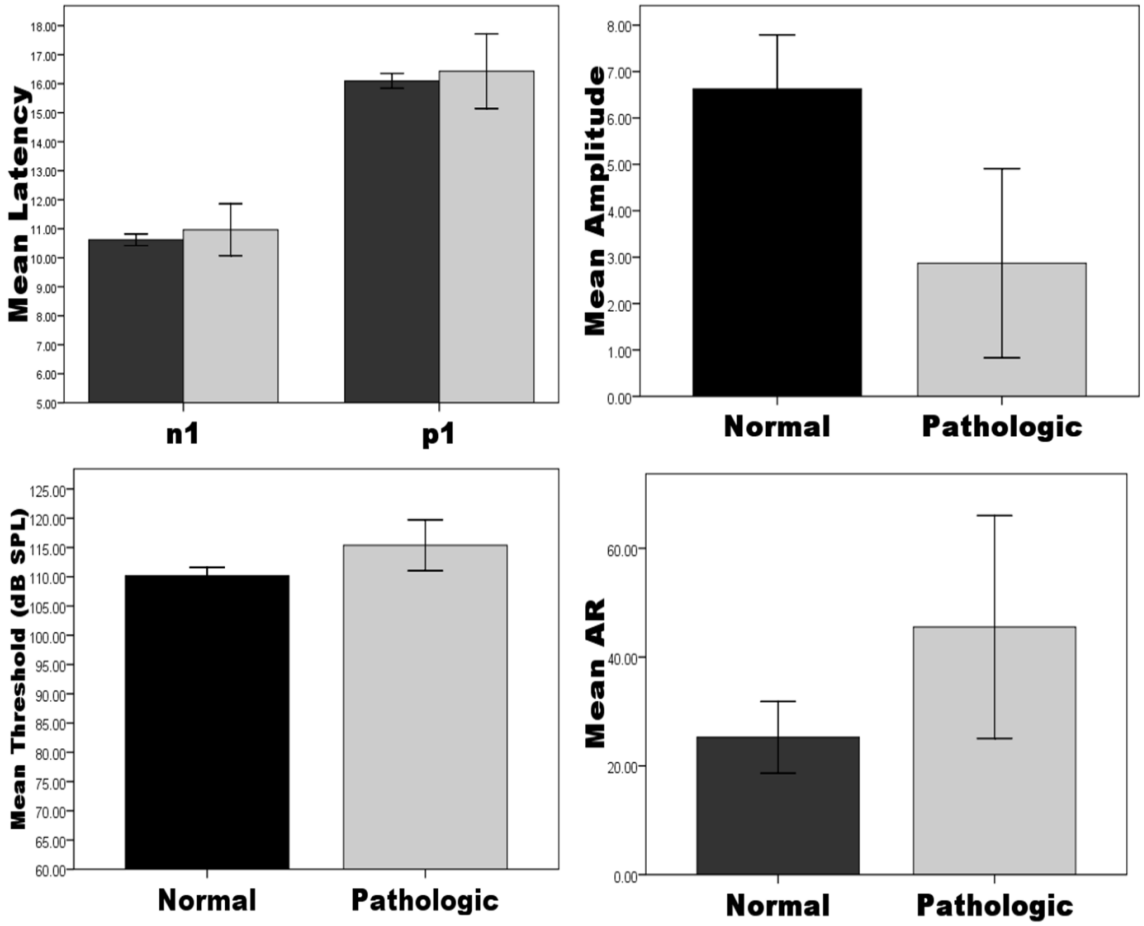

Figure 5: The mean and 95% confidence intervals of n1 and p1 latencies (upper left panel), peak-to-peak amplitude (upper right panel), thresholds (lower left panel) and inter aural amplitude ratio (lower right panel) for binaural recordings. 'AR': Asymmetry ratio

Tests-retest reliability and time efficiency of binaural recordings

The binaural oVEMP recordings were repeated on randomly selected 10 of the healthy individuals to check for the test-retest reliability. The response rate for binaural recordings was 100% during both the test and retest conditions. The mean and standard deviations were calculated of latency measures, amplitude measures and threshold for test and re-test conditions .The mean and standard deviation of each

parameter for test and re test condition for binaural oVEMP recordings in both the ears are given in Table 4.

Table 4.

Test retest values of mean, standard deviation and coefficient measure of binaural oVEMP recording

Parameter	Test		Retest		Correlation coefficient (r)		Chronbach's alpha (α)	
Ear	Right	Left	Right	Left	Right	Left	Right	Left
n1 (in ms)	10.49 (0.90)	10.23 (0.42)	10.61 (0.83)	10.33 (0.41)	0.942	0.848	0.96	0.90
p1 (in ms)	15.74 (0.64)	15.48 (1.05)	15.89 (0.81)	15.68 (1.08)	0.794	0.782	0.86	0.84
Amplitude (in μV)	5.60 (2.90)	8.56 (4.94)	5.6 (3.04)	8.40 (4.94)	0.981	0.977	0.98	0.98
Threshold (in dB SPL)	112.5 (6.34)	107.5 (4.24)	112.5 (5.40)	109.5 (3.68)	0.770	0.797	0.87	0.88
Asymmetry ratio (in %)	23.10 (13.46)		22.27 (11.14)		0.942		0.96	

Note: The values in brackets represent standard deviation; 'ms': milli seconds; 'μV': micro volts

The data obtained for binaural recordings were assessed for test- retest reliability using Chronbach's alpha test. The interpretations of alpha values were based on the classification by Versino, Colnaghi and Callieco (2001). As per this, alpha values greater 0.7 were considered to have excellent reliability, lesser than 0.4

to have poor reliability and intermediate values were considered to have fair/moderate reliability. In the present study, the values of α for various parameters of binaural recording ranged from 0.87 to 0.98, showing excellent test-retest reliability for binaural recordings. A pearson's correlation analysis was also done between the two recording sessions. The results revealed highly significant positive correlation ($p < 0.01$) between test and retest sessions for binaural recordings in both right and left ears. The 'α' and 'r' values for each of the parameters are mentioned in Table 4. The mean and 95% confidence intervals for various binaural oVEMP parameters have been shown in Figure 6 for comparison between the first and second testing sessions in order to project test-retest reliability.

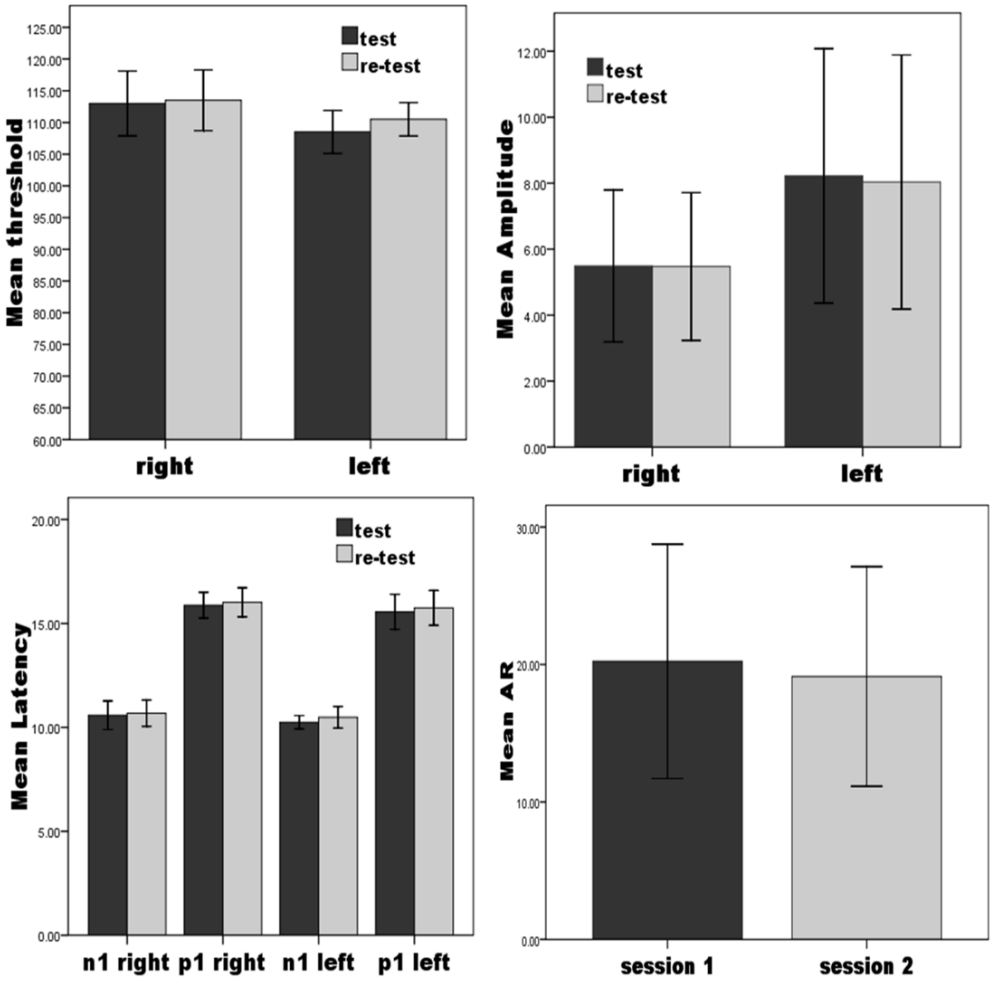

Figure 6: Mean values for different parameters for binaural stimulation in test and retest conditions. The mean and 95% confidence intervals of n1 and p1 latencies (upper left panel), peak-to-peak amplitude (upper right panel), thresholds (lower left panel) and inter aural amplitude ratio (lower right panel) for binaural recordings. 'AR': Asymmetry ratio.

Monaural and binaural oVEMP responses were recorded for 200 sweeps of 500 Hz tone burst presented at the rate of 5.1 Hz. The time taken for single recording with these parameters would be approximately 40 seconds. By providing 1 minute of rest time between each recording for both the binaural and monaural stimulations, the approximate time taken for obtaining monaural oVEMP from both the ears (2 recordings per ear) was 7 minutes whereas it amounted to 3 minutes for binaural

recording. Hence, the time required to record binaural oVEMP is nearly half as that required for recording monaural oVEMP.

Chapter 5

Discussion

In the present study, oVEMPs were recorded for monaural and binaural acoustic stimulations across two groups- a healthy individuals group and a vestibular pathology group which consisted of individuals with Meniere's disease and Benign paroxysmal positional vertigo. The response rate, absolute latencies (n1 & p1), peak-to-peak amplitude and the thresholds were measured for both the stimulations and the obtained data was subjected to statistical analysis.

Comparison of responses from monaural and binaural recordings in healthy individuals

The results in the present study showed an overall response rate of 100% for monaural stimulations in healthy individuals. The binaural recordings replicated the response rates obtained of the monaural recordings. The studies in literature report response rates of 91% (Iwasaki et al., 2013), 92.3% (Kim & Ban, 2012) and 85% (Wang et al., 2008) for binaural recordings of oVEMP. The results of the present study are therefore in consonance with the findings of previous studies (Iwasaki, 2007; Wang et al, 2008; Kim & Ban, 2012) which also report of no differences in the prevalence rates between monaural and binaural oVEMP recordings. Thus, indicating no difference between the two stimulation conditions for response rate. The response rates observed in the present study is also consistent with the findings for response rates for monaural recordings of oVEMP which were reported to range from 72% to 100% (Chihara et al., 2007; Cheng et al., 2009; Wang et al., 2009; Welgampola et al., 2009; Nguyen et al., 2010; Park et al., 2010; Murnane et al., 2011; Piker et al., 2011; Rosengren et al., 2011; Winters et al., 2011; Cheng et al., 2012; Piker, 2012). Of

these, some of the studies (Welgampola et al., 2009; Park et al., 2010) obtained 100% prevalence for monaural oVEMP recordings. The finding of 100% response rate could be attributed to the presence of normal utricular system. The age range of participants in the healthy individuals group was 18 to 30 years in the present study and this age range has been associated with 100% response rate for 500 Hz tone-bursts (Welgampola et al., 2009; Park et al., 2010; Singh, Supreetha, Kashyap, & Sahana, 2013).

The absolute latencies were measured for both monaural and binaural stimulation conditions. The latencies of n1 and p1 were found to be similar between monaural and binaural recordings. Previous studies in this regard also reported no significant difference between the monaural and simultaneous binaural acoustic stimulation for n1 and p1 absolute latencies (Wang, Jaw and Young, 2008; Iwasaki et al., 2013), which shows similarity in the findings between the present study and those reported in the literature. However, contradictory findings were also reported in one of the studies (Kim & Ban, 2012), which demonstrated similar inter-peak latencies but statistically significant difference in n1 and p1 latency between monaural and binaural stimulation conditions. The absolute latencies of both n1 and p1 in this study were reported to be longer for binaural recordings. The authors attributed the delay in latencies to the ipsilateral cross-over effect which might have contaminated the contralateral oVEMP responses. If this were to be the reason, the above study should have also found a difference in the amplitude, which they did not. Additionally, studies in the literature have reported the prevalence of ipsilateral responses to be in the range of 25% to 44% (Chihara et al, 2007; Govender et al, 2009; Wang et al, 2009; Murnane et al, 2011). The mean scores for n1 and p1 latencies obtained in the present study for binaural acoustic stimulations were found to be within the range of

normal values reported for the monaural recording (Wang et al., 2008; Iwasaki et al., 2013).

The present study also revealed existence of no significant difference between the monaural and the simultaneous binaural oVEMP recordings obtained for the amplitude measures (peak-to-peak amplitude as well as asymmetry ratio) in healthy individuals group. This is in consonance with those reported previously in this regard (Wang et al., 2008; Kim & Ban, 2012). In contrast, Iwasaki et al (2013) obtained poorer asymmetry ratios for monaural stimulations than binaural stimulations. The difference in asymmetry ratios between the two stimulation conditions was attributed to greater differences in the background electromyogenic activity during discrete recording sessions required for monaural stimulations. However, the mean asymmetry ratio for the monaural as well as binaural recording in the present study was within the normal limits (< 40%) reported for monaural recordings (Piker et al., 2011).

A non-significant difference was revealed between monaural and binaural oVEMP recordings for oVEMP thresholds. The results of the present study conformed to those obtained in Wang et al (2008). Contralateral threshold for healthy individuals in the present study ranged from 105 dB SPL to 125 dB SPL. Previous studies have reported threshold values ranging from 83 dB nHL (nearly equal to 110 dB SPL) to 129 dB $_{p}$SPL (Chihara et al, 2007; Wang et al, 2009; Park et al, 2010). Thus the range of threshold values for monaural as well as binaural recordings fall very close to the values reported in literature.

The possible explanation for similar findings in all parameters in monaural and binaural recordings can be attributed to the existence of majorly a contralateral neuronal pathway for the generation of oVEMP (Rosengren et al., 2005; Chihara et

al., 2007, 2009). As mentioned before, studies have reported the ipsilateral responses for oVEMP recordings to be less than 50% (Chihara et al, 2007; Govender et al, 2009; Wang et al, 2009; Murnane et al, 2011). Also, no increase in the ipsilateral oVEMP amplitude was reported as a function of gaze elevation (Murnane et al., 2011), which was believed to indicate the mediation of ipsilateral responses from muscle fibres other than inferior oblique muscles, contraction of which is necessary for recording contralateral oVEMP (Chihara et al, 2007; Govender et al, 2009; Wang et al, 2009; Murnane et al, 2011). Had ipsilateral and contralateral responses been mediated by the same pathway, the responses for contralateral binaural recording could be contaminated by the ipsilateral responses. Because of lack of such contamination, the responses from monaural recordings are similar to that of binaural recordings.

Comparison of responses from monaural and binaural recordings in pathologic group

The prevalence of oVEMP responses for both monaural and binaural stimulations was exactly the same (60%). Presence of unilateral response alone was seen in 20% of the individuals whereas 40% of the individuals demonstrated bilateral presence of oVEMP responses. The remaining 40% of the individuals showed complete absence of responses in both their ears. The recordings from simultaneous binaural acoustic stimulations followed the same trend. Infact, not only was the percentage exactly same between the groups but also the pattern in each individual. The individual who had absence of response in right ear but presence of response in left ear for monaural recording, he/she also had exactly this pattern for binaural recording of oVEMP. The literature search from various search engines revealed only one study (Iwasaki et al, 2013) that was conducted in pathologic group to compare the

findings of monaural and binaural recordings. The findings of the present study in terms of the response rate are not in complete agreement with findings of Iwasaki et al (2013) who found response rates of 92.9% for both monaural and binaural recordings of oVEMP in pathologic ears. The differences between the studies could be attributed to the use of subjects with different pathologies in the two studies. While Iwasaki et al (2013) conducted the oVEMP recordings on subjects with vestibular schwannoma and vestibular neuritis, the present study recorded oVEMPs in subjects with Meniere's disease and BPPV. Vestibular schwannomas have less often been reported to be associated with complete absence of oVEMP. They have rather been reported to produce reduction in amplitude and more importantly, prolongation of latencies (Iwasaki et al., 2009). This might be the reason behind higher response rate in Iwasaki et al (2013) compared to the present study. The present study shares similar findings with some of the previous studies which reported of response rate of 60% in a group with Meniere's disease and 50% in a group with BPPV (Nakahara, Yoshimura, Tsuda & Murofushi, 2011).

The n1 and p1 latencies were similar for both the stimulation conditions revealing similar results as that by Iwasaki et al (2013). The pathologic group values of amplitude and asymmetry ratio did not vary between monaural and binaural recordings, which is also in agreement with Iwasaki et al (2013). The results for oVEMP thresholds replicated the findings of other parameters showing no significant difference between the monaural and binaural recordings. Literatures search shows no study conducted to compare the thresholds between monaural and binaural recordings.

The similarity of findings between the monaural and binaural recordings in pathologic group as well can be attributed to the discrete contralateral pathways for oVEMP response generation, as explained earlier. Since monaural and binaural response parameters were found to be similar for all the recording parameters in pathologic group as well, binaural recordings of oVEMP can be as efficient as monaural recordings to detect the abnormalities in disease populations as well.

Comparison of binaural responses of healthy group and pathologic Group

The prevalence rates of binaural oVEMP recordings were significantly different between the healthy individual and the pathologic group. The healthy individuals had 40% greater presence of oVEMP response compared to pathologic group. oVEMP abnormalities in Meniere's disease and BPPV have been reported to include declined prevalance, abnormal reponses, prolonged latencies and reduced amplitude (Winters et al, 2011; Murofoshi et al, 2011; Huang et al, 2011).

The present study failed to detect any abnormalities in absolute latencies of n1 or p1 in pathologic group. The absolute latencies were similar to that obtained from normals in both affected and unaffected ears of pathologic group for binaural stimulation condition. Since, the pathologic group consisted of individuals with peripheral vestibular lesions (MD & BPPV), normal latency values were obtained. Studies on various peripheral vestibular pathologies like BPPV (Seo et al., 2013), Meniere's disease (Murofushi et al. 2011; Taylor et al. 2011), superior semicircular dehiscence syndrome (Chiarovano et al., 2011), vestibular neurinitis (Chiarovano et al., 2011) have reported normal-like latency values. The abnormalities of latency are reflected in diseases affecting the central vestibular pathways like multiple sclerosis

(Gabelic et al. 2013) or in older individuals owing to age related changes in the vestibular system (Iwasaki et al. 2008; Tseng et al. 2010).

The absolute amplitude in the affected ears was found to be significantly lesser than that of the normal group, which is in accordance with the results of previous studies using monaural recordings (Curthoys et al., 2009; Manzari et al., 2010; Chiarovano et al., 2011). A higher asymmetry ratio was obtained for the individuals in pathologic group compared to the normal group. Threshold values were significantly higher in the affected ears of pathologic group when compared to the ear matched normals. These are similar to those reported in the pathologic group using monaural recording technique (Winters et al, 2011; Jacobson et al., 2011; Talaat et al., 2013). The similarity in the findings of present study to those reported previously confirms the validity of the binaural recording method of oVEMP.

Test-retest reliability and time efficiency in binaural oVEMP

When the binaural recordings were repeated in 10 individuals of the healthy group, excellent test-retest reliability was obtained for all the parameters. The findings of the present study are in concordance with those reported by Kim & Ban (2012) in this regard. They obtained better test-retest reliability for binaural recordings compared to monaural recordings. This was accredited to maintenance of similar inferior oblique muscle concentration during binaural recordings since it does not require separate testing for the two ears as is the case for monaural recording. This also suggests that binaural recording can be used as a reliable test procedure for the recording of oVEMP.

In addition to similar findings provided by binaural recordings as that of monaural recordings, this technique has also proved to be time effective. Binaural

testing takes approximately less than half the time (3 minutes) when compared to monaural testing (7 minutes). The present study shares similar findings as that of Kim and Ban (2012). Taking into consideration patient fatigue and cost effectiveness, binaural recordings hold a major advantage over the monaural recordings.

Chapter 6

Summary and Conclusion

Ocular VEMPs are biphasic responses elicited for loud acoustic stimuli. They are produced from the inferior oblique muscles and can be recorded from electrodes placed beneath the eye contralateral to the ear of stimulation. Elevation of gaze brings the inferior oblique in close proximity to the recording electrode, thereby, increasing the amplitude of oVEMP. However, continuous upward gaze leads to muscle fatigue and involuntary eye blinks and hence would deteriorate the quality of waveforms. Also, the differences in the electromyogenic activity may lead to differences in the responses between the two recording sessions required for recording oVEMP with monaural stimulations. Thus, the feasibility of binaural recordings needs to be assessed to overcome these difficulties.

Few previous studies have compared the responses of oVEMP obtained from monaural and simultaneous binaural recordings (Wang et al., 2008; Kim & Ban, 2012; Iwasaki et al., 2013). However, equivocal findings exist between them. While some studies reported no difference between the two stimulation conditions on any of the oVEMP parameters (Wang et al., 2008; Kim & Ban, 2012), Iwasaki et al (2013) reported significantly prolonged latencies for binaural condition than monaural one with no difference in other parameters. Additionally most studies have only been conducted on healthy subjects with only Iwasaki et al (2013) using actual clinical population also. However, in order to establish a good validity of binaural recordings of oVEMP, more studies are required. Hence, the present study was aimed at evaluation of the effect of the two stimulation conditions (monaural and binaural) on absolute latencies, peak-to-peak amplitudes, thresholds and asymmetry ratio of

oVEMP. The study also aimed to compare the findings of binaural recordings between healthy and pathologic ears in order to establish its validity.

Two- channel monaural and binaural recordings of oVEMP were obtained from 36 healthy individuals, 15 individuals with Meniere's disease and 15 individuals with BPPV, using positive and negative electrodes placed on skin surface 1cm and 3 cm below the centre of each eye and ground on forehead. Alternating polarity 500 Hz (1 ms rise/fall time with 2 ms plateau time) tone burst at 125 dB SPL were presented at a rate of 5.1Hz. The electromyogenic activity was recorded for 200 sweeps using an epoch of 64 ms which was inclusive of 10 ms pre-stimulus recording. The participants were instructed to elevate their gaze at at 30^{o}-35^{o} during recording. Only the contralateral responses were considered for response analysis. The testing was repeated on 10 of the healthy individuals to determine the test retest reliability.

The response rates, absolute latencies of n1 and p1, peak-to-peak amplitude, threshold and asymmetry ratio were measured for each stimulation condition and each ear. One-way repeated measures ANOVA was administered to compare the findings between presentation modes (monaural vs binaural). This was done separately for each peak latency, peak-to-peak amplitude and threshold of oVEMP. The comparison of asymmetry ratio between the conditions was achieved using one-way ANOVA. Comparison between the groups for binaural recordings only was done using MANOVA. Chronbach's alpha and Pearson's correlation analysis were carried out to check for the test-retest reliability of the binaural oVEMP responses.

The results of the study indicated no significant difference between recordings obtained from monaural and binaural conditions across all the oVEMP parameters measured. The results were true for healthy as well as pathologic groups. The

probable explanation for similarity in findings between monaural and binaural oVEMP is the involvement of only the contralateral pathway in generation of oVEMP (Rosengren et al., 2005; Chihara et al., 2007, 2009). Hence it can be hypothesized that ipsilateral responses are not contaminating the contralateral responses resulting in similarity of findings between monaural and binaural recordings. Since, all the oVEMP parameters measures were found to be similar between the monaural and binaural oVEMP recordings in pathologic group as well, it can be interpreted that binaural recordings of oVEMP can be as efficient as monaural recordings to detect the abnormalities in disease population as well.

The binaural oVEMP findings of healthy individual group were compared with the binaural oVEMP data obtained from the affected ear of the pathologic group. The results revealed no difference between the groups in latency which was in agreement with the studies using monaural recordings (Seo et al., 2013; Murofushi et al. 2011; Taylor et al. 2011; Chiarovano et al., 2011). However amplitude values were found to be lesser and asymmetry ratios and threshold were found to be higher in the pathologic group. Studies in literature report of similar findings in pathologic group using monaural recordings (Talaat et al, 2013; Winters et al, 2011; Jacobson et al,2011). Thus, abnormalities detected by binaural recording in the pathologic group confirm the validity of binaural recording method of oVEMP.

The statistical analysis on the data from test-retest sessions showed excellent test retest reliability for oVEMP recordings, suggesting high reliability of the binaural for recording of oVEMP. Additionally, the study revealed recording of oVEMP with binaural stimulations consumed half the time as that required for monaural recordings.

Therefore, binaural recording can be accredited as a more time saving procedure than the monaural recording.

The findings of the present study revealed no difference between the monaural and binaural recordings of oVEMP in healthy as well pathologic groups. It also demonstrated the validity of the binaural procedure in identifying the vestibular pathologies. It also produced high test-retest reliability. Therefore, with similar validity and reliability in diagnosis to monaural procedure but with lesser constraint on time, simultaneous binaural recording could be a more useful way for recording oVEMPs than the monaural stimulation.

Clinical implication

In the present study, the results revealed no difference between monaural and binaural recordings of oVEMP in healthy as well as clinical population. The test-retest reliability of the binaural recording of oVEMP was excellent. This suggests that binaural oVEMP is at least as good as the monaural oVEMP recording, if not better. Considering the considerably shorter testing time required for the binaural recording than the monaural one, the results of study paves a way for the proposal of simultaneous binaural oVEMP recording rather than separate monaural ones for each ear.

Future directions

The findings of the present study confirmed equal utility of binaural recording to monaural recording of oVEMP. However, the results were obtained for healthy individuals and individuals with Meniere's disease and BPPV. Thus the results can be directly applied only for these populations. Future studies need to evaluate the

efficacy of binaural recording of oVEMP in other clinical populations like Multiple sclerosis, vestibular schwannoma, labyrinthitis and vestibular neuritis in order to be absolutely sure regarding binaural replacing monaural recording one day.

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