EFFECT OF THE STIMULUS INTENSITY USED FOR FREQUENCY TUNING OF cVEMP ON HEARING

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This Dissertation is submitted as part fulfilment

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CERTIFICATE

This is to certify that this dissertation entitled **'Effect of the stimulus intensity used for frequency tuning of cVEMP on hearing'** is the bonafide work submitted in part fulfilment for the degree of Master of Science (Audiology) of the student Registration Number: 18AUD017. This has been carried out under the guidance of the faculty of the 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 master's dissertation entitled **'Effect of the stimulus intensity used for frequency tuning of cVEMP on hearing'** has been prepared under my supervision and guidance. It is also being certified that this dissertation has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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DECLARATION

This is to certify that this dissertation entitled **'Effect of the stimulus intensity used for frequency tuning of cVEMP on hearing' i**s the result of my own study under the guidance of Dr. Niraj Kumar Singh, Reader in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru
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CHAPTER - I

INTRODUCTION

Vestibular-evoked myogenic potentials (VEMP) are biphasic potentials. VEMPs can be recorded from several muscles of the body. When recorded from the sternocleidomastoid muscle, these ipsilateral potential are called the cervical VEMP (cVEMP) (Colebatch, Halmagyi, & Skuse, 1994). When they are recorded from the extra ocular muscles, specifically the inferior oblique muscle, these potentials of contralateral dominance are referred as the ocular VEMP (oVEMP) (Rosengren, Todd, & Colebatch, 2005).

cVEMPs can be recorded using several types of stimuli. These stimuli include air-conducted sound (Basta, Todt, & Ernst, 2005; Colebatch et al., 1994), bone-conducted vibration (Basta., et al 2005; Miyamoto, Seo, Node, Hashimoto, & Sakagami., 2006; Sheykholeslami, Murofushi, Kermany, & Kaga, 2000; Welgampola, Rosengren, Halmagyi, & Colebatch., 2003), and electrical stimulation (Chang, Young, & Cheng, 2013; Cheng, Yang, Huang, & Young, 2008), but air-conducted stimulation is the most widely used technique of cVEMP in clinical settings (Felipe &Kingma, 2014).

VEMP has become an integral part of the test battery for vestibular assessments because it is among few tests that allow for the assessment of the functional integrity of the otolith organs. In fact, cVEMP is the only means to assess the functional integrity of saccule and the sacculocollic pathway (Kantner & Gurkov, 2012; Young, 2003; Zhou, 2009). Further, it is easy to record, and the robust nature of its peaks allows for ease in their identification (Colebatch & Halmagyi, 1999; Colebatch et al., 1994; Mc Cue & Guinan, 1994).

VEMPs have been found useful in the diagnosis of various disorders, a few of which are Meinere's Disease (Kingma & Wit, 2011; Node et al., 2005; Rauch et al., 2004; Sandhu, Low, Rea, & Saunders, 2012; Taylor, Zagami, Gibson, Black, Watson, & Halmagyi, 2012), vestibular neuritis (Adamec, Skoric, Handzic, Barusic, Bach, & Gabelic, 2014; Lin & Young,2011; Walther & Blodow, 2013) and semicircular canal dehiscence (Janky, Nguyen, Welgampola, Zuniga, & Carey, 2013; Minor, 2005). VEMP also finds its clinical application in the diagnosis of benign paroxysmal positional vertigo (Hornibrook, 2011; Korres, Gkoritsa, Giannakakou-Razelou, Yiotakis, & Riga, 2011; Murofushi, 2016; Xu et al., 2016), vestibular migraine (Gozke, Erdal, & Ozkarakas, 2010; Hong, Kim, Park, & Lee, 2011; Zaleski, Bogle, Starling, Zapala, Davis, & Wester, 2015; Toshihisa & Murofushi, 2015), idiopathic otolithic vertigo (Toshihisa & Murofushi 2015), and vertigo/dizziness arising out of pathologies of the central balance control mechanism (Toshihisa & Murofushi 2015). It also helps in ruling out brainstem involvement in several central pathologies (Bogle, 2018; Venhoven, 2016). Nonetheless, despite its numerous clinical applications, there is a growing concern regarding the possible ill-effects associated with high stimulus intensity needed to elicit VEMP responses.

Need for the study

VEMPs are elicited using high intensity signals, usually 125 dB peSPL to 140 dB peSPL (Murofushi, Matsuzaki, & Wu, 1999; Ochi, Ohashi, & Nishino, 2001; Welgampola, Rosengren, Halmagyi, & Colebatch, 2000; Mattingly et al., 2015). The use of such high signal levels has raised concern among the professionals about their possible ill-effects on hearing function and paved way for a series of investigations in this regard. The concerns regarding the stimulus safety of VEMP arise from the findings of studies on auditory brainstem response (ABR) which showed detrimental effects of stimulus levels used for ABR on distortion product otoacoustic emissions (DPOAE) (Soni & Jain, 2017). Most often, 80-90 dB nHL (equivalent to 115-120 dB peSPL) of stimulus intensity is needed for several applications of ABR, whereas VEMP recordings require much higher levels, usually ≥95 dB nHL or ≥125 dB peSPL for almost all their applications. While, ABR recording requires the use of 1500 to 2000 stimuli presented in a rapid sequence (Buchsbaum & Silverman, 1968), VEMP needs only 100 to 200 stimuli presented in a rapid sequence (Basta et al., 2005; Rodriguez et al., 2018; Young, 2009). Nonetheless, it is not known whether the reduction in the number of stimuli can offset the increase in the intensity in case of VEMP recording. Therefore, there was a need to investigate whether or not such detrimental effects are associated with VEMP eliciting stimuli.

Krause et al (2013) and Stromberg et al (2016) studied the impact of acoustic stimuli (133 dB peSPL& 130 dB peSPL, respectively) for recording cVEMP on pure tone thresholds and DPOAE amplitude. They reported significant post-VEMP reduction of DPOAE amplitudes at certain frequencies. Further, the DPOAE amplitudes were reported to return to pre-VEMP levels within 24 hours. In terms of the pure tone thresholds, the authors noticed no significant change in pure tone thresholds after cVEMP testing. However, these studies did not include the extended high frequencies beyond 8 kHz. Since the frequencies >8 kHz are more sensitive to loud sound-induced changes in the hearing thresholds (Prabhu, Dutta, Goyal, Varma, & Kumar, 2016), not using these frequencies might be a possible reason behind the findings of spared hearing thresholds despite the significantly altered DPOAE amplitudes.

Meanwhile, in a shocking revelation to the scientific community, Mattingly et al (2015) reported a case in which the degree of hearing loss increased (worsened) after cVEMP and oVEMP testing using 123-135dBpeSPL tone burst intensities. However, the presence of the uncontrollable extraneous factors such as age and pre-existing hearing and vestibular deficits could have possibly played a role, as no other report of such an occurrence has been reported before and after this study.

Recently, Rodriguez, Thomas, Fitzpatrick and Janky (2018) used 125 dB peSPL intensity of 500-Hz tone-burst to elicit cVEMP responses and found no significant change in the amplitude of DPOAE after the cVEMP testing. However, the authors of the study cautioned that even an intensity of 125 dB peSPL, when delivered to children's ear canal for cVEMP testing, could be potentially hazardous to their hearing. This was assumed because the smaller ear canal volume could bring about larger sound pressure level in children. Most recently, Singh, Keloth and Sinha (2019) also reported no significant alteration to DPOAE amplitude at any frequency after cVEMP testing. They further observed no significant change in the pure tone thresholds up to the frequency of 16000 Hz. Therefore, they concluded that use of 125 dB peSPL stimulus intensity for a 500-Hz tone-burst was a safe stimulus level for eliciting cVEMPs in adults.

The above mentioned studies showed rapid recovery or no detrimental effects of VEMP eliciting stimulus levels on audiological tests. However, normal OAEs and normal hearing thresholds do not always imply normal auditory system. Numerous animal studies have shown evidences for progressive synaptic loss between inner hair cell and auditory nerve (especially the spiral ganglion cells) despite there being no significant change in the pure tone thresholds after exposure to loud sounds (Kujawa, & Liberman, 2009). This is usually referred to as ‘cochlear neuropathy’ or ‘hidden hearing loss’ (Kujawa, & Liberman, 2009). In such a condition, pure tone hearing thresholds of the noise-exposure sufferers hover within the normal range; however, these victims continue to show poor performance on tests of speech perception in the presence of background noise and those of temporal resolution. Therefore, individuals can have deficit in supra-threshold discrimination and neural temporal coding, despite a non-detectable hearing loss (Plack, Barker, & Prendergast, 2014; Bharadwaj et al., 2014). Thus, keeping this perspective along with the reports that 125-135 dB peSPL was found safe for recording VEMPs, it may be hypothesized that these levels of exposure might still be associated with hidden hearing loss, which unfortunately has not been explored in the context of VEMP eliciting stimuli. The tests such as the Gap detection threshold (GDT) and speech perception in noise (SPIN) were found sensitive for detection of hidden hearing loss (Kujawa & Liberman, 2015). GDT helps in tapping the damage to the auditory pathway, especially for temporal resolution (Samelli & Schochat, 2007). Therefore inclusion of GDT could possibly help unravel this mystery surrounding the safety of VEMP eliciting stimuli.

Further, certain applications of VEMP, such as frequency tuning and inter-frequency amplitude ratio (IFAR), require VEMPs to be tested at multiple frequencies (Rauch et al., 2005; Sandhu et al., 2012). These applications were found especially useful for identification of Meniere’s disease and its differential diagnosis from BPPV (Rauch et al., 2005; Sandhu et al., 2012). These measures were also found useful in differentiating Meniere’s disease from vestibular migraine (Taylor et al., 2012). Nonetheless, these measures require recording VEMPs at multiple frequencies between 250 Hz and 2000 Hz. This would mean implicate in multiple fold increase in the exposure duration, leading to a possibility of more damage than the single frequency exposure studied in the above mentioned investigations concerning VEMP eliciting stimulus and its safety for hearing mechanism. Therefore, there is a need to take a fresh look at the stimulus safety of VEMP for measures such as frequency tuning.

Aim

The above discussion points at the gaps in the existing literature regarding the safe levels of VEMP eliciting stimuli on the auditory system. therefore, the present study aimed to identify safe stimulus level, if any, for obtaining frequency tuning of cVEMP.

Objectives

1. To compare the pre-VEMP gap detection threshold against obtained at various points of measurement after VEMP testing for frequency tuning.
2. To compare the gap detection threshold at various measurement points between the ears in each group.
3. To compare the gap detection thresholds at various measurement points between the study groups.

CHAPTER II

REVIEW OF LITERATURE

Vestibular evoked myogenic potential (VEMP) reflects vestibular system's sensitivity to the acoustic vibrations. When elicited from the SCM muscle, this ipsilateral potential is called cervical VEMP (Colebatch et al., 1994). It is elicited by loud sounds and detected as a change in the post-stimulus time histogram of the SCM (Zhou and Cox, 2004). VEMP is an important part of the test battery as it allows the assessment of otolith organs.

Despite being the only test to evaluate abnormality of the otolith organs, the test is of concern to the scientific community due to the requirement of high stimulus intensity for eliciting discernible peaks in the response. Price (1981) reported that any stimulus beyond 140 dB SPL causes damage to cochlear or middle ear structure and might cause acoustic trauma. VEMPs are generally elicited using high intensity signals, usually between 120 dB peSPL to 145 dB peSPL (Winters, Campschroer, Grolman, & Klis, 2011 Murofushi et al., 1999; Ochi et al., 2001; Welgampola et al, 2001; Rosen µçgren, Welgampola, Colebatch, 2010). Exposure to high levels of sound for even a short duration can cause adverse effects on the auditory system. Investigations have revealed that exposure to loud sounds may cause permanent hearing loss (Oosterveld et al., 1982; Mattingly., 2015), or even create a temporary change at the level of cochlea (Krause et al., 2013; Stromberg et al., 2016). This curiosity therefore became a promising investigation area.

2.1 Effect of loud sounds on the auditory system up to cochlea

The effect of VEMP stimulus intensity was always perceived as a concern, nonetheless, Krause et al (2013) were the first to show scientific evidence in this regard. This study took 30 healthy participants, age ranging from 20-40 years. They administered a single frequency, Hanning window gated 500Hz tone burst (duration = 10 ms) using 133 dB peSPL sound intensity presented at the rate of 3.3 Hz. They presented 200 sweeps of such stimuli for recording cVEMP. DPOAE was assessed before the cVEMP administration, immediately after VEMP and 24 hours later. They reported reduced DPOAE amplitudes at high frequencies (4-6 kHz). These amplitudes however recovered to pre-VEMP levels within 24 hours of the exposure. While this was a landmark study in this area, the possible confounds would have been possible because of the use of unusually high stimulus intensity (133 dB peSPL), rarely used Hanning window and unusually large stimulus duration.

Following the reports of Krause et al (2013), another study by Stromberg et al (2016) examined the effects of VEMP eliciting stimulus intensity of 130 dB peSPL (frequency = 500 Hz, duration = 6 ms, repetition rate = 5 Hz, number of sweeps = 192 in chunks of 64 ms) on DPOAE amplitude in 24 healthy individuals with normal hearing sensitivity. The DPOAE I/O functions were recorded at 750 Hz and also at 3 kHz for various intensity levels ranging from 50 to 80 dB SPL, thrice before and once immediately after the VEMP test. DPOAE showed a lowering of amplitude of about 2.1 dB after the VEMP testing. They recommended lesser stimulus repetitions in order to avoid noise induced cochlear injury. The study ensured that the repeated baselines accounted for the variations without the intervention. This therefore, also accounts for test retest reliability. But they failed to follow-up their subjects to rule out the possible permanent shift in the DPOAE amplitudes.

In yet another study, Rodriguez et al (2018) examined the effect of VEMP eliciting stimuli of 125 dB peSPL and 120 dB peSPL (frequency = 500 Hz, duration = 4 ms, repetition rate = 5 Hz, number of sweeps = 150 & 100 for oVEMP & cVEMP respectively) on 10 adults and 15 children, respectively. They found no significant difference in DPOAE amplitude between the pre- and post-VEMP measurements in either of the two groups. However, despite not using 125 dB peSPL intensity for children, they concluded that use of 125 dB peSPL might have potential deleterious effects on cochlear functions in them. Further, the generalization of the results of the study would be questionable, considering the sample size was limited

The first study to be done on Indian population was by Singh, Keloth et al (2019). They used a conventional and standardized protocol for recording VEMP (intensity = 125 dB SPL, type = tone burst, frequency = 500Hz, gating function = modified Blackman, repetition = 5.1 Hz, number of sweeps = 200). The functional integrity of the cochlea was checked using DPOAEs before and after VEMP test (immediately after VEMP, 1 hour later, 24 hours later and 7 days later). They found no significant change in DPOAE amplitudes following VEMP recordings. The study however made a conclusion about the safe intensity level only by assessing OAEs and not looking for changes at the synaptic junction, either temporary or permanent.

2.2 Effect of VEMP eliciting stimuli on clinical pure tone thresholds

Krause et al (2013) used air conduction testing (250 Hz to 10,000 Hz including mid-octave frequencies) and bone conduction testing (250 Hz to 6000 Hz along with mid- octave frequencies) for examining the effects of VEMP eliciting stimuli in the clinical range of pure tone frequencies. The stimulus parameters used for eliciting cVEMP and participant related details have been mentioned in the previous section. They reported no significant deterioration of the pure tone thresholds at any frequency till 8 kHz after cVEMP testing. They did not talk about the effects on 10000 Hz. Further, the study has its own pitfalls related to the choice of stimulus related parametres, as mentioned above.

Stromberg et al., (2016), in their study, obtained pure tone threshold from 125 Hz to 8 kHz (including the mid-octave frequencies) using Bekesy audiometry procedure. The stimulus parameters for eliciting VEMP and subject related information is already mentioned in the above section. They found no significant difference in the pure tone thresholds from the baseline at any frequency. A major concern to the results might be the less number of participants in the study. Further, the Bekesy audiometry is known to have substantial individual variations (Jerger, 1960), and therefore the generalization of the results could be questionable.

Rodriguez et al (2018) used routine pure tone audiometry (500 Hz to 6000 Hz including mid-octave frequencies) and Singh et al used pure tones up to 16 kHz (at all octave and mid-octave frequencies) to study the effects of VEMP eliciting stimuli of 125 dB peSPL on the pure tone thresholds. They found no significant change in the pure tone thresholds after the VEMP testing. Based on these results, they recommended 125 dB peSPL as safe stimuli for recording cVEMPs, especially among adults. However, they did not include any measures of cochlear synaptopathy which can be present despite normal hearing thresholds.

Meanwhile in the year 2015, Mattingly et al reported permanent increase in the degree of hearing loss in a 75 years old lady after she had undergone cVEMP and oVEMP testing using a range of tone burst intensities (123-135 dB peSPL) . While this was a remarkable revelation, the presence of other predisposing factors such as old age, presence of pre-existing inner ear pathology and use of unusually high stimulus intensities (>125 dB peSPL) might have been the confounding variables. Also till date, this remains the only instance of such a finding. Therefore, it appears highly unlikely that VEMP evaluations were solely responsible for the permanent worsening of hearing in their study.

2.3 Effect of VEMP eliciting stimuli on extended high frequency pure tone thresholds (8-20 kHz)

There is a clear dearth of studies relating to the effects of VEMP eliciting stimuli on the pure tone thresholds in the extended high frequency range of audibility (8-20 kHz). The only study in this regard (Singh, Keloth et al., 2019) reported no significant changes to hearing thresholds in the extended high frequency range even until 7 days after the exposure to the VEMP eliciting stimuli of 125 peSPL. While extended high frequency pure tone thresholds are more sensitive than the pure tone thresholds up to 8 kHz, there are evidences for normal results in the entire hearing range of frequencies despite a hidden hearing loss shown by abnormal findings in tests such as GDT, SPIN at low signal-to-noise ratio etc. (Kuwaja & Liberman., 2009). However, Singh, Keloth et al (2019) did not use any test for the detection of hidden hearing loss. Therefore, it would be unreasonable to assume 125 dB peSPL as the safe stimulus intensity for clinical recordings of VEMP.

So, overall the review of literature shows a number of studies on the effects of various intensities of the VEMP eliciting stimuli on the auditory function. However, there are clear gaps in the knowledge about whether or not a particular intensity is completely safe for eliciting and recording VEMPs. The gaps are even more glaring when it comes to the other measures of VEMP such as the frequency tuning and the inter-frequency amplitude ratios. In fact, there are no studies regarding the safety of the exposure to the stimulus used for these purposes (frequency tuning & IFAR) on the auditory system.

CHAPTER III

METHOD

The present study aimed to identify the safe stimulus level, if any, for obtaining frequency tuning of cVEMP. In order to achieve the above aim, a multiple group time series quasi-experimental research design was used.

3.1 Participants

The study included 60 healthy individuals in the age range of 18-40 years (mean= 22, SD=2.9). They were randomly divided into 3 groups of 20 participants. Each one group of 20 participants underwent cVEMP using 133 dB peSPL tone-bursts (hereafter called Group 1) and the other group of 20 participants underwent cVEMP using 125 dB peSPL tone-bursts (hereafter termed Group 2). Both these groups underwent GDT, before and after cVEMP testing. The participants of Group 3 (n = 20) did not undergo cVEMP testing. A schematic representation of the distribution of participants to various groups is shown in Figure 3.1.1. Each participant in the study was explained about the experiment, possible consequences of being a participant of the study and the option of dropping out of the study at any point of time if they wished to. All participants signed the informed written consent. None of the participants were paid for their participation in the study.

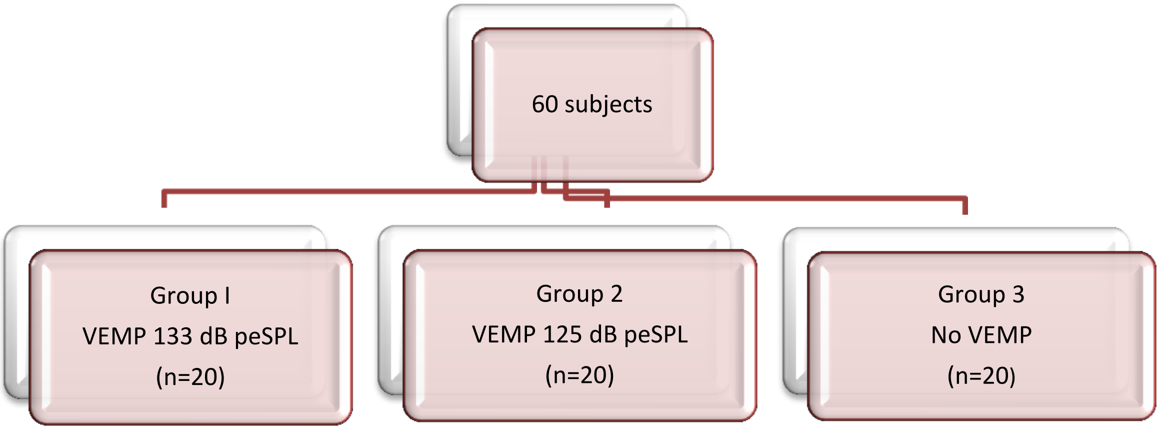

Figure 3.1.1: A schematic representation of the distribution of participants to the various experimental groups.

3.1.1 Subject selection criteria

. Individuals with normal hearing and no complaint/history of middle ear disorders were recruited tothe study. Results within the normative range on a series of audiological tests ensured a normal auditory system. These tests included pure tone audiometry (thresholds ≤15 dBHL at octave and mid-octave frequencies from 250 to 8000 Hz), speech audiometry [speech recognition threshold (SRT) within ±12dB of the four-frequency pure tone average threshold and speech identification scores (SIS) ≥ 95%], immittance evaluation (type-A tympanogram with presence of acoustic reflexes at 100 dBHL for a tonal stimulus of 1000 Hz), and transient evoked otoacoustic emission (>6 dB global SNR). The subject selection criteria also included normal vestibular function, which was ascertained through no complaint/history of vertigo, tinnitus, motion sickness, migraine and balancing issues. Further, they had normal results on Romberg test (absence of sway), Fukuda stepping test (angle of deviation<45^{o} along with <1 meter distance covered from initial point), past pointing test (no undershooting/overshooting of the target and absence of tremors) and diadokinetic test (able to perform rapid alternate pronation and supination of the palm). They also did not have any obvious vestibular pathology which was ascertained using the diagnostic criteria laid out for the diagnosis of vestibular pathologies. These are described in detail in the 'procedure' section later.

3.2 Instrumentation

A calibrated Piano inventis clinical audiometer was used with impedance matched Telephonic TDH-50 supra-aural headphones and Radioear B-71 bone vibrator for pure tone audiometry. A calibrated GSI- tympstar clinical immittance meter was used for tympanometry and reflexometry. To obtain VEMPs, a calibrated Neurosoft Neuro-audio evoked potential system was used with default Etymotic research ER3A insert ear phones. The GDT was tested using the Maximum likelihood procedure (MLP) toolbox, a toolbox developed by Green (1990, 1993), on the MATLAB platform. For the GDT testing, a set of calibrated Sennheiser HDA 200 circum-aural headphones was coupled to a commercially available laptop computer with inbuilt octa-core processor, 4GB RAM, 64-bit memory and pre-installed Windows 8 operating system.

3.3 Procedure

A detailed case history in the form of an interview was taken from all the participants before the commencement of the audiological evaluation. During this, the individuals were asked about the history of auditory problems such as otitis externa, occlusion due to ear wax, and otitis media. The structural abnormalities, such as the presence of stenosis, atresia etc., was ruled out through visual inspection. The participants were also asked if they had ear pain, itching sensation, presence of tinnitus or any ear related surgeries. The participants were also enquired for blocked nose and fullness in the ear due to cold present during the time of testing. If so, the participants were either excluded from the study or asked to report back once the cold resolved. The participants who had complaint of motion sickness were not included in the study. Also, the tympanic membrane was viewed under the otoscope to rule out any perforation, scar or infection

The questionnaire part of the "Vestibulogram" developed by Singh (2018) at the Department of Audiology, All India Institute of Speech and Hearing (AIISH), was filled to rule out vestibular problems. The questionnaire includes important questions for quick screening of the vestibular problems. It seeks information related to type of vertigo, duration of the problem, triggering mechanism, associated problems etc. The criteria described for diagnosis of various vestibular pathologies were used to rule out presence of benign paroxysmal positional vertigo (Bhattacharya et al., 2008), Meniere's disease (Escamez et al., 2015), vestibular migraine (Lempert et al., 2012), and vestibular paroxysmia (Strupp et al., 2016). Questions regarding balance issues after upper respiratory tract infection were asked to eliminate vestibular neuritis and labyrinthitis. Individuals with medical factors such as, diabetes, hyper/ hypotension, thyroid disorder or any other hormonal disorders were also excluded from the study.

Pure tone audiometry was obtained using modified Hughson-Westlake procedure (Carhart & Jerger, 1959) for the octave frequencies from 250 to 8000Hz for air conduction and from 250 to 4000Hz for bone conduction stimuli. SRT was obtained using spondee word list and SIS was obtained using phonetically balanced word list in the participant’s native language. Immittance evaluation (tymapanometry & reflexometry) was done to rule out middle ear pathology. Tympanometry was carried out using a probe tone frequency of 226 Hz. For this, the pressure in the ear canal was varied from -400 daPa to +200 daPa at the rate of 50 daPa/s. Using the same probe-tone frequency, both ipsilateral and contralateral acoustic reflexes were obtained for stimulus frequency of 1000Hz presented at 100 dBHL.

Behavioral tests of posture & equilibrium tests were done to rule out the balance dysfunction. Romberg test was carried out by instructing the participant to stand with his/her feet together and arm stretched forward so that they were parallel to the ground and also to each other. The test was carried out in both eyes open (vision enabled) and eyes closed (vision denied) conditions. Presence of sway/imbalance was considered as an abnormal result. During the Fukuda stepping test, the participant was asked to march for 50 steps at the same place with his/her eyes closed and arms stretched forward (similar position as that used during the Romberg test). Finding of deviation greater than 45^o towards either side and/or distance of >1m from original starting point was considered abnormal. Tandem gait test was performed with the participant walking heel-to-toe with the head held straight for about 5 meters on an imaginary straight line. The presence of sway or loss of balance was considered an abnormal finding. During the past-pointing test, the participant was asked to touch his/her nose tip and the clinician’s fingertip with his/her fingertip alternately. The position of the clinician’s finger was varied in the space in such a way that the distance and the direction were both unpredictable. Citing of undershoot/overshoot of the target and/or presence of evident tremors was considered abnormal.

3.3.1 Recording of cVEMP.

In this study, cVEMP was recorded using Neurosoft Neuro-audio evoked potential system. Default ER-3A insert ear phones of the above mentioned evoked potential system were used for stimulus delivery to the ear canal. The participant was seated on a comfortable chair in an upright position. Sternocleidomastoid muscle was identified by palpating and finding the stiff part when the head was turned to the opposite side. The electrode placement sites were scrubbed with a commercially available abrasive gel. The inverting (negative / reference) electrode was placed at the sterno-clavicular junction, the non-inverting (positive / active) electrode at the upper one-third of the sternocleidomastoid muscle and the ground (common) electrode on the forehead. These electrodes were secured with surgical tape. The absolute impedance and inter-electrode impedance were ensured within 5 kΩ and 2 kΩ, respectively. Table 3.3.1.1 shows the stimulus and acquisition parameters for recording cVEMP.

Table 3.3.1.1.

Stimulus and acquisition parameters for cVEMP testing.

Parameter's name	Parameter type or its value
Stimulus type	Tone burst
Stimulus frequency	250,500,750,1000,1500 and 2000 Hz
Repetition rate	5.1 Hz
Gating function	Modified Blackman window

Stimulus duration	5 ms (2-ms of rise/fall time and 1-ms of plateau time)
Intensity	125 dB peSPL or 133 dB peSPL
Transducer	Insert ear phones
No. of averages	200 per stimulus frequency
Polarity	Rarefaction
Filter	10 to 1500 Hz
Analysis time	74 ms (pre-stimulus= 20 ms)
Amplification	5000X

Electromyography (EMG) monitoring and EMG normalization were used to control the effects of variable muscle tension on cVEMP responses. The participants were given visual feedback by asking them to maintain the needle deflection within the green zone which was equated to an EMG range of 30-70 µV. Further, the raw amplitude was divided by the root mean square of the pre-stimulus EMG in order to achieve EMG normalized cVEMP amplitude. cVEMP was obtained only from one ear of each participant, with half of the participants in each group undergoing recording from his/her right ear and the other half from left ear. This was done in order to avoid ear order effect, if any.

3.3.2 Gap detection test (GDT).

The GDT was done using the MLP toolbox (Green, 1990, 1993) on the MATLAB platform. The MLP toolbox for GDT testing uses a 750-ms long Gaussian noise with 0.5-ms cosine ramps at the beginning and end of the gap. It has a silent interval placed at its temporal center. The toolbox inherently requires a three alternate forced choice procedure to be used with a two-down one-up roving criteria. Gap duration is varied according to the listener’s performance. The minimum gap that a person can hear is estimated and taken as threshold. During this test, the participant’s task was to click on keyboard numbers 1, 2 or 3 based on the identification of the position of the signal with the gap.

Groups 1 and 2 were tested in the same manner, irrespective of the intensity at which they were being tested. Each individual had to undergo 2 baseline assessments to account for the test-retest reliability and the variability, if any, even without an intervention. This was followed by cVEMP testing for obtaining frequency tuning of cVEMP. This was further followed by the same tests as per their group assignment at various time frames (5 minutes after cVEMP, 1 hour after cVEMP, 24 hours after cVEMP and 7 days after cVEMP). Group 3 was evaluated using GDT and PTA, both using same time lines as the other groups. Figure 3.3.3.2 shows the schematic representation of the timeline during the experiment.

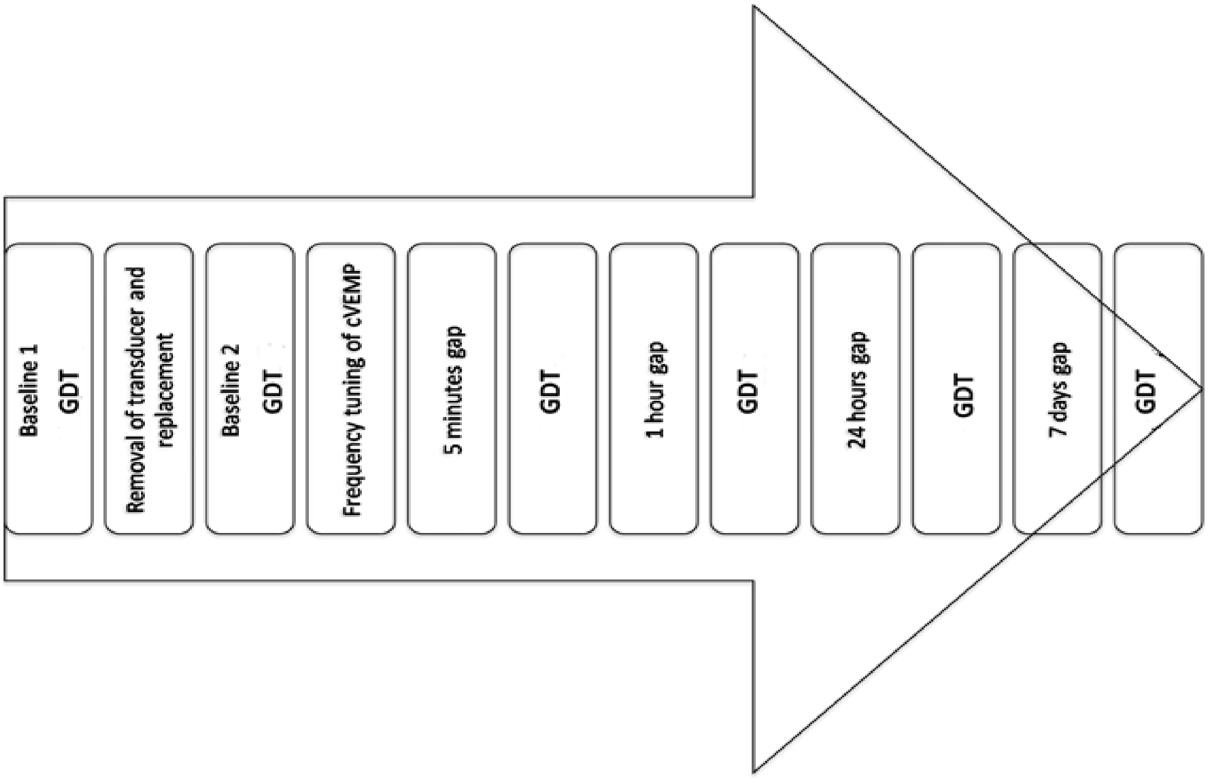

Figure 3.3.3.2: Schematic representation of the timeline of the experiment.

3.4 Statistical analyses

For the statistical analyses, Statistical package for social sciences (SPSS) software version 20 and Smith's statistical package (SSP) software were used. Freidman's test was done for the within group comparisons of GDT between the measurement points. If data showed significant difference among the measurement points, the Wilcoxon signed rank test was administered for pair-wise comparison between the measurement points. The Wilcoxon signed rank test was also used for the within group comparison between the ears. The Kruskal-Wallis test was done for the comparison among the groups. In case of a significant difference among the groups, the Mann-Whitney U test was done for pair-wise comparison between the groups. The

Equality of test for proportions was used for the between groups' comparison of the proportions of individuals with significant changes in GDT post VEMP stimulus exposure. All statistical analyses, except the equality of test for proportions, were done using the SPSS software version 20. The Equality of tests for proportions was done using the Smith's statistical Package.

CHAPTER IV

RESULTS

The present study aimed to identify the safe stimulus level, if any, for obtaining the frequency tuning of cVEMP. In order to achieve the above aim, gap detection test (GDT) was administered as an outcome measure. A total of 60 healthy adults participated in the study. Among them, 40 underwent VEMP testing for obtaining frequency tuning, whereas the remaining 20 formed the control group. The participants in the control group were not subjected to VEMP testing for frequency tuning. All participants of both the experimental groups (Group 1 underwent cVEMP testing at 133 dB peSPL & Group 2 underwent testing at 125 dB peSPL) had to undergo GDT twice before VEMP testing in order to obtain the baseline. In order to assess the effects of VEMP eliciting stimuli on hearing, these participants also underwent GDT measurements at four pre-selected time points after obtaining the frequency tuning of cVEMP. These pre-selected time points were 5 minutes, 1 hour, 24 hours, and 7 days after the VEMP testing for frequency tuning. The participants in the control group (Group 3) also underwent GDT evaluation at 6 time points, including the two baseline assessments, while ensuring same inter-session intervals as that in the experimental groups.

4.1 The within group comparison of GDT between the measurement points

All individuals in the experimental groups underwent Gap detection threshold assessment from both ears, before and after unilateral cVEMP recording for obtaining frequency tuning. The GDT obtained at various measurement points were subjected to descriptive statistics in order to obtain mean, median, standard deviation and range. The outcomes of the descriptive statistics are shown in Table 4.1.1, Table 4.1.2 and Table 4.1.3. The mean and the 95% confidence intervals of GDT of both the ears of all the three groups are shown in Figure 4.1.1.

Table 4.1.1.

Gap detection thresholds at various measurement points in the VEMP-ears (ears that underwent frequency tuning assessment of the cervical vestibular-evoked myogenic potential) of Group1 and Group 2

Measurement points	VEMP eliciting stimulus: 133 dB peSPL (Group 1)					VEMP eliciting stimulus: 125 dB peSPL (Group 2)				
	Mean	Median	SD	Range		Mean	Median	SD	Range	
				Minimum	Maximum				Minimum	Maximum
Baseline1	2.99	2.95	0.63	1.78	4.37	3.0	3.03	0.72	1.55	4.15
Baseline2	2.83	2.79	0.54	2.12	3.85	2.93	2.87	0.54	1.67	3.74
After 5minutes	3.37	2.97	0.99	2.34	6.61	2.86	2.80	0.61	1.75	4.12
After 1 hour	3.25	3.34	0.57	2.41	4.12	2.93	2.95	0.67	1.74	4.20
After 24 hours	3.22	3.14	0.55	2.12	4.26	3.08	3.11	0.60	1.73	4.17
After 7 days	3.26	3.17	0.50	2.17	4.25	3.04	3.02	0.59	1.74	4.15

Note: ‘SD’- standard deviation

Table 4.1.2.

Gap detection thresholds at various measurement points in non-VEMP ears of Group 1 and Group 2

Measurement points	VEMP eliciting stimulus: 133 dB peSPL (Group 1)					VEMP eliciting stimulus: 125 dB peSPL (Group 2)				
	Mean	Median	SD	Range		Mean	Median	SD	Range	
				Minimum	Maximum				Minimum	Maximum
Baseline1	2.88	2.67	0.53	2.10	3.90	2.70	2.80	0.63	1.45	3.85
Baseline2	2.84	2.75	0.52	2.10	3.91	2.70	2.71	0.63	1.79	3.90
After 5minutes	2.87	2.69	0.62	1.99	4.10	2.72	2.72	0.65	1.76	3.89
After 1 hour	2.88	2.75	0.57	1.99	3.89	2.70	2.72	0.62	1.85	3.88
After 24 hours	2.85	2.76	0.58	2.10	3.91	2.77	2.70	0.61	1.97	4.12
After 7 days	2.86	2.77	0.57	2.10	3.91	2.76	2.75	0.60	1.89	4.17

Note: ‘SD’- standard deviation

Table 4.1.3.

Gap detection thresholds at various measurement points in both ears of the control group (Group 3)

Measurement points	Right ear					Left ear				
	Mean	Median	SD	Range		Mean	Median	SD	Range	
				Minimum	Maximum				Minimum	Maximum
Baseline1	2.64	2.65	0.34	1.86	3.12	2.65	2.75	0.51	1.48	3.50
Baseline2	2.51	2.46	0.41	1.95	3.12	2.65	2.66	0.51	1.86	3.68
After 5minutes	2.63	2.80	0.43	1.62	3.12	2.63	2.60	0.49	1.96	3.66
After 1 hour	2.80	2.80	0.37	1.95	3.25	2.64	2.68	0.40	1.95	3.43
After 24 hours	2.71	2.80	0.36	1.75	3.12	2.67	2.75	0.40	2.14	3.50
After 7 days	2.65	2.83	0.40	1.79	3.54	2.73	2.70	0.40	2.05	3.51

Note: ‘SD’- standard deviation

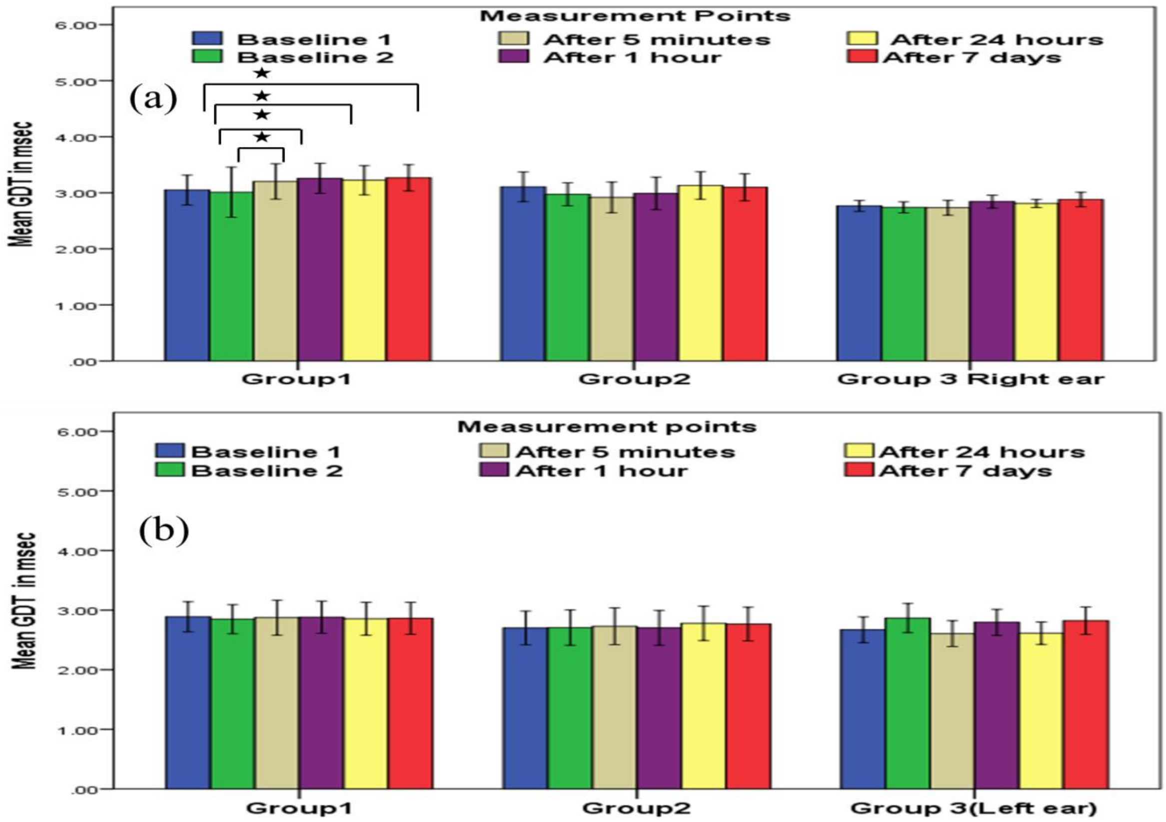

Figure 4.1.1.: The mean and 95% confidence intervals of GDT obtained at various measurement points in (a) VEMP ears of Group 1 and Group 2 and right ears of the Group 3; (b) Non-VEMP ears of the Group 1 and Group 2 and left ears of the Group 3. Note -Star in the graph shows the significance between the measurement points.

GDT after VEMP were compared against the pre-VEMP GDT. This comparison was made between the measurement points using Friedman's test, separately in the VEMP ears and the non-VEMP ears. In case of Group 3, the comparison between the measurement points were made in right and left ears separately. Table 4.1.4 shows the outcome of the Friedman's test.

Table 4.1.4.

The outcome of the Friedman's test for comparison between the measurement points in the experimental groups (Group 1 and 2) and the control group (Group 3)

Group	VEMP-eliciting stimulus (in dB peSPL)	VEMP ear / Right ear*			Non-VEMP ear / Left ear#		
		N	$\chi^2(2)$-value	*p*-value	N	$\chi^2(2)$-value	*p*-value
Group 1 and 2	125	20	7.89	0.16	20	5.38	0.37
	133	20	15.81	0.007	20	0.280	0.998
Group 3	NA	20	4.42	0.49	20	4.80	0.440

Note: *VEMP ear in case of experimental groups and right ears in case of control group;#Non-VEMP ear in case of experimental groups and left ears in case of control group; NA- not applicable; N- sample size.

The comparisons between measurement points using Friedman's test showed significant difference among the measurement points in the VEMP ears of Group1 because of which the data of Group 1 was further subjected to pair-wise comparison using the Wilcoxon signed ranked test. The results revealed significant difference in the GDT of baseline 2 and those obtained after 5 minutes (Z = -3.11, *p*= 0.002), after 1 hour (Z = -3.28, *p*=0.001), after 24 hours (Z = -2.61, *p*=0.09) and after 7 days (Z = -2.81, *p*=0.05) of the exposure to the VEMP eliciting stimuli.

4.2 Within group comparison of GDT between the ears

The GDT was obtained from VEMP ear and Non- VEMP ear in the experimental groups (Group 1 and Group 2) and both ears in the control group (Group 3). The GDT of both the ears in each of the three groups are shown in Table 4.2.1, Table 4.2.2 and Table 4.2.3. The mean and 95% confidence intervals of GDT of the two ears are shown in Figure 4.2.1.

Table 4.2.1.

Mean, median, standard deviation and range of GDT in VEMP and Non-VEMP ears in the experimental group that underwent unilateral VEMP acquisition using stimulus intensity of 133 dB peSPL (Group 1)

Measurement points	VEMP ear					Non-VEMP ear				
	Mean	Median	SD	Range		Mean	Median	SD	Range	
				Minimum	Maximum				Minimum	Maximum
Baseline1	2.99	2.95	0.63	1.78	4.37	2.88	2.67	0.53	2.10	3.90
Baseline2	2.83	2.79	0.54	2.12	3.85	2.84	2.75	0.52	2.10	3.91
After 5 minutes	3.37	2.97	0.99	2.34	6.61	2.87	2.69	0.62	1.99	4.10
After 1 hour	3.25	3.34	0.57	2.41	4.12	2.88	2.75	0.57	1.99	3.89
After 24 hour	3.22	3.14	0.55	2.12	4.26	2.85	2.76	0.58	2.10	3.91
After 7 days	3.26	3.17	0.50	2.17	4.25	2.86	2.77	0.57	2.10	3.91

Note: ‘SD’- standard deviation

Table 4.2.2.

Mean, median, standard deviation and range of GDT at various measurement points in VEMP and Non-VEMP ears in the experimental group that underwent unilateral VEMP acquisition using stimulus intensity of 125 dB peSPL(Group 2)

Measurement points	VEMP ear					Non-VEMP ear				
	Mean	Median	SD	Range		Mean	Median	SD	Range	
				Minimum	Maximum				Minimum	Maximum
Baseline1	3.0	3.03	0.72	1.55	4.15	2.70	2.80	0.63	1.45	3.85
Baseline2	2.93	2.87	0.54	1.67	3.74	2.70	2.71	0.63	1.79	3.90
After 5minutes	2.86	2.80	0.61	1.75	4.12	2.72	2.72	0.65	1.76	3.89
After 1 hour	2.93	2.95	0.67	1.74	4.20	2.70	2.72	0.62	1.85	3.88
After 24 hours	3.08	3.11	0.60	1.73	4.17	2.77	2.70	0.61	1.97	4.12
After 7 days	3.04	3.02	0.59	1.74	4.15	2.76	2.75	0.60	1.89	4.17

Note: ‘SD’- standard deviation

Table 4.2.3.

Mean, median, standard deviation and range of GDT at various measurement points in both ears of the control group (Group 3)

Measurement points	Right ear					Left ear				
	Mean	Median	SD	Range		Mean	Median	SD	Range	
				Minimum	Maximum				Minimum	Maximum
Baseline1	2.64	2.65	0.34	1.86	3.12	2.65	2.75	0.51	1.48	3.50
Baseline2	2.51	2.46	0.41	1.95	3.12	2.65	2.66	0.51	1.86	3.68
After 5minutes	2.63	2.80	0.43	1.62	3.12	2.63	2.60	0.49	1.96	3.66
After 1 hour	2.80	2.80	0.37	1.95	3.25	2.64	2.68	0.40	1.95	3.43
After 24 hours	2.71	2.80	0.36	1.75	3.12	2.67	2.75	0.40	2.14	3.50
After 7 days	2.65	2.83	0.40	1.79	3.54	2.73	2.70	0.40	2.05	3.51

Note: ‘SD’- standard deviation

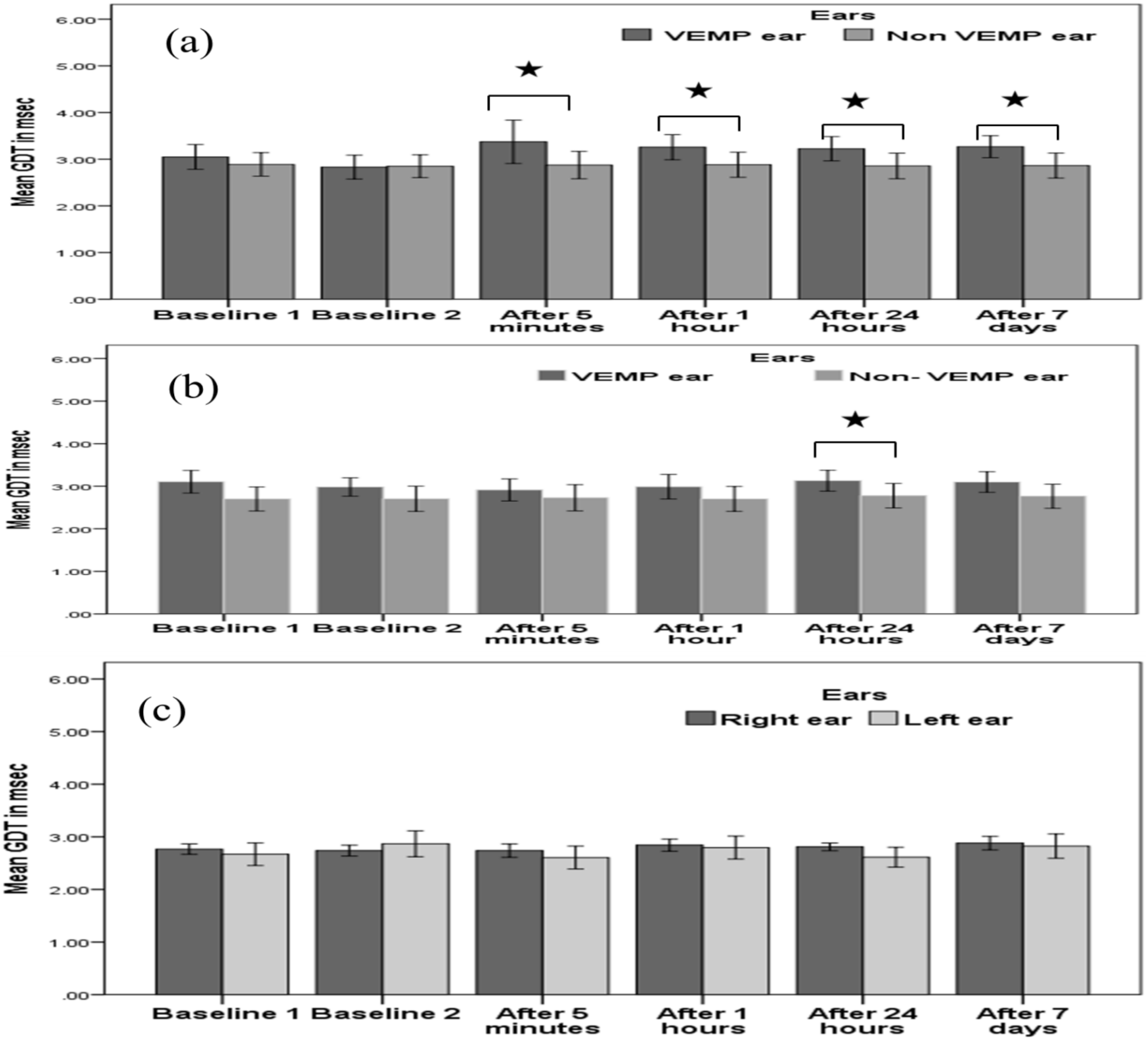

Figure 4.2.1.: Mean and 95% confidence intervals of GDT obtained at various measurement points in (a) VEMP ears and Non-VEMP ear Group 1; (b) VEMP ears and Non-VEMP ears of Group 2; and (c) right and left ears of Group 3. Note -Star in the graph shows the significance between the measurement points.

Wilcoxon signed ranked test was carried out for comparison of GDT between the ears within each group. The results are displayed in Table 4.2.4.

Table 4.2.4

The outcome of the Wilcoxon's signed rank test for pair-wise comparison between the ears at each measurement in each group.

Measurement point	133 dB peSPL (Group 1)		125 dB peSPL (Group 2)		Control (Group 3)	
	Z	*P*	Z	*p*	Z	*p*
Baseline 1	-1.23	0.21	-1.97	0.04	-0.52	0.60
Baseline 2	-0.12	0.90	-1.28	0.19	-0.89	0.37
After 5minutes	-1.97	0.04	-0.724	0.46	-0.46	0.64
After 1 hour	-2.10	0.03	-1.38	0.16	-0.89	0.67
After 24 hours	-2.13	0.03	-1.99	0.04	-1.58	0.11
After 7 days	-2.38	0.01	-1.81	0.07	-.0.37	0.70

As can be seen from the Table 4.2.4, the GDT was significantly larger in the VEMP ear than the Non-VEMP ear in Group 1 at all post-VEMP measurement points ($p < 0.05$). In case of the Group 2, the significant difference was observed only at baseline 1 and after 24 hours of the VEMP stimuli exposure.

4.3 The comparison of GDT between the groups

The groups at each of the measurement points were compared with each other. The GDT of all three groups are shown in Table 4.3.1 and Table 4.3.2. Further, Figure 4.3.1 and Figure 4.3.2 show mean and 95% confidence intervals of GDT in order to portray the comparison among the groups.

Table 4.3.1.

Mean, median, standard deviation and range of GDT at various measurement points in the ears undergoing VEMP testing of experimental groups (Group 1 and Group 2) and Right ear of control group (Group 3)

	Baseline 1			Baseline 2			After 5 minutes			After 1 hour			After 24 hours			After 7 days		
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD
133 dB peSPL (Group 1)	2.99	2.95	0.63	2.83	2.79	0.54	3.37	2.97	0.99	3.25	3.34	0.57	3.22	3.14	0.55	3.26	3.17	0.50
125 dB peSPL (Group 2)	3.00	3.03	0.72	2.93	2.87	0.54	2.86	2.80	0.61	2.93	2.95	0.67	3.08	3.11	0.60	3.04	3.02	0.59
Control (Group 3)	2.64	2.65	0.34	2.51	2.46	0.41	2.63	2.80	0.43	2.80	2.80	0.37	2.71	2.80	0.36	2.65	2.83	0.40

Note: ‘SD’- standard deviation

Table 4.3.2.

Mean, median, standard deviation and range of GDT thresholds at various measurement points in the ears undergoing Non-VEMP testing of experimental groups and Left ear of control group.

	Baseline 1			Baseline 2			After 5 minutes			After 1 hour			After 24 hours			After 7 days		
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD
133 dB peSPL (Group 1)	2.88	2.67	0.53	2.84	2.75	0.52	2.87	2.69	0.62	2.88	2.75	0.57	2.85	2.76	0.58	2.86	2.77	0.57
125 dB peSPL (Group 2)	2.70	2.80	0.63	2.70	2.71	0.63	2.72	2.72	0.65	2.70	2.72	0.62	2.77	2.70	0.61	2.76	2.75	0.60
Control (Group 3)	2.65	2.75	0.51	2.65	2.66	0.51	2.63	2.60	0.49	2.64	2.68	0.40	2.67	2.75	0.40	2.73	2.70	0.40

Note: ‘SD’- standard deviation

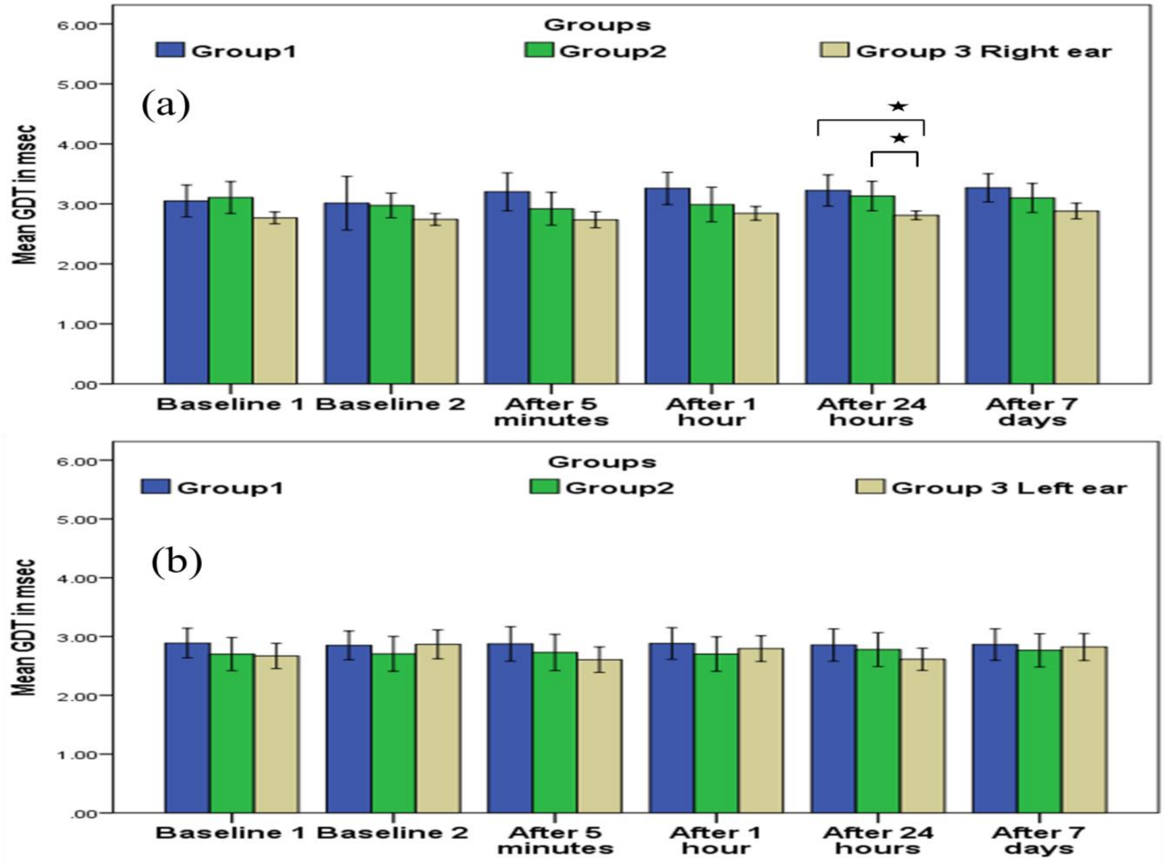

Figure 4.3.1.: Mean and 95% confidence intervals of GDT obtained among the groups in (a) VEMP ears of the experimental groups(Group 1 and Group 2) and right ears of the control group (Group 3); (b) Non-VEMP ears of the experimental groups (Group 1 and Group 2) and left ears of the control group (Group 3). Note – Star represents the significant difference among 2 groups.

The Kruskal-Wallis test was carried out for comparison among the groups. There was no significant difference among the groups for the Non-VEMP ears at Baseline 1 [$\chi^2(2)$ =1.39, p= 0.49)], Baseline 2 [$\chi^2(2)$ = 1.07, p=0.58], after 5minutes [$\chi^2(2)$ = 1.05, p = 0.59] after 1 hour [$\chi^2(2)$ = 0.90, p = 0.63] after 24 hours [$\chi^2(2)$ = 1.18, p = 0.55] and after 7 days[$\chi^2(2)$ = 0.39, p= 0.82]. In the VEMP ear also, the Kruskal-Wallis test showed no significant difference at Baseline 1 [($\chi^2(2) = 5.69$, $p = 0.05$], Baseline 2[$\chi^2(2) = 3.16$, $p = 0.20$], after 5 minutes [$\chi^2(2) = 4.85$, $p = 0.08$] and after 1hour [$\chi^2(2) = 4.66$, $p = 0.09$]. However, Kruskal Wallis test showed significant difference after 24 hours [$\chi^2(2) = 8.22$, $p = 0.016$] and after 7 days [$\chi^2(2) = 8.22$, $p = 0.016$] of the stimulus exposure in the VEMP ear. This warranted pair- wise comparison. So the data for 24 hours after VEMP and after 7 days after VEMP were subjected to pair-wise analysis using Mann-Whitney *U* test. Results of Mann Whitney U test are shown in Table 4.3.3.

Table 4.3.3.

The outcome of the Mann-Whitney U test for comparison among the groups

Pairs	After 24 hours		After 7 days	
	Z	P	Z	P
133 dBpeSPL(Group 1) vs Control (Group 3)	-2.57	0.01	-3.113	0.002
125dBpeSPL(Group 2) vs Control (Group 3)	-2.33	0.02	-1.08	0.27
133 dBpeSPL(Group 1) vs 125 dBpeSPL (Group 2)	-0.44	0.65	-1.25	0.20

The group data showed significant difference in GDT between the groups, after the exposure to the VEMP eliciting stimuli. This, however, need not necessarily implicate that VEMP eliciting stimuli used for obtaining frequency tuning cause GDT to increase in every individual. Therefore, the individual data was also compared between the groups in order to quantify the number of individuals in whom these stimuli caused significant increase in the GDT. The values beyond “mean + 2 standard deviation” of the GDT of baseline 2 was used as a criteria for classifying significant worsening of the

GDT after the exposure to the VEMP stimuli. For this purpose, baseline 2 was used so that any practice effects from the first to the second test session could be countered. The mean + 2 standard deviation of baseline 2 was found to be 3.80 ms and therefore any value of GDT >3.80 ms was deemed abnormal. Using this value for comparison, the number of individuals with abnormal results was identified at each point of measurement in all three groups. Figure 4.3.2 shows the number of individuals with abnormal GDT values at each point of time in each group.

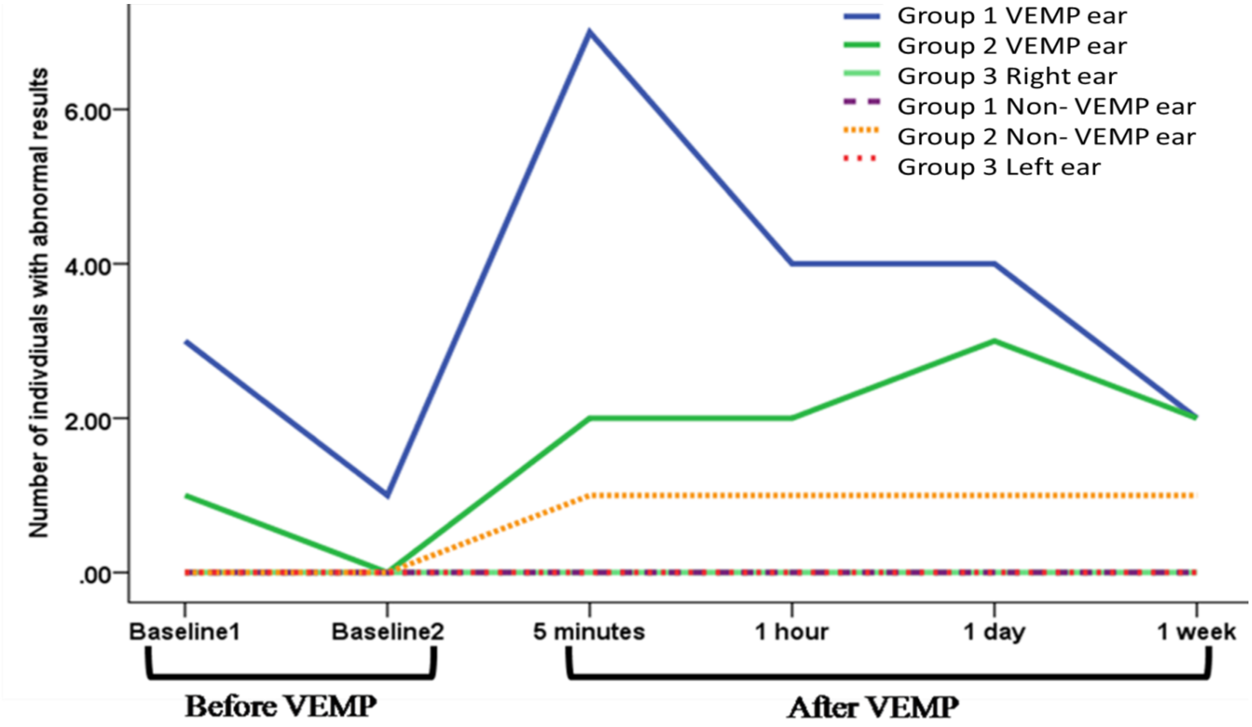

Figure 4.3.2.: The number of individuals with abnormal GDT (>3.8 ms) at various measurement points in both ears of all three groups.

The proportion of abnormal results between the groups was compared using the Equality of test for proportions. The results revealed that significantly higher proportion of ears undergoing VEMP test for Group 1 had abnormal GDT at 5 minutes, 1 hour and

24 hours after VEMP the test than the individuals in Group 3 at the same points ($p < 0.05$). There was no significant difference between the groups at any other measurement point in either ear. The results of the Equality of test for proportions are shown in Table 4.3.4

Table 4.3.4.

The comparison of the proportion of individuals with abnormal GDT (GDT > 3.80 ms) between the groups at various measurement points

Ear	Groups for comparison	Before VEMP				After VEMP							
		Baseline1		Baseline2		5 minutes		1 hour		24 hours		7 days	
		Z	*P*	Z	*p*	Z	*P*	Z	*p*	Z	*P*	Z	*p*
VEMP Ear	Group 1 Vs Group3	1.80	0.071	1.01	0.311	2.91	0.003	2.10	0.035	2.10	0.035	1.45	0.146
	Group 1 Vs Group 2	1.05	0.291	1.01	0.311	1.89	0.058	0.88	0.370	0.41	0.677	0.00	1.00
	Group 2 Vs Group 3	1.01	0.311	0.00	1.00	1.45	0.146	1.45	0.146	1.80	0.071	1.45	0.146
Non-VEMP Ear	Group 1 Vs Group 3	1.01	0.311	1.45	0.146	1.80	0.071	1.80	0.071	1.45	0.146	1.45	0.146
	Group 1 Vs Group 3	0.00	1.00	0.60	0.548	0.00	1.00	1.05	0.291	0.00	1.00	0.60	0.548
	Group 2 Vs Group 3	1.01	0.311	1.01	0.311	1.80	0.071	1.01	0.311	1.45	0.146	1.01	0.311

To summarize, the results of the present study shows significant persistent worsening of the GDT in the VEMP ears after the exposure to the VEMP eliciting stimuli of 133dB peSPL. The significant worsening of GDT was also observed after the exposure to 125 dB peSPL; however it was observed only after 24 hours of the exposure to the VEMP eliciting stimuli.

CHAPTER V

DISCUSSION

The present study included 60 healthy adult participants. Among them, 20 underwent VEMP testing for obtaining frequency tuning using 133 dB peSPL stimuli (Group 1), whereas 20 were tested using 125 dB peSPL (Group 2). The remaining 20 formed the control group (Group 3). The participants in Group 3 were not subjected to VEMP testing. Group 1 and Group 2 had to undergo GDT twice before VEMP testing in order to obtain baseline. In order to assess the effects of VEMP eliciting stimuli on hearing, these participants also underwent GDT measurements at four pre-selected time points after obtaining the frequency tuning of cVEMP. These pre-selected time points were 5 minutes, 1 hour, 24 hours, and 7 days after the VEMP testing for frequency tuning. The participants of Group 3 also underwent GDT evaluation at 6 time points, including the two baseline evaluation while ensuring same inter-session intervals as that in Group 1 and Group 2.

5.1 The comparison of GDT between the measurement points

Group 3 was the control group in the present study. The participants of this group were not exposed to the VEMP eliciting stimuli. In this group, the results of comparison between the measurement points revealed no significant change in the GDT in either ear. This possibly points at highly repeatable responses. In other words, the GDT showed high degree of test-retest reliability. The studies on test-retest reliability of GDT have shown excellent test-retest reliability (Shinn, Jennifer, Chermak, & Musiek, 2009; Wang & McPherson, 2015). Therefore, the findings of the present study are in accordance with those reported previously.

The participants of Group 2 in the present study underwent VEMP testing at various frequencies using tone bursts of 125 dB peSPL in order to obtain frequency tuning. They also underwent GDT before and after VEMP testing at various time intervals. The results of VEMP ear as well as Non-VEMP ear showed no significant difference in GDT among the measurement points. This means that the exposure to 125 dB peSPL did not cause any significant change to the GDT. There are no previous studies about the effects of VEMP eliciting stimuli on GDT. However, studies have explored the effects of exposure to 125 dB peSPL of VEMP eliciting stimuli on other tests of hearing function, such as pure tone audiometry, extended high frequency pure tone audiometry and DPOAE (Rodriguez et al., 2018; Singh., Keloth, et al., 2019). They showed no significant alterations in the audiometric thresholds and the amplitudes of DPOAE after the exposure to VEMP eliciting stimuli. This possibly indicates that the VEMP eliciting stimuli of 125 dB peSPL represent safe levels. However, these studies were done on single frequency VEMPs. In the present study VEMPs were recorded in response to six different frequencies using the same stimulus intensity as those in the above mentioned studies. Despite the increase in the amount of stimulus exposure, the GDT did not change significantly in the present study. Therefore, this again points at 125 dB peSPL being safe stimulus intensity for obtaining frequency tuning of cVEMP.

In Group 1, the participants underwent frequency tuning assessment using 133 dB peSPL intensity at all frequencies. The GDT was significantly increased (became worse) at 5 minutes post-VEMP stimulus exposure and remained significantly increased at all subsequent measurement points till 7 days. As stated before, there are no studies investigating the effect of VEMP stimulus on GDT. However, studies using other behavioural measures have shown equivocal findings (Krause et al., 2013; Rodriguez et al., 2018; Stromberg et al., 2016; Singh, Keloth, et al., 2019). While the majority of the studies showed no significant change in pure tone thresholds after VEMP test (Krause et al., 2013; Rodriguez et al., 2018; Stromberg et al., 2016), the study by Singh, Kumar, and Keloth (2019) showed significant deterioration of pure tone thresholds of 14 kHz and 16 kHz after VEMP test. Therefore, the findings of present study are in consonance with those of Singh, Kumar et al (2019), whereas they show disagreement with the others (Krause et al., 2013; Rodriguez et al., 2018; Stromberg et al., 2016). The difference in the findings of the present study from the above mentioned ones could be related to the relative sensitivity of the frequencies used in identifying the effects of loud sounds on auditory function. These studies used frequencies up to 6 kHz (Rodriguez et al., 2018) and 8 kHz (Stromberg et al., 2016). It is well known that the frequencies up to 8 kHz are less susceptible to deleterious effects of noise, whether temporary or permanent, than the extended high frequencies (Barbee et al., 2014; Mehrparvar et al., 2014; Moore, Hunter, & Munro, 2017).The only known study to have incorporated extended high frequencies to investigate the effects of VEMP eliciting stimuli on puretone audiometry was done by Singh, Kumar et al (2019). They reported significant change in high frequency puretone thresholds, especially at 14 kHz and 16 kHz, after exposure to the VEMP eliciting stimuli. However, the findings of the present study are in slight disagreement with those of even Singh, Kumar et al (2019). While Singh, Kumar et al (2019) showed the temporary threshold shift to last for less than an hour, the significant changes in GDT in the present study have lasted even up to the duration of 7 days. These differences can be explained using a combination of two facts- (i) Singh, Kumar et al (2019) used single frequency tone bursts to elicit VEMPs, whereas the present study evaluated frequency tuning of VEMP which exposed the ears to 6 different frequencies. Therefore it is possible that larger duration of exposure could have caused longer lasting deleterious impact on GDT. (ii) Singh, Kumar et al (2019) used extended high frequency pure tone audiometry, whereas the present study used GDT as an outcome measure of the effects of VEMP eliciting stimuli on hearing function. The studies comparing the effects of hazardous noise levels on hearing thresholds, including those using extended high frequencies (Guest, Munro, &Plank, 2018; Moore, Hunter, & Munro, 2017; Plack, Guest & Carcagno, 2019), have shown signs of cochlear synaptopathy even before the deterioration of the hearing thresholds can be noticed at any frequency. Since GDT has evolved as a test for detecting cochlear synaptopathy (Song et al., 2016), it is only logical to assume that GDT will be more sensitive than the extended high-frequency pure tone audiometry. This, in combination with the previous point about more amount of loud sound exposure, explains the longer lasting impact on the GDT in the present study than on pure tone thresholds on the extended high frequency region in the study by Singh, Kumar et al (2019).

5.2 The within group comparison of GDT between the ears

In Group 3, the results showed no significant difference in GDT between the ears. Similar findings of no significant difference in GDT between the ears have been reported in normal hearing children and adults with no auditory processing deficits

(Shinn et al., 2009; Wong & McPherson, 2014; Samelli & Schochat, 2007). This is due to symmetrical representation of the temporal processing abilities between the ears.

In Group 2, the results revealed a significant difference in the GDT between the ears at Baseline 1 and after 24 hours after the exposure to the VEMP eliciting stimuli. However, the difference in the GDT between the ears at Baseline 1 appears to be mainly because of the practice effect / chance effect. This does not seem to be an actual difference in GDT between the ears because there was no significant difference at baseline 2, despite no intervention between the two baselines. Post-VEMP stimuli exposure of 125 dB peSPL across the frequencies, the GDT was consistently larger (worse) in the VEMP ear than the Non-VEMP ear; however, the statistically significant difference was observed only at 24 hours. The finding of larger GDT in the VEMP ear than the Non-VEMP ear is most likely caused by the unilateral VEMP testing. While the VEMP ear received stimuli of 125 dB peSPL (equivalent to 105 dB SPL), the Non-VEMP ear in all likelihood would have received an intensity of 55 dB peSPL or less considering that the minimum value of the inter-aural attenuation for the insert earphones is 65 dB (Munro & Angew, 1999). Any exposure duration to such small intensity stimuli cannot cause a temporary or permanent change in hearing function. However, long duration exposure to 105 dB SPL, which was the intensity used in the VEMP ear, may cause temporary or permanent change in the hearing thresholds. This explains the unilateral nature of GDT change after exposure to the VEMP eliciting stimuli. Since the difference between the ears was significant only at 24 hours, and not before or after that, it can be assumed that the effect of exposure to the VEMP eliciting stimuli of 125 dB peSPL is short-lived. Generally, the studies on the effect of noise exposure on hearing have shown the maximum temporary threshold shift in the immediate vicinity after the noise exposure, and the amount of temporary threshold is reported to decline as a function of the duration since exposure (Liberman & Kujawa, 2017; Liberman et al., 2016; Song et al., 2016). However, in Group 2 in the present study, the maximum change in GDT was observed at 24 hours after the exposure. While this is not a usual finding, a study has shown that the maximum temporary change in the thresholds did occur at 24 hours post exposure in their data set (Lobarinus, Spankovich & Prell, 2017). The studies on cochlear synaptopathy after noise exposure have observed that the temporary synaptopathy between the inner hair cell and the auditory nerve takes a while (≥ 4 hours) to develop and it is followed by rapid recovery within 1-2 weeks (Khuwaja & Liberman, 2009; Miyakita, Hellstrom, Frimanson & Axelsson, 1992). Therefore the findings of the present study are in accordance with those reported previously.

The participants of Group 1 had undergone VEMP testing using 133 dB peSPL tone bursts. The results of comparison between the ears showed significantly larger GDT in the VEMP ear at all post-VEMP measurement points than the Non-VEMP ears. This is in consonance with other reports pertaining to the use of 133 dB peSPL stimuli to generate VEMP and its consequence on the auditory function (Krause et al., 2013; Singh, Kumar et al., 2019). This finding might be explained on the basis of the amount of crossed-over energy to the Non-VEMP ear and its effect on hearing. The equivalent sound pressure for the VEMP stimuli was measured at 110 dB SPL. As explained above, the maximum crossed-over energy reaching the Non-VEMP ear would have been 60 dB SPL, which is not sufficient to cause a temporary or permanent threshold shift.

However, exposure to 110 dB SPL in the VEMP ear could have caused changes to the hearing mechanism, thereby causing significant worsening of the GDT in the VEMP ear. This would have in turn produced significant difference between the ears.

The changes observed in the study by Krause et al (2013) and Singh, Kumar et al (2019) were transient and returned to the pre-VEMP exposure levels within 1-24 hours. However, the significant difference between the ears in the present study was observed even until 7 days. Therefore, there was slight disagreement of the findings of the present study to those reported before. The differences could be attributed to the differences in the nature of the outcome measures in the studies. GDT is a test to detect the presence of cochlear synaptopathy, whereas OAEs and pure tone audiometry (including the extended high frequency audiometry) are tests of outer hair cell functioning and hearing, respectively. It has been reported that cochlear synaptopathy may be observed despite the intact OAEs and the presence of normal hearing thresholds at all frequencies up to 16 kHz (Liberman et al 2016). This makes GDT more sensitive test for subtle auditory system damage. Since it is more sensitive, the impact of loud acoustic stimuli may remain longer on these than on the OAEs or the pure tone thresholds. This explains the reason behind longer lasting effects on GDT, the test used in the present study, than the tests used in the other studies (Krause et al., 2013; Singh, Kumar et al., 2019).

The differences between the ears remained significant even till the last measurement point in the present study. So does it mean that the exposure of 133 dB peSPL caused a permanent cochlear synaptopathy in these participants? While, the present study did not assess GDT beyond 7th post-exposure day, studies in literature have reported the temporary changes lasting for as long as 14-16 days (Liberman &

Liberman, 2015; Lobarinus, Spankovich, & Prell, 2017). This shows that there is still hope for the complete recovery by the end of 2 weeks from the exposure.

5.3 The comparison of GDT between the groups

The results for the between group comparisons showed no significant change in GDT in the Non-VEMP ear. There was no significant difference between the groups at the two baselines, at 5 minutes after the exposure and 1 hour after the exposure to the VEMP eliciting stimuli for obtaining frequency tuning of cVEMP. However, there was significant difference between Group 1 and Group 3 at two measurement points – after 24 hours and after 7 days of the VEMP test. This means that there was significant worsening of GDT after 24 hours of the exposure, which continued to be significant even 7 days after the exposure. These findings are in disagreement with the previous studies which reported recovery from temporary threshold shift within 1-24 hours of the exposure to an intensity of 133 dB peSPL for eliciting VEMP (Krause et al, 2016; Singh, Kumar et al 2019).These findings open up possibility for two assumptions- (i) use of the 133 dB peSPL for obtaining frequency tuning of cVEMP causes permanent cochlear synaptopathy; (ii) the cochlear synaptopathy caused by the above mentioned stimuli is longer lasting, yet temporary, considering that there are previous evidences of complete recovery till as long as 2 weeks after the exposure (Liberman & Liberman, 2015; Lobarinus, et al., 2017). Since the last measurement point in the present study was 7 days after the exposure, one hopes for the latter rather the former. This positive hope arises from the analysis of individual participant’s data where the number of individuals with abnormally large GDT after 5 minutes of VEMP stimulus exposure was 7, and it progressively reduced to 4, 4 and 2 at the measurement points of 1 hour, 24 hours and 7 days after the exposure, respectively. However, this does pose a major limitation to the methods used in the present study. Had there been one more measurement point at about 16 or 20 days from the exposure in the present study, the uncertainty over the temporary/permanent nature of the change in GDT would have been clearer.

The comparison between the VEMP ears of Group 2 and Group 3 showed significant increase (deterioration) of GDT only by 24 hours after the exposure to the VEMP eliciting stimuli. Since there was no significant difference between these 2 groups at any point before or after 24 hours from the exposure, it can be safely assumed that the effect was temporary. Therefore, the present study shows slight disagreement with the studies of Rodriguez et al (2018), Singh, Keloth et al (2019) and Singh, Kumar et al (2019), all of which found no deleterious effect of VEMP eliciting stimuli on OAEs and extended high frequency audiometry after the exposure to 125 dB peSPL sound for eliciting VEMP. The possible reason of such a difference can be- (i) the difference in the amount of VEMP stimuli exposure; (ii) the differences in the sensitivity of the tests used as the outcome measure.

In the studies of Rodriguez et al (2018), Singh, Keloth et al (2019) and Singh, Kumar et al (2019), the participants underwent single frequency VEMP (500Hz tone-burst), whereas the participants of the present study underwent VEMP using 6 different frequencies (250 Hz, 500 Hz, 750 Hz, 1000 Hz, 1500 Hz, 2000 Hz), one after the other. Therefore the cumulative impact (relative noise dose) was more for participants in the present study than the studies mentioned above (Rodriguez et al., 2018; Singh, Keloth et al., 2019;Singh, Kumar et al., 2019). Further, The studies by Rodriguez et al (2018), Singh, Keloth et al (2019) and Singh, Kumar et al (2019) used distortion product OAEs, puretone audiometry and extended high frequency audiometry upto 16 kHz whereas, the present study used GDT as the test for outcome measure. While there is no study on direct comparison of the sensitivity of GDT, OAEs, puretone and extended high frequency audiometry in detecting the effects of exposure to impulse noise, the studies have shown abnormal GDT in the noise exposed ears despite normal OAEs and normal hearing thresholds across the entire range of hearing frequencies. Therefore there might be likelihood that the findings of the present study and the differences of the present study from that reported before might probably be an example of temporary cochlear synaptopathy affecting the GDT yet sparing the OAEs and puretone thresholds. The evidence for the presence of cochlear synaptopathy of temporary nature percolates from a study on anatomical and structural changes at the synaptic level after the short duration exposure to loud impulsive clicks of about 106dB SPL (A), (Henry & Munroy., 1995). The authors observed reduction in the number of synaptic vesicles, decrease in the number of synapses, reduction in the packing density of synaptic vesicles around the synaptic body and reduction in the size of the synaptic body. These changes were found to be temporary in nature. Since GDT is sensitive to the changes at the level of synapse, owing to similar change after the exposure to VEMP eliciting stimulus they were found to be affected in the present study. In fact, there is a possibility that a combination of higher load of exposure and better sensitivity of GDT could have yielded the findings of the present study in Group 2.

There was no significant difference between Group 1 and Group 2 at any measurement point. This probably points towards a continuum between no exposure, medium loud exposure and loud exposure, where there is no significant change from

Group 3 to Group 2 and from Group 2 to Group 1, although Group 1 and 3 are significantly different.

CHAPTER VI

SUMMARY AND CONCLUSION

Vestibular-evoked myogenic potential (VEMP) are biphasic potentials. VEMP can be recorded from several muscles of the body. If recorded from the sternocleidomastoid muscle, the potential is called cervical VEMP (cVEMP). VEMP has found its extensive clinical utility in the test battery for vestibular assessment in the recent years, as it is the only test for estimating the functional integrity of the saccule and the sacculocollic pathway. cVEMP has been extensively used for the diagnosis and differential diagnosis for numerous conditions such as Meniere’s disease, benign paroxysmal positional vertigo, vestibular migraine, vestibular neuritis and superior semi-circular canal dehiscence (Kingma, & Wit, 2011; Node et al., 2005; Rauch et al., 2004; Sandhu et al., 2012; Taylor et al., 2012).

While the utility of cVEMP has gained popularity because of its high sensitivity in the diagnosis of vestibular disorders, the concerns regarding the safety of the stimuli used for eliciting VEMP have been growing rapidly, considering that the successful repeatable recording of cVEMP requires very high intensity, usually $\geq$ 120 dB SPL or $\geq$ 95 dB nHL. In order to search for an answer to such questions about the safety of VEMP eliciting stimuli, a few studies were carried out using otoacoustic emissions or puretone audiometry before and after the exposure to the VEMP eliciting stimuli. These studies showed significant decline in the amplitudes of DPOAE (Krause et al., 2013; Rodriguez et al., 2018; Stromberg et al., 2016) or worsening of pure tone thresholds at some frequencies(Krause et al., 2013; Rodriguez et al., 2018; Stromberg et al., 2016). However, a few other studies have also no significant deleterious effect of the VEMP eliciting stimuli on the outcomes of the tests of auditory function (Singh, Keloth et al., 2019). Based on such outcomes, these studies concluded that 125 dB peSPL represents a safe level for eliciting cVEMP. However, the finding of no significant change of OAE amplitude or pure tone thresholds after cVEMP test does not necessarily ensure no ill-effects of these stimuli on the hearing mechanism. Numerous animal studies have shown evidences for progressive synaptic loss between the inner hair cells and the auditory nerve (especially the spiral ganglion cells) despite there being no significant change in the thresholds after exposure to loud sounds (Kujawa, & Liberman, 2009). This phenomenon was termed “hidden hearing loss” or “cochlear synaptopathy” (Kujawa, & Liberman, 2009). Therefore, it is possible that an individual can have deficit in supra-threshold discrimination and neural temporal coding, despite a non-detectable hearing loss after an exposure to high intensity cVEMP eliciting stimuli. The Gap detection test (GDT) and speech in noise test (SPIN) are believed to be sensitive for detection of this hidden hearing loss, either temporary or permanent. Keeping such reports in mind, GDT was chosen as a test to check the auditory system for any possible damage from the VEMP eliciting stimuli. Moreover, the studies in literature have used single frequency VEMPs for establishing the ill-effects on the auditory system. This cannot account for the cumulative damage that can be caused by measures such as frequency tuning, as these require cVEMP recordings in response to 6-8 stimulus frequencies, one after the other. Therefore, the aim of the present study was to identify safe stimulus level, if any, for obtaining frequency tuning of cVEMP using GDT as an outcome measure for investigating the effects on the auditory mechanism.

In order to fulfill the aim, 60 healthy adults with normal hearing sensitivity and vestibular function,in the age range of 18-40 years (mean = 22, SD =2.9), were enrolled as participants. Of these, 40 participants were divided into 2 experimental groups (20 in each group) which were called as Group 1 and Group 2. The participants of Group 1 underwent VEMP using 133 dB peSPL, whereas those in Group 2 were evaluated using 125 dB peSPL for obtaining frequency tuning of cVEMP. The remaining 20 participants formed the control group (Group 3). The participants in Group 3 were not subjected to VEMP testing. The participants of Group 1 and Group 2 underwent GDT twice before VEMP testing in order to obtain a stable baseline and counter for adulteration of outcomes by practice effect. In order to assess the effects of VEMP eliciting stimuli on hearing, these participants also underwent GDT measurements at four pre-selected time points after obtaining the frequency tuning of cVEMP. These pre-selected time points were 5 minutes, 1 hour, 24 hours, and 7 days after the cVEMP testing for frequency tuning. The participants in Group 3 also underwent GDT evaluation at 6 time points while ensuring the same inter-session intervals as that in the two experimental groups.

cVEMP testing for obtaining the frequency tuning of cVEMP was done using the Neurosoft Neuro-audio evoked potential system. cVEMP recordings were carried out at 6 different tone burst frequencies (250Hz, 500Hz, 750 Hz, 1000Hz, 1500Hz,&2000 Hz). The tone bursts were gated through the modified Blackman window such that the stimulus duration was 5 ms (2-ms rise/fall times and 1-ms plateau time). Two hundred sweeps of stimuli were delivered at the rate of 5.1Hz for each tone burst frequency. Filter settings and amplification for cVEMP was set at 10 to 1500 Hz and 5000 times, respectively. The stimuli were delivered through the default insert earphones, either at 133 dB peSPL or at 125 dB peSPL, across the frequencies.

For the statistical analyses, the Freidman's test was done for the within group comparisons of GDT between the measurement points. In case of a significant difference among the measurement points, the Wilcoxon signed rank test was administered for pair-wise comparison between the measurement points. The Wilcoxon signed rank test was also used for the within group comparison between the ears. The Kruskal-Wallis test was done for the comparison among the groups. In case of a significant difference among the groups, the Mann-Whitney U test was done for pair-wise comparison between the groups. The Equality of test for proportions was used for the between groups' comparison of the proportions of individuals with significant alterations of the GDT after the VEMP stimulus exposure. All statistical analyses, except the Equality of test for proportions, were done using the SPSS software version 20. The Equality of tests for proportions was done using the Smith's statistical Package.

The within group comparison between the measurement points was significant only in the VEMP ears of Group 1. The GDT was found to be significantly smaller at baseline 2 than all the other measurement points after the exposure to the cVEMP eliciting stimuli. All the previous studies had either shown no significant effects on hearing mechanism or the effect lasted for less than 1-24 hours (Rodriguez et al., 2018, Singh, Kumar et al., 2019, Singh, Keloth et al., 2019). The reason for such discrepancy in findings could be the difference in the exposure duration due to the use of 6 frequencies in the present study as opposed to single frequency to elicit cVEMPs in the previous studies (Rodriguez et al., 2018, Singh, Kumar et al., 2019, Singh, Keloth et al., 2019). Another reason that can explain such a finding is the difference in the test used for the outcome measure. Previous studies used DPOAEs or pure tone audiometry with or without extended high- frequency audiometry; however, the present study used GDT as the test for outcome measure. Since GDT has evolved as a measure to detect cochlear synaptopathy, which can occur despite no noticeable change in pure tone thresholds or DPOAE amplitudes (Guest et al., 2018; Moore et al., 2017; Plack et al., 2019), the difference in the results between the studies can be expected.

The GDT was also compared between the ears at each point within each group. The results showed a significant difference between the ears at baseline 1 and after 24 hours of VEMP stimuli exposure in Group 2. The results of comparison between the ears in Group 1 showed significant difference at all post-exposure time points. Since there was no intervention between the two baselines, and the ear differences at baseline 2 were not statistically significant, it appears that the significant ear difference at baseline 1 in Group 2 was a chance result. However, the significant difference between the ears after 24 hours of the exposure to cVEMP eliciting stimuli in Group 2 could have resulted from temporary effects of the impulse noise exposure that can sometimes take up to 24 hours to develop and disappears within 1-2 weeks (Khuwaja & Liberman, 2009; Miyakita et al.,1992). Since the stimulus intensity was about 8 dB higher in Group 1 than in Group 2, a more widespread and longer lasting effects of exposure can be understood.

The results for the comparison between the groups showed that Group 2 and 3 had a significant difference at the measurement point of 24 hours. Group 1 and 3 showed significant difference at the measurement point of after 24 hours and after 7 days. The possible reason for such a finding can be attributed to majorly two facts (i) the difference in the amount of VEMP stimuli exposure- single frequency used for other studies versus frequency tuning of cVEMP needing exposure to 6 frequencies in the present study; (ii) the differences in the sensitivity of the tests: GDT used in the present study versus OAEs, pure tone audiometry or extended pure tone audiometry used in other studies as the outcome measure. The reasons for increase in GDT post-VEMP stimulus exposure could be the structural changes at the synaptic level, such as reduction in the number of synapses, number of synaptic vesicles, packing density of synaptic vesicle surrounding the synaptic body, and the size of the synaptic body, as observed in an animal study on effects of the short-term exposure to impulsive stimuli of about 106 dB SPL (Henry & Munroy, 1995). Similar temporary changes might be possible at the synapses in the humans. Since GDT is sensitive to the changes at the synapse, GDT were temporarily affected after exposure to VEMP eliciting stimuli of 133 dB peSPL (equivalent to about 110 dB SPL) in the present study.

The findings of the present study point at longer lasting effects of exposure to 133 dB peSPL tone bursts for obtaining frequency tuning of cVEMP than 125 dB peSPL. There was clear evidence for return of GDT to normal levels when 125 dB peSPL was used, but the effects were persistent till even 7 days for 133 dB peSPL. While there is a possibility that GDT could return to pre-stimulus levels by about 2 weeks, it was not measured in the present study and is therefore it is at the best, a speculation. Therefore, 125 dB peSPL appears to be safe level for obtaining frequency tuning of oVEMP. This also points fingers at the lacunae in the method used in the study, especially for the choice of the last measurement point. Therefore, the future studies could benefit from keeping the last measurement point at or beyond 2 weeks in order to make clear segregation between temporary or permanent effects of the stimulus levels on hearing mechanism.

Clinical implication of the study

Despite the lacunae in the methods, the present study helps us to understand that 125 dB peSPL can be safely used for a single frequency tone burst testing. However, for using 125 dB peSPL as a stimulus for obtaining frequency tuning, one should follow caution and optimize the testing in such a way that the acoustic load from the VEMP stimuli on the ears is minimal. This might be either possibly eliminating the use of a few frequencies which are of lesser clinical use, such as 250Hz. There is enough evidence in literature which shows that the resonant frequency of the otolith organs is between 450-750 Hz. Also, for a differential diagnosis of semicircular canal dehiscence or Meniere's disease, it is only reasonable to do a frequency tuning till only 2000Hz, as most often the tuning is between 1000-2000 Hz (Taylor et al., 2012). The study also showed that 133 dB peSPL, when used for frequency tuning of cVEMP, has a potential to cause permanent cochlear synaptopathy. Therefore, this intensity should be avoided, at least for frequency tuning of cVEMP, until more conclusive evidence is obtained for the GDT change being temporary in nature.

Limitations of the study and future directions

The present study included follow-up of the participants till 7 days after the exposure to VEMP eliciting stimuli for obtaining frequency tuning of cVEMP. While the group data showed significantly worse GDT even until the last measurement point, the individual data showed such an occurrence in only 2 individuals, with the remaining 5 individuals showing return to the pre-exposure baselines. However, it is not clear about whether or not the GDT in these two individuals returned to pre-exposure values at any point later. It is well known that temporary effects of short-term noise exposure can last up to 2 weeks after the exposure. Had the study incorporated another measurement point 16/20 days post the exposure, a clearer picture regarding the safety of stimulus level would have been obtained. Therefore, it is recommended that future studies include one more measurement point beyond 2 weeks. This will help to understand regarding any permanent possible damage to the auditory structures.

The study also did not have groups with OAE and extended high frequency audiometry as the outcome measure. Inclusion of these groups, in addition to GDT, will be helpful in understanding the relative sensitivity of these measures to the effects of loud impulsive sound exposures of short durations. Further, the present study found 125 dB peSPL as a safe intensity level and 133 dB peSPL as unsafe. Had there been a mid-intensity between 125-133dB peSPL, the puzzle regarding optimization of a safe stimulus level could be better solved. Therefore, the future studies in this regard should ensure against such limitations before commenting on the safe stimulus levels for obtaining frequency tuning of cVEMP.

All the previous studies on the effect of VEMP eliciting stimuli on the puretone thresholds have used changes in AC thresholds as an outcome measure for the detection of the effects of VEMP eliciting stimuli on hearing. It is worth noting that the air conduction thresholds are affected both by a middle ear pathology and/or cochlear pathology, whereas bone-conduction relates directly to the response from the cochlea (sensorineural mechanism). While conductive hearing loss is temporary entity and is completely curable using medical and or surgical options, the damages in the cochlea, especially if permanent, are not curable. Therefore use of bone-conduction thresholds as outcome measures could be better for understanding the effects of VEMP eliciting stimuli on cochlea.

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