ESTIMATING SAFE STIMULUS LEVEL FOR 500 HZ TONE BURST EVOKED CERVICAL AND OCULAR VESTIBULAR EVOKED MYOGENIC POTENTIALS

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CERTIFICATE

This is to certify that this dissertation entitled **‘Estimating safe stimulus level for 500 Hz tone burst evoked cervical and ocular vestibular evoked myogenic potentials’** is the bonafide work submitted in part fulfilment for the degree of Master of Science (Audiology) of the student Registration Number: 18AUD013. 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.

Mysuru
July 2020

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CERTIFICATE

This is to certify that this masters dissertation entitled **'Estimating safe stimulus level for 500 Hz tone burst evoked cervical and ocular vestibular evoked myogenic potentials'** 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 **'Estimating safe stimulus level for 500 Hz tone burst evoked cervical and ocular vestibular evoked myogenic potentials'** is the result of my own study under the guidance of Dr. Hemanth N, 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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Unto thee, O God, do we give thanks
Unto thee do we give thanks
For that thy name is near thy wondrous work declare
Psalms 75:1 (KJV)

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CHAPTER 1

INTRODUCTION

Vestibular evoked myogenic potentials (VEMP) are sound-induced electrical impulses that are recorded as inhibitory or excitatory modulations of some specific muscles of the body. They gained clinical popularity after the twin publications by Colebatch and colleagues in the early 1990s (Colebatch & Halmagyi, 1992; Colebatch, Halmagyi, & Skuse, 1994). Among the several sub-types, based on the muscle of response recording, cVEMP and oVEMP remain clinically most explored and understood. The cVEMP is recorded using surface electrodes overlying the sternocleidomastoid (SCM) muscle and it assesses the functional integrity of the saccule and the sacculocollic pathway (Colebatch et al., 1994). The oVEMP is recorded from the surface electrodes over the inferior oblique muscle and it assesses the functioning of the utriculo-ocular pathway (Bogle, 2018; Kantner & Gurkov, 2012; Young, 2006). Therefore, the use of both cVEMP and oVEMP provides information about the functionality of the two otolith organs and the reflex pathways originating from them.

cVEMP and oVEMP have been recorded in response to several different stimuli such as, clicks, tone burst, and modulated tones presented via air-conduction (Basta, Todt, & Ernst, 2005; Colebatch et al., 1994) or bone-conduction modes (Basta, Todt, & Ernst, 2005; Miyamoto, Seo, Node, Hashimoto, & Sakagami, 2006; Sheykholeslami, Murofushi, Kermany, & Kaga, 2000; Welgampola, Rosengren, Halmagyi, & Colebatch, 2003). They have even been reported in response to the galvanic (electrical) stimulation (Chang, Young, & Cheng, 2013; Cheng, Yang, Huang, & Young, 2008). Among these stimuli, the tone burst presented through air-conduction mode is commonly used in clinical settings, as other types of stimuli require additional equipment to carry out the testing or compromise on the response prevalence.

Various peripheral and central vestibular disorders are assessed using cVEMP and oVEMP. These include Meniere’s disease (Kingma & Wit, 2011; Sandhu, Low, Rea, & Saunders, 2012; Taylor et al., 2012), benign paroxysmal positional vertigo (Hornibrook, 2011; Korres et al., 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), vestibular neuritis (Adamec et al., 2014; Lin & Young, 2011; Walther & Blodow, 2013), superior semicircular canal dehiscence (Janky, Nguyen, Welgampola, Zuniga, & Carey, 2013; Minor, 2005). In fact, cVEMP is the only known test of saccular function (Colebatch & Halmagyi, 1992; Colebatch, Halmagyi, & Skuse, 1994; Welgampola, & Colebatch, 2001) and oVEMP is among a very few tests of utricular function (Curthoys, Vulovic, & Manzari, 2012; Govender, Rosengren & Colebatch, 2011; Manzari, Tedesco, Burgess, & Curthoys, 2010; Taylor, Wijewardene, Gibson, Black, Halmagyi, & Welgampola, 2011; Valko, Hegemann, Webber, Straumann, & Bockisch, 2011).

Obtaining replicable and robust cVEMP and oVEMP requires high intensity stimuli, usually ≥120 dB peSPL or ≥95 dB nHL (Murofushi, Matsuzaki, & Wu, 1999; Ochi, Ohashi, &Nishino, 2001; Welgampola, Rosengren, Halmagyi, & Colebatch, 2001). But this intense stimulus level has now become a concern for professionals due to the possibility of its ill-effects on the hearing mechanism.

1.1 Need for the study

Any auditory stimulus level beyond 140 dB SPL causes damage to cochlear or middle ear structures and stimuli below this level are considered safe, as far as the effects on hearing mechanism are concerned (Price, 1981). This report probably was the basis behind frequent clinical and research utility of sound levels between 120 and 140 dB peSPL for eliciting cVEMP and oVEMP. However, a case report by Mattingly, Portnuff, Hondorp and Cass (2105) showed progression in a patient's degree of hearing loss after cVEMP and oVEMP testing. It is quite possible that other factors could have led to the progression of hearing loss in this patient, as there has been no report of such an occurrence in the 4 years since the publication of this report or even before it. In fact, other studies have shown temporary effects or no effects of VEMP eliciting stimuli on the cochlear function.

In a study, one of the first of its kind on VEMP, Krause et al (2013) observed no change in pure-tone auditory thresholds after cVEMP testing using 500-Hz tone bursts presented at 133 dB peSPL. However, they did observe short-lived reduction of DPOAE amplitude, lasting for less than 24 hours, at high frequencies. Subsequently, Stromberg, Olofsson, Westin, Duan and Stenfelt (2016) reported reduction of DPOAE amplitude in the frequency region of 750 Hz and 3000 Hz after recording cVEMP using 500-Hz tone bursts of 130 dB peSPL intensity. A few years later, Rodriguez Thomas, Fitzpatrick and Janky (2018) used 125 dB peSPL intensity of 500-Hz tone burst to elicit cVEMPs and reported no significant change in DPOAE amplitude in adults' ears after cVEMP testing. However, they 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 owing to the smaller ear canal volume. Most recently, Singh, Keloth and Sinha (2019) reported that 125 dB peSPL was safe for recording cVEMP in adults as this intensity for 500-Hz tone burst produced no significant change in hearing threshold up to 16 kHz and DPOAE amplitude till the same frequency in their study.

From the above discussion, it can be safely assumed that either there is no significant effect of VEMP stimuli on hearing or, at the worst, there is a temporary effect on DPOAE amplitude alone. This notwithstanding, animal studies have shown a progressive synaptic loss between inner hair cells and spiral ganglion cells after loud sound exposure (100 dB SPL for 2 hours) (Kujawa & Liberman, 2009). This is commonly referred as ‘cochlear neuropathy’ or ‘hidden hearing loss’, as there is no documented hearing loss along the conventional test frequencies on the pure-tone audiometry (Kujawa & Liberman, 2009). Nevertheless, such people may have deficits in supra-threshold discrimination and neural temporal coding (Bharadwaj, Verhulst, Shaheen, Liberman, & Shinn-Cunningham, 2014; Plack, Barker, & Prendergast, 2014). However, changes in the supra-threshold discrimination and the neural temporal coding were not explored in any of the above studies on effect of VEMP eliciting stimuli on hearing function. Therefore, there is a need to study, not only the effect of VEMP eliciting stimuli on pure-tone threshold and DPOAE, but also the effect of VEMP eliciting stimuli on test of discrimination and temporal coding such as gap detection test (GDT) and speech perception in noise (SPIN).

Further, the above mentioned studies exploring the effect of VEMP eliciting acoustic stimuli on hearing and cochlear function used only cVEMP. However, most clinics carryout both cVEMP and oVEMP recordings routinely for all patients with vestibular issues. Addition of oVEMP would double the exposure dose and therefore it is imperative that effects of both tests be explored in order to understand the true potential effects in actual clinical settings.

1.2 Aim

To identify a safe stimulus level for recording 500 Hz tone burst evoked cVEMP and oVEMP.

1.3 Objectives

1. To compare the pre-VEMP gap detection threshold against those obtained 5 minutes, 1 hour, 24 hours and 7 days after cVEMP and oVEMP testing.

2. To compare the gap detection threshold at all measurement points between ears.

3. To compare the gap detection threshold at various measurement points between the groups.

CHAPTER 2

REVIEW OF LITERATURE

Vestibular evoked myogenic potential assess the saccule's and utricle's functioning. It makes use of the loudness of the stimulus to elicit the myogenic response. Price (1981) reported that as far as hearing mechanism is concerned, any stimulus beyond 140 dB SPL causes damage to cochlear or middle ear structure and might cause acoustic trauma. Various authors have recorded replicable robust VEMPs using high intensity stimulus usually ≥120 dB peSPL or ≥95 dB nHL (Murofushi et al, 1999; Ochi et al, 2001 & Welgampola et al, 2001). This makes case for a potential investigation for loud sound induced temporary cochlear damage, or potential hearing loss. This has been explored in a few studies.

2.1 Effect of VEMP eliciting stimuli on cochlear function

Attention towards the adverse effect of intensity used for recording VEMP was bought to light by Krause et al (2013) who for the first time investigated the effect of high intensity cVEMP stimuli on hearing abilities. This study was carried out on 30 young adults who were free from all audio-vestibular issues. Unilateral cVEMPs were recorded with 500 Hz tone burst with a duration of 10 ms produced using Hanning window. The stimulation rate was fixed at 3.33 Hz. A total of 200 stimuli were delivered at 133 dB SPL. The pure tone thresholds and DPOAEs were measured before, immediately after, and 24 hours after cVEMP testing. DPOAE amplitudes were measured at the above mentioned time points using fours stimulus level combinations as DPOAE eliciting stimuli (63/60, 59/50, 55/40, & 51/30 dB SPL). They found significant decline in the DPOAE amplitudes at 4 and 6 kHz immediately after the VEMP testing. They also observed complete recovery of DPOAE amplitudes by 24 hours from testing. The study did a commendable work in choosing DPOAE as outcome measure; nonetheless, the choice of stimulus parameters for eliciting

VEMP left much to be desired. Choice of 133 dB peSPL as tone burst intensity, Hanning window as gating function, and 10-ms as stimulus duration could all have confounded the results, as most studies use 125 dB peSPL (95 dB nHL), Blackman gating function and ≤5-6 ms stimulus duration for eliciting cVEMPs (Janky & Shepard, 2009; Takeichi, Sakamoto, Fukuda & Inuyama, 2001).

In the year 2016, Stromberg et al investigated the effects of VEMP stimulus of 130 dB peSPL (frequency 500 Hz) on cochlear functioning of 24 normal hearing adults. The stimulus duration of 5 ms, repetition rate of 5 Hz and 192 sweeps (in groups of 64) rounded-off the other major stimulus parameters used for eliciting cVEMPs. The DPOAE (I/O functions at 750 Hz & 3 kHz at various intensity levels from 50 to 80 dB SPL) was used as an outcome measure. DPOAEs were administered before and soon after the VEMP test. The DPOAE amplitudes were found to reduce by about 2.1 dB after the VEMP testing. The major strength of the study was the use of 3 baselines for DPOAE in order to avoid the variations due to changes caused by replacing the probe tube and account for test-retest reliability. But they failed to follow-up their participants to rule out the possibility of a permanent decline of the DPOAE amplitudes.

Later in 2018, Rodriguez et al used lower stimulation level to see its effect on hearing potentials. Both cVEMP and oVEMP were evaluated on 10 adults and 15 children. A 500-Hz tone burst stimulus of 4-ms duration were presented at 125 dB peSPL for adults and 120 dB peSPL for children. DPOAE were recorded at 750 Hz to 8000 Hz with a stimulus level of 65/55 dB SPL before and after the VEMP recording. They found no change in DPOAE amplitude for both adults and children. High point of this study was that they carried out the testing at the intensity which is usually used in the clinical set-up. Further, they also included paediatric population for the study which was not done in the preceding studies. The sample size taken for the study was less which may prevent from generalization of the results of this study. Further, the study might have benefited from evaluating the effects of higher intensity VEMP stimuli on hearing.

In a recent study by Singh et al (2019), the authors investigated the effect of cVEMP eliciting stimuli of 125 dB peSPL (500 Hz tone burst) on cochlear function of 60 individuals with normal audio-vestibular system. Standard protocol was utilized for recording cVEMP (repetition rate= 5.1 Hz, number of stimuli= 200 & stimulus duration= 5 ms). As an outcome measure, DPOAE amplitude was used. Measurements were done before and at several points of time after the VEMP recordings. They found no change in DPOAE amplitude following VEMP recordings. This was the only study to have included a control group to make sure that changes in the outcome measures were solely due to the VEMP eliciting stimuli. The major limitation was the use of only 125 dB peSPL, prevents from accepting that the VEMP stimuli of other higher intensities are unsafe and that the difference in results from the preceding studies are not affected by racial differences. Further, they did not consider evaluating for hidden hearing loss.

2.2 Effect of VEMP eliciting stimuli on clinical pure-tone thresholds (up to 8 kHz)

Krause et at (2013), along with DPOAE as an outcome measure, also used pure tone thresholds to evaluate the effect of high intensity VEMP stimuli on hearing abilities. The subject and stimulus related parameters are already described above. Air conduction thresholds (250 Hz to 10,000 Hz including mid-octaves) and bone conduction thresholds (250 Hz to 6000 Hz along with mid-octaves) were measured before, immediately after and 24 hours after VEMP testing. They found no change in the thresholds obtained using pure audiometry after the VEMP testing. Even though air conduction threshold were measured till 10,000 Hz, results up till 6,000 Hz were mentioned in the result section. Results of bone conduction thresholds were also not mentioned in the article.

Later, Stromberg et al (2016) carried out the study in a similar fashion using 500 Hz tone burst of 130 dB peSPL VEMP stimuli. Protocols set for the VEMP recording are explained in previous section. Bekesy audiometry was chosen as an outcome measure and the thresholds were measured thrice before and once immediately after VEMP testing. Frequencies considered were between 125 Hz to 8000 Hz. The results revealed no significant change in hearing thresholds after the VEMP test. The high point of the study was the repeated recording of the baseline thresholds so as to counter the variation due to changes caused by replacing the probe tube. It also helped in accounting for the test-retest reliability. The use of extended high frequency audiometry could have given more information about the effect of the stimuli on hearing abilities, which however was not used in this study.

In the year 2018, Rodriguez et al measured the effect of 125 dB peSPL of VEMP eliciting stimulus on pure tone thresholds. Details of the study along with the VEMP protocol were mentioned in the above section. Pure tone thresholds 500 to 6000 Hz (inclusive of mid-octave frequencies) were measured pre and post cVEMP and oVEMP recordings. They found no significant change in the thresholds from the baseline. Point to note from the study was that they carried out the testing at the intensity which is usually used in the clinical set-up. Further, the study included paediatric population for the study. However, the sample size taken for the study was limited and therefore prevents the generalization of the results with any degree of confidence.

Finally in the year 2019, Singh et al investigated the effects of VEMP stimuli on hearing mechanism. Details of the study along with the VEMP protocol were mentioned in the above section. The thresholds at the pure tone frequencies from 250 to 8000 Hz were measured before and after the VEMP recordings. They found no significant change in the thresholds after undergoing VEMP testing. The major highlights of the study included the use of a control group to make sure that changes in the outcome measures were solely due to the

VEMP eliciting stimuli. However, the study was limited by the non-use of extended high frequencies which are more sensitive than the frequencies up to 8000 Hz.

While most of the studies showed no significant change or at best a temporary change in the hearing function after the exposure to VEMP eliciting stimuli, Mattingly et al (2015) reported the finding of permanent change in hearing thresholds after cVEMP and oVEMP testing in a 75 years-old woman. cVEMP and oVEMP were recorded using 500 or 1000 Hz tone burst using a range of intensities from 123 dB peSPL to 135 dB peSPL. The other stimulus parameters were: stimulus duration 3 ms, 70-90 sweeps per recording, and repetition rate of 5.1 Hz. Pure tone audiometry and speech audiometry were done before the testing and after the arousal of hearing difficulties post VEMP recording. It was found that hearing threshold deteriorated to moderate degree of hearing loss along with worsening of speech scores. Major reason for this variation of results from the other studies could be subject and testing factors. The subject in the study was a 75 years old who was previously diagnosed with presbycusis, peripheral neuropathy and decline in vision. And for the testing, two trails were obtained at each intensity ranging from 123 dB to 135 dB peSPL.

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

Krause et al (2013) measured pure tone thresholds till 10 kHz, however, they failed to report the outcomes beyond 6 kHz. Singh, Kumar et al (2019) measured extended high frequency pure tone thresholds till 16000 Hz and found temporary yet significant change in the thresholds at 14 and 16 kHz frequencies after exposure to 133 dB peSPL but not after the exposure to 125 dB peSPL. Based on these results, the authors concluded that 125 dB peSPL represent safe stimulus intensity for VEMP recordings. However, these comments could be unreasonable considering that normal pure tone thresholds can be observed in cases of cochlear synaptopathy, the tests for which were not included in this study.

2.4 Effect of loud sounds beyond the level of cochlea – (Hidden hearing loss)

From the above discussion, it can be safely assumed that either there is no significant effect of VEMP stimuli on hearing or at worst there is a temporary effect on DPOAE amplitude alone. This notwithstanding, animal studies have shown a progressive synaptic loss between inner hair cells and spiral ganglion cells after loud sound exposure (Kujawa et al, 2009). This is commonly referred as cochlear neuropathy or hidden hearing loss, as there is no documented hearing loss (Kujawa et al, 2009). Nevertheless, such people can have deficits in supra-threshold discrimination and neural temporal coding (Bharadwaj et al, 2014; Plack et al, 2014). However, changes in supra-threshold discrimination and neural temporal coding was not explored in any of the above studies on effect of VEMP eliciting stimuli on hearing function which points at the gaps in the concurrent literature on stimulus safety of the VEMP eliciting stimuli.

CHAPTER 3

METHODS

3.1 Participants

Sixty healthy individuals in the age range of 15 to 40 years were included as the participants in this study. Before recruiting them to the study, a written informed consent was obtained. Further, these individuals were not paid for their participation in the study. Individuals with history or complaint of ear discharge, ear pain, itching sensation, tinnitus, vertigo, migraine, headache or any other medical or surgical history related to ear were excluded.

All participants of the study had normal audio-vestibular system which was ascertained through an audio-vestibular test battery. The auditory functions were evaluated using pure tone audiometry, immittance evaluation and transient evoked oto-acoustic emissions. Their hearing thresholds were measured from 250 Hz to 8000 Hz and were within 15 dB HL at each of the octave and mid-octave frequencies within the above mentioned range of frequencies. Further, all participants obtained 'type-A' tympanogram with both ipsilateral and contralateral acoustic reflex thresholds for tones within 100 dB HL at 500, 1000, 2000 and 4000 Hz. The global signal-to-noise ratio of transient non-linear click-evoked oto-acoustic emission was ≥ 6 dB. The tests for posture and equilibrium included Romberg test, Fukuda stepping test, tandem gait test, and past-pointing test. Normal results were obtained on Romberg test (absence of sway), Fukuda stepping test (angle of deviation $\leq 45^{o}$ and distance moved <1 meter from the initial point), tandem gait test (no imbalance while walking heel-to-toe on an imaginary straight line), and past-pointing test (absence of overshooting & overshooting of targets, & lack of tremors).

3.2 Test environment

All the tests were carried out in well-illuminated, air-conditioned sound treated rooms with the ambient noise levels within the acceptable limits of the specifications of the American National Standard Institute (ANSI S3.1, 1999, R2013). Among the tests mentioned above, pure tone audiometry was carried out in a double room set-up, whereas the remaining tests were performed in a single room set-up.

3.3 Instrumentation

The equipment used in the study included a Grasson-Stadler Incorporated-61 (GSI-61) clinical audiometer, GSI Tympstar immittancemeter, ILO-V6 oto-acoustic emission system, Neurosoft neuro-audio evoked potential system and a personal laptop with MATLAB software. The GSI-61 clinical audiometer, withTelephonicsTDH-50 supra-aural headphone was used for conventional audiometry. The GSI-Tympstar with default probe assembly and contralateral insert earphone was used to assess the middle ear functioning. To record the transient evoked oto-acoustic emission, ILO-V6 was used along with its default probe assembly. VEMP recordings were carried out with Neurosoft neuro-audio evoked potential system with Etymotic Research ER-3A insert ear phones. This system had an inbuilt cVEMP protocol which allowed for monitoring EMG levels and performing EMG normalization to obtain rectified cVEMP responses. Gap detection test was done with the help of MATLAB software using maximum likelihood adaptive procedure (MLP) which was developed and modified by Green (1990, 1993).

3.3 Procedure

Initially, all participants underwent detailed case history which tapped on the history or the presences of the hearing or the vestibular related problems. Individuals with the history or the presence of the auditory problems such as otitis externa, occlusion due to ear wax, any structural deformities like stenosis or atresia, acute, chronic or serous otitis media, perforated tympanic membrane, scared tympanic membrane, Eustachian tube dysfunction, any traumatic insult to the ear or any surgeries related to ears were excluded. To rule out the vestibular issues, the “vestibulogram” developed at All India Institute of Speech and Hearing by Singh (2018), was used. The questions based on the recent recommendations of the Barany society were used to exclude benign paroxysmal positional vertigo, Meniere’s disease, vestibular migraine, labyrinthitis, vestibular neuritis, stroke etc. (Bhattacharya et al., 2008; Von Brevern et al., 2017; Lopez-Escamez et al., 2017; Lempert et al., 2012; Strupp et al., 2016). These disorders are screened by few questions from the questionnaire such as type of giddiness, triggering factor, duration of vertigo, frequency of occurrence, associated symptoms, nature of problem or any history which induced vestibular symptoms. Considering the medical factors, any individual with a history of diabetics, hyper/ hypotension, thyroid disorder or any other hormonal disorders will be excluded from the study.

Hearing thresholds were obtained using the modified Hughson and Westlake procedure (Carhart & Jerger, 1959). The thresholds were obtained using the above method at the octave frequencies from 250 Hz to 8,000 Hz.

In order to rule out the middle ear pathology, immittance evaluation was carried out. Probe was placed in the ear canal and hermetic seal was ensured. Tympanometry and reflexometry were done using a probe frequency of 226 Hz. The pressure in the ear canal was swept from – 400 daPa to + 200 daPa, at the rate of 50 daPa/s during tympanometry. Ipsilateral and contralateral acoustic reflexes were obtained in response to pure tones of 500, 1000, 2000 and 4000 Hz. The minimum change of admittance to be considered for the presence of an acoustic reflex was 0.03 mmho.

For recording TEOAE, non-linear clicks were delivered at 80 dB peSPL through the probe assembly placed in the ear canal. The parameter noted was the global signal-to-noise ratio. The global signal-to-noise ratio of >6 dB was considered for the presence of TEOAEs.

Behavioural vestibular testing was done to ensure a normal vestibular functioning. As mentioned above, the tests for posture and equilibrium included Romberg test, Fukuda stepping test, tandem gait test and past-pointing test.

For the Romberg test, the participant was instructed to stand with the feet together and arms stretched forward. This was carried out in both eye opened and closed condition. Presence of any sway or imbalance was considered as abnormal. The test was aborted at the end of 30 seconds if no sway or imbalance was observed. In such a case, the result was classified as normal.

The Fukuda stepping test was done with 50 steps. The participant was instructed to march at a place with eyes closed. An angle of deviation $>45^0$ and/or distance moved >1m from the initial position were considered abnormal results.

In the tandem gait test, the participant was asked to walk by placing the heel of the front foot in front of the big toe of the back foot such that they touch each other. They were asked to cover a distance of 5 metres on an imaginary straight line using this walking method. Presence of sway or imbalance was considered an abnormal outcome.

In the past pointing test, the participant was asked to touch his/her nose tip and clinician’s finger-tip alternately using his/her index finger. Position of the clinician’s finger, both in terms of distance and position in space, was varied in an unpredictable manner. Presence of undershoot or overshoot of the target and/or tremors of the participants’ fingers was considered an abnormal result.

This 60 individual who fulfilled the inclusion criteria were randomly split into 3 groups. Each group consist of 20 individuals each. Twenty individuals (Group I) underwent cVEMP and oVEMP using 133 dB peSPL of stimulus intensity whereas other 20 individuals were tested using 125 dB peSPL (Group II). Both groups were tested using GDT as an outcome measures. The remaining 20 individuals formed Group III which served as the control group. The participants of Group III did not undergo VEMP testing; however, they were evaluated using gap detection test using similar time lines as the other groups. Figure 3.3.1 depicts a schematic representation of the group division.

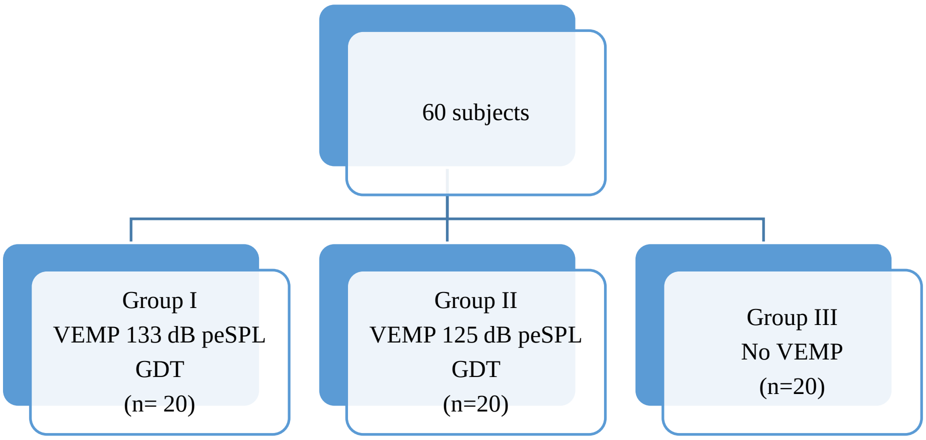

Figure 3.3.1: Schematic representation of the group division used in the study.

Every individual in the study had two baseline assessments before the VEMP testing. Double baselines were taken for evaluating test-retest reliability and checking variability without any intervention. After cVEMP testing, the groups underwent their outcome measurement tests (audiometry or GDT) at different points of time (5 minutes, 1 hour, 24 hours, & 7days) after VEMP testing. As described above, Group III underwent pure-tone audiometry and gap detection test using similar time lines as the other groups. Figure 3.3.2 shows a schematic representation of the time lines and interventions used for various groups in the present study.

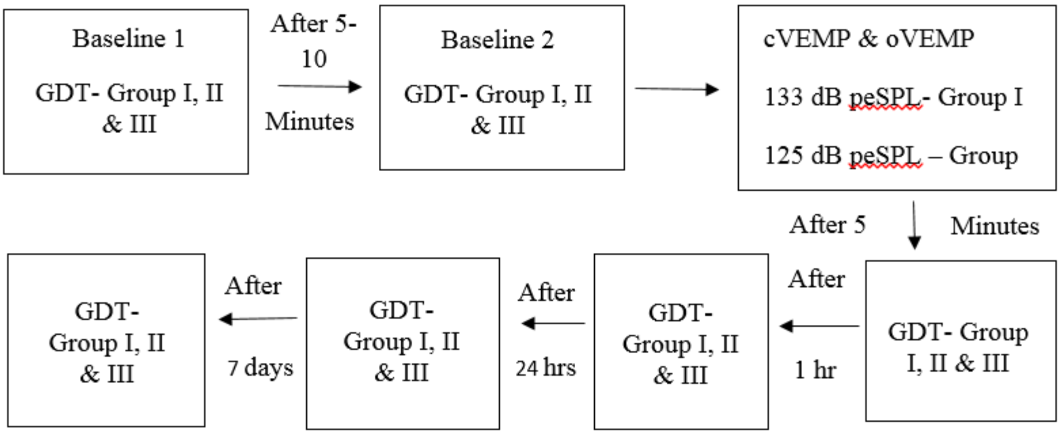

Figure 3.3.2: Schematic representation of the time lines and intervention of various groups of study

3.3.1 Recording of cVEMP and oVEMP.

For recording cVEMP, the participant was seated on a comfortable chair in an upright position. The SCM muscle was identified and the recording site was scrubbed with a commercially available abrasive gel. The inverting (negative / reference) electrode was placed at the sterno-clavicular junction where the SCM muscle joins the bone, the non-inverting (positive / active) electrode at the upper one-third of the SCM muscle and the ground (common) electrode on the forehead. For recording oVEMP, the non-inverting electrode was placed 1-cm below the lower eyelid directly below the pupil when in centre forward gaze. The inverting electrode was placed 2-cm below the non-inverting electrode and the ground one was positioned on the forehead. These electrodes were secured in place using commercially available surgical tape. All cVEMP and oVEMP electrodes were placed at once, in the beginning, in order to ensure against large variability in the time gap between cVEMP and oVEMP testing. The absolute and inter electrode impedance was ensured within 5 kΩ and 2 kΩ, respectively. Ipsilateral responses were obtained for cVEMP whereas contralateral responses were acquired for oVEMP. All the other stimulus and acquisition related parameter for recording cVEMP and oVEMP are shown in Table 3.3.1.1.

Table 3.3.1.1.

Stimulus and acquisition related parameters for recording cVEMP and oVEMP.

Parameter	cVEMP	oVEMP
Stimulus type	Tone burst	Tone burst
Stimulus frequency	500 Hz	500 Hz
Window	Modified Blackman window	Modified Blackman window
Stimulus duration	5 ms	5 ms
Rise /fall time	2 ms each	2 ms each
Plateau	1 ms	1 ms
Intensity	125 dB peSPL or 133 dB peSPL	125 dB peSPL or 133 dB peSPL
Repetition rate	5.1 Hz	5.1 Hz
No. of stimulus	200	200
Polarity	Rarefaction	Rarefaction
Filter	10 to 1500 Hz	0.1 to 1000 Hz
Analysis time	74 ms (pre-stimulus = 20 ms)	74 ms (pre-stimulus = 20 ms)
Amplification	5000 X	30000 X
Transducer	Insert phone	Insert phone

For cVEMP recording, the participant was asked to turn his/her head away from the side of stimulation in order to tense the SCM muscle for ipsilateral recording of cVEMP. EMG monitoring and EMG normalization was used to control the effect of variable muscle tension on the cVEMP responses. The target EMG range was set to 30-70 µV for EMG monitoring. For EMG normalization, the software divides the raw amplitude by the root-mean-square of baseline (pre-stimulus) EMG. In case of oVEMP recording, the participant was instructed to raise his/her gaze angle to 30^0 in the mid-line. Stimuli was delivered to only one ear of each participant for eliciting cVEMP and oVEMP, with one half of the participants undergoing recording from right side (stimulus ear) and the other half from left side in order to avoid ear order effect. The parameters noted were the individual peak latencies and peak-to-peak amplitude.

3.3.2 Gap detection test.

The MLP toolbox for GDT uses 750-ms long Gaussian noise with a 0.5-ms cosine ramp. Gaps are given within the noise and its duration is varied according to the listener's performance. A three interval three alternate forced choice procedure was used with a two down one up roving criteria. Here the patient was instructed to identify the stimulus with the gap and accordingly press the designated button for that token (1, 2 or 3). As the test progresses, the duration of silence reduces until the subject fails to detect the gap any further. This toolbox estimates the minimum duration of gap which a subject can identify. This was documented as his/her gap detection gap detection threshold. The same instrumentation and procedure were used at all different points of measurement.

3.4 Statistical analyses

For analysis, SPSS version 20 was utilized. Shapiro Wilk's test of normality was used to check for normality of the distribution of gap detection threshold. It was found that the date distribution was not normal ($p > 0.05$) hence, the non-parametric tests were carried out. For within group comparisons, Friedman's test was administered wherever multiple comparisons were needed. Wilcoxon signed rank test was also administered in case of pair-wise comparisons. For between group comparisons, the Kruskal Wallis test was used.

CHAPTER 4

RESULTS

The current study aimed to find a safe stimulus to record 500 Hz tone burst-evoked cVEMP and oVEMP. A total of 60 individuals participated in this study. Among them, 40 underwent cVEMP and oVEMP test (Group I & Group II), whereas 20 served as control (Group III). The participants in the control group did not undergo cVEMP and oVEMP. All participants of the Groups I and II underwent GDT twice before VEMP testing in order to obtain baseline and at four specified points of time after VEMP testing (5 minutes, 1 hour, 24 hours, and 7 days post-VEMP recordings) in order to assess the effects of VEMP eliciting stimulus on hearing. Participants of the Group III maintained the same time gaps between the GDT sessions as that in the two experimental groups. The GDT were obtained from both test and non-test ear.

4.1 Comparison of the gap detection threshold among various measurement points

All participants of all the three groups underwent GDT at several pre-specified measurement points. The GDT of these groups 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 vestibular-evoked myogenic potential testing) of the Group I and II.

Measurement points	VEMP eliciting stimulus: 133 dB peSPL (Group I)					VEMP eliciting stimulus: 125 dB peSPL (Group II)				
	Mean	Median	SD	Range		Mean	Median	SD	Range	
				Minimum	Maximum				Minimum	Maximum
Baseline1	2.96	2.95	0.48	2.16	4.37	2.71	2.72	0.45	1.95	3.48
Baseline2	2.62	2.85	0.48	1.42	3.12	2.83	2.80	0.49	1.70	3.68
After 5minutes	2.51	2.52	0.55	1.48	3.68	2.69	2.74	0.53	1.48	3.90
After 1 hour	2.60	2.58	0.50	1.70	3.29	2.57	2.65	0.39	1.86	3.12
After 24 hours	2.77	2.65	0.43	1.83	3.48	2.78	2.87	0.48	2.05	3.90
After 7 days	2.71	2.80	0.36	1.95	3.12	2.65	2.80	0.43	1.95	3.12

Note: ‘SD’- standard deviation

Table 4.1.2.

GDT at various measurement points in the non-VEMP ear (ears that didn't undergo vestibular-evoked myogenic potential testing) of the Group I and II.

Measurement points	VEMP eliciting stimulus: 133 dB peSPL (Group I)					VEMP eliciting stimulus: 125 dB peSPL (Group II)				
	Mean	Median	SD	Range		Mean	Median	SD	Range	
				Minimum	Maximum				Minimum.	Maximum.
Baseline1	2.52	2.27	0.61	1.65	3.48	2.56	2.58	0.54	1.86	3.68
Baseline2	2.58	2.66	0.46	1.86	3.29	2.65	2.70	0.48	1.95	3.68
After 5 minutes	2.58	2.58	0.51	1.65	3.65	2.60	2.65	0.44	1.70	3.68
After 1 hour	2.50	2.45	0.47	1.65	3.29	2.62	2.58	0.56	1.86	3.90
After 24 hours	2.57	2.52	0.35	1.86	3.12	2.76	2.75	0.43	1.86	3.90
After 7 days	2.58	2.52	0.37	1.95	3.29	2.69	2.70	0.41	1.95	3.48

Note: 'SD'- standard deviation

Table 4.1.3.

GDT at various measurement points in both ears of the Group III

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	0.31	1.95	3.12	2.65	2.66	0.51	1.86	3.68
After 5 minutes	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	2.74	2.80	0.40	1.79	3.54	2.73	2.70	0.40	2.05	3.51

Note: ‘SD’- standard deviation

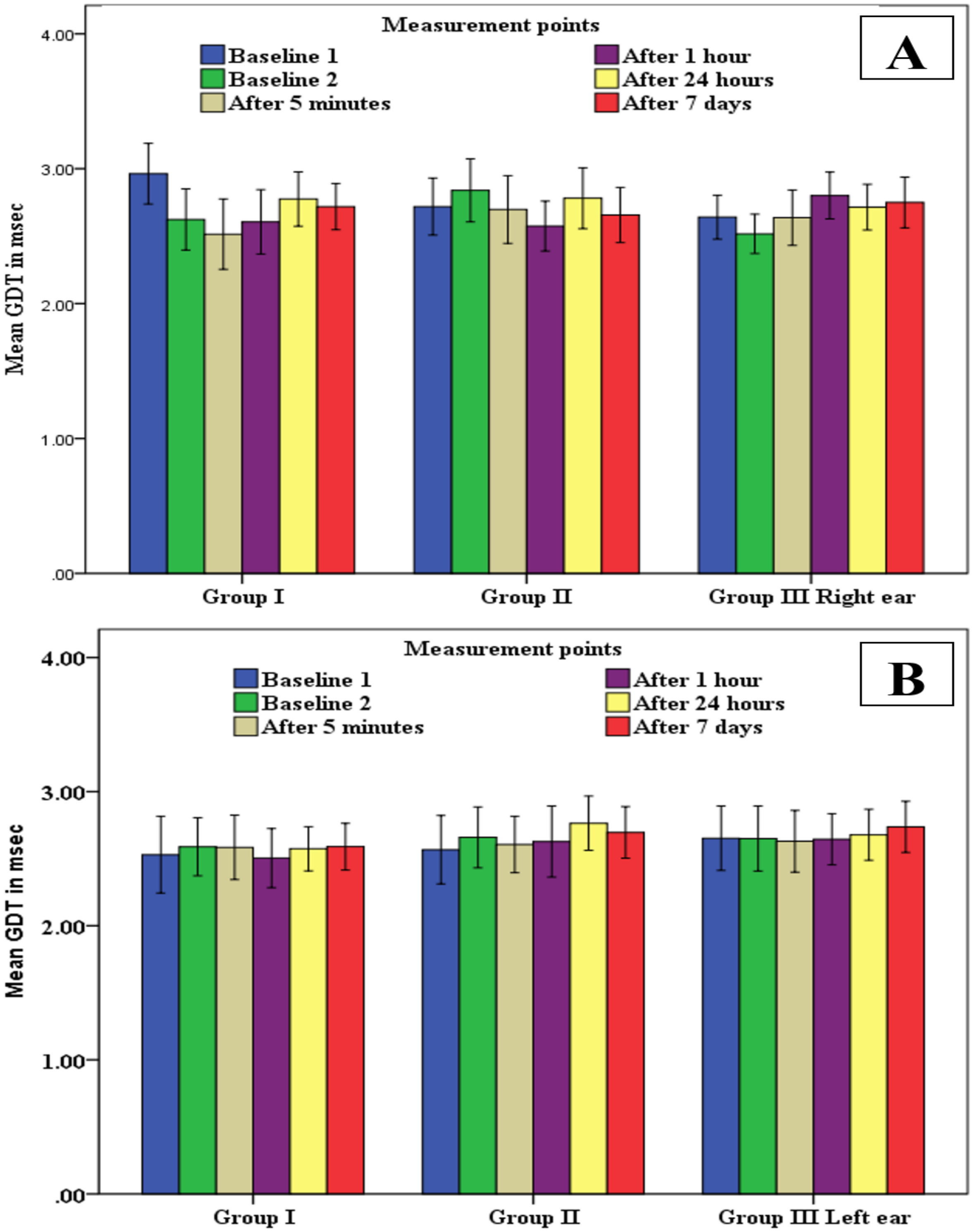

Figure 4.1.1.: Mean and 95% confidence intervals of GDT obtained at various measurement points in (A) VEMP ears of the Group I and II and right ears of the Group III; (B) Non-VEMP ears of the Group I and II and left ears of the Group III.

The GDT after VEMP testing were compared against that obtained before VEMP. This comparison was made between the measurement points using Friedman’s test, separately in the VEMP ears and the Non-VEMP ears. For this, and for all other comparisons involving the ears of participants in the Group III, right ears of were used with VEMP ears and left ears with non-VEMP ears. The results revealed no significant difference between the measurement points in any group ($p > 0.05$). Table 4.1.4 shows the outcome of the Friedman’s test for comparison among the measurement points in both ears of each group.

Table 4.1.4.

Outcome of Friedman's test for comparison between measurement points in each group

Group	VEMP-eliciting stimulus (in dB SPL)	VEMP ear / Right ear*			Non-VEMP ear / Left ear#		
		N	$\chi^2(5)$-value	*p*-value	N	$\chi^2(5)$-value	*p*-value
Group I	133	20	7.36	0.19	20	1.00	0.96
Group II	125	20	4.54	0.47	20	6.61	0.25
Group III	NA	20	7.95	0.15	20	5.49	0.35

Note: *VEMP ear in case of Group I and II and right ears in case of Group III; #Non-VEMP ear in case of Group I and II and left ears in case of Group III; NA- not applicable; N- sample size.

4.2 Comparison of gap detection threshold between the ears

The comparison of GDT was done between the ears at all measurement points and in each group separately. 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 GDT thresholds and the 95% confidence intervals at various measurement points in VEMP / right ear and Non-VEMP / left ear are shown in Figure 4.2.1.

Table 4.2.1.

GDT at various measurement points in VEMP and Non-VEMP ears in the Group I that underwent unilateral VEMP acquisition using stimulus intensity of 133 dB peSPL

Measurement points	VEMP ear					Non-VEMP ear					Wilcoxon signed rank test for between the ears comparison	
	Mean	Median	SD	Range		Mean	Median	SD	Range			
				Minimum	Maximum				Minimum	Maximum	Z-value	*p*-value
Baseline1	2.71	2.72	0.45	1.95	3.48	2.56	2.58	0.54	1.86	3.68	-1.70	0.08
Baseline2	2.83	2.80	0.49	1.70	3.68	2.65	2.70	0.48	1.95	3.68	-1.37	0.17
After 5 minutes	2.69	2.74	0.53	1.48	3.90	2.60	2.65	0.44	1.70	3.68	-0.15	0.87
After 1 hour	2.57	2.65	0.39	1.86	3.12	2.62	2.58	0.56	1.86	3.90	-0.96	0.33
After 24 hours	2.78	2.87	0.48	2.05	3.90	2.76	2.75	0.43	1.86	3.90	-1.50	0.13
After 7 days	2.65	2.80	0.43	1.95	3.12	2.69	2.70	0.41	1.95	3.48	-1.63	0.10

Note: 'SD'- standard deviation

Table 4.2.2.

GDT at various measurement points in VEMP and Non-VEMP ears in the Group II that underwent unilateral VEMP acquisition using stimulus intensity of 125 dB peSPL

Measurement points	VEMP ear					Non-VEMP ear					Wilcoxon signed rank test for between the ears comparison	
	Mean	Median	SD	Range		Mean	Median	SD	Range			
				Minimum	Maximum				Minimum	Maximum	Z-value	*p*-value
Baseline1	2.96	2.95	0.48	2.16	4.37	2.52	2.27	0.61	1.65	3.48	-1.35	0.17
Baseline2	2.62	2.85	0.48	1.42	3.12	2.58	2.66	0.46	1.86	3.29	-1.24	0.21
After 5 minutes	2.51	2.52	0.55	1.48	3.68	2.58	2.58	0.51	1.65	3.65	-0.37	0.70
After 1 hour	2.60	2.58	0.50	1.70	3.29	2.50	2.45	0.47	1.65	3.29	-0.38	0.70
After 24 hours	2.77	2.65	0.43	1.83	3.48	2.57	2.52	0.35	1.86	3.12	-0.19	0.84
After 7 days	2.71	2.80	0.36	1.95	3.12	2.58	2.52	0.37	1.95	3.29	-0.56	0.57

Note: ‘SD’- standard deviation

Table 4.2.3.

GDT at various measurement points in the group III

Measurement points	Right ear					Left ear					Wilcoxon signed rank test for between the ears comparison	
	Mean	Median	SD	Range		Mean	Median	SD	Range			
				Minimum	Maximum				Minimum	Maximum	Z-value	*p*-value
Baseline1	2.64	2.65	0.34	1.86	3.12	2.65	2.75	0.51	1.48	3.50	-0.13	0.89
Baseline2	2.51	2.46	0.31	1.95	3.12	2.65	2.66	0.51	1.86	3.68	-1.45	0.14
After 5 minutes	2.63	2.80	0.43	1.62	3.12	2.63	2.60	0.49	1.96	3.66	-1.00	0.31
After 1 hour	2.80	2.80	0.37	1.95	3.25	2.64	2.68	0.40	1.95	3.43	-0.41	0.67
After 24 hours	2.71	2.80	0.36	1.75	3.12	2.67	2.75	0.40	2.14	3.50	-1.40	0.15
After 7 days	2.74	2.80	.40	1.79	3.54	2.73	2.70	0.40	2.05	3.51	-0.19	0.98

Note: ‘SD’- standard deviation

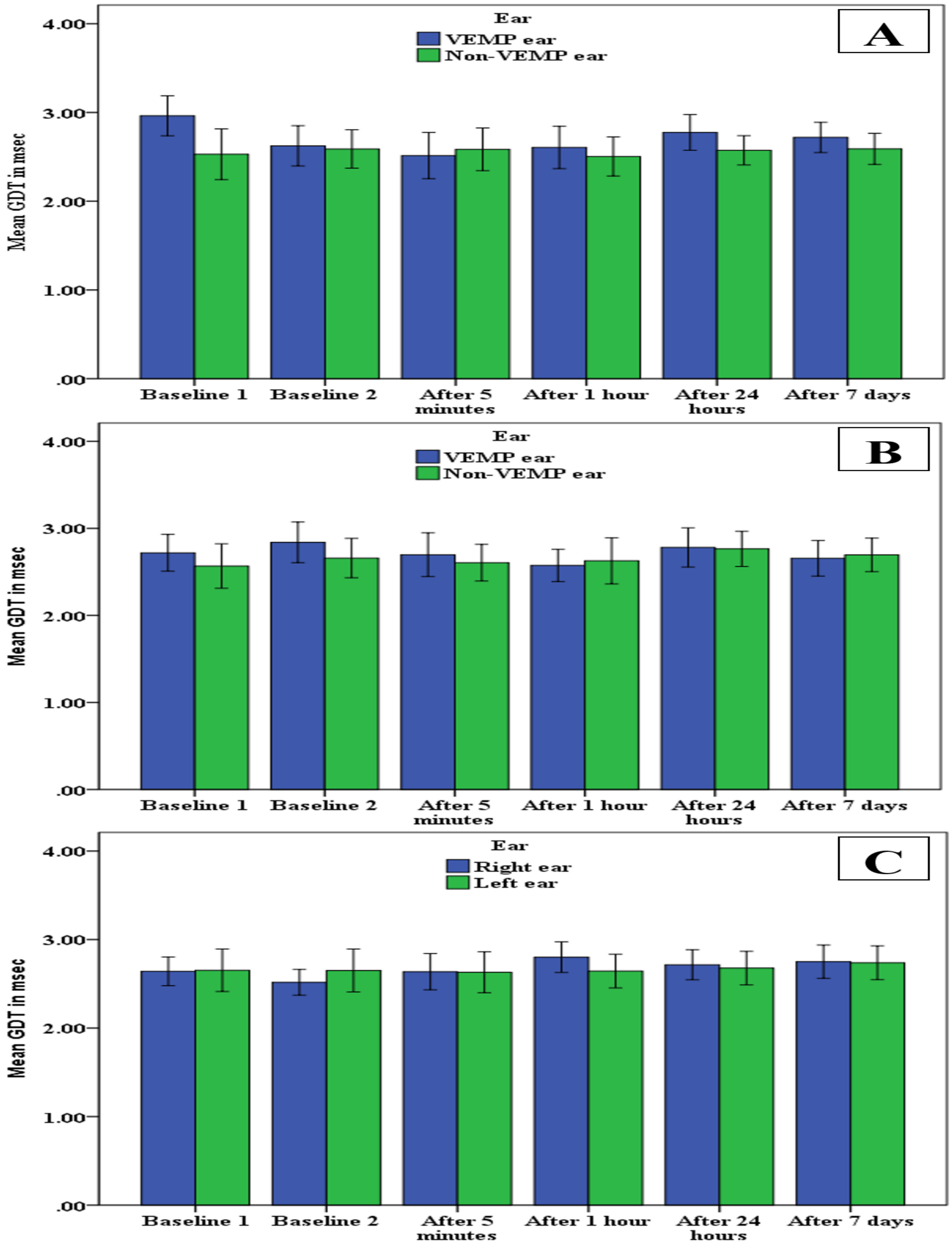

Figure 4.2.1.: Mean and 95% confidence intervals of GDT obtained at various measurement points in (A) VEMP ears and Non-VEMP ear of the Group I, (B) VEMP ears and Non-VEMP ear of the Group II, and (C) Right and Left ears of the Group III.

GDT scores of VEMP/right ear were compared against Non-VEMP/left ear of each groups using separate Wilcoxon signed-rank tests. The results revealed no significant difference in GDT between the ears in any group ($p > 0.05$). The outcomes of these separate Wilcoxon sign rank tests (Z-values &*p*-values) are given in Table 4.2.1, Table 4.2.2 and Table 4.2.3.

4.3 Comparison of gap detection threshold between the groups

The three groups were compared with each other at various measurement points. 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.

GDT at various measurement points in the ears undergoing VEMP testing of Group I and II and Right ear of Group III.

	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
Group I (133 dB peSPL)	2.96	2.95	0.48	2.62	2.85	0.48	2.51	2.52	0.55	2.60	2.58	0.50	2.77	2.65	0.43	2.71	2.80	0.36
Group II (125 dB peSPL)	2.71	2.72	0.45	2.83	2.80	0.49	2.69	2.74	0.53	2.57	2.65	0.39	2.78	2.87	0.48	2.65	2.80	0.43
Group III (Control)	2.64	2.65	0.34	2.51	2.46	0.31	2.63	2.80	0.43	2.80	2.80	0.37	2.71	2.80	0.36	2.74	2.80	0.40

Note: ‘SD’- standard deviation

Table 4.3.2.

GDT at various measurement points in the ears undergoing non-VEMP testing of Group I and II, and *Left ear of Group III.*

	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
Group I (133 dB peSPL)	2.52	2.27	0.61	2.58	2.66	0.46	2.58	2.58	0.51	2.50	2.45	0.47	2.57	2.52	0.35	2.58	2.52	0.37
Group II (125 dB peSPL)	2.56	2.58	0.54	2.65	2.70	0.48	2.60	2.65	0.44	2.62	2.58	0.56	2.76	2.75	0.43	2.69	2.70	0.41
Group III (Control)	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

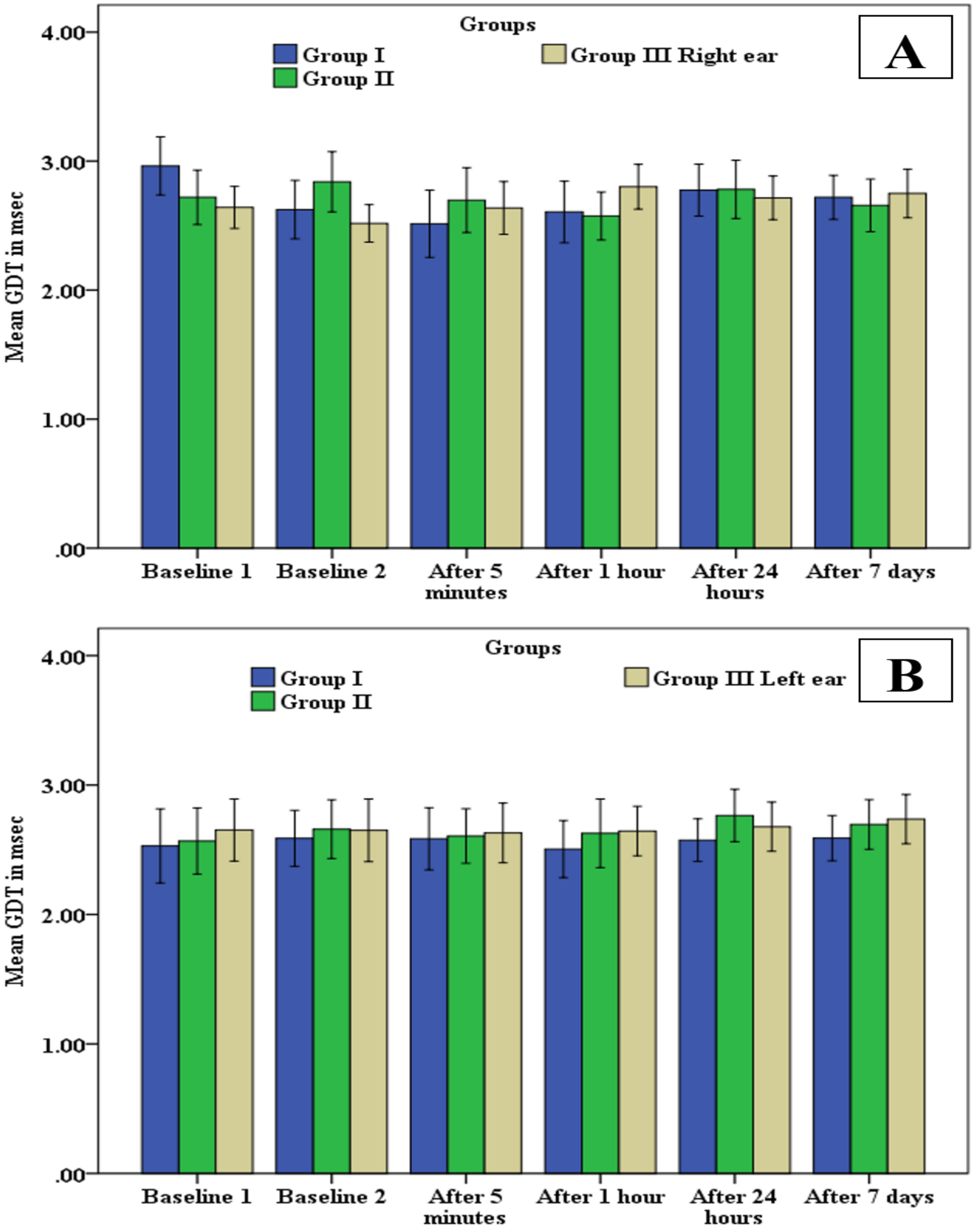

Figure 4.3.1.: Mean and 95% confidence intervals of GDT obtained among the groups in (A) VEMP ears of the Group I and II, and right ears of the Group III; (B) Non-VEMP ears of the Group I and II and left ears of the Group III.

The comparison among the groups was done using Kruskal-Wallis test, separately for the two ears. The results revealed no significant difference among the groups for the VEMP ear/right ear at baseline 1 [$\chi^2(2) = 0.44$, $p = 0.80$], baseline 2 [$\chi^2(2) = 7.06$, $p = 0.28$], after 5minutes [$\chi^2(2) = 1.63$, $p= 0.44$], after 1 hour [$\chi^2(2)= 1.58$, $p = 0.45$], after 24 hours [$\chi^2(2) = 0.33$, $p = 0.84$], and after 1 week [$\chi^2(2)= 0.11$, $p = 0.94$]. There was also no significant difference among the groups for the Non-VEMP ear/left ear at baseline 1 [$\chi^2 (2)= 0.24$, $p = 0.88$], baseline 2 [$\chi^2(2) = 0.37$, $p = 0.83$], after 5 minutes [$\chi^2(2) = 0.52$, $p = 0.76$], after 1 hour [$\chi^2(2) = 1.85$, $p = 0.39$], after 24 hours [$\chi^2(2)= 2.68$, $p = 0.26$], and after 1 week [$\chi^2(2)= 3.45$, $p = 0.17$].

Even though the group results showed no significant difference in any of the above measurements. Yet these results cannot be generalised on individual data. Therefore, individual GDT measures were compared among the groups in order to identify the individuals in whom the GDT scores increased after exposure to VEMP stimuli. The values beyond mean + 2 standard deviation of the GDT of baseline 2 was set as a criteria for classifying significant worsening of the GDT post the exposure to VEMP stimuli. For this purpose, baseline 2 was used so that any practice effects from first to second test session could be countered. The mean + 2 standard deviation of baseline 2 was found to be 3.56 ms and therefore any value of GDT> 3.56 ms .Using this value for comparison, it was found that single participant had an abnormal results in both VEMP and non-VEMP ear for Group I and II at 5 minutes. In Group I, for non-VEMP ear at 1 hour post VEMP recording, an individual showed GDT was above 3.56 ms. Similar result was found in Group II for VEMP ear at 24 hours post VEMP recordings.

CHAPTER 5

DISCUSSION

This study aimed to investigate about the safe intensity of stimulus for recording 500 Hz tone burst evoked cVEMP and oVEMP. The stimulus level chosen for the study were 133 dB peSPL and 125 dB peSPL. This study incorporated 60 participants, who were sub-categorised into three groups - 20 participants underwent VEMP recording using 133 dB peSPL (Group I), 20 participants underwent VEMP recording using 125 dB peSPL (Group II), and the rest served as control (Group III). The gap detection test served the purpose of measuring the outcomes at several measurement points before and after the VEMP recordings. The GDT measurements were compared between measurement points (baseline 1, baseline 2, after 5 minutes, after 1 hour, after 24 hours & after 7 days of VEMP recordings), between VEMP and non-VEMP ear at each measurement point, and between the groups at each measurement point.

5.1 The comparison of gap detection threshold between the measurement points

The GDT at various points of measurements were compared with each other. The results revealed no significant difference in GDT between the measurement points. Presently, there is no study on the effects of VEMP eliciting stimuli on the gap detection threshold. However, gap detection threshold is a behavioural measure of hearing, and therefore the outcomes of the present study can be compared with the effects of VEMP eliciting stimuli on other behavioural measures of hearing. Several studies have obtained pure tone thresholds as a measure to study the effects of VEMP eliciting stimuli on hearing mechanisms (Krause et al., 2013; Mattingly et al., 2015; Stromberg et al., 2016; Rodriguez et al., 2018; Singh et al., 2019). The findings of the present study are in consonance with those reported in majority of the above mentioned studies (Krause et al., 2013; Stromberg et al., 2016; Rodriguez et al., 2018; Singh et al., 2019). All these studies reported no significant change in pure tone thresholds after the exposure to VEMP eliciting stimuli. However, Mattingly et al. (2015) reported a case of hearing threshold deterioration after undergoing cVEMP and oVEMP test. The subject in the study was 75 years old woman who was previously diagnosed with presbycusis, peripheral neuropathy and decline in vision. The predisposing factors such as age, hearing loss and associated conditions might be the possible contributors for worsening of pure tone thresholds in the study by Mattingly et al (2015). The participants in the present study were young adults with no history of hearing or vestibular pathologies, which might have led to preserved gap detection thresholds in the present study. Additionally, the participant in the study by Mattingly et al (2015) underwent threshold evaluation of cVEMP using stimuli ranging from 123 to 135 dB SPL (probably dB peSPL) which would have resulted in cumulative effect of exposure to many more stimuli than in the present study. In the present study, each individual was exposed to only single intensity stimuli. Therefore, the above mentioned reasons could explain the differences in the findings reported in the present study and the study by Mattingly et al (2015).

The outcomes in the Group II (VEMP using 125 dB peSPL) are in agreement with those using physiological and behavioural measures for investigating the outcome (Rodriguez et al., 2018; Singh et al., 2019). Both Rodriguez et al (2018) and Singh et al (2019) found no significant changes in oto-acoutsic emissions and behavioural pure tone thresholds after the exposure to the VEMP eliciting stimuli of 125 dB peSPL. However, the findings of Group I (VEMP testing using 133 dB peSPL) in the present study are in dissonance with those reported using physiological tests such as oto-acoustic emissions. Studies using 130 and 133 dB peSPL stimuli for eliciting VEMP found reduced amplitude of oto-acoustic emissions in the immediate post-stimulus exposure phase than the pre-stimulus one (Krause et al., 2013; Stromberg et al., 2016). Therefore, with no detrimental effect of VEMP eliciting stimuli on

GDT in the present study, even for a stimulus intensity of 133 dB peSPL, the findings of the present study are in disagreement with Krause et al (2013) and Stromberg et al (2016). The reasons for such a discrepancy could be explained on the basis of the generators for the two response types used in these studies. The outer hair cells, which are generators of OAEs, are more susceptible to damage than any other auditory structure due to impulse or high-level sound (Mcgill & Schuknecht, 1976). Due to this reason probably, the DPOAE showed a shift from the baseline despite the pure tone thresholds and GDT remaining intact. However, this must be taken with caution, as there are no published studies on comparison of the relative efficacy of OAEs and GDT in the noise exposed ears. Another contributing factor to this discrepancy could be the variation in the stimulus parameters between the present study and those reporting detrimental impact on oto-acoustic emissions (Krause et al. 2013; Stromberg et al., 2016). Krause et al (2013) used a 10-ms stimulus duration and Hanning window as the gating function, and Stromberg et al (2016) used a stimulus duration 6-ms without mentioning about which gating function was used in their study. In the present study, the tone burst duration was 5-ms and Blackman window was used as gating function. The B-duration, which is an important predictor of the damage to auditory structure in case of impulse noise exposure, tends to depend in part on the stimulus duration (Coles, Garinther, Hodge & Rice, 1968). Ward in 1986 stated “B-duration is the sum of periods in a quasi-oscillating waveform during which the pressure envelope exceeds 10% of the peak pressure value”. It is well known that longer B-durations have more ill effects on hearing systems (Mäntysalo & Vuori, 1984).Singh et al (2019) found that the B-duration of the stimulus used by Krause et al (2013) and Stromberg et al (2016) was 4.8 ms and 2.7 ms, respectively. This duration is longer in comparison with the stimulus used in the current study. This might be one of the reasons for the discrepancies of the results of the present study with those of Krause et al (2013) and Stromberg et al (2016). Further, it is a known fact that Hanning window has higher energy in side lobes than the Blackman window. More energy in the side lobes could possibly also contribute to the effects of the exposure on hearing. Therefore, a combination of the above mentioned parameters might have caused temporary effects on the hearing mechanism in the studies by Krause et al (2013) and Stromberg et al (2016) while sparing damage in the present study.

5.2 The comparison of gap detection threshold between the ears

The GDT was compared between VEMP ears and non-VEMP ears, and the results showed no significant difference in the GDT between the ears at any measurement point. The concurrent literature account has no study on the effects of the VEMP eliciting stimuli on GDT. Since the Gap detection test is a behavioural measure, the findings of the current study can be compared with the studies exploring the impact of VEMP eliciting stimuli on other behavioural measures of hearing.

The studies on pure tone audiometry up to 8 kHz or extended high frequency pure-tone audiometry found no change in the threshold after VEMP recordings (Krause et al., 2013; Stromberg et al., 2016; Rodriguez et al., 2018; Singh et al., 2019). Therefore, the results of the present study are in accordance with the above mentioned studies. However, Mattingly et al. (2015) reported a case of worsening of the pure tone thresholds after VEMP evaluation. Prime reasons for such discrepancy of the present study with that of Mattingly et al (2015) could be the differences in the age of the participants, associated medical condition and repeated recordings of cVEMP and oVEMP at intensity ranging from 123 dB SPL to 135 dB SPL, as described earlier.

The findings of the Group II of the present study are in agreement with those using the same stimulus intensity as the present study (Rodriguez et al., 2018; Singh et al., 2019). These studies, as well as the present study, observed no significant effect of VEMP eliciting stimuli of 125 dB peSPL on GDT (present study), DPOAE and pure-tone audiometry up to 8 kHz (Rodriguez et al., 2018) and DPOAE, pure-tone audiometry up to 8 kHz and extended high frequency audiometry up to 16 kHz (Singh et al., 2019).

The results of the present study for Group I are also in dissociation with the studies using physiological tests as outcome measures for effects of VEMP eliciting stimuli on hearing mechanism (Krause et al., 2013; Stromberg et al., 2016). They reported significant deterioration of the DPOAE amplitude after the VEMP recordings in response to stimulus intensity of 130 dB peSPL (Stromberg et al., 2016) and 133 dB peSPL (Krause et al., 2013). As explained above, the discrepancy in findings of the present study to those reported by Krause et al (2013) and Stromberg et al (2016) could be due to the differences in the use of stimulus parameters (such as type of gating function, B-duration etc.) and the differences in the inherent sensitivity of the tests chosen between the studies.

5.3 The comparison of gap detection threshold between the groups

The between groups comparison of GDT revealed no significant difference among the groups. The previous studies on the effect of VEMP eliciting stimuli of 125 dB peSPL on hearing showed no significant impact of the stimulus exposure on DPOAE, pure-tone audiometry and extended high frequency pure-tone audiometry (Rodriguez et al., 2018;Singh et al., 2019). Therefore, the findings of the present study are in agreement with these studies. However, the studies using 130 or 133 dB peSPL tone bursts to elicit VEMP reported significant reduction of DPOAE amplitude at certain frequencies despite no significant change in the pure-tone thresholds up to 8 kHz (Krause et al., 2013; Stromberg et al. 2016).While the change in DPOAE amplitude produced slight contrast between the findings of present study and those of Krause et al (2013) and Stromberg et al (2016), these effects in these studies were short lived, lasting less than 24 hours. However, Mattingly et al (2015) reported permanent increase in the degree of hearing loss in a patient after she underwent cVEMP and oVEMP testing. Therefore, the findings of the present study are in disagreement with those reported previously. As mentioned before, these differences could be due to a combination of the differences in the use of stimulus parameters and the differences in the inherent sensitivity of the tests used in the studies. The differences from the outcomes of Mattingly et al (2015) could be due to the differences in the cumulative exposure to intense sound, age of the participants and other predisposing factors, as explained in detail in the above sub-sections.

In the present study, the individual participant's data were also analysed in order to investigate whether or not individual participants were affected despite a no significant group difference. For this purpose, an abnormally large GDT was operationally defined as a value beyond 2 standard deviations of the mean. The cut-off for normal GDT was found to be ≤ 3.56 ms. There was one participant with the GDT breaching the criteria for normality defined above at only 5 minutes after VEMP testing and one participant with abnormally large GDT at only 24 hours after VEMP testing. Both showed recovery at the very next measurement point. Therefore, even the individual data suggests no significant deleterious impact of VEMP eliciting stimuli on GDT which represents disagreement with the reports showing significant changes in DPOAE amplitude (Krause et al., 2013; Stromberg et al., 2016). The reason for such differences between the findings could be individual susceptibility caused by possible genetic differences among the races used in the studies. Krause et al (2013) conducted the study in Germany and Stromberg et al (2016) in Sweden. There is a high possibility that the majority of participants in these studies were Europeans. However, all participants in the present study were Indians. Therefore, there is a high possibility of genetic predisposing factors between these two races. Such a difference between the races has been reported previously for the temporary threshold shifts. Rosen, Bergman, Plester, and Satti

(1962) observed that Sudanese had more resistance to temporary threshold shift than to Euro-Americans. Therefore, differences in a host of stimulus and subject related factors explain the unique findings of the present study.

CHAPTER 6

SUMMARY AND CONCLUSION

After the twin publications of Colebatch and his colleagues in the early 1990s, VEMP has gained widespread clinical popularity. Among the known VEMP sub-types, cVEMP and oVEMP are the most frequently used. While cVEMP is a test of the sacculocolic pathway function, oVEMP provides insight in to the functional integrity of the utriculo-ocular pathway. cVEMP and oVEMP can together prove helpful in the diagnosis and differentials diagnosis of several labyrinthine and neural pathologies, such as Meniere's disease, benign paroxysmal positional vertigo, vestibular migraine, vestibular neuritis, superior semi-circular canal dehiscence, strokes of anterior-inferior cerebellar artery, to name a few.

In order to achieve robust and replicable VEMP recordings, high intensity stimuli, usually ≥ 120 dB peSPL or ≥ 95 dB nHL, are used. Use of such high intensity sounds often castes questions about the possible ill-effects on the hearing mechanisms. Literature has shown evidence of a short-lived decline in DPOAE amplitudes immediately after the exposure to VEMP eliciting stimuli of 133 dB peSPL (Krause et al., 2013) and 130 dB peSPL (Stromberg et al., 2016). However, the studies using 125 dB peSPL reported no such changes (Rodriguez et al., 2018; Singh et al., 2019). Based on these outcomes, the authors of these studies recommended that 125 dB peSPL is safe stimulus intensity for obtaining VEMP. However, several animal studies have shown a synaptic loss between inner hair cells and spiral ganglion cells after loud sound exposure despite the retention of normal hearing and normal outer hair cell function in these animals (Kujawa et al, 2009). This condition was termed 'cochlear neuropathy', 'cochlear synaptopathy' or 'hidden hearing loss'. The typical cochlear synaptopathy is characterised by normal hearing thresholds in the clinical range of audiometric frequencies with deficits in the supra-threshold discrimination and neural temporal coding. Keeping this perspective in mind, it is possible that despite no deleterious impact on hearing, as evidenced by no significant alterations of pure-tone thresholds and oto-acoustic emissions, the supra-threshold discrimination or neural temporal coding could be affected in ears undergoing VEMP testing. Since gap detection test is a test of supra-threshold discrimination and neural temporal coding, the present study aimed to examine the effects of VEMP eliciting stimuli on gap detection threshold.

A total of 60 healthy adults in the age range of 15-40 years (mean = 21.97, SD = 2.32) served as the participants in the current study. They had no history of auditory or vestibular disorders. These participants were categorised into three equal groups (20 participants in each group). Gap detection test was used as an outcome measure of the effects of VEMP eliciting stimuli on hearing mechanism. The gap detection test was performed to obtain two baselines with an inter-test interval of 5 minutes, in order to evaluate the test- retest reliability, check variability without any intervention, and avoid adulteration of results due to practice effect. After the baseline assessments, the participants of Group I and Group II underwent cVEMP and oVEMP testing using 133 dB peSPL and 125 dB peSPL tone burst intensities, respectively. Following this, the gap detection test was performed in all of them after 5 minutes, 1 hour, 24 hours and 7 days of VEMP testing. Group III served as a control groups (did not undergo VEMP recordings); nonetheless, GDT assessment was done using same inter-session intervals as that in two experimental groups.

cVEMP and oVEMP was carried out using with Neurosoft neuro-audio evoked potential system (Natus Medical Incorporated, Mundelein). VEMP recordings were carried out with 500 Hz tone burst of 5-ms duration (modified Blackman window). Two hundred sweeps of the tone bursts of rarefaction polarity was delivered at a rate of 5.1 Hz. Filter setting and amplification for cVEMP were set at 10 to 1500 Hz and 5000 times, respectively and for oVEMP, these were set at 0.1 to 1000 Hz and 30000 times, respectively. Depending upon the group, the stimuli of 133 dB peSPL or at 125 dB peSPL were delivered through the default insert earphones of the evoked potential system.

The GDT was compared among the measurement points in each group, between ears at each measurement, and between the groups at each measurement point. Friedman's test was used for the comparison of GDT among the measurement points. Wilcoxon signed rank test was used for comparison of GDT between the ears and the Kruskal-Wallis test was used for the comparison of GDT among the groups.

The results of the present study showed no significant difference among the measurement points within any group, no significant difference between the ears in any group and no significant difference among the groups at any measurement point. Similar results were obtained in other studies using behavioural measures of hearing, although not using GDT as an outcome measure (Krause et al., 2013; Mattingly et al., 2015; Stromberg et al., 2016; Rodriguez et al., 2018; Singh et al., 2019). However, these results were in discordance with studies that used DPOAE as an outcome measure. This disagreement was seen while using VEMP stimuli at 130 dB peSPL and 133 dB peSPL. This disparity might be accounted for by two reasons. First, and the more likely reason could be the differences in the stimulus parameters such as stimulus duration and gating function used for the VEMP eliciting stimuli. Second, and the lesser likely reason could be relatively higher susceptibility of the outer hair cells, the cell responsible for the generation of OAEs, to the damaging impact of impulse or high-level sound than the other auditory structures.

6.1 Implication

In the present study both 133 dB peSPL and 125 dB peSPL intensities were associated with no deleterious impact on GDT. Based on this findings it appears that stimulus intensity up to 133 dB peSPL are safe for VEMP testing.

6.2 Limitation of the study and future direction

Although, the results of present study have shown that both the stimuli are safe (owning to no detrimental effect on GDT), the studies in the past have found temporary decline of DPOAE amplitudes after VEMP test using 130 and 133 dB peSPL. Since these studies were done in European countries, and would probably have used European population, it is possible that racial differences might have resulted in discrepant results. Since the present study did not use DPOAE as an outcome measure, it would be inappropriate to assume this as a reason for the discrepant results. Therefore future studies could benefit from incorporating OAE, in addition to GDT, before commenting on the stimulus safety of VEMP eliciting stimuli. A significant limitation to the present study is the use of a smallish sample size within each group considering that the study was done on normal hearing healthy adults. In order to be more certain of generalization of the results, future studies would also benefit from using larger sample size within each of the groups. Nonetheless, the results of the present study have defined the beginning of a new way to look at the fast emerging test like VEMP and their possible impact on hearing.

So to conclude, both 133 dB peSPL and 125 dB peSPL tone burst intensities were found to be safe in the present study. However, considering that a few reports of deleterious, although temporary, effects of using 133 dB peSPL tone bursts have been published, it might be safer to recommend 125 dB peSPL for clinical recording of cVEMP and oVEMP.

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